



**PD-299,685**

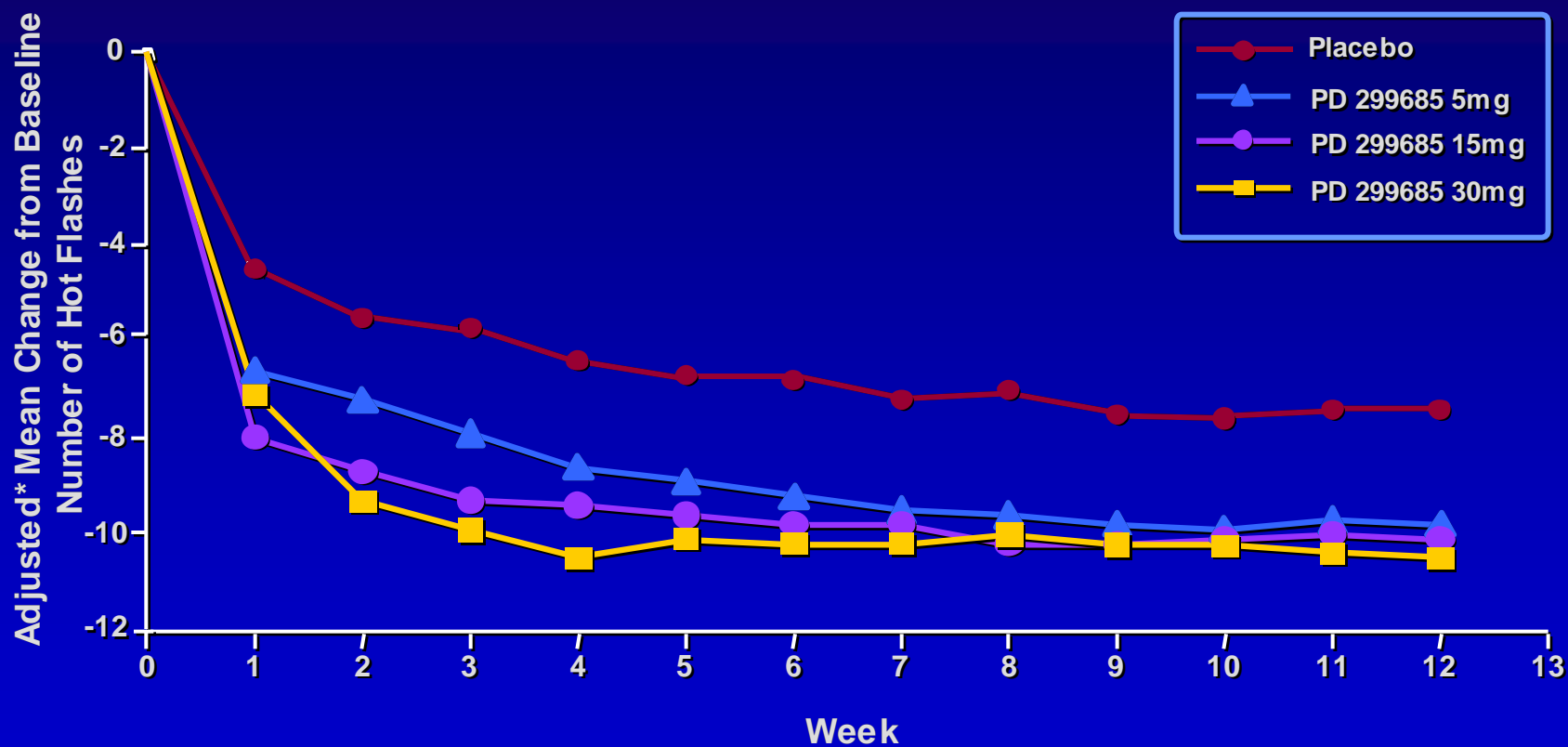
***A Novel Treatment for Hot Flashes***

- ◆ **Treatment of Vasomotor Symptoms Associated with Menopause**
- ◆ **Current Standard of Care is Hormone Replacement Therapy (HRT)**
- ◆ **Non-hormonal Mode of Action Offers an Alternative to Women Concerned About HRT**





# PD-299,685 Reduces the Number of Hot Flashes



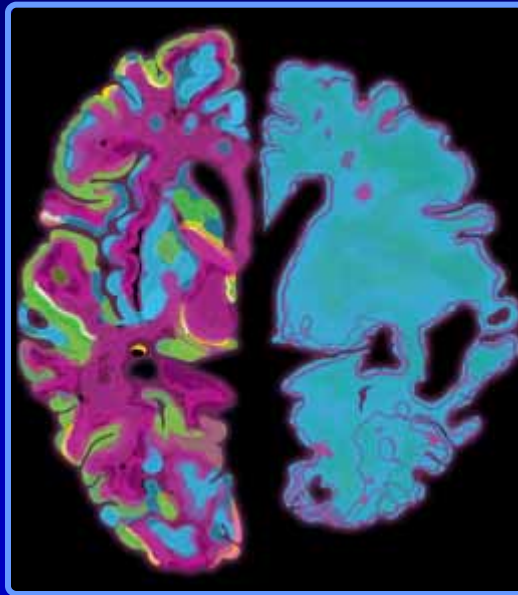


# Alzheimer's Points of Intervention

***A $\beta$  Antibodies and RAGE  
Increase Clearance of A $\beta$***

***Secretase Inhibitors  
Block Production of A $\beta$***

***Tau Kinase  
Inhibitors  
Block Tangle  
Formation***



***Cholesterol  
Modulation  
Lower A $\beta$   
Production***

***Neuroprotection  
Increase Neuron Survival***

***Neurorestoration  
Increase Neuron Function***



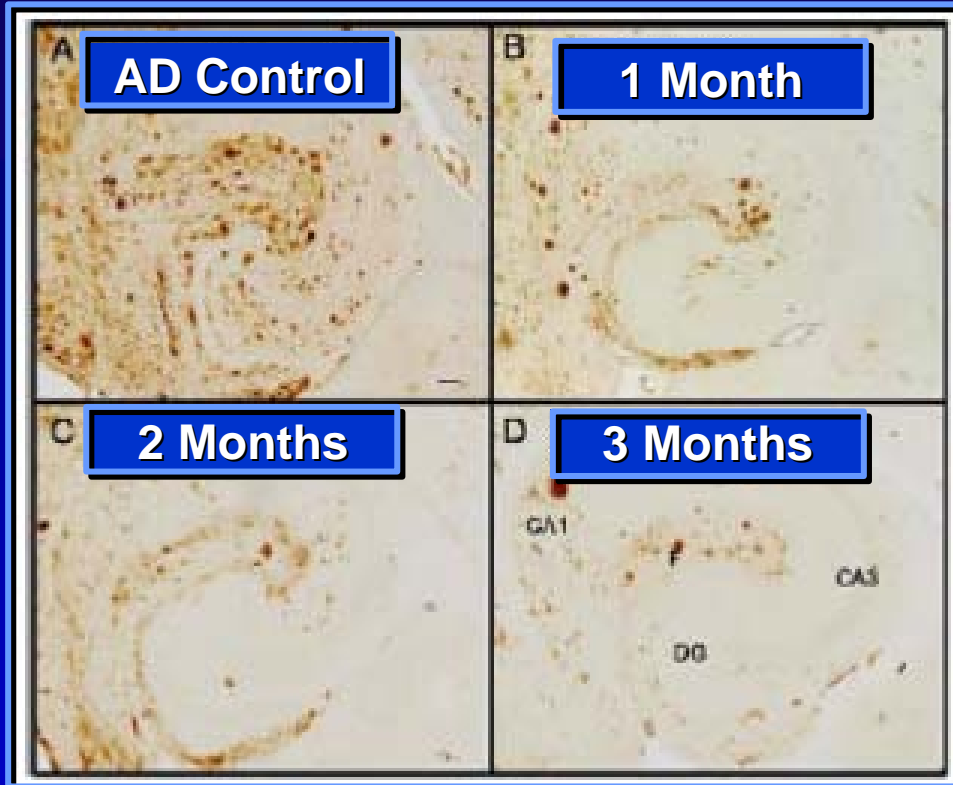
- ◆ **Compelling Approach:  
Potential Best-In-Class  
Therapy for  
Alzheimer's Disease**
- ◆ **Robust Portfolio of  
Other Opportunities**
  - **RN624 – Acute and Chronic  
Pain (Entering Phase 2)**
  - **Antibodies Related to the  
Prevention of Chemo-induced  
Cachexia**
  - **Rich Discovery Pipeline**





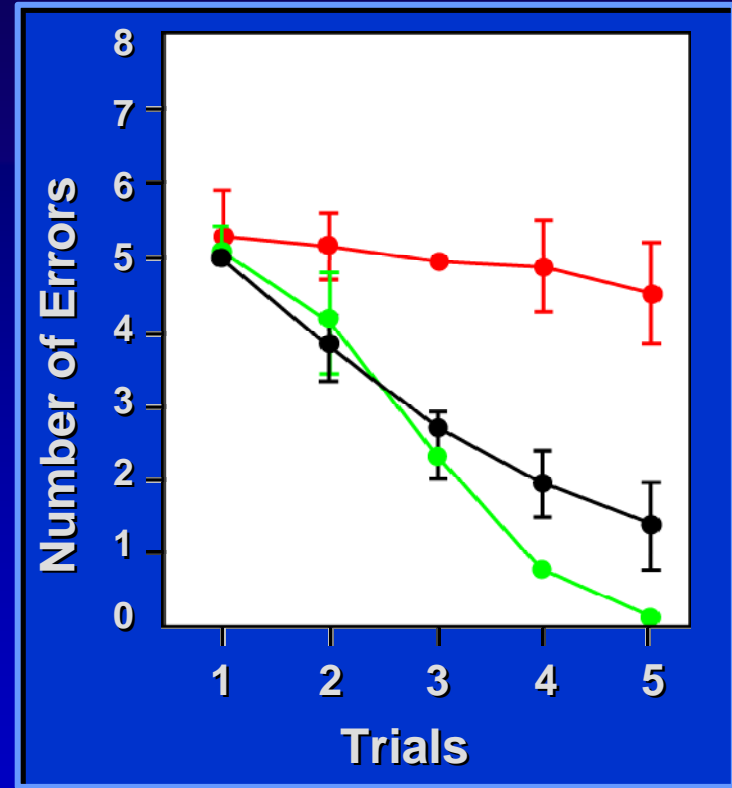
**RN1219**\*

**Reduces Plaque, Improves Cognitive Function**



Wilcock, D.M. et al., *J. Neurosci.* 24(27): 6144-6151 (2004)

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Derived from: Wilcock, D.M. et al *J. Neuroinflamm.* 1:24 (2005)

**AD mice**

**Normal mice**

**Control Rx**

**Control Rx**

**Murine anti-A $\beta$**

*\*Results presented using glycosylated Murine anti-A $\beta$  antibodies - same target as RN1219*

Valid as of November 30, 2006

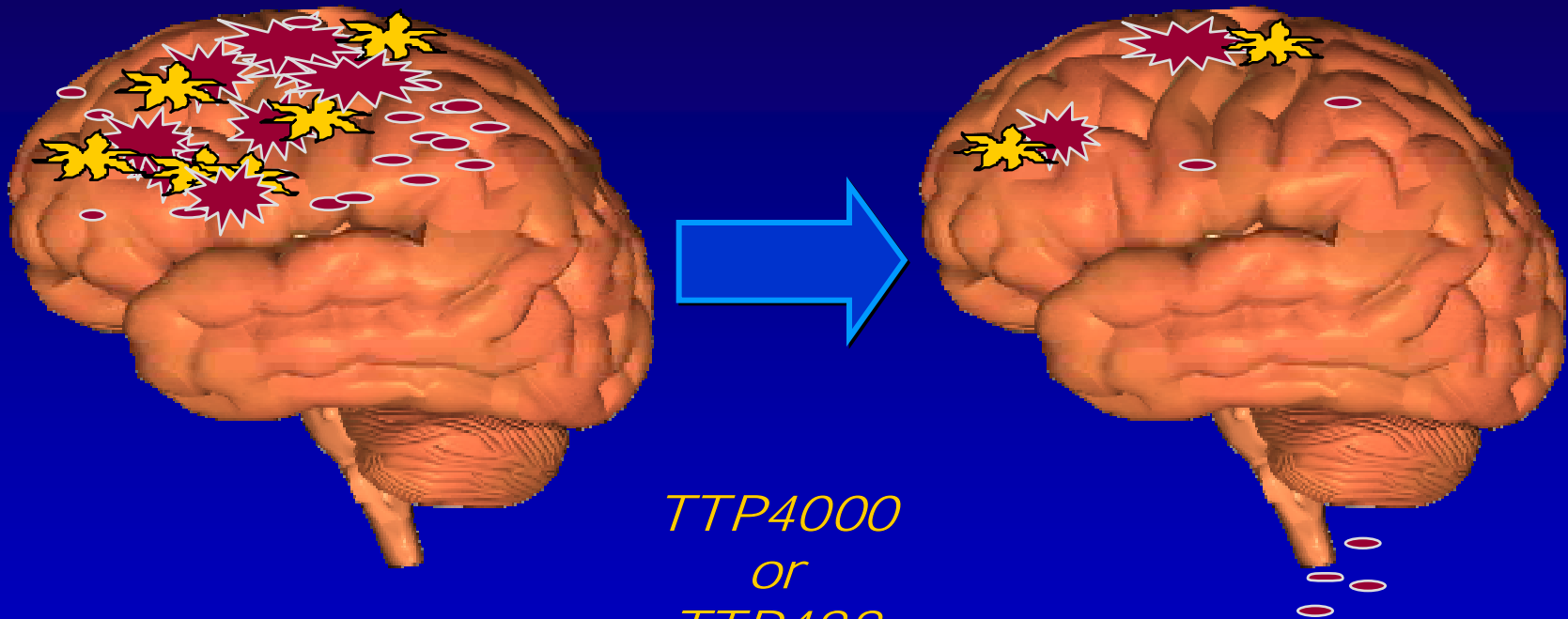


- ◆ **Second Strategic Collaboration in Alzheimer's Disease**
- ◆ **Highly Complementary to Rinat and In-House Approaches**
- ◆ **Novel Mechanism Targeted: Receptor for Advanced Glycation End-products (RAGE)**





# RAGE Therapies



*TTP4000*  
or  
*TTP488*



AD Brain Plaques



Activated Inflammatory Cells

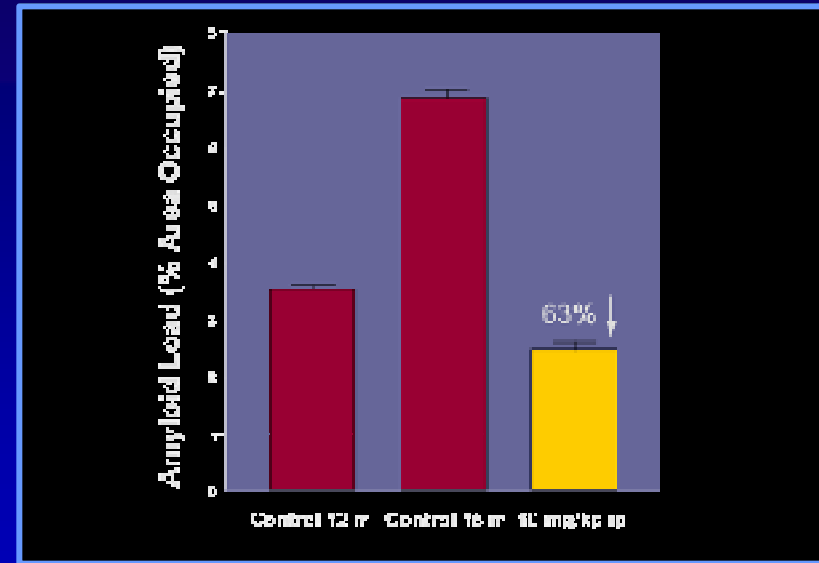
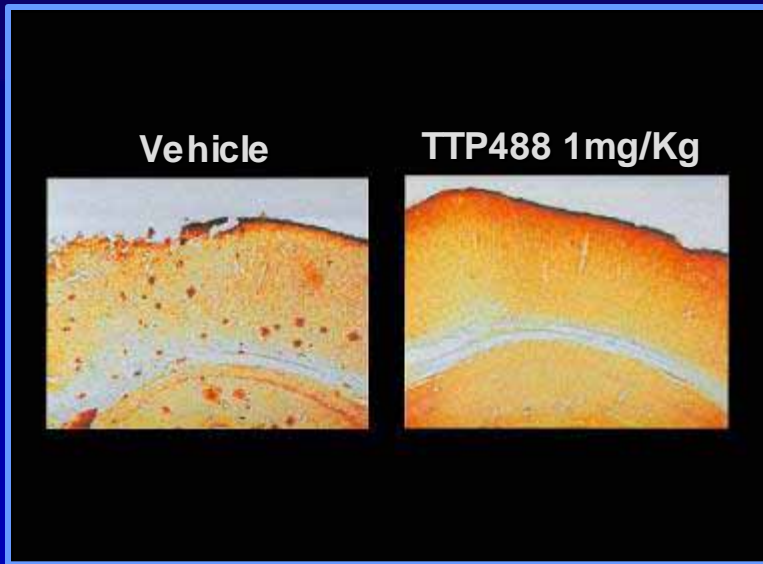


Beta-Amyloid





# TTP488 Results



## *Prevention Model*

Begin Treatment at 6 Months Before  
Plaque Deposition is Initiated

## *Therapeutic Model*

Begin Treatment at 12 Months after  
Plaque Deposition Has Initiated



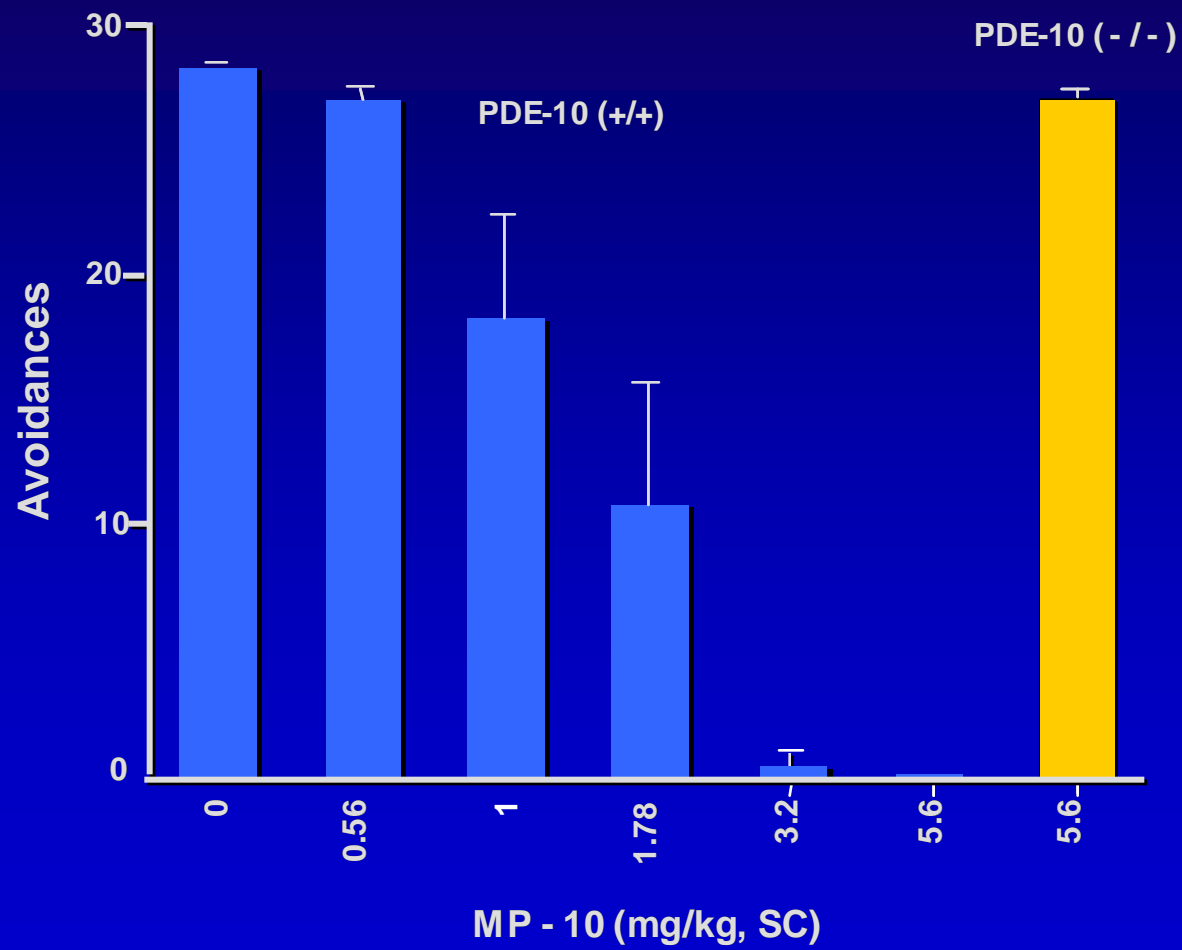






# **PDE-10 Inhibitors**

## **Active in Schizophrenia Models**





## Groundbreaking Collaborations

FOUNDATION  
FOR THE  
National Institutes of Health

### GAIN Program



- ◆ Stephen V. Faraone, SUNY, “International Multi-Center ADHD Genetics Project.”
- ◆ Pablo V. Gejman, Northwestern, “Genome-Wide Association Study of Schizophrenia.”
- ◆ John Rice Kelsoe, UCSD, “Whole Genome Association Study of Bipolar Disorder.”
- ◆ Patrick Francis Sullivan, UNC, “Major Depression: Stage 1 Genome-wide Association in Population-Based Samples.”



## ***Neuroscience Vision***

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***We will Change Society  
by Lifting the Burden of  
Neuropsychiatric Disease***

