

## Company Announcement

### *Journal of Neuroscience* paper further validates Prana science

**Melbourne, Australia 7 April 2004** — Prana Biotechnology Ltd. (ASX: PBT, Nasdaq: PRAN), today announced the publication of a new paper in the current edition of *Journal of Neuroscience*. The results further support Prana's theory that metals in the brain, rather than proteins on their own, are responsible for the pathology of Alzheimer's Disease and that attenuating the action of these metals may hold the key to effective therapeutic intervention.

It is known that zinc reacts with amyloid beta to cause the amyloid plaques around nerve endings in Alzheimer's disease. The role of zinc in the formation of damaging amyloid plaques in blood vessels supplying the brain has, up to now, not been clear.

Amyloid deposits in arteries cause damage to the blood vessel wall resulting in impaired blood flow. If these deposits occur in arteries that supply blood to the brain then this may starve the brain tissue of oxygen compounding the dementia associated with Alzheimer's Disease.

This *Journal of Neuroscience* article demonstrates that zinc plays a central role in the formation of amyloid plaques not only at the nerves but also in the blood vessels of the brains of people with Alzheimer's disease.

Prana's scientific consultants produced a mouse model which lacked a protein from nerve endings that transports and mediates the levels of zinc in the nerves and surrounding tissue. They observed that not only did the blood vessel walls in the brains of these mice have lower levels of zinc, but with less zinc there is also significantly fewer amyloid deposits. These new results show that the same zinc responsible for toxic amyloid deposits around nerves is also responsible for causing amyloid deposits in blood vessels.

Dr Ashley Bush, chief scientific consultant to Prana, and senior author on the publication explained; "These findings strongly support the suitability of Prana's MPAC\* class of drugs for targeting amyloid deposits in Alzheimer's disease, both in the blood vessels in the brain and in the brain tissue around the nerve endings.

"It is yet another piece of evidence that attenuating the interaction of metals and amyloid protein could be beneficial in treating Alzheimer's Disease," said Dr Bush.

Prana's MPAC technology is designed to attenuate the interaction of zinc and amyloid protein in the brain of patients with Alzheimer's Disease.

To view the abstract on the *Journal of Neuroscience* website please visit  
<http://www.jneurosci.org/cgi/content/abstract/24/13/3453>

---

ENDS

**Further information**

Media – Australia	Media – New York	Company
Kate Mazoudier Buchan Phone: +61 3 9866 4722 0403 497 424 <a href="mailto:kmazoudier@bcg.com.au">kmazoudier@bcg.com.au</a>	Ivette Almeida (ext 209) Steven Silver (ext 212) Anne McBride Company Phone: + 1 212 983 1702 <a href="mailto:silver@annemcbride.com">silver@annemcbride.com</a> <a href="mailto:ivette.almeida@annemcbride.com">ivette.almeida@annemcbride.com</a>	Mr Geoffrey Kempler, Executive Chairman, Prana Phone: +61 3 9690 7892 <a href="mailto:gkempler@pranabio.com">gkempler@pranabio.com</a>

***Background: Amyloid beta and amyloid plaques***

\*Prana's MPACs (metal protein attenuating compounds) are chemicals that bind zinc and copper, and have been shown by Prana to lower the levels of amyloid beta and the associated toxicity in the brains of transgenic mice used as a model of Alzheimer's Disease. Prana's scientists first described the metal-based structure of the beta amyloid

The brains of patients with Alzheimer's Disease are affected by the chemical changes associated with the formation of 'clumps' of amyloid beta (plaques) near and around nerve endings and in blood vessels, particularly in the areas used for memory and other cognitive functions. . The normal form of amyloid beta is soluble, but in Alzheimer's Disease, the protein comes out of solution to become a major component of insoluble amyloid plaques. Inappropriate accumulation of amyloid beta in the brain is intimately associated with the loss of neuronal function causing the dementia.

Metals, also a component of the brain, have chemical roles in the development and progression of plaque formation. Abnormal binding of zinc to amyloid beta leads to protein clumping. Abnormal binding of copper to amyloid beta can lead to the formation of hydrogen peroxide through oxidative reactions. Hydrogen peroxide is toxic to brain cells.

Experimentally, the amyloid can be dissolved by the use of metal-binding chemicals such as clioquinol that specifically reverse the copper and zinc interaction with amyloid beta.

**About Prana:**

Prana is a Melbourne-based biotechnology established in 1997 to commercialize research into Alzheimer's disease and other major age-related degenerative disorders (ASX: PBT; Nasdaq: PRAN). Prana's technology was discovered by the company's researchers at prominent international institutions including Massachusetts General Hospital at Harvard Medical School, the University of Melbourne and the Mental Health Research Institute in Melbourne.