This poster presentation was made on May 8, 2007 at the Innovation Corridor Poster Session Abstracts section of the 2007 Bio International convention, Boston, MA, USA.

PROGRESS IN DEVISING A BOWEL BASED PROBIOTIC THERAPY FOR UREMIA.

Natarajan Ranganathan, Ph D[1], Eli A Friedman, M.D.[2] [1]Kibow Biotech Inc, Newtown Square,, PA, United States; and [2] Downstate Medical Center, State University of New York (SUNY), Brooklyn, NY, United States.

To assess the potential of devising a gut-based probiotic formulation as therapy in chronic kidney disease (CKD), we have performed extensive *in vitro* R&D investigations in our labs. We then used the Simulated Human Intestinal Microbial Ecosystem (SHIME, Ghent University, Belgium), a computer controlled gastrointestinal *in vitro* simulated system and validated the ability of the microbial formulation to metabolize and thus reduce the concentration of nitrogenous components including urea, creatinine, and uric acid. Bacterial strains studied were *Streptococcus thermophilus* (KB27), *Lactobacillus acidophilus* (KB31) and *Bifidobacterium longum* (KB35). We then confirmed and reported that these bacterial formulations, fed orally in 5/6th nephrectomized rodent - rat (at Thomas Jefferson University, Philadelphia, PA) and minipig models (at Indiana University, Indianapolis, IN), reduced both blood urea nitrogen (BUN) and serum creatinine (Scr) levels.

Before starting human trials we conducted a study of the effect of our probiotic mixture in clinical renal failure in veterinary practice. Two independent veterinarians initiated trials of Kibow Biotics® in uremic cats and dogs of both genders and varying body weights. Treatment consisted of orally ingesting live bacteria (expressed as Colony Forming Units – CFU) as enterically coated gel caps (15 billion CFU/gel cap) administered twice or thrice daily for a total dose 30 to 45 billion CFU per day (because of difficulties in feeding the whole gel cap to some of the smaller animals, a few pet owners broke the gel cap and mixed the contents with their animal feed). Study animals were solicited from their owners after a clear explanation that the probiotic given had not previously been tested in a clinical setting.

Azotemia declined during therapy; in cats (n=7), BUN fell from 54 13.0 to 45.1+12.0 mg/dl, while Scr decreased from 4.0 1.9 to 2.9 0.7 mg/dl. Similar results were obtained in dogs (n=6), BUN decreased from 64.7 35.4 to 30.4 17.7 mg/dl, while Scr fell from 2.6 1.3 to 2.0 1.5 mg/dl. No adverse effects were noted during 2-6 months of treatment. Survey questionnaires sent to pet owners generated strongly positive results from the respondents, who reported either significant improvement in uremia marker values or, in more advanced cases of kidney failure, stabilization and improved quality of life for their

companion animals. These data are presented as a step in the evolution of a gut- based uremia therapy with possible application in human patients. Currently our product is being marketed and sold as “Azodyl™” by Vetoquinol USA to companion animals, both cats and dogs in moderate to severe kidney failure generating positive results and with improved quality of life across USA.

Our data support the view that testing efficacy of orally administered probiotics in a clinical veterinary practice setting affords a rational opportunity to confirm and validate inferences drawn from partially nephrectomized test animals. A safety study in healthy volunteers has also been accomplished with Kibow Biotics® (identical product formulation as used in cats and dogs with renal failure) by our own group of volunteer employees with required legal documentation. The next step is the initiation of pilot scale human clinical trials in stage III and IV CKD patients. Efforts are in progress towards accomplishing this goal in several countries beginning with USA and Canada.

Contact information:
Natarajan Ranganathan, PhD
rangan@kibowbiotech.com
(610)353-5130