



## **Prana Announces Success in Phase IIa Clinical Trial of PBT2 in Early Alzheimer's Disease**

*PBT2 demonstrates positive biomarker and cognitive effects*

**MELBOURNE, Australia – February 26, 2008: Prana Biotechnology Limited (NASDAQ: PRAN / ASX: PBT)**, a biopharmaceutical company focused on the research and development of treatments for neurodegenerative disorders, today announced that PBT2 has demonstrated safety and tolerability and reduced Abeta 42, in a Phase IIa study of PBT2 in patients with early Alzheimer's Disease. PBT2 also improved Executive Function performance in select cognitive tests.

"This is a very exciting and important milestone for the company, particularly because PBT2, a drug known to inhibit the toxic oligomers of Abeta that cause the functional damage in Alzheimer's Disease, was able to show such a clear effect in a short trial," commented Geoffrey Kempler, Prana's Chairman and CEO.

In this double blind multi-centre clinical trial, 78 patients in Sweden and Australia were randomized to receive either a placebo, PBT2 50mg or PBT2 250mg capsule once per day for 12 weeks.

Analysis of the trial data demonstrated that the safety and tolerability profile of PBT2 at both doses was indistinguishable from that of placebo. There were no study withdrawals related to adverse events. There was no serious adverse event (SAE) in any PBT2 treated patient.

The study also demonstrated the impact of PBT2 on reducing Abeta 42 in the cerebrospinal fluid (CSF) that surrounds the brain and spinal cord, considered a key biomarker for Alzheimer's Disease. Specifically, PBT2 at the 250mg dose showed a highly significant reduction in CSF Abeta 42 compared to placebo ( $p=0.006$ ). The effect of PBT2 was dose related ( $p=0.02$ ).

Professor Jeffrey Cummings, Director of the Easton Centre for Alzheimer's Disease at UCLA, and Head of Prana's Research and Development Advisory Board, commented that "PBT2 has hit what we consider to be the critical target for Alzheimer's Disease, as evidenced by the significant reduction in Abeta 42."

Encouraging signs of cognitive improvement, as measured by the Neuropsychological Test Battery (NTB), were also observed. Statistically significant improvement was evident in two of the four Executive Function NTB tests: the Category Fluency Test ( $p=0.028$ ) and the Trail Making Test part B ( $p=0.005$ ), both after 12 weeks of treatment at the 250mg dose compared to placebo. PBT2, in this study of early disease progression, had no effect on ADAS-cog, a test of cognition not designed to measure Executive Function changes. The NTB is a test of cognition that is more sensitive to the changes in Executive Function that are seen in the early stage of Alzheimer's Disease.

“The impact of this drug on Executive Function is very encouraging as this is likely to predict an improvement in the day to day functioning in the lives of people with Alzheimer’s Disease. The ability to plan and execute everyday activities, even more so than memory, offers great practical and clinical benefit to patients” added Professor Cummings.

These results build on earlier observations using PBT2 in transgenic mouse models of Alzheimer’s Disease, where PBT2: reduced toxic oligomers of Abeta, reversed the Abeta-induced loss of neurotransmission and improved cognition.

Prana now plans to further progress PBT2 into larger and longer clinical trials to investigate its potential as a disease modifying drug.

“We are very hopeful that PBT2 will continue to perform as well as it has in this trial and progress through the development pathway, eventually to bring true benefit to patients with Alzheimer’s Disease. PBT2 is one of many Metal Protein Attenuating Compounds (MPACs) within the Prana pipeline, which we are enthusiastic to develop for a range of neurodegenerative diseases,” concluded Mr. Kempler.

Please refer to the Appendix below which is included in, and forms part of, this announcement.

**Conference call details:**

The company will hold a conference call to discuss the above results and welcomes participation from interested parties.

**Australia**

**Wednesday, February 27, 2008  
9.00am(Eastern Summer Time)**

**Dial in number:**

**1800-002-971**

**USA**

**Tuesday, February 26, 2008  
5.00pm (US Eastern time)**

**Dial in number:**

**888-713-4218 from the US or Canada (toll-free)**

**or +1 617-213-4870 from other locations**

**Dial in at least 10 minutes prior to commencement to access call**

**Reference Prana or conference ID # 64631038**

The call will be webcast and available on the Prana website [www.pranabio.com](http://www.pranabio.com)

**REPLAY OF TELECONFERENCE**

A replay of the call will be available 2 hours later until 11.59pm (US eastern time) on March 3, 2008.

Dial + 1 888-286-8010 from the US or Canada (toll – free) or +1 617-801-6888 from other locations. To enter conference dial ID # 16766828

## **About Prana Biotechnology Limited**

Prana Biotechnology was established to commercialize 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, please visit the Company's web site at [www.pranabio.com](http://www.pranabio.com)

## **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 factors 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.

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## Appendix

### Details of study design and results of the trial in accordance with the reporting guidelines in the Australian Stock Exchange's Code of Best Practice for Reporting by Life Science Companies, section 4.5.

Study Title: PBT2-201-EURO Study Design

<b>Number of patients</b>	78 patients randomized (Intent-to-Treat population); 74 patients completed study.
<b>Key patient selection criteria</b>	<ul style="list-style-type: none"><li>▪ Fulfill National Institute of Neurological and Communication Disorders and Stroke (NINCDS)/Alzheimer's Disease and Related Disorders Association (ADRDA) criteria for probable AD and International Classification of Diseases (ICD)-10 criteria for AD.</li><li>▪ Age over 55 years</li><li>▪ Mini-mental Status Examination (MMSE) score between 20 and 26 inclusive or ADAS-Cog score of 10-25.</li><li>▪ Modified Hachinski score <math>\leq 4</math></li><li>▪ Computerised tomography (CT) or magnetic resonance imaging (MRI) scan within the last 24 months which, in the opinion of the local investigator, does not alter the diagnosis of AD to vascular or multi-infarct dementia.</li><li>▪ Stable dose of donepezil, rivastigmine or galantamine for at least 4 months with clinical evidence of deterioration.</li></ul>
<b>Rationale</b>	The interactions between key metals and $\beta$ amyloid ( $A\beta$ ) in the brains of patients suffering from AD may be related to both the pathogenesis and devastating toxicity of the disease. Because PBT2 interferes with this interaction and inhibits toxic Abeta oligomer production, PBT2 is being developed as a potential disease modifying treatment for AD.
<b>Blinding</b>	Double-blind
<b>Placebo controlled</b>	Yes
<b>Route of administration</b>	Oral (capsules)
<b>Study design</b>	Randomised, double-blind, placebo-controlled, parallel three-group study to assess the safety and tolerability of PBT2 in patients with early AD. A modified dose-escalation element with ongoing Data Safety Monitoring Board (DSMB) review was included at the start of the study. An initial cohort of patients were allocated to either 50mg or placebo and data was monitored by the DSMB. Further patients randomised were allocated to either 50mg, 250mg or placebo, again with ongoing DSMB monitoring.
<b>Dose groups</b>	0mg (placebo capsules of identical appearance), 50mg and 250mg
<b>Duration</b>	12 weeks once daily dosing with 2 week follow-up
<b>Primary endpoints</b>	Safety and tolerability
<b>Secondary endpoints</b>	CSF and plasma biomarkers (including $A\beta_{42}$ , $A\beta_{40}$ , total Tau, P-Tau); cognition readouts
<b>Trial sites</b>	15 clinical trial sites in Australia (7) and Sweden (8)
<b>Contract Research Organisation</b>	Quintiles Limited, Berkshire, UK

Results of the PBT2-201-EURO Study

<p><b>Patient demographics</b></p>	<ul style="list-style-type: none"> <li>• Mean age 72 years (range 58 – 83 years)</li> <li>• 50% male, 50% female</li> <li>• ApoE e4 genotype 75.6%</li>   <li>• Mean ADAScog score at entry             <ul style="list-style-type: none"> <li>• 50mg 18.9</li> <li>• 250mg 18.7</li> <li>• Placebo 18.9</li> </ul> </li>   <li>• Mean MMSE score at entry             <ul style="list-style-type: none"> <li>• 50mg 23.2</li> <li>• 250mg 23.5</li> <li>• Placebo 22.2</li> </ul> </li> </ul> <p>All characteristics similar across dose groups</p>
<p><b>Primary endpoint</b></p>	<p>PBT2 in this study of early AD patients was safe and well tolerated, with no significant findings or trends in any of the safety parameters measured. The safety and tolerability profile of either dose of PBT2 was indistinguishable from placebo.</p>
<p><b>Secondary endpoints - biomarkers</b></p>	<p>PBT2 250mg showed a statistically significant reduction of CSF A<math>\beta</math><sub>42</sub> after 12 weeks of treatment compared with placebo (p=0.006, ITT).</p>
<p><b>Secondary endpoints - cognition</b></p>	<p>PBT 250mg showed statistically significant improvements in both the Trail Making Test part B and the Category Fluency Test (NTB sub-tests) after 12 weeks of treatment compared with placebo (p=0.005 and p=0.028, respectively (ITT)).</p>