

# **ANNUAL GENERAL MEETING**

Chairman & CEO Geoffrey Kempler 28<sup>th</sup> November 2013



#### 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 2010 Form 20-F, filed with the US Securities and Exchange Commission, in particular Item 3, Section D, titled "Risk Factors."

# **A Year of Progress**

- IMAGINE Phase II clinical trial
  - Trial fully recruited and nearing completion.
  - Safety Data Monitoring Board met five times with no recommended change to protocol.
  - Physician requested Extension trial approved allowing all patients to continue for a further 12 months with ALL taking PBT2.
- Reach2HD Phase II clinical trial
  - Trial fully recruited and completed. Results pending.
  - Safety Data Monitoring Board recommended no changes to protocol.
  - New benchmark test to assess patient reported feedback.









### **A Year of Progress**



- Parkinson's and movement disorders
  - Parkinson's UK awards £150k to study PBT434.
  - PBT434 inhibits Parkinson's protein and brain cell death.

#### Corporate

- A\$20m cash at end of Sept.
- A\$5.8 million R&D refund.
- Raised A\$13 million in new capital.





#### **Awareness growing**



PBT2 named Top 10 global neuroscience projects to watch



Prana dominates e-briefing "Targeting Metals in Alzheimer's and Other Neurodegenerative Disease



Journal of Huntington's disease publishes benefits of PBT2

#### Presentations at:









## 13.8 million reasons why

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1 in 3 seniors dies with Alzheimer's or another dementia.



Alzheimer's disease is the sixth-leading cause of death.

One in nine people age 65 and older have Alzheimer's disease.

Today 5.2 million Americans have Alzheimer's Disease. By 2030 it will be 13.8 million.



Costs of caring with people with AD and other dementias will soar from \$203 billion this year to a projected \$1.2 trillion by 2050.



Unpaid caregivers provided ~17.5 billion hours of unpaid care, a contribution valued at over \$216 billion.

All content sourced from 2013 Alzheimer's Disease Facts and Figures

#### **Regulatory environment strengthened**



- FDA Industry Guidance on Early Stage AD Trial Designs.
- In February, the FDA offered draft guidance to assist companies in the development of new Alzheimer's diseases but emphasized the importance of focusing on developing early-stage treatments first

"The purpose of this guidance is to assist sponsors in the clinical development of drugs for the treatment of the various stages of Alzheimer's disease that occur before the onset of overt dementia. Specifically, this guidance addresses the FDA's current thinking regarding the selection of patients with early AD, or patients who are determined to be at risk of developing AD, for enrollment into clinical trials.

> FDA Guidance for Industry: Alzheimer's Disease: Developing Drugs for the treatment of early stage disease



# Huntington's – a smaller market but just as big an opportunity

- Huntington's is an Orphan Disease one that affects a small percentage of the population
  - In Australia = 2000
  - In US = 30,000
- Drugs with Orphan drug status have exclusivity for a defined period and can command much higher product price
- Only one drug approved in HD (Tetrabenazine)
  - FDA approved Tetrabenazine on 2 small pivotal trials
  - Only works on motor symptoms
  - No treatments for cognitive or behavioural symptoms.





## Metal Hypothesis: A Differentiated Novel Therapeutic Strategy

- Copper, zinc and iron are crucial to healthy brain function.
- Due to aging, genetic factors or disease, regulation of these metals is impaired affecting critical neuronal functions.
- The abnormal interaction between brain metals and disease related proteins e.g. Abeta in Alzheimer's disease and Htt in Huntington disease – promotes aggregation, forming amyloid plaques.
- PBT2 is a differentiated novel technology which prevents the toxic consequence of metal binding to proteins, and which also helps restore metal distribution:
  - Anti-amyloid

- Neurorestorative

- Neuroprotective

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- Improves executive function

In Alzheimer's, clinical trial failures of other products support the idea that targeting Abeta only is not enough.



#### How does PBT2 work?

 Preclinical studies have shown that PBT2 has exhibited superior performance which interferes with the toxic mechanisms of Alzheimer's disease & Huntington disease

#### (i) Anti Abeta & mHtt 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
- ✓ Promotes neuronal growth
- ✓ Prevents free radical production
- ✓ Reduces tau hyperphoshorylation
- $\checkmark$  Reduces brain tissue degeneration



#### **PBT2 and Alzheimer's disease**



- The brain requires metals (zinc and copper) to form new memories.
- In Alzheimer's disease, these metals are bound up in amyloid deposits and hence not available.
- PBT2 liberates these metals and restores them to neurons.
- In liberating the metals, PBT2 prevents amyloid toxicity and promotes its clearance.
- But memory is just a part of the problem....



#### **Executive Function**



- Executive Function (EF) is an integrated set of cognitive abilities, including thinking flexibility, concept formation, self-monitoring, multi-tasking and organising.
- EF capacity will allow patients to remain in their own homes.
- PBT2 targets brain metals to keep them available for healthy EF.
- PBT2 significantly improved patients' EF in initial clinical trial.





# Problems begin many years before full dementia





#### **CLINICAL CHANGES (MEMORY)**



#### DISEASE







DISEASE















#### DISEASE





#### **PBT2 - Phase IIa 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
  - 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

\*Lancet Neurol 2008; 7: 779-86 and errata Lancet Neurol 2009; 8: 981

#### BIOTECHNOLOGY Limited

# **Alzheimer's Phase II IMAGINE Trial**

- Double Blind Placebo Controlled
- 42 prodromal/early AD patients ("enriched recruitment")
  - Pre-established by PIB PET SUVR score greater than 1.7.
  - Cognitive deficit measured as episodic memory deficit.
- 12 months treatment period
  - Doses: 250mg and placebo.
- Measures effect of PBT2 on:
  - distribution and amount of amyloid in the brains of AD patients using PIB Imaging;
  - brain volume using MRI;
  - Cognition (NTB); and
  - Brain energy utilisation (reflecting function) using FDG PET scanning.
- Last Patient enrolled November 2012. Trial ends December 2013.
- Data Safety monitoring board recommended no changes to protocol.
- Results expected March 2014.

#### **12 month Extension trial**



- July 2013; IMAGINE Extension open label trial approved allowing all patients who have completed the IMAGINE trial to participate for a further 12 months.
- Initiated at the request of physicians.
- Strong patient conversion.
- All trial participants receive 250mg PBT2.
- Extension trial does not impact on the reporting of the initial IMAGINE trial.
- Significant opportunity to collect a further 12 months data.





# Huntington Phase II Reach2HD trial

- Double Blind Placebo Controlled
- 109 early to mid stage Huntington Disease patients .
- 6 months treatment period
- Doses: 100mg and 250mg and placebo.
- Safety and tolerability primary end point.
- Efficacy: cognition/motor/behavioural/functional.
- 20 sites in USA and Australia.
- FDA Approval for trial Jan 2012.
- Trial completed and results under analysis.
- Results expected early 2014.
- Targeting NDA filing 2016



#### **Prana Asset Pipeline**





#### **Portfolio of potential treatments**

- PBT 434 under development for Parkinson's disease, Parkinsonian syndromes, and other movement disorders
  - Completed the first stage of preclinical toxicology studies, with the support of The Michael J Fox Foundation, and is now completing further toxicology studies to be ready to start Phase 1 clinical trials at the end of 2014.
- PBT 519 in preclinical testing for brain cancer
- A library of more than 900 Metal-Protein Attenuating Compounds (MPACs) which target the interaction between selected metals and target proteins, preventing protein aggregation and corruption.





#### **Thank You**