



## Prana commences US Investor Roadshow

**Melbourne, Australia – Wednesday 22nd January, 2014; San Francisco, United States – Tuesday 21<sup>st</sup> January 2014:** Prana Biotechnology (ASX:PBT/ NASDAQ:PRAN), a leading innovative drug developer targeting disease modification in neurodegenerative disease, is commencing a non-deal investor roadshow in the United States with Credit Suisse.

The Corporate presentation includes:

- Information on the Company's development programs and upcoming catalysts;
- Overview of the Huntington's disease phase 2 clinical trial which is nearing the reporting of major clinical results; and
- Overview of the Alzheimer's disease phase 2 clinical trial, which is expected to report in March 2014.

Mr Geoffrey Kempler, President and Chief Executive Officer and Professor Rudy Tanzi, Prana's Chief Scientific Advisor and Professor of Neurology, Harvard Medical School will be in attendance.

### **About Prana Biotechnology Limited**

Prana Biotechnology was established to commercialise 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](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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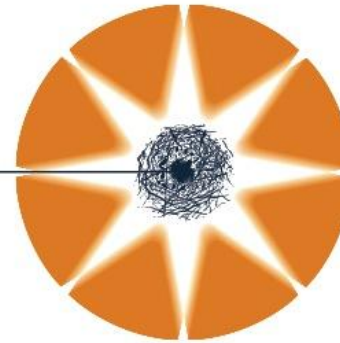
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**PRANA**  
BIOTECHNOLOGY  
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# Company Update

January 21-23, 2014

[www.pranabio.com](http://www.pranabio.com)

ASX: PBT    Nasdaq: PRAN



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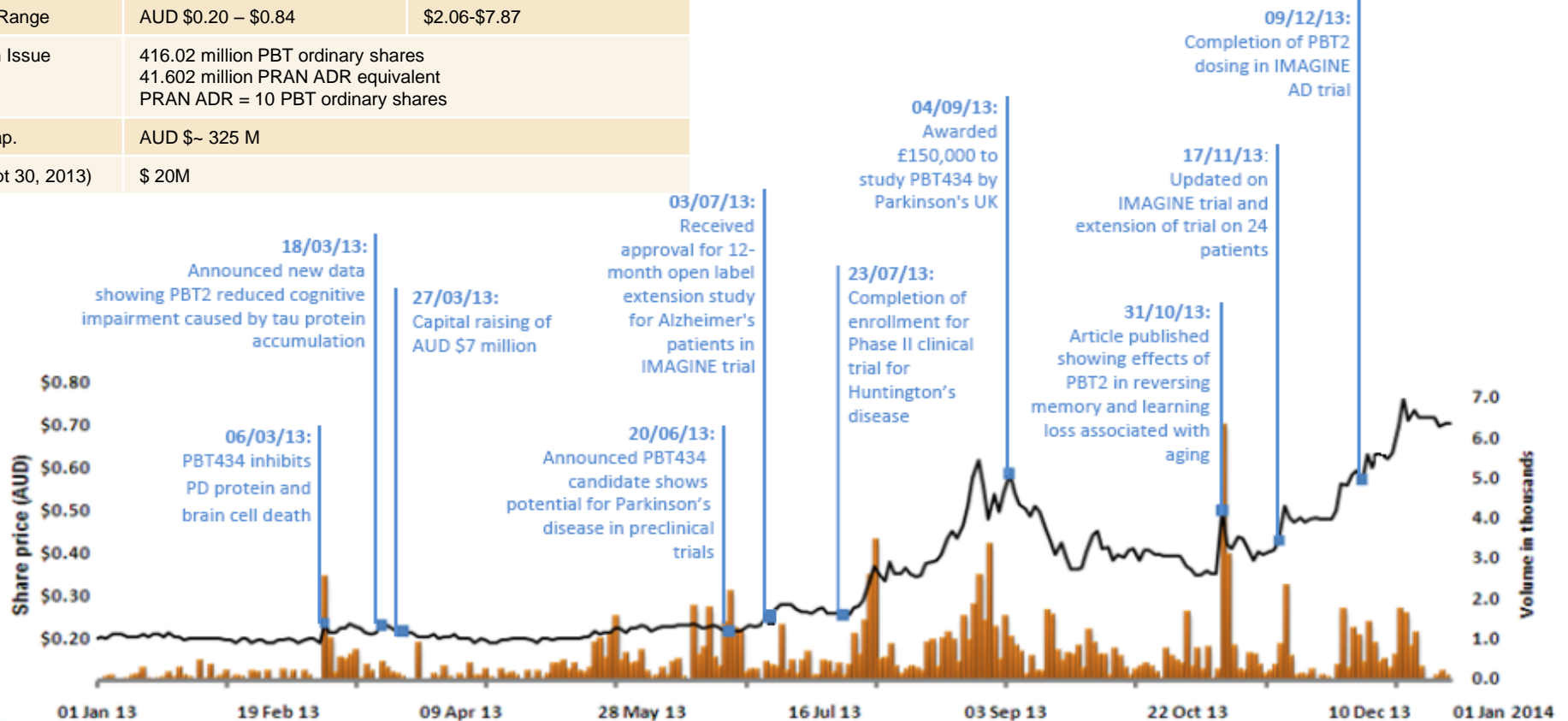
## Safe Harbour

This presentation may contain some statements that may be considered “Forward-Looking Statements”, within the meaning of the US Securities Laws. Thus, any forward-looking statement relating to financial projections or other statements relating to the Company’s plans, objectives, expectations or intentions involve risks and uncertainties that may cause actual results to differ materially. For a discussion of such risks and uncertainties as they relate to us, please refer to our 2013 Form 20-F, filed with the US Securities and Exchange Commission, in particular Item 3, Section D, titled “Risk Factors.”

# Public Market Overview

NASDAQ: PRAN; ASX: PBT (as of 20th January 2014)

	PBT – AU shares (\$ in AUD)	Prana – US ADRs (\$ in USD)
Share Price:	\$0.83	\$7.10
52-Week Range	AUD \$0.20 – \$0.84	\$2.06-\$7.87
Shares on Issue	416.02 million PBT ordinary shares 41.602 million PRAN ADR equivalent PRAN ADR = 10 PBT ordinary shares	
Market Cap.	AUD \$~ 325 M	
Cash (Sept 30, 2013)	\$ 20M	



# MPAC (Metal-Protein Attenuating Compounds) Technology

Age-related neurological conditions involve pathological interactions between selected metals and target proteins.

Metal-Protein Attenuating Compounds (MPACs) inhibit Alzheimer's-like changes in the brain by preventing a build up of beta-amyloid aggregates, which destroy cognitive function.

Alzheimer's Disease (AD), Huntington's Disease (HD) and a range of other neurodegenerative and movement disorders share a common pathological feature; the presence of neurotoxic protein aggregates that deposit in specific brain regions.

Protein aggregates result from metal mediated misfolding of a particular disease-associated protein that causes it to aggregate.

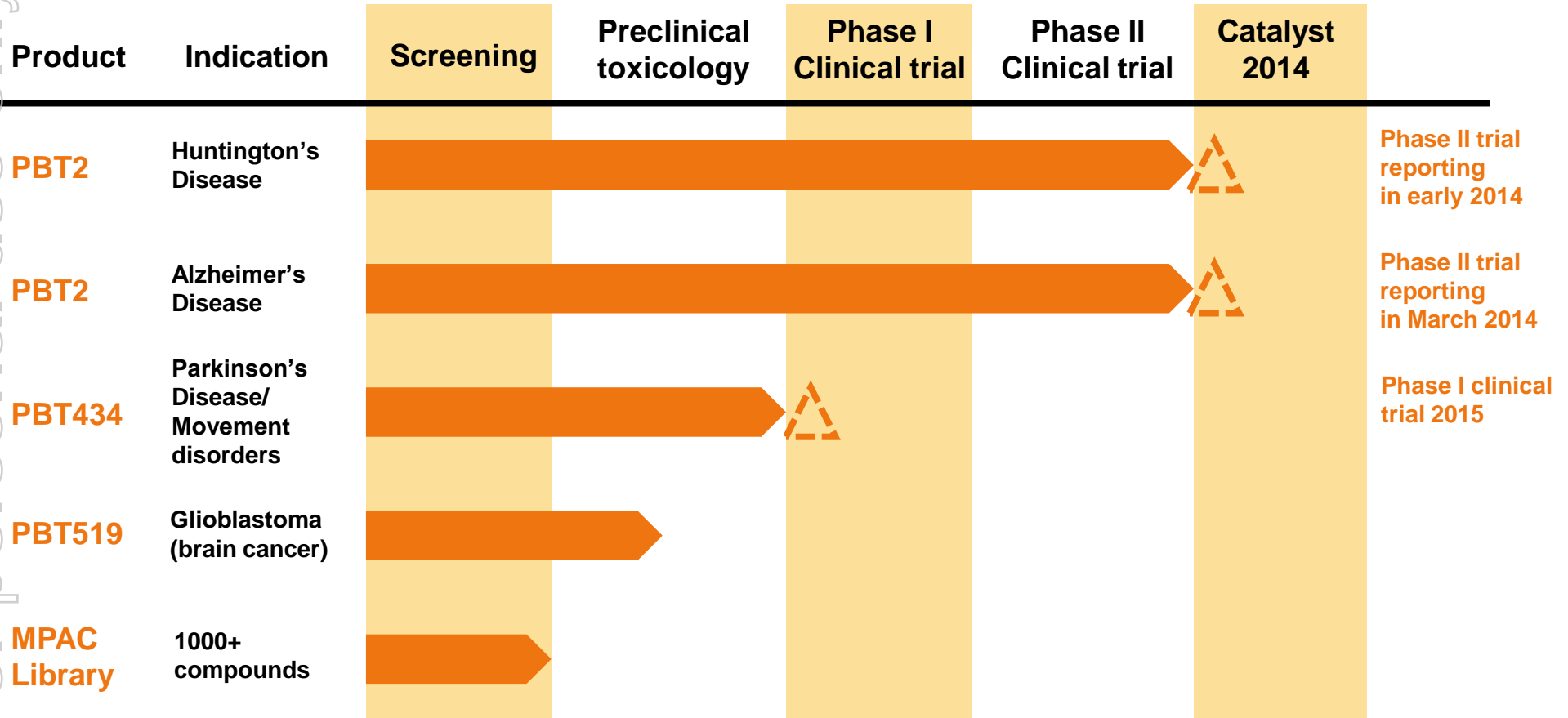
PBT2 is a small molecule that reversibly binds and shuttles copper and zinc away from these aggregates and back into neurons and synapses, where the metals can be used in a beneficial manner.

Prana has a library of more than 1000 MPACs

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# Prana Asset Pipeline

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# How Does PBT2 work?

- Preclinical studies have shown that PBT2 potently interferes with the underlying toxic mechanisms of Alzheimer's Disease & Huntington Disease.

## (i) Anti Abeta (AD) & mHtt (HD) effects:

- ✓ Reduces Abeta aggregation
- ✓ Promotes dissolution
- ✓ Prevents toxicity
- ✓ Promotes Abeta degradation & clearance
- ✓ Redistributes metals
- ✓ Reduces mHtt aggregation

## (ii) Neuroprotective & neurotrophic effects:

- ✓ Redistributes metals into neurons
- ✓ Modulates signalling pathways
- ✓ Reduces potential for glutamate excitotoxicity
- ✓ Reduces neuritic degeneration
- ✓ Reduces free radical generation
- ✓ Reduces tau hyperphosphorylation
- ✓ Reduces brain tissue degeneration



# PBT2 and Huntington's Disease


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- Huntington's Disease is a neurodegenerative disease caused by a mutated gene (Htt).
  - Death of specific brain cells causes gradual loss of cognitive (thinking), physical and emotional function.
  - Most commonly observed symptom is jerky involuntary movements of the arms and legs.
- Only one drug approved in HD – Tetrabenazine:
  - FDA approved on 2 small pivotal trials;
  - Only works on late stage motor symptoms (called 'chorea');
  - 2012 drug sales: US\$216m\*; and
  - Very few drugs under development (E.g. Raptor and Pfizer in Phase 2).
- No treatments for cognitive or behavioural symptoms currently available.
- Low patient numbers globally offer opportunity to develop PBT2 for HD through to approval and marketing, as value adding alternative to licensing.
- Prana's NDA application expected 2016/2017.

\*EvaluatePharma Report 2014

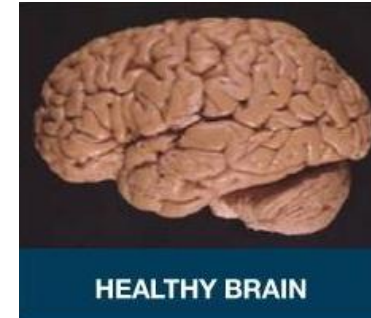
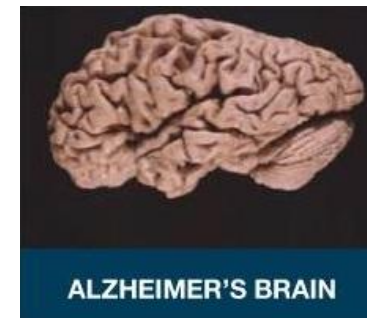
# Phase 2 Huntington's Disease Trial

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Phase	Population	Treatment	Status & Key Points
II 	Early to Mid Stage Huntington's Disease in males/females.  Number of participants: 109	<u>PBT2-203</u> 3 arm study: 100mg and 250 mg PBT2 versus placebo once daily for 26 weeks.	Status: Completed. Results under analysis.  Results due early 2014.  Primary Objective: To evaluate safety and tolerability in patients with HD.  Secondary Objectives: To evaluate the effect of PBT2 on; <ul style="list-style-type: none"> <li>•Cognition.</li> <li>•Motor Function.</li> <li>•Behaviour.</li> <li>•Functional Abilities.</li> <li>•Global Function.</li> <li>•Biomarkers.</li> <li>•Brain Volume and function.</li> <li>•Pharmacokinetics.</li> </ul> Exploratory MRI sub-study on brain metals.

# PBT2 and Alzheimer's Disease

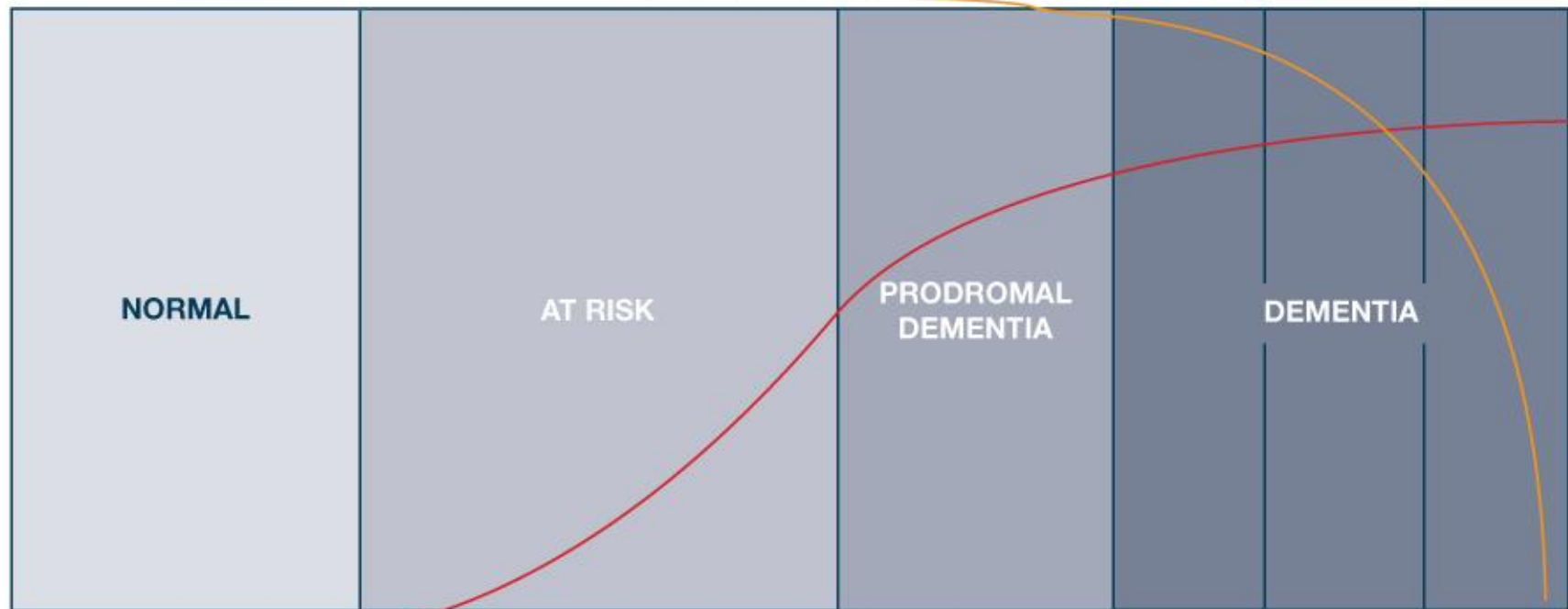
- Brain requires zinc and copper for healthy synaptic function and cognition.
- In AD these metals become sequestered by amyloid deposits; hence not available.
- PBT2 liberates these metals and restores them to usable pool in neurons.
- In liberating the metals, PBT2 prevents amyloid toxicity and promotes its clearance.
- **But memory is just a part of the problem....**
- Executive Function (EF) is an integrated set of cognitive abilities, including thinking flexibility, concept formation, self-monitoring, multi-tasking and organising.
- Potential accelerated approval mechanism under FDA Industry Guidance on Early Stage AD Trial Designs.



# Targeting Executive Function and Memory

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## CLINICAL CHANGES (MEMORY)



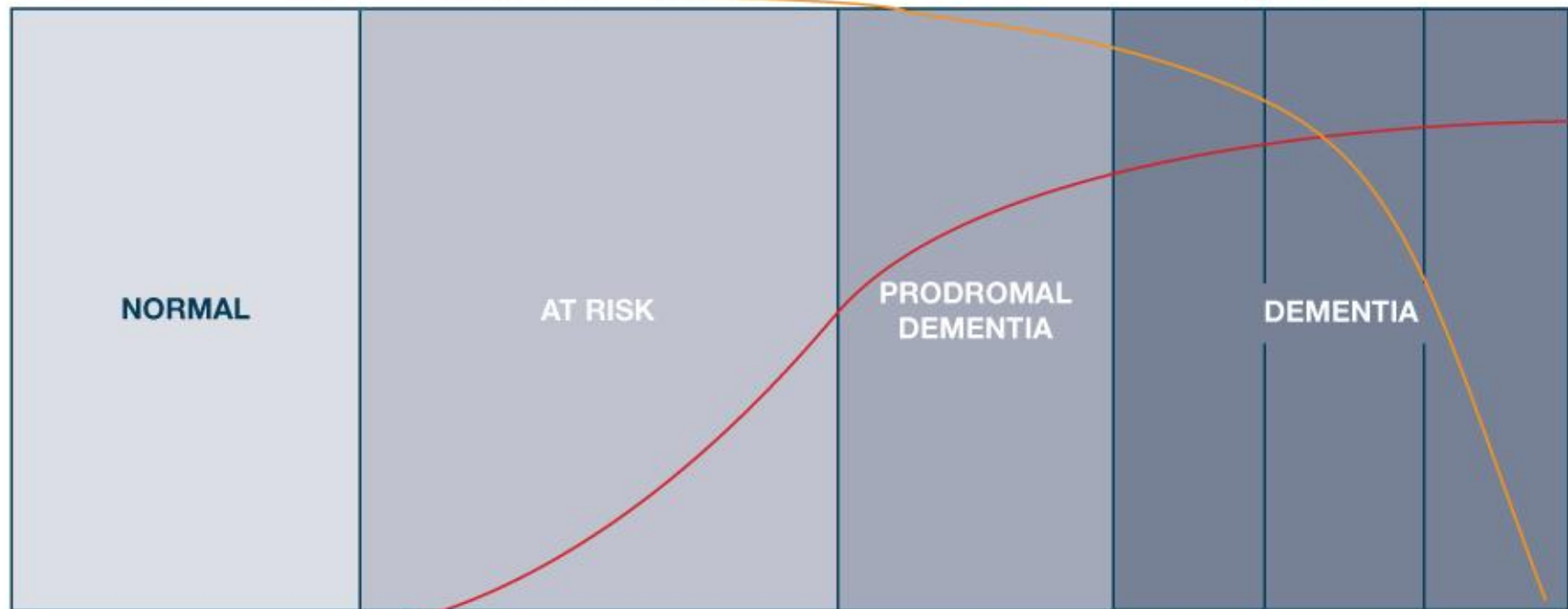
DISEASE

# Targeting Executive Function and Memory

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CLINICAL CHANGES (EXECUTIVE FUNCTION)

Current Drug Rx  
Target Memory



DISEASE

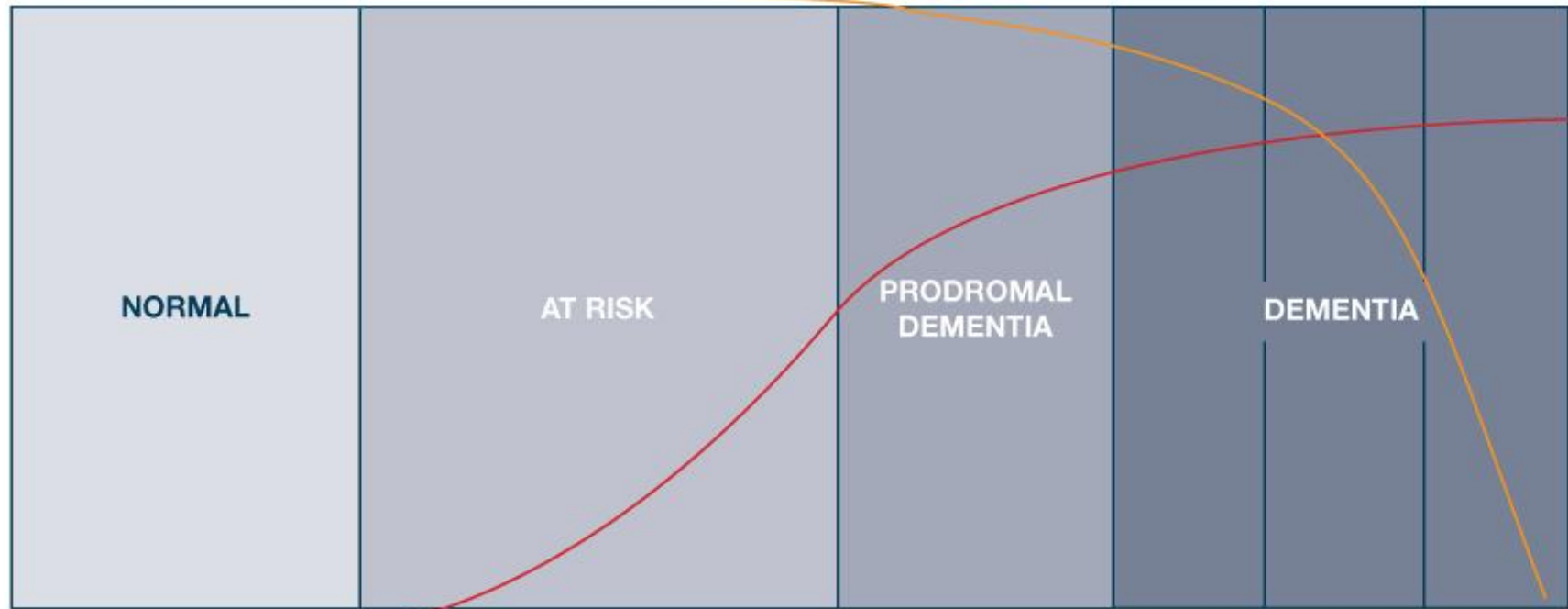
# Targeting Executive Function and Memory

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CLINICAL CHANGES (EXECUTIVE FUNCTION)



PBT2 Rx Target EF  
and Memory



DISEASE

# Alzheimer's Disease Market

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Six drugs approved, primarily for memory symptoms (Exelon, Aricept, Memary, Rivastach, Razadyne, Ebixa).

\$5.3 Billion in drug sales in 2012\*.

No approved drug for disease modification.

Global market for AD ~US\$10 billion#

Multiple phase 3 trial failures/challenges (J&J/Pfizer, Eli Lilly, Baxter, BMS) – all with different MOA to Prana.

Drivers for the Alzheimer's Disease market and impact on global drug market:

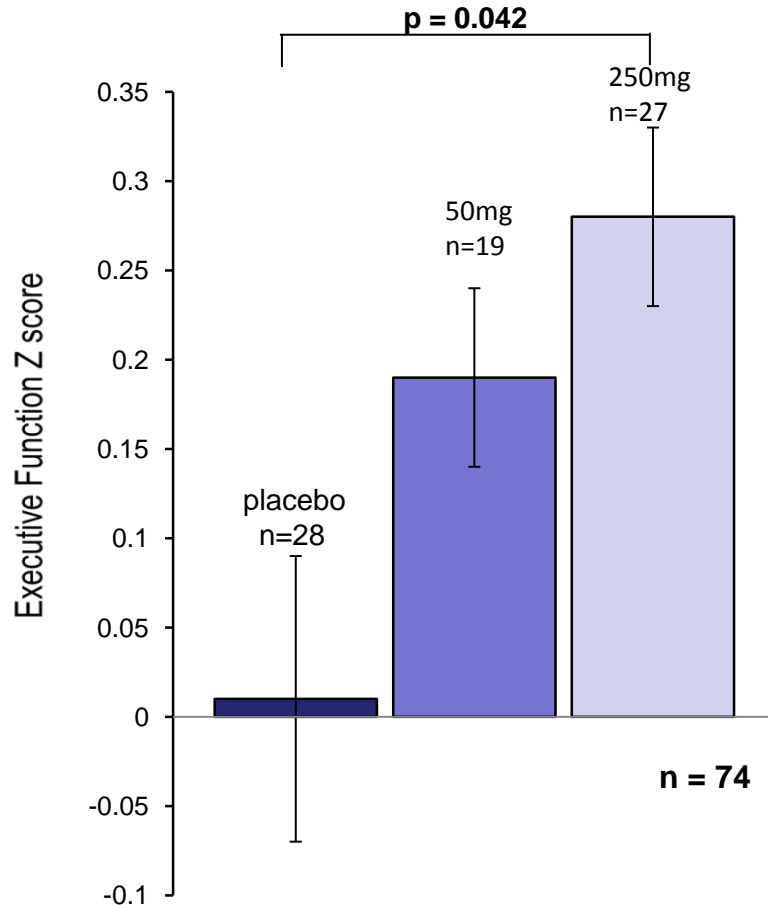
- Steady increase in elderly population and subsequent prevalence of AD;
- Increasing disease awareness among the general population; and
- Government and society initiatives.

\*EvaluatePharma Report, 07012014

# Profound Market Intelligence Report, BCC Research, Wellesley MA USA.

# Phase 2a Trial Results\*

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- 78 mild AD patients; placebo (29), 50mg PBT2 qd (20), 250mg PBT2 qd (29):
  - ADAS-cog 10-25, MMSE 20-26;
  - 74 patients completed study;
  - 12 weeks of treatment; and
  - Double blind trial design.
- Primary outcome; PBT2 was safe and well tolerated.
- Significant improvement in Executive Function Z score (p=0.042) for 250mg dose.
- Decrease in  $A\beta_{42}$  (p=0.006) and  $A\beta_{40}$  (p=0.092) in the CSF for 250mg dose.

**Executive Function : The overarching control of cognitive processes**




# Phase 2 Alzheimer's Disease Trial

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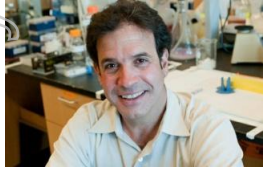
Phase	Population	Treatment	Status & Key Points
II 	Prodromal or Mild Alzheimer's Disease in males/females over 55 years.  Number of participants: 42	PBT2-204 2 arm study: 250mg PBT2 versus placebo once daily for 52 weeks	<p><b>Status:</b> Complete. Results under analysis.</p> <p>95% patient retention.</p> <p>Data safety monitoring board (met 5 times) recommended no changes to protocol.</p> <p>Results due March 2014.</p> <p><b>Primary Objective:</b> To evaluate brain amyloid levels by imaging.</p> <p><b>Secondary Objectives:</b> To evaluate the effect of PBT2 on:</p> <ul style="list-style-type: none"> <li>•Safety and tolerability.</li> <li>•Brain metabolic activity.</li> <li>•Brain volumes.</li> <li>•Cognition.</li> <li>•Functional abilities.</li> </ul>

# 12 month IMAGINE extension trial

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Phase	Population	Treatment	Status & Key Points
<p>II</p> 	<p>Prodromal or Mild Alzheimer's Disease in males/females over 55 years.</p> <p>Number of participants: 33</p>	<p>PBT2-204 Open Label - 250mg PBT2 daily for further 52 weeks</p>	<p><b>Status:</b> Commenced July 2013. Open to all patients who have completed the IMAGINE trial.</p> <p>Initiated at the request of physicians.</p> <p><b>Primary Objective:</b> To evaluate brain amyloid levels by imaging.</p> <p><b>Secondary Objectives:</b> To evaluate the effect of PBT2 on:</p> <ul style="list-style-type: none"> <li>•Safety and tolerability.</li> <li>•Brain metabolic activity.</li> <li>•Brain volumes.</li> <li>•Cognition.</li> <li>•Functional abilities.</li> </ul>

# Key Opinion Leaders



## *Prof. Rudy Tanzi*

- Scientific Co-Founder of Prana; Member Prana R&D Board
- Joseph P. and Rose F. Kennedy Professor of Neurology at Harvard University and Director of the Genetics and Aging Research Unit at Massachusetts General Hospital (MGH)



## *Prof. Ira Shoulson, MD*

- Clinical investigator on Prana's Reach2HD trial
- Professor of Neurology, Pharmacology and Human Science and Director of the Program for Regulatory Science and Medicine (PRSM) at Georgetown University, Washington, DC
- Founded the Parkinson's and Huntington's study groups



## *Prof. Jeffrey Cummings, MD*

- Chairs Prana R&D Board
- Prof. Neurotherapeutics & Drug Development, Neurological Institute, Cleveland Clinic; Director Cleveland Clinic Lou Ruvo Center for Brain Health, and Professor Neurology at UCLA



## *Prof. Colin Master, MD*

- Member Prana R&D Board
- Mental Health Research Institute and Laureate Professor, University of Melbourne
- Awarded Lifetime Achievement Award in Alzheimer's Disease Research at the 10th International Conference on Alzheimer's Disease



**Targeting Metals in Alzheimer's and Other Neurodegenerative Disease** symposium hosted by New York Academy of Sciences in January 2013. Significant body of evidence supporting PBT-2.

Visit:

<http://www.nyas.org/Publications/Ebriefings/Detail.aspx?cid=1fc1b1f4-1c78-46ba-85a1-0763632fa129>

## Thank you

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