PRANA BIOTECHNOLOGY Limited

Reach2HD Phase 2 Clinical Trial
Top Line Results

Investor Conference Call 19th February 2014

Reach2HD
A Huntington Disease Research Trial

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."

Introduction

Mr Geoffrey Kempler, Chairman and Chief Executive Officer

Dr Ray Dorsey, Professor of Neurology, University of Rochester; Principal Investigator

Dr Ira Shoulson, Professor of Neurology, Georgetown University; Chair, Huntington Study Group

Dr Rudy Tanzi, Professor of Neurology, Harvard Medical School; Prana Chief Scientific Advisor

Diane Angus, Chief Operating Officer, Prana.

Mr Geoffrey Kempler, Chairman and Chief Executive Officer

Dr Ray Dorsey, Professor of Neurology, University of Rochester; Principal Investigator

Outline

- Huntington disease and cognition
- Reach2HD study
- Results

Huntington disease (HD) is a rare, inherited neurodegenerative disorder

Who	•Approximately 30,000 Americans and over 80,000 individuals globally •Affects both sexes equally
What	•Inherited disorder that causes involuntary movements (chorea), behavior changes, and cognition decline •Only one FDA-approved treatment for chorea (tetrabenazine) is available
When	•Disease onset is typically between 30 to 50 years of age •Rarer, childhood onset forms occur
Where	•Higher prevalence in Europe and North America •Lower prevalence in Japan and Africa
Why	•Disease is caused by a trinucleotide (CAG) expansion in *huntingtin* gene •The huntingtin protein is expressed in higher concentrations in the brain; its exact function remains unclear, but it is involved in regulation of gene expression

Sources: Walker FO. Lancet 2007;369:318-28, Subramaniam S et al. Science 2009;324:1327-30; Fisher E, Semaka A. How many people have Huntington disease? Available at: http://www.e-digitaleditions.com/issue/47322

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 promote aggregation of mutant huntingtin
- PBT2 belongs to a class of metal-protein attenuating compounds that reduce metal-induced toxicity of mutant huntingtin

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

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

Trail Making Test Part B is a test of executive function, which is impaired in HD

Executive function and Trail Making Test Part B

Cognitive decline is universal in Huntington disease

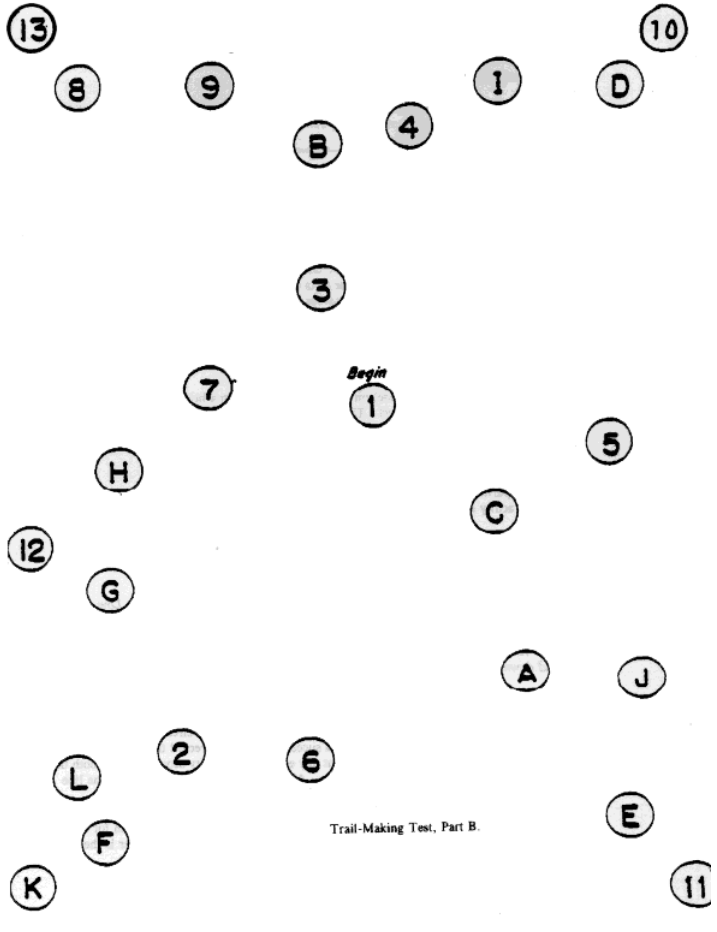
- Cognitive decline begins before diagnosis and is progressive
- Cognitive decline predicts impairments in everyday function

Executive cognitive decline in HD

- Refers to cognitive control processes, such as planning, problem solving, flexibility of behaviour when situational demands change.

Trail Making Test Part B

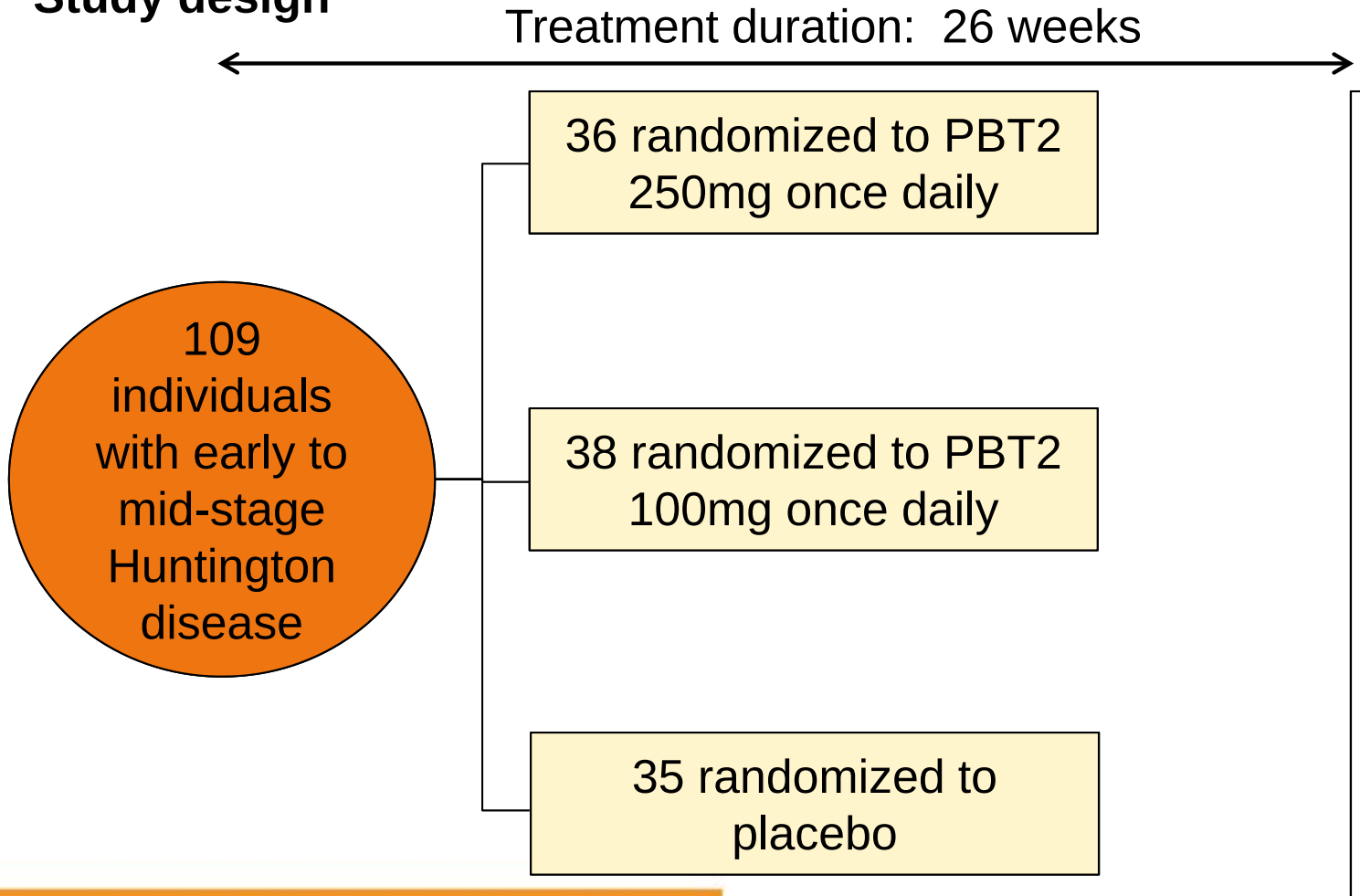
- Timed executive function measure (flexibility), impaired in HD
- Patients 'Connect the dots' alternating numbers and letters (1→A→2→B→3…)
- Slowing indicates impaired flexibility



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]

The 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

Baseline characteristics of participants were well balanced across groups

Baseline characteristics of the Reach2HD study population

Characteristic	Placebo (N=35)	PBT2 100mg (N=38)	PBT2 250mg (N=36)	All (N=109)
Mean age in years (range)	51.2 (30-66)	54.1 (31-79)	50.3 (28-70)	51.9 (28–79)
Percent men	45.7%	50.0%	52.8%	49.5%
Mean CAG repeat length (of the expanded allele)	44.1	43.2	44.4	43.9
Mean score on Montreal Cognitive Assessment (range is 0-30)	22.5	23.5	22.9	23.0
Mean Total Functional Capacity (range is 0-13)	9.0	9.3	9.3	9.2

PBT2 was well tolerated ...

Tolerability

PBT2 250mg daily	•32 (88.9%) of the 36 individuals randomized to PBT2 250mg completed the study
PBT2 100mg daily	•38 (100%) of the 38 individuals randomized to PBT2 100mg completed the study
Placebo	•34 (97.1%) of the 35 individuals randomized to placebo completed the study

Overall, 95% of participants completed the 26-week study

... and generally safe in the study

Safety of PBT2

Serious adverse events	•Ten serious adverse events occurred during the study •Nine were in the PBT2 groups (6 in PBT2 250mg and 3 in PBT2 100 mg) •Only one (on PBT2 250mg) was deemed related to study drug by the site investigator
Adverse events	•Frequency of adverse events did not differ significantly across the three study groups •Most common adverse event was diarrhea, and the rate was similar across groups

PBT2 250mg significantly improved performance on Trail Making Test Part B

Change in Trail Making Test Part B

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

Trend toward improvement on the executive function composite z-score

Other cognitive outcomes

Executive function composite	Among all participants, there was a trend toward improvement in the composite executive function for those randomized to PBT2 250mg (p=0.069) that was significant among those with mild Huntington disease (p=0.038)
Remaining cognitive measures	No other significant differences were observed at 26 weeks on the other cognitive measures

Cognitive improvement was also accompanied by a trend toward improvement on functional capacity

Other efficacy outcomes

Total Functional Capacity

- Total Functional Capacity is a key measure of function in occupation, finances, domestic chores, activities of daily living, and care level that is used in almost all in clinical studies in Huntington disease
- Score ranges from 0 (most impaired) to 13 (normal)
- In Reach2HD, individuals randomized to PBT2 had a favorable signal on slowing functional decline over 6 months

Remaining efficacy measures

No other statistically significant differences were observed on other efficacy measures

Source: Huntington Study Group. Mov Disord 1996;2:136-42

Small, exploratory neuroimaging study suggested decreased atrophy among those exposed to PBT2

Exploratory outcome

Imaging results	•In a small (n=6), pilot sub-study, individuals randomized to PBT2 (n=4) had reduced brain atrophy compared to those randomized to placebo
Context	•Brain atrophy is known to begin in the prodromal phase of Huntington disease and progresses along with the disease •Brain atrophy and cortical thinning are associated with cognitive decline in Huntington disease •A recent Huntington disease clinical trial suggested that pharmacological treatment could reduce cortical thinning relative to placebo

Sources: Tabrizi SJ et al. Lancet Neurol 2013;12:637-49, Scahill RI et al. Hum Brain Mapp 2013;34:519-29, Rosas HD et al. Neurology 2005;65:745-7, Rosas HD et al. Neurology 2014;82:1-8

PBT2 is a promising therapy for a cardinal feature of HD

Summary

Tolerability and safety

- PBT2 was well tolerated and generally safe 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

These promising results require confirmation in a larger phase 3 clinical trial

Dr Ira Shoulson, Professor of Neurology, Georgetown University; Chair, Huntington Study Group

PRANA BIOTECHNOLOGY Limited

Q&A

Reach2HD
A Huntington Disease Research Trial