# Prana Receives Approval For Alzheimer's Trial

*12 month Phase II Imaging study with PBT2 in early Alzheimer's patients*

**Melbourne – 22 November, 2011: Prana Biotechnology (NASDAQ:PRAN; ASX:PBT)** today announced that it has received approval from the Austin Health Research Ethics Committee to commence a 12 month Phase II Imaging trial testing PBT2, the Company's drug in development for Alzheimer's Disease. The purpose of the trial, which builds on the success of an earlier Phase IIa clinical trial of PBT2, is to measure physical changes in the brains of participants treated with PBT2 for 12 months, and to consolidate the evidence, over a longer period, of the positive effects of PBT2 on patients' cognition reported in the earlier trial.[1,2]

"This is an important milestone for the Company. Given that PBT2 has already been shown both to significantly change Abeta levels in spinal fluid and improve the cognition of Alzheimer's Disease patients in a 12 week trial, we believe that in this 12 month trial PBT2 will establish its credentials as a safe and effective treatment for Alzheimer's Disease", commented Prana's Executive Chairman, Mr Geoffrey Kempler.

The double blind placebo controlled trial will enroll 40 patients with prodromal or mild Alzheimer's Disease in 3 sites in Melbourne, Australia. Brain Imaging will be used to measure PBT2's effect on amyloid deposits in the brain (using PiB-PET scanning) and effects on increasing brain activity (F-FDG PET). Cognition effects will be measured by the Neuropsychological Test Battery (NTB). The protocol synopsis appears below in Appendix 1.

## Funding and Key Opinion Leader support

The trial has received funding from the Alzheimer's Drug Discovery Foundation (ADDF).

Howard Fillit, MD, the ADDF's Executive Director commented that "PBT2 stands out as one of the few remaining orally available agents with clinical trial evidence of cognitive benefit for Alzheimer's patients. Success in this trial will demonstrate target engagement by PBT2 in the brain of people with Alzheimer's Disease, and accelerate the clinical development of PBT2 to patients".

## Commercial Strategy

AD and dementia affects over 26 million people worldwide. The cost to society has been reported as $600 billion per annum. Currently all available treatments are approved to provide some degree of symptomatic relief. None change the course of the disease and the eventual decline in patient's cognition and health. Over the past few years several high profile Phase III trials have failed to reach their primary endpoints. PBT2 has the potential to be an effective treatment for AD that is supported by an extensive body of scientific and clinical work. Prana's earlier clinical data was for a 12 week trial in 78 patients, the new PBT2 Imaging Trial provides the opportunity to treat patients for 12 months, providing significantly more safety data as well as efficacy data. The study design aims to demonstrate PBT2's potential as an effective disease modifying treatment available to patients.

## Previous Clinical Evidence

Patients with mild AD treated with 250mg of PBT2 (a once-a-day capsule) demonstrated a significant improvement in cognition *(NTB Executive Function Composite z-score, p=.042)*. The effect was noteworthy because of the sample size of patients on the effective dose *(n=27)* and the period of treatment (12 weeks). The new PBT2 Imaging Trial will have the same number of patients treated with the same effective dose *(n=27)* but for the much longer period of 12 months. The clinical data from earlier trials can be viewed here[a].

## Strong Scientific Evidence

The scientific data supporting the belief that PBT2 will bring meaningful clinical benefit to patients is extensive. A position paper on PBT2's mechanism of action can be viewed here[b]. PBT2 restores neuronal health by selectively binding and redistributing brain metals (copper, zinc) that have become imbalanced due to disease or the ageing process. The positive effects on brain function delivered by PBT2's actions are:

(i) Anti amyloid effects

- ✓ Reduces Abeta Aggregation[4]
- ✓ Promotes Dissolution of Abeta Oligomers[4]
- ✓ Prevents toxicity of Abeta oligomers (preventing binding to NMDA receptors)[4]
- ✓ Promotes Abeta Degradation and Clearance[4,6]
- ✓ Redistributes Abeta-Sequestered Metals back into neurons and other cells[4,6]

(ii) Neuroprotective and neurotrophic effects

- ✓ Redistributes metals into neurons and modulates intracellular signalling pathways[4,6]
- ✓ Reduces potential for glutamate excitotoxicity
- ✓ Restores Synaptic Plasticity (LTP and Spine Density) ie promotes neuronal regrowth[4,5]
- ✓ Prevents free radical production (silences redox activity of redox active metals)[4]
- ✓ Reduces tau hyperphosphorylation[4]

Links

a. Mechanism paper available at: http://www.pranabio.com/downloads/Prana%20Positioning%20statement%20November%202010%20FINAL.pdf
b. Clinical data available at: http://www.pranabio.com/default.asp?contentID=625

References


1. Lannfelt *et al.* "Safety, Efficacy, and biomarker findings of PBT2 in targeting Abeta modifying therapy for Alzheimer's disease: a controlled phase IIa, double-blind, randomized, placebo-controlled trial", Lancet Neurology (2008) vol. 7, pp. 779-86.
2. Lannfelt *et al.* **Errata:** Lancet Neurology (2009) vol. 8, pp. 981.
3. Faux *et al* "PBT2 Rapidly Improves Cognition in Alzheimer's Disease: Additional Phase II Analyses", Journal of Alzheimer's Disease (2010) vol. 20 pp. 509-516
4. Adlard *et al*. ''Rapid Restoration of Cognition in Alzheimer's Transgenic Mice with 8-Hydroxy Quinoline Is Associated with Decreased Interstitial Aβ Analogs", Neuron (2008) vol. 59, pp. 43-55
5. Crouch *et al.* "The Alzheimer's therapeutic PBT2 promotes amyloid-B degradation and GSK phosphorylation via a metal chaperone activity", Journal of Neurochemistry (2011) vol. 119, pp.220-230

6. Adlard et al "Metal Ionophore Treatment Restores Dendritic Spine Density and Synaptic Protein Levels in a Mouse Model of Alzheimer's Disease", PLoS ONE (2011) 6(3): e17669. doi:10.1371/journal.pone.0017669 (2011) e17669

## Appendix 1 – Protocol Synopsis

**Protocol synopsis**

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| **Title** | **A randomised, double-blind, placebo-controlled study to assess the safety and tolerability of PBT2, and its effect on amyloid deposition in the brains of patients with prodromal or mild Alzheimer's disease** |
| **Study Number** | **PBT2-204** |
| **Study Design** | **Randomised, double-blind, placebo-controlled, Phase IIa study** |
| **Objectives** | ***Primary Objective***<br>**To evaluate the effect of PBT2 compared to placebo on brain amyloid levels after 52 weeks of treatment in patients with prodromal or mild Alzheimer's disease**<br>***Secondary Objectives***<br>• **To evaluate the safety and tolerability of PBT2 compared to placebo after 52 weeks**<br>• **To evaluate the effect of PBT2 compared to placebo on brain metabolic activity after 52 weeks**<br>• **To evaluate the effect of PBT2 compared to placebo on brain volumes after 52 weeks**<br>• **To evaluate the effect of PBT2 compared to placebo on cognition after 52 weeks**<br>• **To evaluate the effect of PBT2 compared to placebo on functional abilities after 52 weeks** |
| **Number of Patients** | **It is planned that 40 patients will be randomised in to the study** |
| **Key Patient Criteria** | • **Prodromal or mild Alzheimer's disease**<br>• **$^{11}$C-PiB PET positive (SUVR > 1.7)**<br>• **MMSE ≥ 20** |
| **Doses** | **Placebo (0mg PBT2) and 250mg PBT2, once daily capsules** |
| **Per Patient Duration** | **60 weeks: Four week Screening period, 12 months (52 weeks) Treatment period and Follow-up 4 weeks post treatment** |
| **Endpoints** | ***Primary***<br>• **$^{11}$C-PiB PET neocortical SUVR**<br>***Secondary***<br>• **Safety and Tolerability**<br>• **$^{18}$F-FDG PET: SUVR**<br>• **MRI: Total brain, hippocampal and ventricular volumes**<br>• **Cognition: NTB and MMSE**<br>• **Functional: ADCS-ADL-23** |
| **Trial Locations** | **Approx. 3 sites in Melbourne, Victoria** |
| **Trial Standard** | **Study will be conducted according to ICH GCP** |

## About Prana Biotechnology Limited

Prana Biotechnology was established to commercialize research into age-related neurodegenerative disorders. The Company was incorporated in 1997 and listed on the Australian Securities 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 please visit the Company's web site at www.pranabio.com.

**About the Alzheimer's Drug Discovery Foundation**

The Alzheimer's Drug Discovery Foundation (ADDF) is the only non-profit organization whose sole mission is to accelerate the discovery and development of drugs to prevent, treat and cure Alzheimer's Disease, related dementias and cognitive aging. Since 1998, the ADDF has granted more than $50 million to fund over 325 Alzheimer's drug discovery programs in academic centers and biotechnology companies in 18 countries. For more information about the Foundation, please visit www.AlzDiscovery.org.

**Forward Looking Statements**

*This press release contains "forward-looking statements" within the meaning of section 27A of the Securities Act of 1933 and section 21E of the Securities Exchange Act of 1934. The Company has tried to identify such forward-looking statements by use of such words as "expects," "intends," "hopes," "anticipates," "believes," "could," "may," "evidences" and "estimates," and other similar expressions, but these words are not the exclusive means of identifying such statements. Such statements include, but are not limited to any statements relating to the Company's drug development program, including, but not limited to the initiation, progress and outcomes of clinical trials of the Company's drug development program, including, but not limited to, PBT2, and any other statements that are not historical facts. Such statements involve risks and uncertainties, including, but not limited to, those risks and uncertainties relating to the difficulties or delays in financing, development, testing, regulatory approval, production and marketing of the Company's drug components, including, but not limited to, PBT2, the ability of the Company to procure additional future sources of financing, unexpected adverse side effects or inadequate therapeutic efficacy of the Company's drug compounds, including, but not limited to, PBT2, that could slow or prevent products coming to market, the uncertainty of patent protection for the Company's intellectual property or trade secrets, including, but not limited to, the intellectual property relating to PBT2, and other risks detailed from time to time in the filings the Company makes with Securities and Exchange Commission including its annual reports on Form 20-F and its reports on Form 6-K. Such statements are based on management's current expectations, but actual results may differ materially due to various factions including those risks and uncertainties mentioned or referred to in this press release. Accordingly, you should not rely on those forward-looking statements as a prediction of actual future results.*

**Contacts:**

*Australia*
Prana Biotechnology Ltd
T: +61 3 93494906
E: info@pranabio.com

*US – Investor Relations*
Leslie Wolf-Creutzfeldt
T: 646-284-9472
E: leslie.wolf-creutzfeldt@grayling.com

*US - Media*
Ivette Almeida
T: 646-284-9455
E: ivette.almeida@grayling.com