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## **SPHERIX ANNOUNCES POST-HOC ANALYSIS OF PHASE 3 TRIAL WITH D-TAGATOSE IN DIABETES**

***D-Tagatose May Be More Effective In Patients With Higher Body Mass Indexes;  
Postulated Mechanism Of Action Also Suggests Use In High Triglycerides***

**BETHESDA, MD (December 2, 2010) – Spherix Incorporated (NASDAQ: SPEX)**, an innovator in biotechnology for therapy in diabetes, metabolic syndrome and atherosclerosis; and providers of technical and regulatory consulting services to food, supplement, biotechnology and pharmaceutical companies, today announced results from its first Phase 3 trial post hoc analysis in which the higher body mass index (BMI) of the U.S. population relative to the Indian population was a likely key contributor to the more positive effects of D-tagatose in the lowering of HbA1c levels in the U.S. population. Initial results were announced on October 7.

The first post hoc analysis done of the Biospherics Phase 3 NEET clinical trial suggests that the larger reduction in HbA1c observed in the Per Protocol population in the USA may be the result of D-tagatose acting at the level of metabolic control mediated by adipocytes (fat cells). In other words, in patients with sufficient numbers and size of adipocytes for dietary carbohydrate effects to be manifested, there is a role for adipocytes in the mechanism of D-tagatose in the control of blood glucose and plasma triglyceride levels.

“Tagatose appears to be more effective in Type 2 diabetes patients with adipocyte dysfunction that no longer permits the adipocytes to act appropriately as an endocrine organ controlling HbA1c,” said Dr. Robert Lodder, President of Spherix.

Results from the first post hoc analysis of the Biospherics Phase 3 70971-004 clinical trial showed a correlation between HbA1c and BMI through all of the monthly visits (v1-v14) in the trial (see Table 1). Results of the Phase 3 trial, as previously reported, showed a greater lowering of HbA1c with tagatose treatment in patients from the US cohort (-1.1 vs. placebo at 10 months of therapy in the Per Protocol population) compared with India (-0.2 vs. placebo at 10 months of therapy in the Per Protocol population). BMI is an indirect measure of adiposity, which in turn measures the ratio of fat mass to the mass of the whole body. Differences in BMI may have contributed to the changes seen in HbA1c reduction in the two cohorts, because patients must have enough adipocytes that are large enough to enable body fat to act as an endocrine organ.

Differences in BMI between the US and India have been well documented; according to the 2010 WHO Global Database on BMI, 66.9% of the population of the USA was overweight (defined as BMI>25), while only 4.5% of the population of India had a BMI>25. Consistent with WHO data, in the Biospherics Phase 3 trial the BMI of patients from India was lower than in patients from the US. The mean BMI across all visits was lower in the Indian population than in the US, and the distribution was essentially Gaussian (“bell-shaped”) (see Table 2). In the US population, the mean BMI across all visits (v1-v14) was significantly higher than in India and the BMIs were skewed toward higher values (i.e., BMIs>28.3). As a result, the US population is more likely to have sufficient adipocytes that are large enough to enable body fat to act as an endocrine organ.

Triglycerides are used by the body to transport fats from one location to another. Interestingly, the mean serum triglycerides for patients in India at randomization was lower than the mean for the patients in the US (Table 2). Serum triglycerides were also directly correlated with BMIs through all of the months on tagatose therapy (Table 1). In addition, as observed in other studies [Khan, 2007], serum triglycerides were directly correlated to HbA1c. Patients with higher HbA1c (poorer glucose control) tended to also have higher triglycerides.

The mean BMI is an important factor in interpreting results from the current Phase 3 Type 2 diabetes trial because BMI is an indirect measure of the amount of fat stored in adipocytes in the body [van Harmelen, 2003]. Adipose tissue has an important role in the control of glucose homeostasis. When fatty acid and triglyceride metabolism in adipocytes is altered by obesity, primary insulin resistance in skeletal muscle can occur [Guilherme, 2008]. Impaired responsiveness of skeletal muscle to insulin is a precondition for the onset of Type 2 diabetes. Literature has documented the probable causal relationship between weight gain and decreasing insulin sensitivity and weight loss and increasing insulin sensitivity [Parks, 2002]. Therefore, adipocytes have been hypothesized to be a contributing factor to the insulin response to plasma glucose.

Adipocytes synthesize and store triglycerides during feeding as well as release fatty acids, transported in the blood as triglycerides during fasting. In the normal homeostatic state, the balance of triglyceride storage and lipolysis is maintained at a rate appropriate to the caloric intake. During a disruption of the normal metabolic and secretory function of the adipocyte, for example in the overweight (high BMI) diabetic individual, a prolonged caloric surplus contributes to a lipid excess, enhanced lipolysis and consequent overload of free fatty acids in the skeletal muscle and liver contributing to decreased insulin sensitivity [Guilherme, 2008].

The significance of adipose tissue in regulating whole-body metabolism by sequestering lipid is demonstrated in the literature [Sovik, 1996] [Moitra, 1998] [Laustsen, 2002] [Shimomura, 1998]. The physical size of the adipocytes affects their function as well. Subcutaneous adipocytes have been reported to be heterogeneous in size and intrinsic insulin sensitivity [Varlamov, 2010]. Smaller adipocytes normally respond to insulin by increasing lipid uptake, but adipocytes with cell diameters larger than 80–100 micrometers are insulin resistant. It appears that, when cell size approaches a critical boundary, adipocytes lose insulin-dependent fatty acid transport mediated by GLUT-4. This negative feedback mechanism may protect adipocytes from lipid overload and restrict further expansion of adipose tissue, which leads to obesity and metabolic complications. However, when the negative feedback mechanism is activated, fatty acid transport in the enlarged cells is inhibited, and the enlarged cells are in a sense no longer available to participate in glucose homeostasis.

The association between high carbohydrate diet and hypertriglyceridemia is stronger for those who are overweight (BMI >28). Insulin resistance is more common among the overweight and the obese (BMI >30) and is suspected to be a result of carbohydrate-induced hypertriglyceridemia. [Parks, 2002] In the adipocyte, glucose is transported into the cell mediated by the glucose transporter type-4 (GLUT-4). Glucose can be converted to alpha-glycerol phosphate, the main source of the glycerol backbone of triglycerides. These triglycerides, during adipocyte dysfunction, are broken down and released back into circulation resulting in free fatty acid overload at skeletal muscle and insulin resistance [Guilherme, 2008].

It is hypothesized that reducing glucose transport into the adipocyte could decrease triglyceride deposition, thus making less triglyceride available for release during a metabolically dys-regulated state. D-tagatose shares common metabolic pathways with other sugars and it is possible that it may compete with glucose for transport into the adipocytes via the GLUT-4 transporter. Once in the cell, it may interfere with lipolysis of the formed triglycerides. If this occurred, D-tagatose would be most effective in those patients whose diabetes control was impaired (resulting in high HbA1c levels) to a larger extent by metabolic dysregulation of the adipocytes.

As a result of this analysis of the Phase 3 clinical trial results, Biospherics is currently designing new studies in cell culture, animal models and humans to clarify the mechanism of action of D-tagatose in modulating triglycerides and glucose in the metabolic syndrome.

**Table 1. Correlations Between Clinical Measures**

	<b>HbA1c</b>	<b>BMI</b>	<b>TG</b>
<b>HbA1c</b>	1	0.722	0.801
<b>BMI</b>	0.722	1	0.718
<b>TG</b>	0.801	0.718	1

Values are Pearson product-moment correlation coefficients,  $p \leq 0.10$

**Table 2. Differences Between Countries**

	<b>USA</b>	<b>India</b>	
	<b>mean</b>	<b>mean</b>	<b>p</b>
<b>BMI</b>	28.3	25.8	<0.00001
<b>TG</b>	189	171	0.43

**Units:** HbA1c %, BMI kg/m<sup>2</sup> , TG mg/dl

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## **About Spherix**

Spherix Incorporated was launched in 1967 as a scientific research company under the name Biospherics Research. The Company now leverages its scientific and technical expertise and experience through its two subsidiaries – Biospherics Incorporated and Spherix Consulting, Inc. Biospherics recently completed a Phase 3 clinical trial to study the use of D-tagatose as a treatment for Type 2 diabetes. Its Spherix Consulting subsidiary provides scientific and strategic support for suppliers, manufacturers, distributors and retailers of conventional foods, biotechnology-derived foods, medical foods, infant formulas, food ingredients, dietary supplements, food contact substances, pharmaceuticals, medical devices, consumer products and industrial chemicals and pesticides. For more information, please visit [www.spherix.com](http://www.spherix.com).

## **Forward-Looking Statements**

This release contains forward-looking statements which are made pursuant to provisions of Section 21E of the Securities Exchange Act of 1934. Investors are cautioned that such statements in this release, including statements relating to planned clinical study design, regulatory and business strategies, plans and objectives of management and growth opportunities for existing or proposed products, constitute forward-looking statements which involve risks and uncertainties that could cause actual results to differ materially from those anticipated by the forward-looking statements. The risks and uncertainties include, without limitation, risks that product candidates may fail in the clinic or may not be successfully marketed or manufactured, we may lack financial resources to complete development of D-tagatose, the FDA may interpret the results of studies differently than us, competing products may be more successful, demand for new pharmaceutical products may decrease, the biopharmaceutical industry may experience negative market trends, our continuing efforts to develop D-tagatose may be unsuccessful, our common stock could be delisted from the Nasdaq Capital Market, and other risks and challenges detailed in our filings with the U.S. Securities and Exchange Commission, including our current report on Form 8-K filed on October 10, 2007. Readers are cautioned not to place undue reliance on any forward-looking statements which speak only as of the date of this release. We undertake no obligation to publicly release the results of any revisions to these forward-looking statements that may be made to reflect events or circumstances that occur after the date of this release or to reflect the occurrence of unanticipated events.

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