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Probiotic Symposium Honors Dr. Eli Metchnikoff

Reno, NV, November 16, 2007 — On September 14th and 15th, the University of Nevada School of Medicine hosted a Symposium on Clinical Applications of Probiotics in Human Health. The Symposium commemorated the centennial of the publication in English of *The Prolongation of Life* by Dr. Eli Metchnikoff, the Nobel laureate father of probiotic research. The Symposium was organized and sponsored by Klair Labs™, a division of ProThera®, Inc. An international faculty provided attendees with cutting edge information on the use of probiotics to enhance health.

Dr. Stephen Olmstead, the Chief Science Officer for Klair Labs™, introduced the concept of the human intestinal microbiota organ critical for immune and gastrointestinal system maturation, colonization resistance, modulation of immune responses, and nutritional needs. He noted that the importance of *Lactobacillus* and *Bifidobacterium* microorganisms to human health is highlighted by dendritic and lymph cell-mediated transfer of a mother's microflora from her intestines to her infant's by way of secretion of microorganisms into breast milk. Dr. Olmstead discussed probiotic production and outlined methods including the InTactic® technology used to enhance delivery of viable probiotic microorganisms to the distal bowel. Dr. Olmstead concluded with practical recommendations on probiotic dosing and administration such as consuming probiotics with food rather than on an empty stomach.

Dr. Lynne McFarland, a world-class authority on probiotics, *Clostridium difficile*, and antibiotic-associated diarrhea from the University of Washington, summarized the history of probiotic use and outlined guidelines to assess probiotic health claims, safety, and product quality. In a second lecture, Dr. McFarland reviewed data from 216 clinical trials of probiotics in health conditions ranging from antibiotic-associated diarrhea to allergies and eczema. She noted that clinical research has substantiated the efficacy of *Saccharomyces boulardii* for recurrent *C. difficile* disease, pediatric diarrhea, and traveler's diarrhea. She also reviewed highly positive data for the use of *Lactobacillus rhamnosus* GG, *L. casei*, and multispecies probiotics in a variety of clinical

conditions including the prevention of antibiotic-associated diarrhea and reduction of the risk of pediatric allergic diseases.

Dr. José Saavedra, Associate Professor of Pediatrics at Johns Hopkins University School of Medicine and pioneer in pediatric probiotic research, closed the first day of the symposium by presenting compelling data on the importance of the intestinal microbiota for immune system maturation and modulation and the role of microbiota disruptions in the current epidemic of childhood allergic diseases. He reviewed mechanisms by which the normal microbiota modulates the immune system through the function of regulatory T cells. Dr. Saavedra highlighted the importance of *Bifidobacterium lactis* to improve secretory immune function and enhance gut maturation in preterm infants, decrease rotavirus shedding in children, and enhance innate cellular immunity and phagocytosis in adults.

Dr. David Traver, a pediatrician specializing in the biomedical treatment of children with autism spectrum disorders began the second day of the Symposium by reviewing the high prevalence of gastrointestinal disorders that afflict children with autism. He noted that alterations in gut barrier function are common and well-documented in these children and that the absorption of exorphins from incompletely digested casein and gluten may significantly contribute to the neurological manifestations of autism. Dr. Traver presented data showing that exposure to broad spectrum antibiotics may be a trigger in the development of autism and findings that the intestinal microbiota of children with regressive autism is disrupted with an increase in *Clostridium* and *Ruminococcus* species. Dr. Traver reported that the use of probiotics has become a cornerstone in the biomedical treatment of autism spectrum disorders and observed that clinical trials are sorely needed.

Dr. Stig Bengmark, chief of surgery for over 20 years at Lund University Hospital in Sweden and now Visiting Professor at University College London, gave a highly engaging lecture on the combined use of prebiotics, food fiber that stimulates the growth and/or activity of healthful bacteria, with probiotics for the control of acute and chronic diseases. Dr. Bengmark stated that his research interest in probiotics began in 1986 when he and colleagues reviewed the incidence of infections in their patients undergoing liver resection and found that all the post operative infections occurred in those treated with antibiotics and no infections developed in patients who had not received antibiotics. He speculated that many of the chronic diseases now prevalent in industrial societies are related to lack of dietary consumption of important probiotic species such as *Lactobacillus plantarum* and *L. paracasei*. Dr. Bengmark presented new data on the beneficial

use of a new a symbiotic, a multispecies probiotic and prebiotic formulation, for chronic liver disease, decreasing the incidence of infections in patients undergoing surgery for intraabdominal malignancies, and reducing infection, intensive care unit days, need for mechanical ventilation, and mortality in patients with severe multiple trauma.

Dr. William Marks, Robert B. McMillen Chair of the Department of Organ Transplantation and the Laboratory for Transplantation Biology at Swedish Medical Center in Seattle reviewed the problem of immunosuppressant-induced diarrhea in patients following kidney transplantation. Dr. Marks presented an elegant overview of how, in collaboration with Klaire Labs™, he conceived a double-blind, placebo-controlled clinical trial of probiotics to reduce the incidence of immunosuppressant-induced diarrhea. He has hypothesized that the short chain fatty acids produced by probiotic microorganisms may improve entero- and colonocyte function thereby reducing the incidence of diarrhea. Klaire Labs™ is supplying Dr. Marks and his coworkers with the probiotic formulation and placebo used in the study. Dr. Marks presented preliminary data although the study is ongoing and remains blinded.

Dr. Philippe Marteau, Professor of Gastroenterology at Paris 7 University and Lariboisière Hospital in Paris, France and world-renowned authority on the use of probiotics in inflammatory bowel disease, delivered the final lecture of the Symposium. Dr. Marteau presented the clinical data demonstrating that the clinical efficacy of a probiotic formulation containing 8 species for the management of ulcerative colitis, pouchitis, a complication of the surgical management of ulcerative colitis, and Crohn's disease. Although the response of Crohn's disease has been disappointing overall, Dr. Marteau outlined the evidence for the efficacy of *Saccharomyces boulardii* and *Escherichia coli* Nissle 1917 for reducing the incidence of relapse in Crohn's disease. He presented study data indicating the efficacy of probiotics in inflammatory bowel disease appears to be contingent on the immune modulating properties of unmethylated sequences of portions of bacterial DNA containing high cytosine-guanine sequences known as CG or CpG islands. How much remains to be discovered and understood about probiotic activities and benefits was underscored as Dr. Marteau presented data showing that *Lactobacillus acidophilus* is effective at providing relief for mild to moderate abdominal pain through a mechanism that involves induction of intestinal cannabinoid and opioids receptors.

A set of CDs and the accompanying Symposium syllabus are available for order at www.ProbioticSymposium.com or by calling 1-888-488-2488. Klaire Labs™ will organize and fund the second annual Probiotic Symposium entitled Probiotics, Prebiotics and Enzymes:

Clinical Applications in Human Health. The second annual Probiotic Symposium is planned for October 17th and 18th of 2008 to be held in Reno-Lake Tahoe.

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