PRANA BIOTECHNOLOGY Limited

Annual General Meeting

13 November 2015

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."

Prana Portfolio

PBT2:
Huntington disease

PBT2:
Alzheimer's disease

PBT434:
Parkinsonian diseases

MPAC library

PBT2 – Huntington Disease Program

- Reach2HD Phase II trial met its primary end points
- Results published in *Lancet Neurology*, Nov 2014
- Further drug exposure studies show a trend to increased improvement in the cognitive tests with increasing drug exposure
  - consistent with the findings of the Reach2HD trial
  - support the proposition that the improvement in cognitive performance in the Reach2HD trial was attributable to PBT2
- Orphan drug designation granted in US and Europe
- Planning underway for global clinical trial in EU, Aust, US (US subject to FDA partial clinical hold)
  - Aim is to demonstrate the clinical benefit with PBT2 with a much larger patient cohort of sufficient size for regulatory purposes

PBT2 – Alzheimer's Disease

Phase 2 'EURO' clinical trial

- Demonstrated significant improvement in Executive Function
- Results published *Lancet Neurology* (Lannfelt et al 2008, 2009)

Support for the PBT2 Mechanism Of Action grows

- Targeting both abeta and tau, reducing abeta oligomers and phosphorylated tau, improving neuronal function, growth (plasticity) and survival

PBT2 – IMAGINE Open Label extension

- 52 week Clinician-initiated Open Label Extension Trial expanded strong safety package
- 82% of originally included IMAGINE trial participants completed the full 24 months of treatment (12 months placebo-controlled phase + 12 months extension)
- 12 month “IMAGINE’ study did not significantly reduce amyloid deposition
  - unexpected and confounding decline in placebo group
- Analysis of the extension data (unpublished) reveal no significant differences and did not distinguish between 12 months v 24 months of exposure to PBT2 on any of the measured trial outcomes
- For the cohort of 27 trial participants (16 were on PBT2 for 24 months) completing 24 months on the trial, deposited amyloid levels decreased compared to an historical control group from the Australian Imaging Biomarker Lifestyle (AIBL) study

PBT434 – Parkinsonian conditions

- Over the past 2 years PBT434 has been profiled in mouse models of orphan and non-orphan Parkinsonian conditions including:
  - Parkinson's disease
  - Multiple System Atrophy
  - Tauopathies (e.g. Corticobasal Degeneration, Progressive Supranuclear Palsy)

- Comprehensive IND-enabling non clinical program has been conducted to evaluate the pharmacologic and pharmacokinetic profile of PBT434

- Anticipated commencement of PBT434 Phase 1 program in 2016 (subject to regulatory approval)

- Key activities: prevents neuronal loss (5 different typical and atypical models), reduces alpha-synuclein, iron and tau (incl. by PET scan), improves cognition and motor function in tg mouse models

MPAC Library

- 2000+ potential compounds
- PBT519 Brain Cancer (GBM)
  - Reduced tumor growth in both mouse and human GBM cell lines
  - Spared non cancerous astrocytes
  - Effect additive with Temozolamide (SOC)
- Two tiered research program:
  - Undertake new MPAC design and synthesis; and
  - Translational animal modelling programs to test and validate new candidate MPACs in orphan indications

Strong safety package

- PBT2 has completed four Phase I trials and four Phase II trials with good recruitment, high retention and completion rates
- Each was reviewed by the independent Data Safety Monitoring Board. No safety concerns identified or changes to the protocols
- Based on this strong safety profile, a robust safety monitoring plan for future trials in HD is being developed for the FDA
- Notwithstanding the clinical safety demonstrated to date for PBT2, US FDA has placed a Partial Clinical Hold based on non-clinical findings in dog studies

Partial Clinical Hold (PCH)

What does it mean?

- FDA placed PBT2 on PCH in Feb 2015 based on particular non-clinical neurotoxicology findings in dog studies
- Dose of PBT2 has been limited to an amount that is not considered clinically relevant and therefore has resulted in delays to the commencement of our next trial
- We are required to establish how the dog study is not relevant to future PBT2 trials or in humans and to describe a strategy to safely proceed with clinically relevant dosages in future clinical trials

How has Prana responded?

- Response to FDA will draw upon reports from specialist clinical safety physicians and pharmacometricians, to understand the relationship between increasing drug exposure and safety outcomes
- Anticipate submitting response to FDA early 2016

Orphan drug designation granted

- PBT2 has been granted Orphan Drug designation for Huntington's disease:
  - European Commission: June 2015
  - US FDA: September 2014

- To achieve Orphan designation, the drug must have the potential to offer plausible benefits to patients for indications affecting a small percentage of the population, that are not currently being met with effective treatments

- Orphan drug designation entitles Prana to:
  - an extended seven-years of market exclusivity in the US and ten years in Europe - for the use of PBT2 in the treatment of Huntington disease;

  - protocol assistance by the FDA to optimize drug development in the preparation of a dossier that will meet regulatory requirements; and

  - reduced fees associated with applying for market approval

Conclusion

- The need for treatments for neurodegenerative disease remains critical to patients, families and the healthcare economy
- Based on the promising safety and efficacy data package, Prana remains committed to the further development of PBT2, PBT434 and new clinical leads from our MPAC library
- Primary focus: Initiation of the next clinical trial of PBT2 in HD well underway. Anticipate sites in EU, Aust and US (subject to PCH)
- All efforts are being directed to finalising the submission to the FDA to lift the current PHC
- PBT434 will be moving into the clinic 2016, leveraging Prana's MPAC library and CNS orphan and non-orphan R&D expertise in additional indications
- Cash position remains strong with $33M cash at hand (as of 30 Sept 2015)

Ira Shoulson MD

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Cognitive Decline and Dementia

Progressive intellectual decline in adults resulting in serious and seemingly irreversible disability

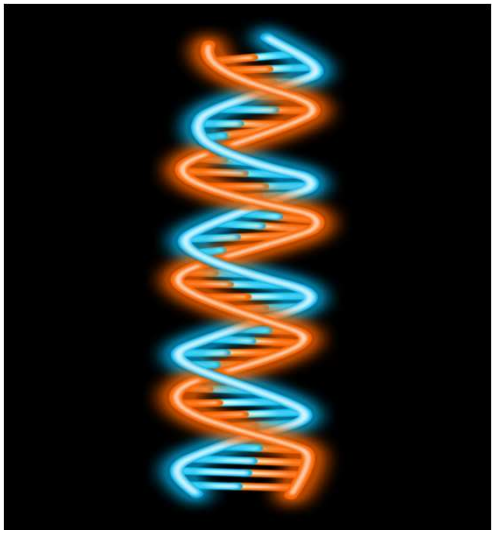
Many types and causes

- Degenerative diseases wherein brain nerve cells (neurons) loose their vitality and capacity to function
- Vascular diseases causing repeated injury to nerve cells
- Genetic
- Other

Degenerative Diseases Causing Dementia and Worldwide Prevalence (2010, 2030, 2050)

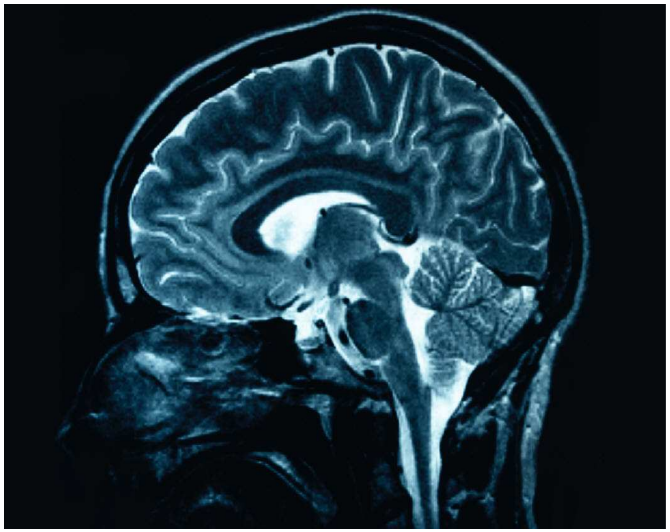
- Alzheimer (36 million, 66 million, 115 million)
- Parkinson (5 million, 9 million, 15 million)
- Huntington (100,000)
- Others

Huntington Disease



Expanded CAG_n on Chromosome 4

Genetic Etiology



Selective Neuronal Degeneration

Brain Phenotype & Pathogenesis

Cognitive Impairment

Behavioral Disorders

Clinical Consequences

Clinical Phenotype

Huntington Disease

- Unmet treatments needs for HD
- Status of R&D for HD
- Why PBT2 is worth pursuing

FDA Huntington Disease Public Meeting on Patient Focused Drug Development Sept 22, 2015

Important and recurrent themes expressed by patients and families

- Cognitive impairment is the most important problem and unmet need in HD, cited by 66% of patients in the room and 80% patients on the webcast.
- Examples of cognitive impairment mentioned: inability to concentrate and complete tasks, problems balancing a checkbook and making change, following sequences of directions, irrationality, inattentiveness, memory loss, problems making decisions, word-finding difficulties
- Behavioral and psychiatric problems and sleep disturbances were also common concerns.

HD RCTs Underway or Completed

- 25 HD RCTs in various phases of activity per *HD Insights,* June 2015
- per www.Clinicaltrials.gov 19 placebo-controlled RCTs initiated, active or completed between January 2005 and June 2015
  - Collectively involved 3152 research participants
  - About 40% these RCTs have not yet reported results in full peer-reviewed publications.

Clinical Trials Update

SPONSOR	STUDY NAME/ IDENTIFIER	STUDY AGENT	PHASE	PRINCIPAL INVESTIGATOR, CONTACT	DESIGN	TRIAL LENGTH	SITES	STATUS
Charité University	ETON-Study	Epigallocatechin gallate	II	Josef Priller, MD +49 (0)30 450 617209	Randomized double-blind study testing the efficacy and tolerability of (2)-epigallocatechin-3-gallate (EGCG) in changing cognitive function in HD patients	1 year	4 total - Germany	*Enrollment complete, study ongoing*
Charité University	Action-HD	Bupropion	II	Josef Priller, MD +49 (0)30 450 617209	Randomized double-blind study testing the efficacy and tolerability of bupropion in changing apathy in patients with HD	10 weeks	3 total - Germany	*Study complete*
Ipsen	NCT02231580	BN82451B	II	Bruno Padrazzi, MD clinical.trials@ipsen.com	Dose escalation, proof of concept study to investigate the safety and tolerability, the pharmacokinetic and the pharmacodynamic properties of twice daily BN82451B for four weeks in male patients with HD	28 days	1 total - Germany	*Currently enrolling*
Omeros Corporation	NCT02074410	OMS643762	II	Albert Yu, MD 206-676-5000	Randomized, double-blind, placebo-controlled, sequential cohort study to evaluate safety and efficacy of OMS643762 in subjects with HD	28 days	4 total - United States	*Trial suspended*
Prana Biotechnology	REACH2HD	PBT2	II	Ray Dorsey, MD	Randomized double-blind safety and tolerability study of PBT2 of individuals with mild to moderate HD	6 months	20 total - Australia and United States	*Results published*
Pfizer	NCT01806896	PF-0254920	II	Pfizer CT.gov Call Center, 800-718-1021	Randomized, double-blind, placebo-controlled study to evaluate the safety, tolerability and brain cortico-striatal function of 2 doses of PF-02545920 in individuals with early HD	28 days	Paris, France	*Study complete*
Pfizer	NCT02197130	PF-0254920	II	Pfizer CT.gov Call Center, 800-718-1021	Randomized, double-blind, placebo-controlled proof of concept study of the efficacy and safety of PF-02545920 in HD	26 weeks	23 total - Europe and United States	*Currently enrolling*

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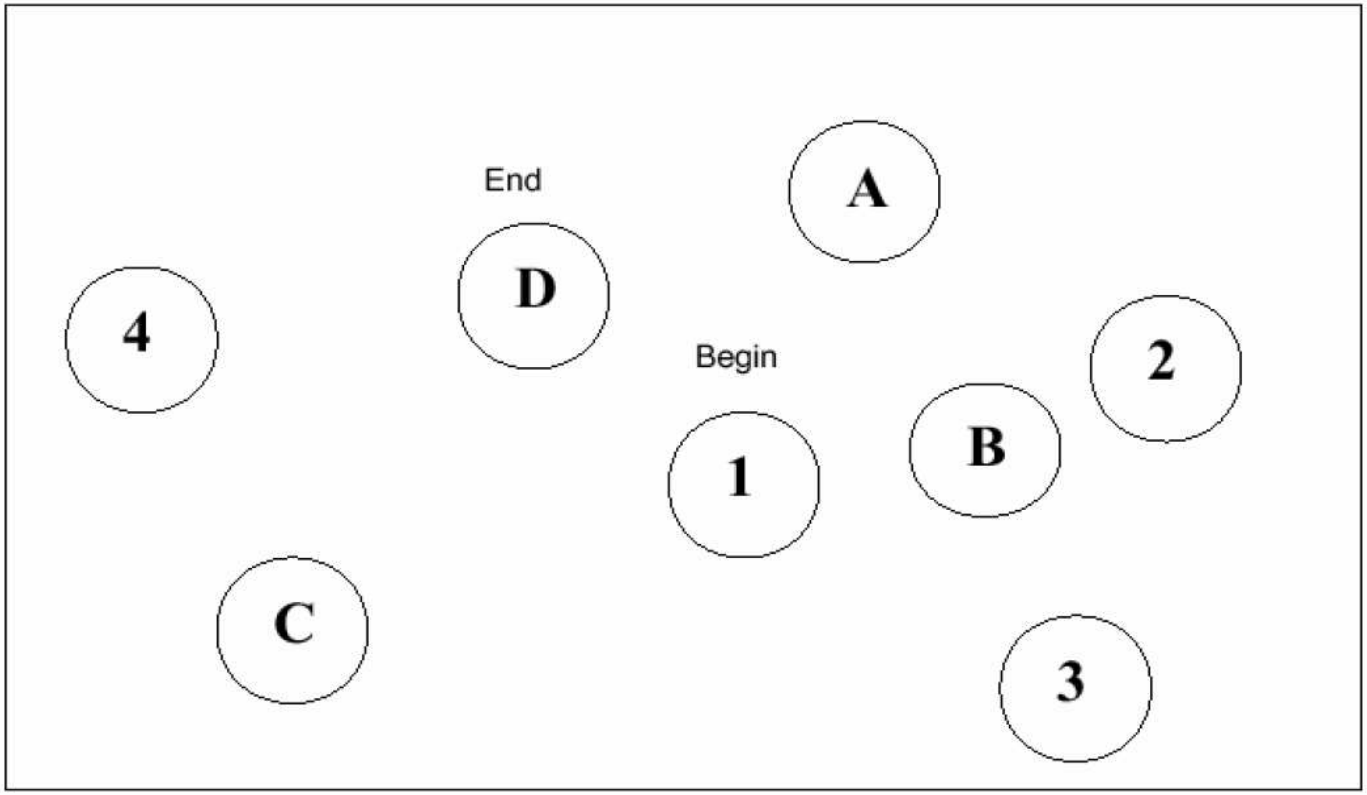
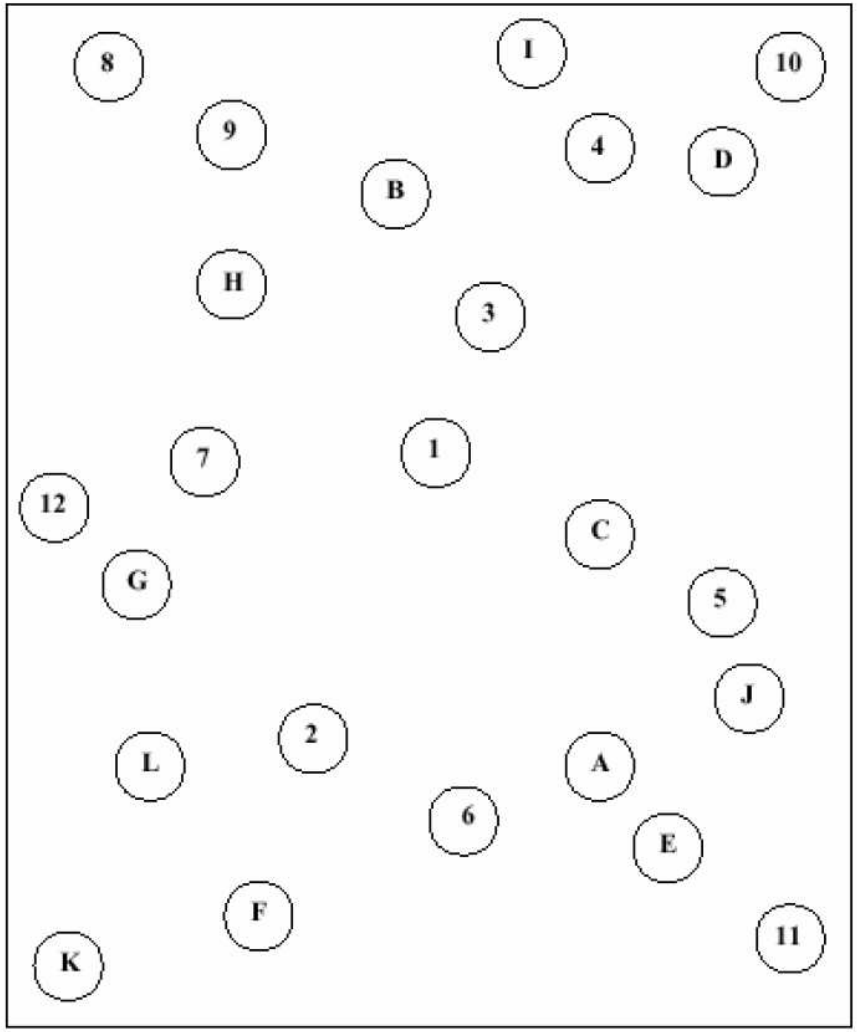
Trail Making Test Part B – *SAMPLE*



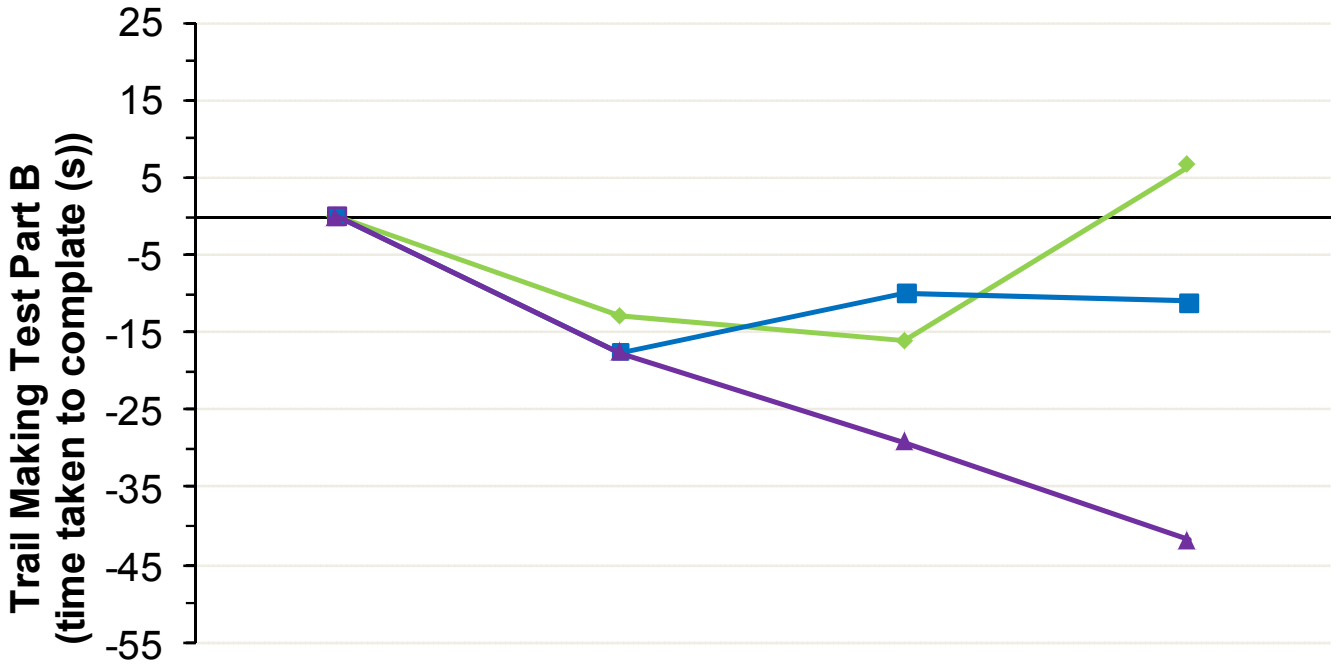
Trail Making Test Part B

Patient's Name: _____ Date: _____



PBT2-201-EURO Study

Trail Making Test Part B:
LSMean Change from Screening over 12 weeks (ITT)



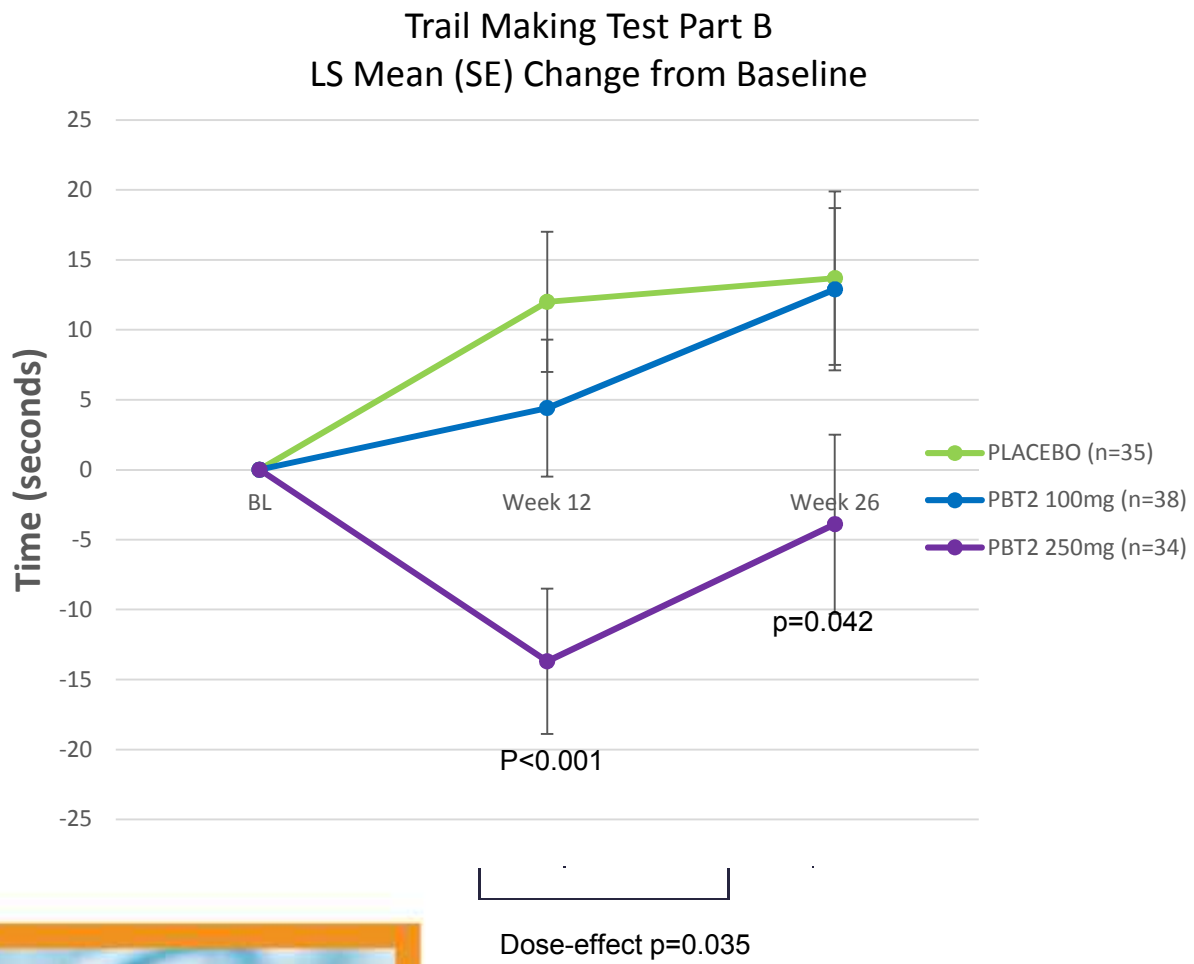
Decreased time to complete = improvement

*** Compared with placebo**

Lancet Neurology (Lannfelt et al 2008, 2009)

High-Dose PBT2 in Early HD Significantly Improves Trails Making Test B Cognition

(Huntington Study Group REACH2HD Investigators, *Lancet Neurology*, Nov 2014)



Decreased time to complete = improvement

Lancet Neurology, Nov 2014

12 November, 2015

Dear Friends,

I am writing this letter, first, to express my appreciation for your support of Prana Biotechnology and, more generally, drug development aimed at preventing and treating this terrible disease called Alzheimer's disease (AD). Second, I would like to take the opportunity to update you on how recent studies modelling AD, using human stem cell-derived neurons grown in 3D cultures, have dramatically enhanced and clarified our understanding of the pathogenic events underlying AD-related neurodegeneration.

The past year of AD research has arguably been one of the most exciting in the last two decades. I say this in references to new revelations coming out of genetic studies of AD, as well as the insights regarding the etiology and pathogenic events underlying AD, emerging from our new model of the disease dubbed "Alzheimer's-in-a-Dish". We have developed this new model of AD using human stem cell-derived neural cultures grown in petri dishes in a gel that resembles the milieu of the brain. This is referred to as 3-D neural culture and we used it to recreate for the first time, the two major pathological hallmarks of AD - deposits of beta-amyloid protein, which appear as senile plaques (outside neurons), and twisted aggregates of tau proteins that manifest as neurofibrillary tangles (inside neurons). While those in the AD research field agree that it is the tangles and inflammation that kill neurons, heavy debate has raged for thirty years in the Alzheimer's research community as to what initiates the tangles and deadly neurodegenerative cascade—the beta-amyloid or something else.

While our and other's genetic studies of AD over the last three decades have strongly supported the notion that beta-amyloid acts as a trigger for tangle formation and neurodegeneration, evidence against this idea was suggested by two repeated findings. First, when the early-onset familial AD gene mutations in the amyloid precursor protein (APP), presenilin 1 (PSEN1) and presenilin 2 (PSEN2) were introduced into mice in attempts to create animal models for AD, plaques were observed, eventually leading to neuroinflammation, cell death, and cognitive deficits. However, no tangles were produced. This suggested beta-amyloid does not lead to tangles - at least, in mice. Second, many anti-amyloid therapies failed in clinical trials.

Now, Alzheimer's-in-a-dish, using human (not mouse) neurons, has clearly shown that beta-amyloid is sufficient to lead directly to tangles (after ~9 weeks in culture). Furthermore, we showed that if you stop the deposition of beta-amyloid, you also stop the tangles. Regarding the numerous failed clinical trials targeting beta-amyloid, we now know that beta-amyloid accumulates 10-20 years before any cognitive symptoms of AD and that treating AD by only targeting amyloid in mid-late stage patients is too little-too late. Beta-amyloid deposition must be targeted as early as possible, preferably at the pre-dementia stage of the disease process.

Recent discoveries in AD genetics have also strongly implicated neuroinflammation as the third pillar of AD pathology (in addition to beta-amyloid deposition (e.g. as senile plaques and neurofibrillary tangles). In 2008, we discovered the new AD gene, CD33, and in 2012, Decode (Iceland) discovered the AD gene, TREM2. We now know that these two genes play a major

role in controlling neuroinflammation in AD. These are now serving as drug targets for regulating neuroinflammation in AD. This is particularly important in patients with mid-late stage AD.

The newest combined genetic, imaging, biomarker, and Alzheimer's-in-a-Dish data now collectively illustrate a path for Alzheimer's pathology in which first, beta-amyloid accumulates in the brain, decades before cognitive impairment. Beta-amyloid then triggers the production of tangles that kill neurons from within as well as neuro-inflammation, which kills more neurons. As increasing numbers of neurons die, there is more neuro-inflammation driven by microglial cells (regulated by the genes, CD33 and TREM2). Inflammation then drives even more plaques and tangles, and a vicious cycle ensues.

We have been using Alzheimer's-in-a-Dish to find drugs that will slow or halt plaque and tangle formation. Among those that are being tested is PBT2. Studies of PBT2 are still in progress and once confirmed, will be submitted for publication. So far, the preliminary findings show that PBT2 has the following effects in Alzheimer's-in-a-Dish: 1. A trend in the direction of attenuation of the aggregation and fibrillization of the Abeta peptide into beta-amyloid, 2. significantly reduced tangle formation, and 3. significantly increased cell viability. Once these results are confirmed, PBT2 would become the only compound tested in Alzheimer's-in-a-Dish to achieve all three of these effects on AD pathology.

In closing, based on recent findings, I firmly believe, that beta-amyloid remains the best target for preventing and treating AD, but this must be achieved in the earliest stages of the disease process. Based on the combined data, I continue to believe that PBT2 carries great potential for curbing plaque and tangle formation, while also enhancing neuronal cell viability as an AD therapeutic.

Sincerely yours,

Rudolph E. Tanzi, Ph.D.

Reference:

Choi SH, Kim YH, Hebisch M, Sliwinski C, Lee S, D'Avanzo C, Chen H, Hooli B, Asselin C, Muffat J, Klee JB, Zhang C, Wainger BJ, Peitz M, Kovacs DM, Woolf CJ, Wagner SL, Tanzi RE, Kim DY. A three-dimensional human neural cell culture model of Alzheimer's disease. Nature. 2014 Nov 13;515(7526):274-8. doi: 10.1038/nature13800. Epub 2014 Oct 12.