PRANA BIOTECHNOLOGY Limited

34th Annual Cowen Healthcare Conference

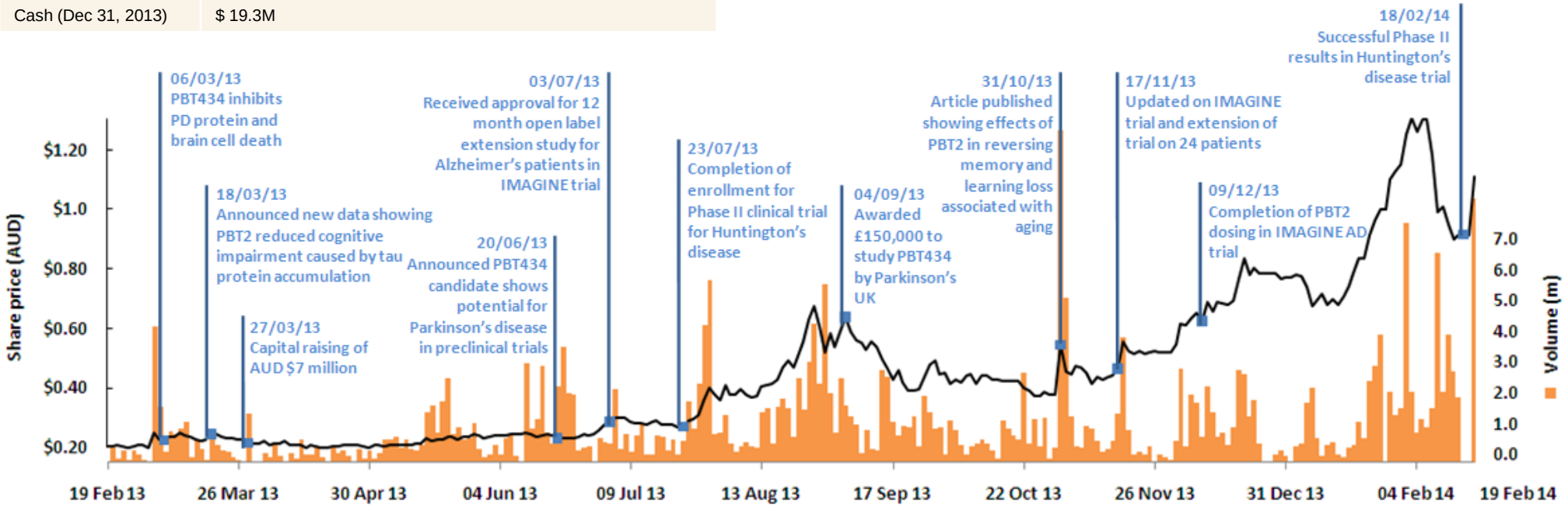
March 3-5, 2014

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 28 February 2014)		
	PBT – AU shares ($ in AUD)	**Prana – US ADRs ($ in USD)**
Share Price:	$1.26	$11.31
52-Week Range	AUD $0.20 – $1.37	$2.11-$13.29
Shares on Issue	422.66 million PBT ordinary shares 42.266 million PRAN ADR equivalent PRAN ADR = 10 PBT ordinary shares	
Market Cap.	~AU$ 500M / US$440M	
Cash (Dec 31, 2013)	$ 19.3M	



Metal Hypothesis

- Copper (Cu), zinc (Zn) and iron (Fe) are crucial to healthy brain function.
- Due to aging, genetic factors or disease, **distribution and uptake of these metals into neurons may be impaired**, resulting in:
    - impaired neurotransmission;
    - increased metal mediated amyloid formation (e.g.. Abeta in Alzheimer's and mHtt in Huntington disease); and
    - elevated production of toxic radicals.
- PBT2 and other Metal Protein Attenuating Compounds (MPACS) have demonstrated activity in numerous animal models of neurodegeneration. They target the target proteins, but unlike other approaches, also address the diminished functional capacity of neurons.

Metal Hypothesis – Alzheimer's

- Deposition of plaques formed from β-amyloid (Aβ) are the primary pathological feature of the disease.
  - Amyloid plaques contain high concentrations of Cu and Zn ("metal incarceration").
- In-vitro, Aβ will bind Cu and Zn which promotes aggregation.
- In-vitro, Cu catalyzes the formation of di-tyrosine crosslinks between Aβ molecules.
  - Cross-linked β-amyloid is resistant to degradation by proteases.
  - Recent data suggests Cu/ Aβ oligomers are highly toxic.
- Cu complexed with Aβ can catalyze the formation of hydroxyl radicals
- Aβ plaques can be disaggregated by removing metals

PBT2 competes with Abeta and mHtt for these metals, reduces their oligomerisation, reduces toxic radical formation, and liberates these metals making them available for normal biological processes

How Does PBT2 work?

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

- ✓Inhibits Abeta aggregation[1]
- ✓ Promotes dissolution of amyloid plaques[1]
- ✓ Prevents Abeta and mHtt toxicity [2,3]
- ✓Reduces mHtt aggregation and toxicity[3]
- ✓Promotes Abeta degradation & clearance[4]
- ✓ Reduces free radical generation[1]

(ii) Neuroprotective & neurotrophic effects:

- ✓ Redistributes metals to correct neuronal compartments[5,6]
- ✓ Modulates signalling pathways[6]
- ✓ promotes synaptic plasticity[6]
- ✓Reduces tau hyperphoshorylation[1]
- ✓ Reduces brain tissue degeneration[3]

1. Adlard et al Neuron (2008) 59: .43-55
2. McColl et al Mol Neurodegen. (2013) 7:57. DOI: 10.1186/1750-1326-7-57
3. Cherny et al J Hunt Dis (2012) 1: 211-219.
4. Crouch et al J Neurochem (2011) 119: 220-230
5. Adlard et al Aging Cell (2013) Doi:10.1111/acel.12178
6. Adlard et al PloS One (2011) Doi:10.1111/acel.12178

PBT2 – Phase 2a Trial *

- 78 mild AD patients; placebo (n=29), 50mg PBT2 qd (20), 250mg PBT2 qd (29).
  - Patients recruited in Sweden (8 centers) and Australia (7 centers)
- Study was well balanced for demographics and treatment history.
- Entry criteria/study design.
  - ADAS-cog 10-25, MMSE 20-26.
  - 12 weeks of treatment.
  - Double blind, placebo controlled.
- 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) CSF for 250mg dose.

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

Executive function is impaired in HD & AD

Cognitive decline is universal in HD and AD

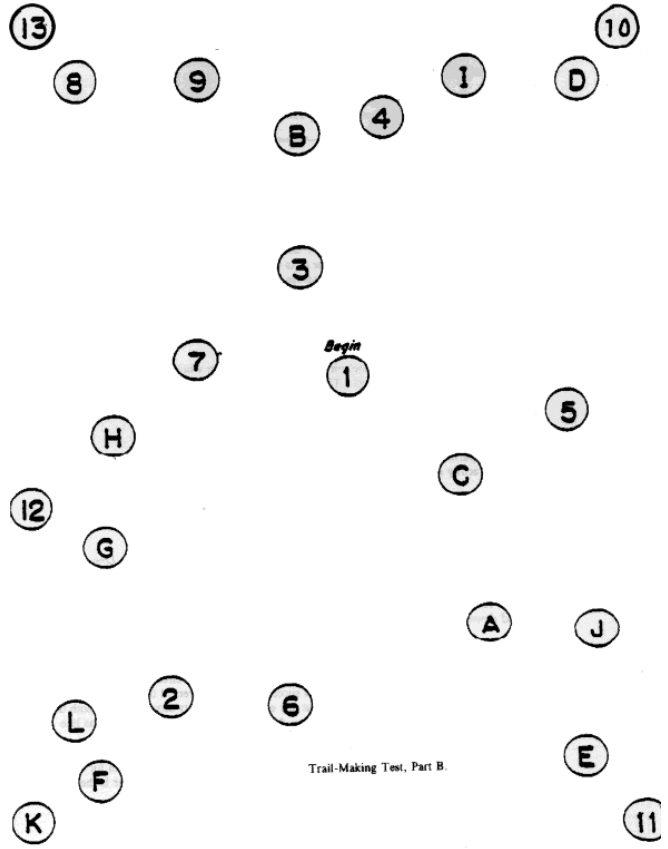
- Cognitive decline begins before diagnosis and is progressive
- Cognitive decline predicts impairments in everyday function

Trail Making Test Part B

- Timed executive function measure (flexibility), impaired in HD and AD
- Slowing indicates impaired mental flexibility

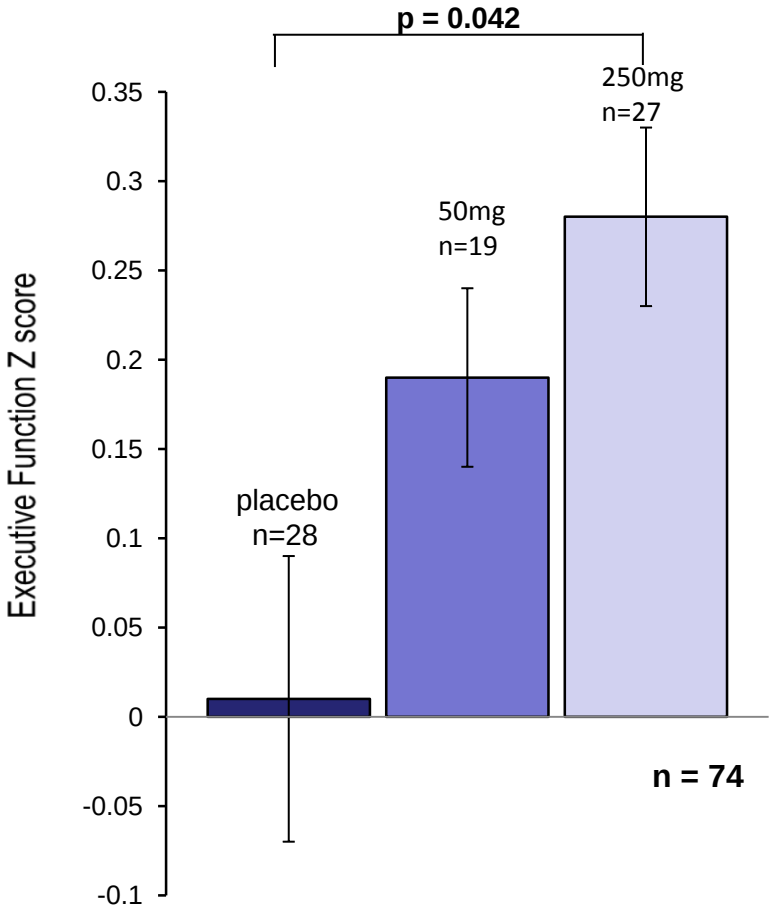
PBT2 is being targeted to treat patients early in the disease

Trail Making Test Part B



Sources: Tabrizi SJ et al. Lancet Neurol 2013;12:637-49, Dorsey ER et al. JAMA Neurol 2013;310:1520-30, Paulsen JS et al. JNNP 2013;84:1233-9, Stout JC et al. Cogn Behav Neurol 2007;20:212-8, O'Rourke JJ et al. J Clin Exp Neuropsychol 2011;33:567-79, Beglinger LJ et al. Mov Disord 2013 [epub ahead of print]

Phase 2a Trial Results in Alzheimer's*

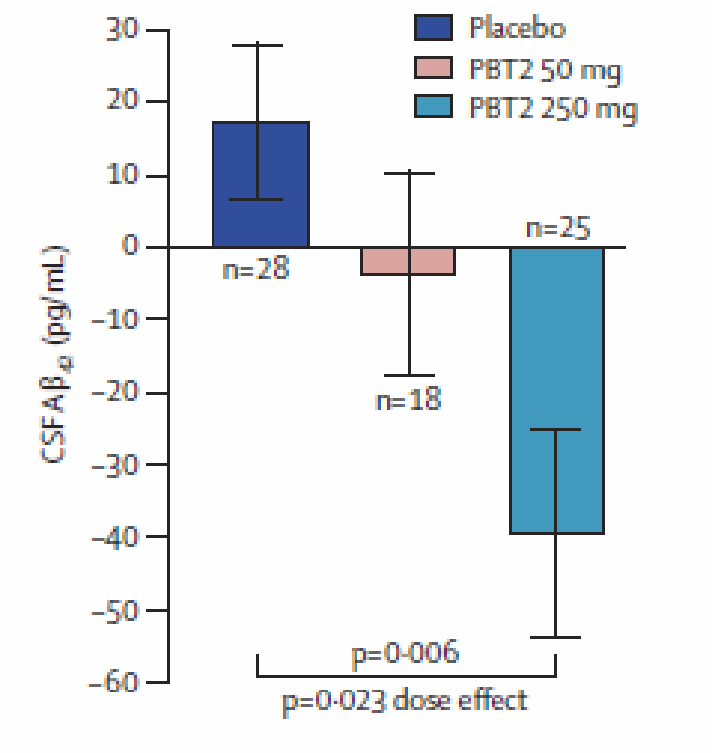


- 78 mild AD patients; placebo (29), 50mg PBT2 qd (20), 250mg PBT2 qd (29):
  - ADAS-cog 10-25, MMSE 20-26;
  - 74 patients completed study;
  - 12 weeks of treatment; and
  - Double blind trial design.
- Primary outcome; PBT2 was safe and well tolerated.
- Significant improvement in Executive Function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

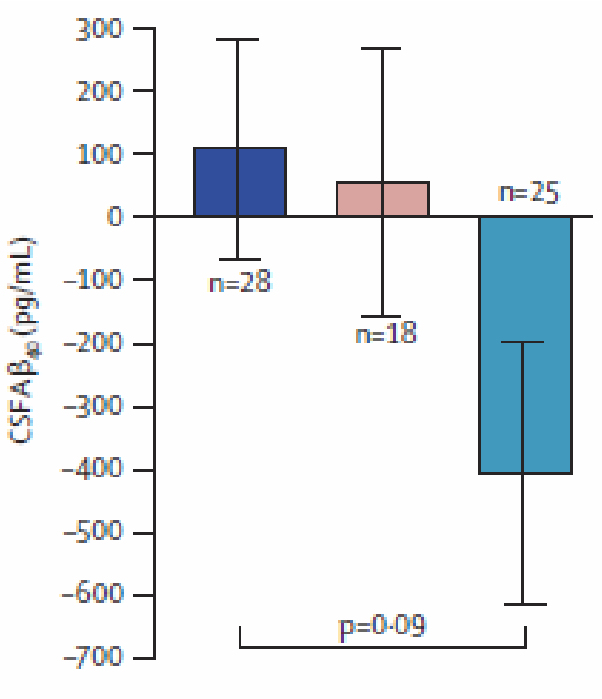
**Lancet Neurol 2008; 7: 779–86* and errata *Lancet Neurol 2009; 8: 981*

PBT2 - Phase 2a trial Results

Changes in CSF biomarkers at 12 weeks



$A\beta_{42}$



$A\beta_{40}$

AD – Phase 2 IMAGINE Trial

- 42 prodromal/early AD patients, aged >55yrs.
  - Stable acetylcholinesterase inhibitor use.
  - ^{11}C-PiB PET SUVR score > 1.7.
  - MMSE ≥20.

- 12 months treatment.
  - Doses: 250mg PBT2 qd or placebo; randomised 2:1.
  - Double blind, placebo controlled.

- Primary endpoint – change in ^{11}C-PiB PET neocortical SUVR.

- Secondary endpoints.
  - Safety and Tolerability.
  - ^{18}F-FDG PET: SUVR.
  - MRI: Total brain, hippocampal and ventricular volumes.
  - Cognition: NTB.
  - Functional: ADCS-ADL-23.

- DSMB has met 5 times and recommended no changes to protocol.
- Trial completed December 2013. 95% retention rate.
- Results expected March 2014.

AD - Phase 2 Extension Study

- Open label extension study
  - All patients receiving study drug 250mg PBT2 qd
  - 12 month treatment period
- 33 of 40 eligible patients chose to enrol into extension study (83%)
- First patient enrolled July 2013
- Follow-up imaging, NTB and biomarker analysis continuing over 12 months
- Provides up to 2 years of safety and efficacy data
- Trial expected to complete December 2014 with final data 1H2015

Preclinical and clinical data supported the study of PBT2 in HD

Study rationale

Mechanism

- In Huntington disease, copper concentrations are elevated in the brain (basal ganglia) where they could bind mutant huntingtin and promote its aggregation.

Preclinical study

- In the R6/2 mouse model of Huntington disease, PBT2 improved motor performance, increased body and brain weight, and increased lifespan by 26%
- PBT2 also delayed the onset of paralysis in C. elegans worm model of HD

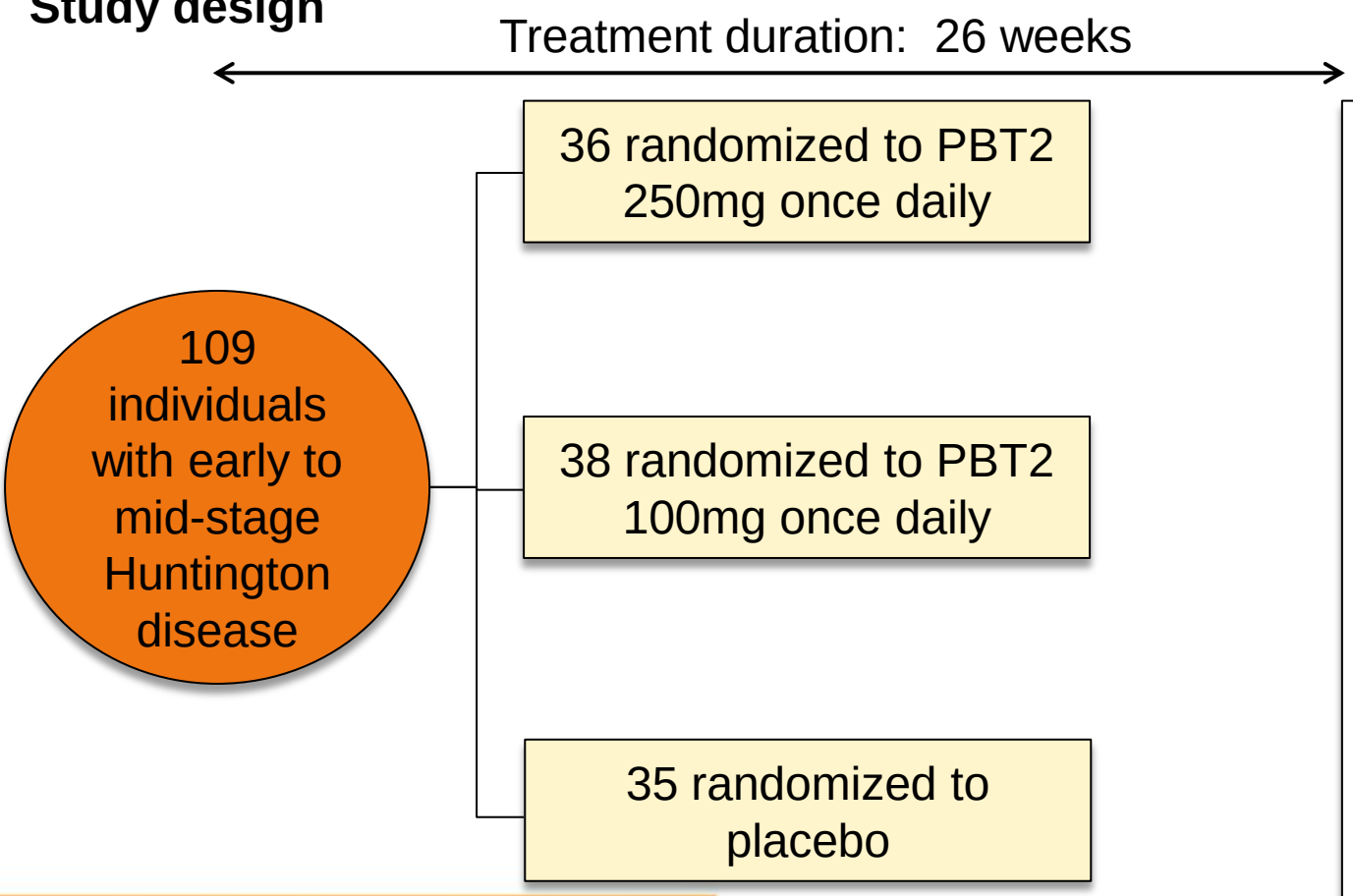
Clinical study

- In a 12-week, phase 2, randomized controlled study in 78 individuals with Alzheimer disease, PBT2 was well tolerated and safe
- Individuals receiving PBT2 250 mg performed significantly better on two executive function tests – Category Fluency and Trail Making Test Part B – and on the Executive Factor composite z-score – ***key cognitive deficits in Huntington disease***

Sources: Butcher LL and Fox SS. Science 1968;160:1237-9, Nguyen T et al. PNAS 2005;102:11840-5, Cherny RA et al. J Hunt Dis 2012;1:211-9, Lannfelt L et al. Lancet Neurology 2008;7:779-86. Erratum in Lancet Neurology 2009;8:981

Reach2HD: Phase 2, randomized, double-blind placebo-controlled study

Study design



Study Objectives

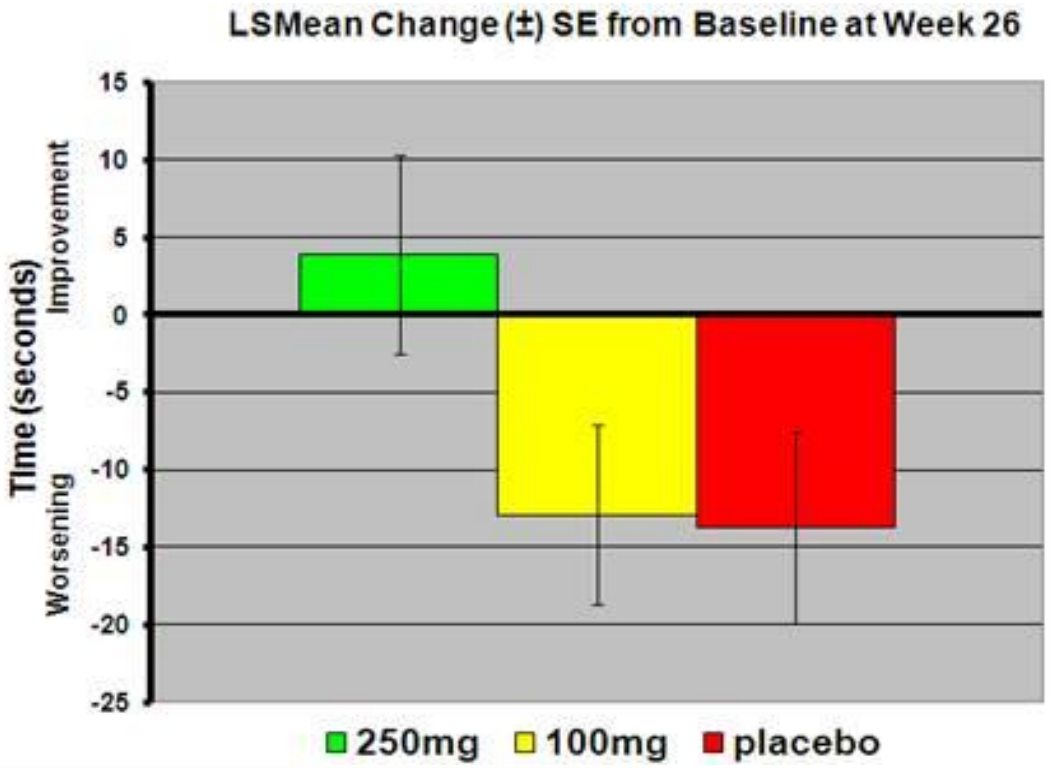
Primary: To evaluate the tolerability and safety of PBT2

Secondary: To evaluate the effect of PBT2 on the following:

- Primary efficacy variables were cognition
- Secondary efficacy variables were motor, behavior, function, and global outcomes
- Additional biomarker and imaging outcomes

PBT2 250mg significantly improved performance in HD Phase 2 trial

Change in Trail Making Test Part B



Improvement Trail Making Test Part B was significant at 12 ($p<0.001$) and 26 weeks ($p=0.042$)

PBT2 is a promising therapy for HD

Tolerability and safety

- PBT2 was well tolerated and safe in this trial over 26 weeks in individuals with early to mid-stage Huntington disease.

Efficacy

- PBT2 250mg daily significantly improved cognition on a key measure of executive function.
  - Trails Making Test B significantly improved from Baseline to Week 26 in PBT2 250 mg treatment group.
  - Improvement in executive function has never been previously demonstrated in a Huntington disease clinical trial.
  - Results observed are consistent with that seen in the prior phase 2 trial of PBT2 in Alzheimer disease.
- Cognitive improvement was accompanied by a favorable signal in functional capacity.

Imaging

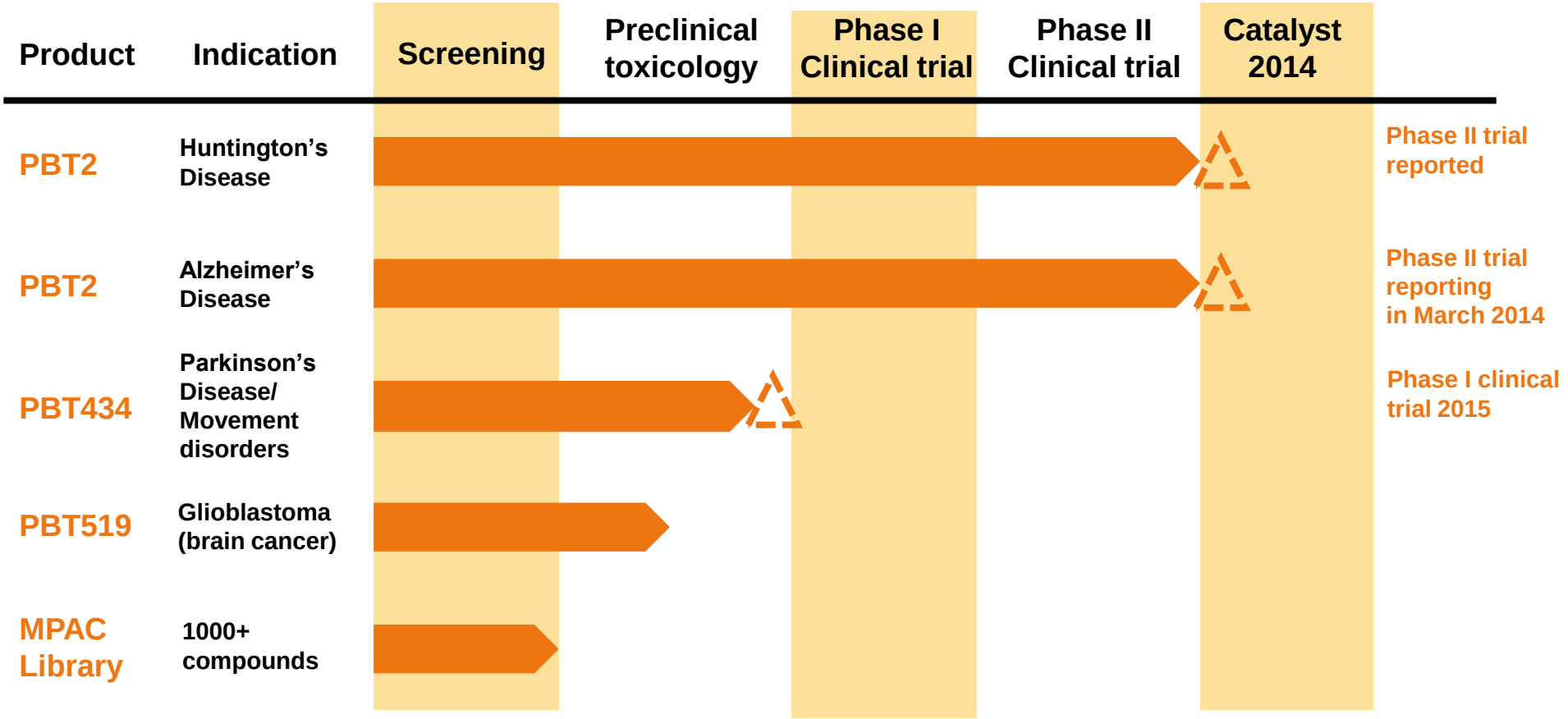
- Small sub-study suggested reduced brain atrophy among those exposed to PBT2.

Source: Mestre TA, Ferreira JJ. Parkinsonism Relat Disord 2012;18:316-20; Beglinger LJ et al. Mov Disord 2013 [epub ahead of print]

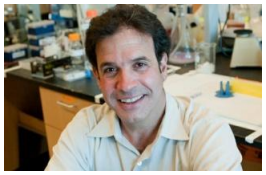
Path to Market – HD

- 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 behavioral symptoms.
- Huntington's is an Orphan Disease - ~30,000 patients in US.
- PBT2 – Company preparing to advance PBT2 into a confirmatory Phase 3 clinical trial.
- **Targeting NDA filing 2016/17.**

Multiple potential applications



Academic Advisors



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

Mr Geoffrey Kempler
Chairman and CEO
Prana Biotechnology
gkempler@pranabio.com