Press Release: Prana Biotechnology's PBT2 is in development for HD and AD

The published research on HD, copper, and clioquinol or its derivative PBT2 is not new. However, with its new press release (below) it looks like Prana's progress with Alzheimer's disease has caused them to take another look at the HD data so we may see some forward movement with clinical development.

In 2007, Dr. Steven Hersch and colleagues showed that concentrations of copper are elevated in HD and provided evidence that interactions between copper and the HD protein and highly copper-sensitive lactate dehydogenase (LDH) contribute to HD pathology.

In 2005, Dr. Steven Massa and colleagues first found that clioquinol looked promising in a cell model and then administered it to R6/2 mice. As compared to untreated R6/2 mice, the clioquinol group experienced less atrophy of the striatum, lost less weight, performed better on the rotarod, and lived twenty percent longer.

Clioquinol is an old antibiotic which is currently used as a topical cream for skin infections. Clioquinol was at one time given internally in Japan but was banned in 1970 after it was discovered to cause neurotoxicity, a syndrome called subacute myelo-optico-neuropathy (SMON). The mechanism which caused the neurotoxicity was never determined. Copper deficiency, Vitamin 12 deficiency, and impurities have all been hypothesized to have been the source of the problem. Prana first began its research with clioquinol but was unable to remove impurities in the manufacturing process. It then developed a second-generation version of the drug which has in clinical trials for Alzheimer's patients. In a twelve-week phase IIa trial with early AD patients, PBT2 was found to be safe and well-tolerated and to improve cognition.

References:

Jonathan H. Fox, Jibrin A. Kama, Gregory Lieberman, Raman Chopra, Kate Dorsey, Vanita Chopra, Irene Volitakis, Robert A. Cherny, Ashley I. Bush, Steven Hersch. **"Mechanisms of copper ion mediated Huntington's disease progression."** PLoS ONE 2(3): e334. doi:10.1371/journal.pone.0000334

Trent Nguyen , Aaron Hamby, and Steven M. Massa**. "Clioquinol down-regulates mutant huntingtin expression in vitro and mitigates pathology in a Huntington's disease mouse model."** Proceedings of the Nat'l Academy of Sciences of the USA. August 16, 2005 , vol. 102, 11840-5.

- *Marsha L. Miller, Ph.D., July 1, 2010*

Press Release:

New PBT2 data in 2010 Hot Topics Session at International Conference on Alzheimer's Disease

- *Evidence of Complementary and Beneficial Effects in the Treatment of Alzheimer's and Huntington's Disease*

- *PBT2, promotes neuronal growth and prevents brain deterioration in both Alzheimer's disease and Huntington's disease transgenic mice*

- *Exciting prospects for a second neurological indication for PBT2*

MELBOURNE, Australia – July 1, 2010 : Prana Biotechnology Limited (NASDAQ: PRAN / ASX: PBT), today announced that its Head of Research, Assoc. Prof. Robert Cherny, will present new data on PBT2, the Company's lead compound in development for Alzheimer's disease, at the Hot Topics Therapeutics/Intervention session on July 14th at the International Conference of Alzheimer's Disease (ICAD) in Honolulu. The presentation is entitled "Novel molecular mechanisms for the neurotrophic and neuroprotective effects of PBT2 in Alzheimer's disease and Huntington's disease".

The new findings show that the effectiveness of PBT2 lies in a unique combination of complementary activities. PBT2 acts to detoxify A-beta by disarming it of copper and zinc and returns these crucial metals to neurons. Assoc. Prof. Cherny will present data* showing that by returning these metals to neurons, important cell signaling pathways are activated that prevent neuronal death and promote neuronal function. In addition, data will be presented linking the neuroprotective qualities of PBT2 with beneficial effects evident in an animal model of Huntington's disease.

In collaboration with the University of California San Francisco, PBT2 was tested in the R6/2 transgenic model of Huntington's disease. The mice exhibited significant improvement in coordination, motor function and lifespan**. Significantly, examination of the brains of treated mice showed marked reduction in atrophy of the striatal tissue. In Huntington's disease, this tissue degenerates resulting in the loss of brain volume, a hallmark of the disease.

Prof. Rudy Tanzi, co-founding scientist of Prana and Professor of Neurology at Harvard University Medical School said "The ability of PBT2 to promote normal neuronal function and prevent degeneration of the brain tissue further indicates the disease modifying potential of PBT2". "Prana's mission is to create a library of compounds that can offer therapies to treat neurodegenerative disorder of high unmet medical need. We are very excited about the potential opportunity to treat these two devastating neurodegenerative disorders" commented Geoffrey Kempler, Prana's CEO.

About Prana Biotechnology Limited

Prana Biotechnology was established to commercialise research into Alzheimer's disease and other major age-related neurodegenerative disorders. The Company was incorporated in 1997 and listed on the Australian Stock Exchange in March 2000 and listed on NASDAQ in September 2002. Researchers at prominent international institutions including The University of Melbourne, The Mental Health Research Institute (Melbourne) and Massachusetts General Hospital, a teaching hospital of Harvard Medical School, contributed to the discovery of Prana's technology.

For further information, and descriptions of the peer-reviewed journals, please visit the Company's web site at www.pranabio.com.

*8 month old APP/PS1 mice were treated for 11 days oral PBT2 30 mg/kg (n=7) or vehicle (n=7), In the brains of drug treated animals statistically significant ($P<0.05$) increases were detected in levels of neuronal markers TrkB,

NMDAR1, NMDAr2a, NMDAR2b and CAMKII compared with untreated controls. Primary mouse cortical neurons cultured in the presence of 10μMPBT2 and 10μM zinc were protected against the toxic effects of 30μM glutamic acid ($P<0.01$).

**R6/2 (transgenic HD) mice were administered 30mg/kg PBT2 orally (n=10) or vehicle (N=10) for up to 8 weeks. Significant improvements ($P<0.05$) were observed in performance in the rotorod and hindlimb clasping tasks in the drug treated animals compared with the untreated controls. The average cumulative lifespan of the PBT2 treated animals was around 40% longer than that of the untreated controls ($P<0.05$)