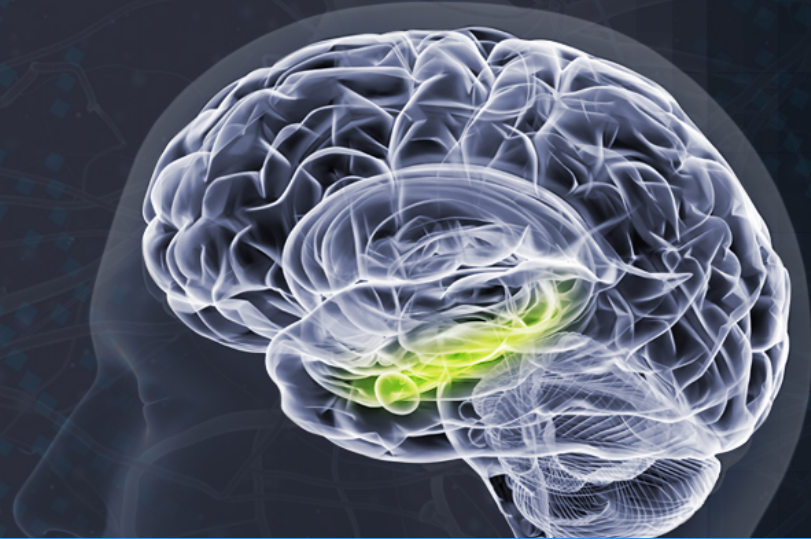


AGENE^{BIO}™

AgeneBio is dedicated to developing innovative therapeutic solutions for unserved patients at risk of **neurodegeneration**.



March 2016

Experienced Leadership Team

Management



Jerry McLaughlin

President, CEO, Board of Directors

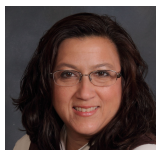
25-year veteran of the pharmaceutical industry: Merck, Endo, NuPathe



Michela Gallagher, PhD

Founder, Scientific Advisor, Board of Directors

>20 years researching the neurobiology of aging: Johns Hopkins University, UNC-Chapel Hill



Sharon Rosenzweig-Lipson, PhD

VP, R&D

>20 years developing compounds for neurologic indications: Pfizer, Wyeth, AHP



Richard Mohs, PhD

VP, Clinical Development

>30 years in clinical development: Eli Lilly, Mount Sinai School of Medicine

Led Eli Lilly's Phase 3 development team for Alzheimer's candidates solanezumab and semagacestat



Steven Mulcahy, MS

Director, Clinical Operations

>20 years managing clinical trials: Consolidated Clinical Trials, INC Research, U of Pitt Cancer Institute, Cephalon

Board of Directors (non-management)

Pat LePore, Chairman

Former Chairman & CEO, current Director of Par Pharmaceuticals

Floyd Bloom, MD

Founder and Director of Alkermes, former Editor-In-Chief of *SCIENCE*

Charles Clavitt

Former CEO of Vinci Partners US, former Co-Head of BlackRock Alternative Advisors, Johns Hopkins Trustee

Ronald Nordmann

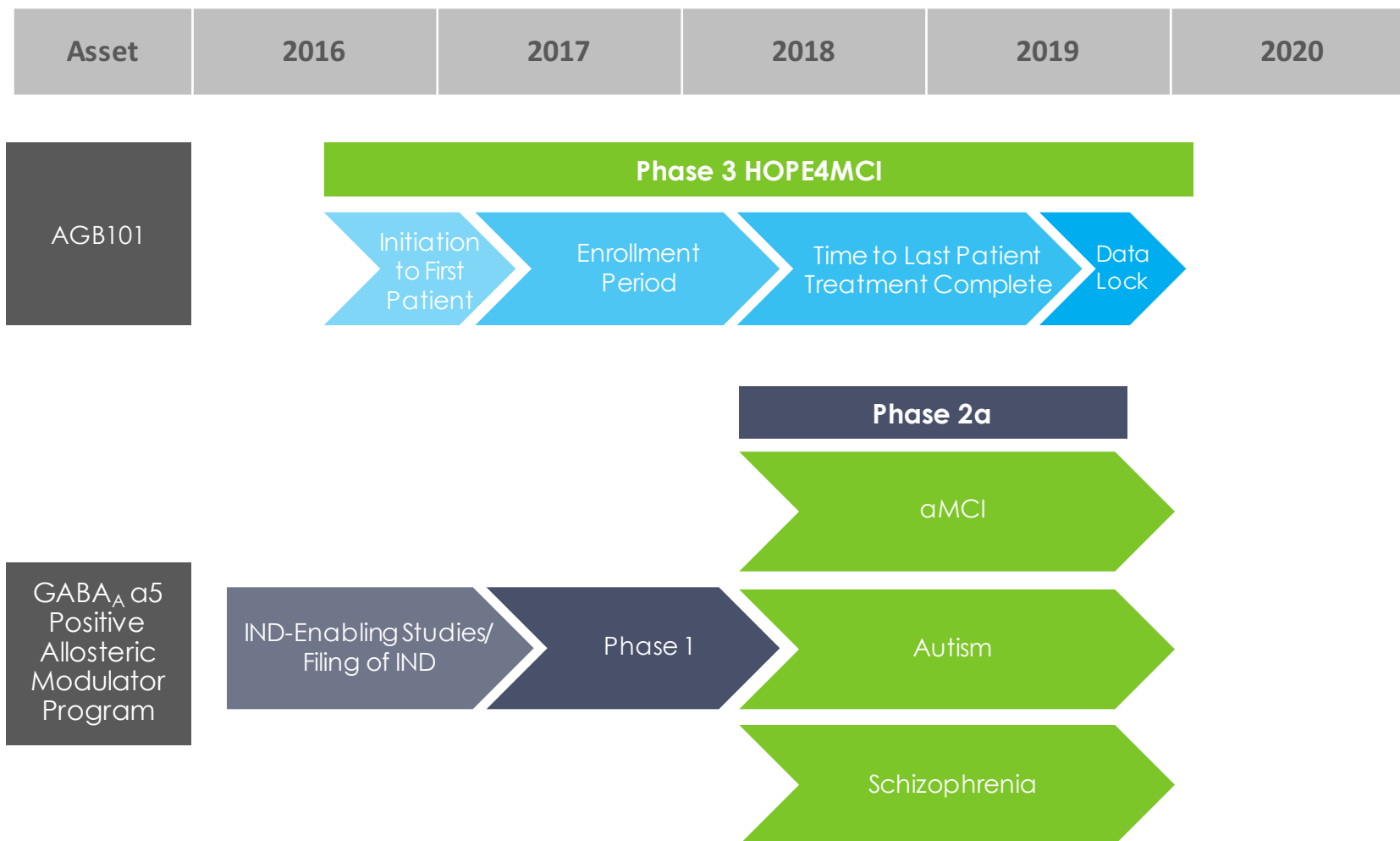
Former Partner at Deerfield Management, PaineWebber Group, Johns Hopkins Trustee Emeritus

De-Risked, Late-Stage Product Candidate for aMCI* Due to Alzheimer's Disease (Prodromal AD)

Phase 3 ready program: **AGB101**

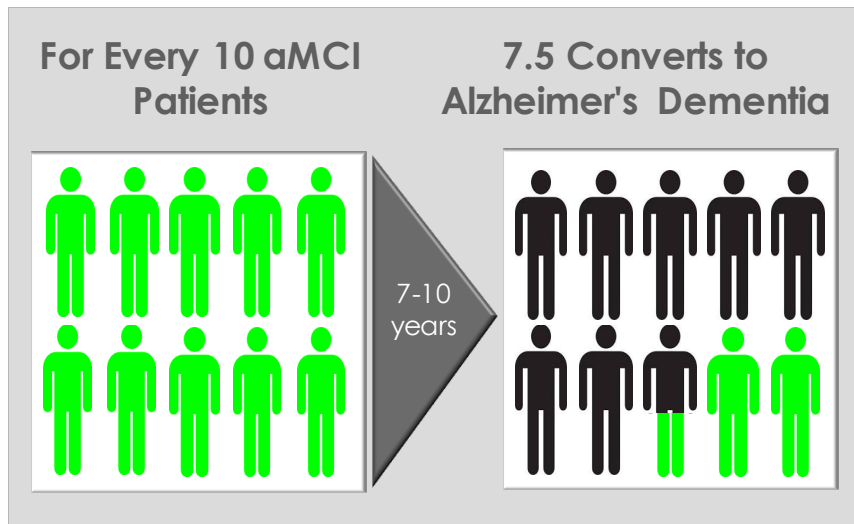
- Targets large patient population with aMCI due to AD – earliest symptomatic stage characterized by memory loss
 - No treatments exist for the 5 million US patients
- First and only product candidate addressing brain network imbalance that leads to memory loss and brain atrophy
 - Multiple animal models demonstrate efficacy
 - Phase 2 trial positive results
- Active ingredient levetiracetam marketed for 17 years as anti-epileptic Keppra (daily doses of 1,000 - 3,000 mg)
 - AGB101 is dosed once daily as a single extended-release 220 mg tablet
 - AGB101 is expected to demonstrate an excellent safety profile
- FDA supported Phase 3 manufacture
- Capital efficient manufacturing process, low cost of goods
- Extensive IP providing broad application protection and coverage

Company Pipeline and Milestones 2016 - 2020



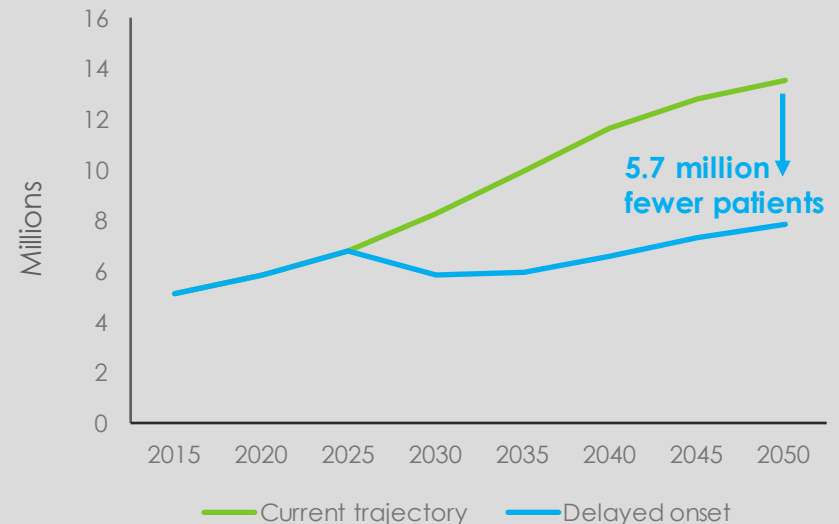
5 Million in US with aMCI – Projected to Double to 10 Million by 2050 and Exceed \$1 Trillion in Medical Costs

- aMCI is the first symptomatic clinical condition between normal aging and Alzheimer's dementia characterized by impaired memory
- Majority of patients with aMCI progress to Alzheimer's dementia within 7-10 years
- Delaying conversion to Alzheimer's dementia dramatically reduces disease burden



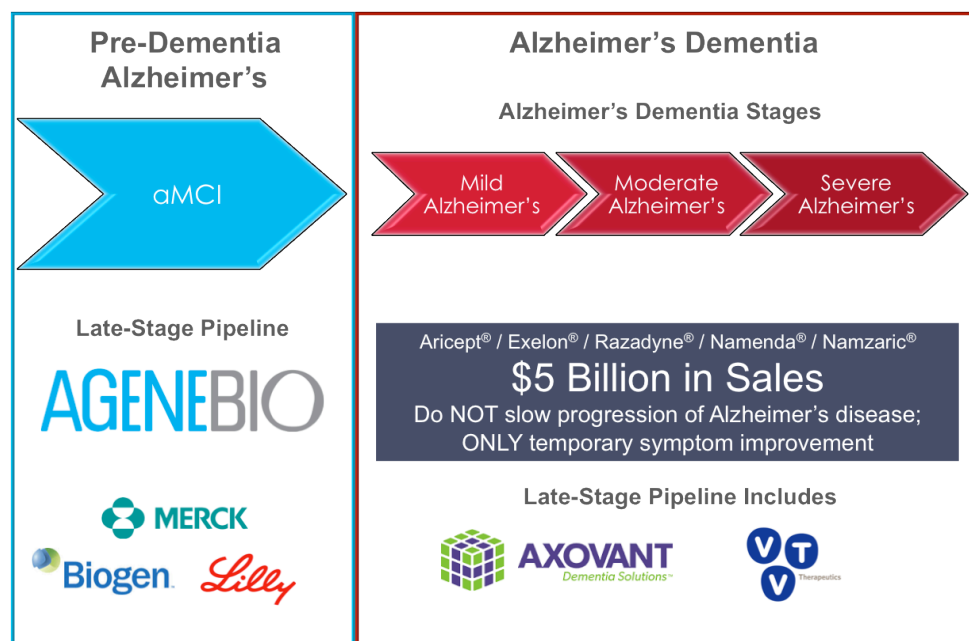
Delaying Onset of Alzheimer's Dementia by 5 Years

Impact on Number of Americans Age 65+ Living with Alzheimer's Dementia



Today's Treatments Offer Modest and Temporary Symptom Benefit; Toxicity Has Been a Barrier for Pipeline Candidates

No Approved Treatments for aMCI and Nothing Today Slows Disease Progression



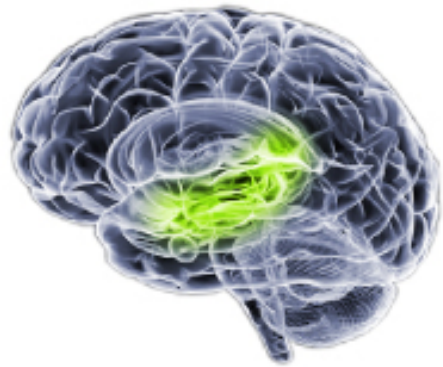
Select Alzheimer's Programs Halted or Terminated Due to Toxicity or AEs

Company & Candidate	Target & Mechanism of Action	Safety/Toxicity Issue
Eli Lilly (LY2886721)	BACE Inhibitor	Liver toxicity
Roche (RG7129)	BACE Inhibitor	Undisclosed
BI/Vitae (BI-1181181)	BACE Inhibitor	Skin reactions
Janssen/Pfizer AN-1792	Active Immunotherapy	Aseptic meningo-encephalitis
Forum Pharma (Encenicline)	Alpha 7 Receptor Agonist	Serious GI adverse events

5

aMCI: Earliest Pathophysiology of AD Cascade in the Brain Coinciding with Worsening of Memory Impairment

aMCI



Hippocampus and
Entorhinal Cortex
(Medial Temporal Lobe/MTL)

Episodic Memory Loss

Alzheimer's Dementia

Mild

Spreads to Lateral Temporal &
Parietal Lobes

Reading problems
Poor direction sense
Worsening memory loss

Moderate

Spreads to Frontal Lobe

Poor judgment
Impulsivity
Short attention

Severe

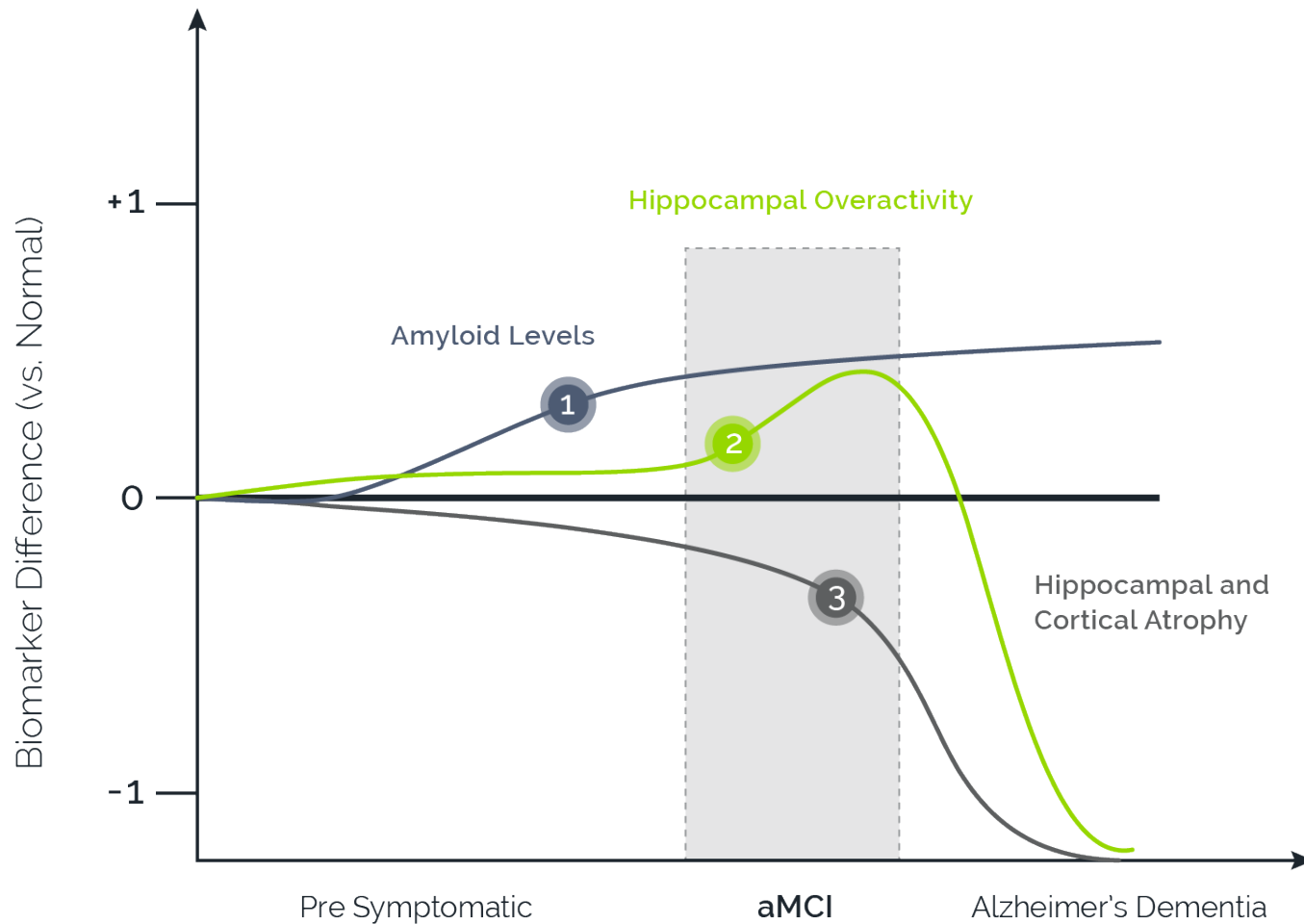
Widespread Brain Atrophy

Loss of language
Loss of basic motor skills

Episodic Memory

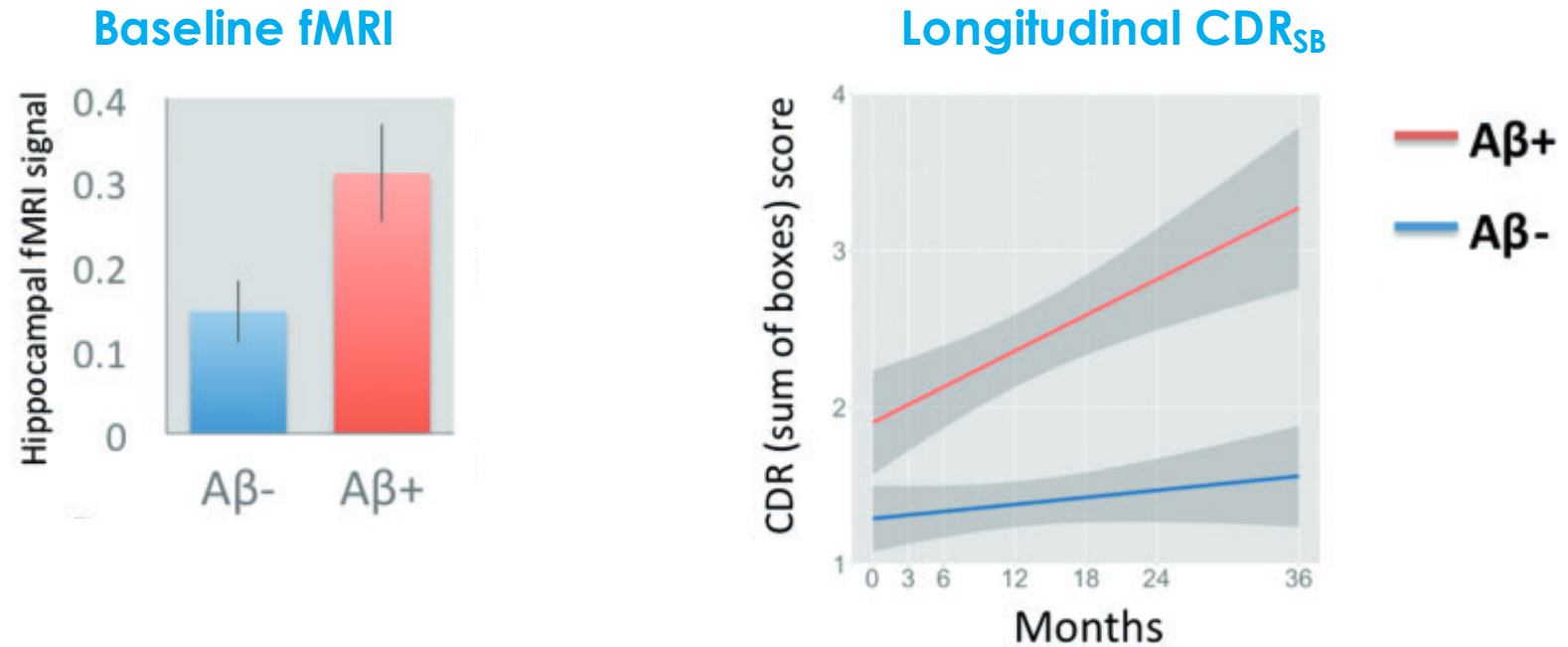
- Memory for events and episodes that can be recollected
- Ability to recollect specific events
 - Where are my keys?
 - Where did I park my car today?
 - What was last night's dinner conversation?
 - What were the events surrounding my daughter's last birthday party?

aMCI: Period of Rapid Changes in Brain Activity and Memory Decline



Adapted from Ewers et al., Trends in Neuroscience 34:430-442, 2011.

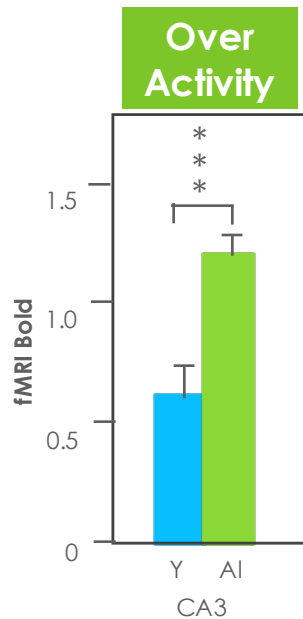
Amyloid ($A\beta$ +) in aMCI: Hippocampal Overactivity, Increased CDR-SB, and CDR-SB Progression



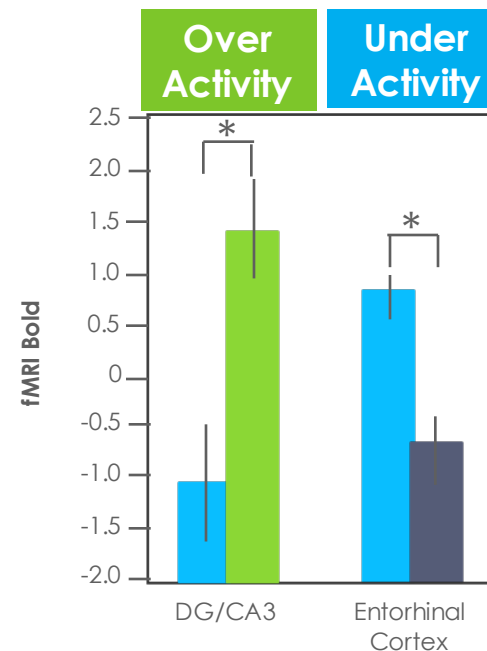
- aMCI patients with amyloid have enhanced hippocampal overactivity
- These patients have a rapid and pronounced clinical progression

Successful Translation on the Basis for Memory Impairment

Rat Age-Impaired



Human aMCI

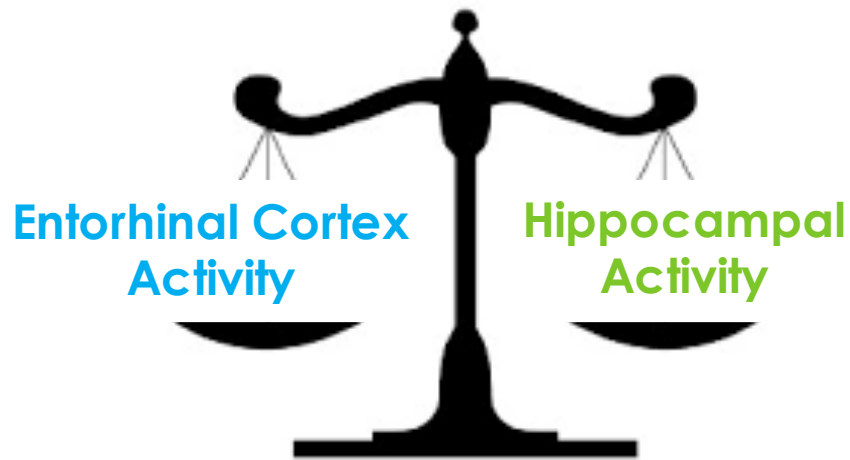


Yassa et al. 2010

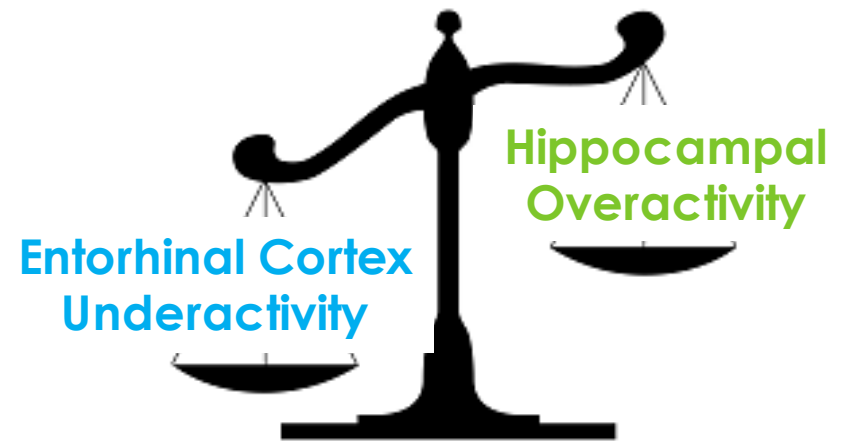
- Elevated neural activity discovered in memory-impaired aged rats (firing rates with *in vivo* recording) are the same location of elevated fMRI activation in aMCI.
- aMCI patients also have reduced activation detected by fMRI in the entorhinal cortex.

Hippocampal/Entorhinal Network Imbalance

Healthy Aging



aMCI due to AD



The Solution: AGB101

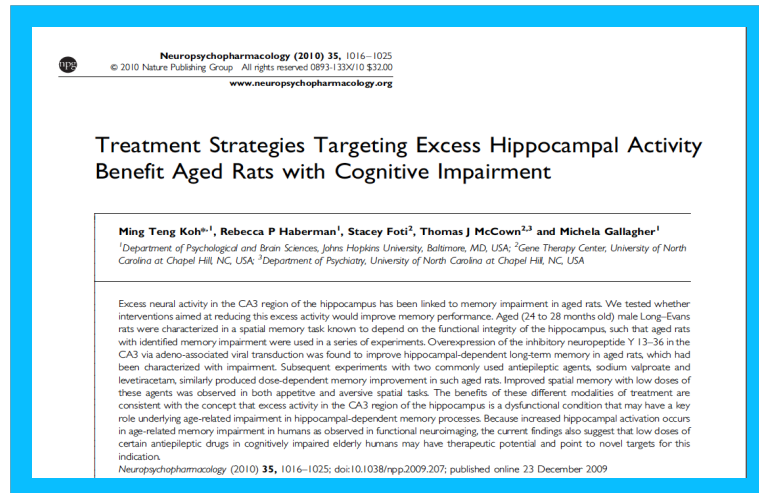
Addresses Brain Network Imbalance Driving Brain Atrophy

Levetiracetam at 1/5th to 1/12th the anti-epileptic dose

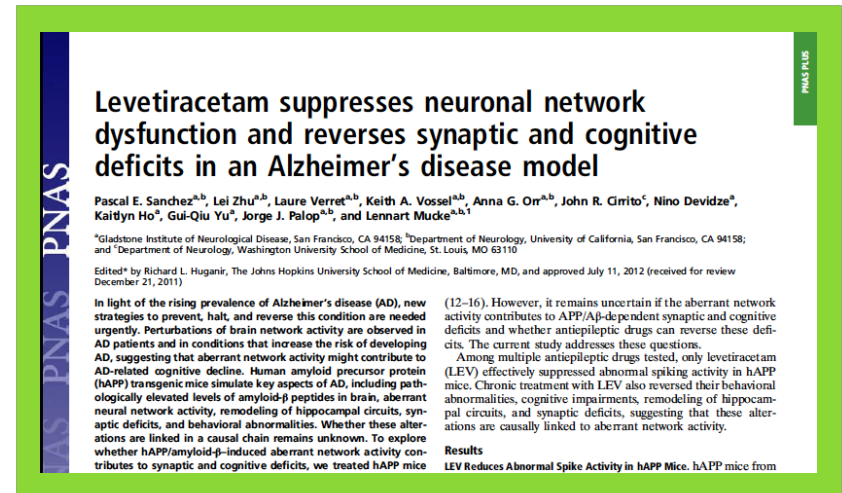
- Therapeutic target: normalizes neuronal firing in the hippocampus, restoring balance to key brain network
- Mechanistic target: SV2A inhibitor (other anti-epileptics do not share this profile)
- Favorable compound characteristics
 - ✓ 100% orally bioavailable
 - ✓ Linear pharmacokinetics
 - ✓ Readily penetrates the brain
 - ✓ No active metabolites
 - ✓ Minimal plasma protein binding (<10%)
 - ✓ No induction or inhibition of the P450 system or other enzyme systems
 - ✓ Eliminated from circulation by renal excretion as unchanged drug
 - ✓ No known drug interactions

AGB101 Demonstrates Efficacy across Animal Models for Alzheimer's Disease

Rat Model of Memory Impairment in Aging (Gallagher, Johns Hopkins)



Alzheimer's Disease Mouse Models (Mucke, Gladstone Institute, UCSF)



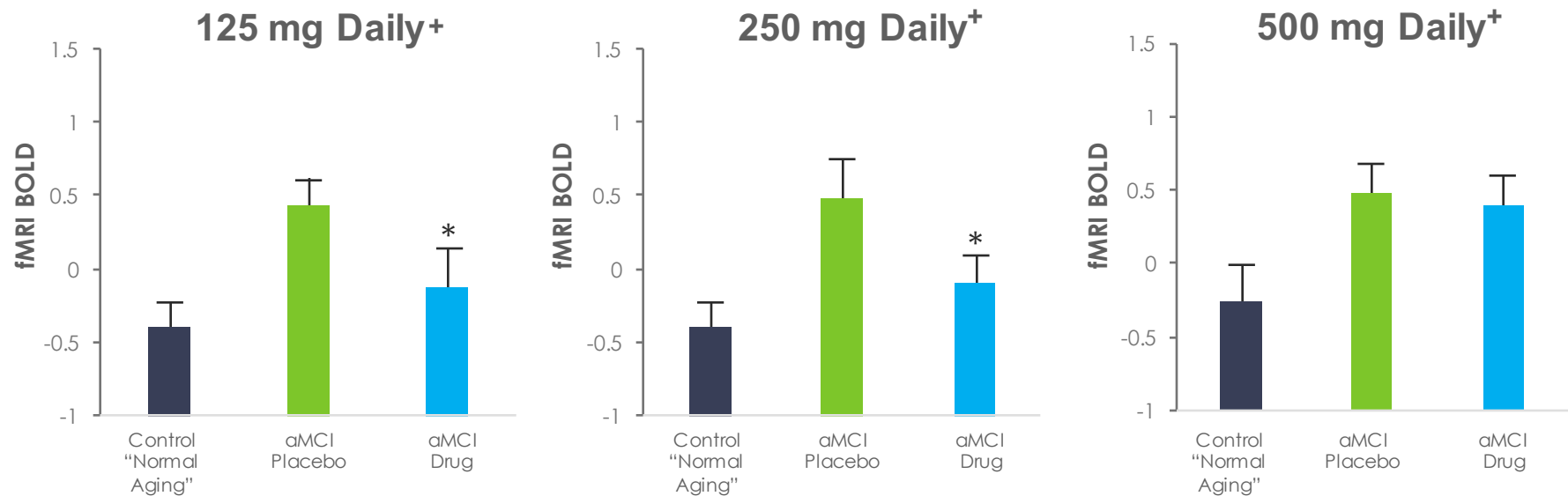
- Converging behavioral, network, synaptic and molecular data on neurocognitive basis of memory deficit
- Treatment effects demonstrated on behavioral, network, synaptic and molecular endpoints
- Therapeutic window at low doses of AGB101 (low ceiling dose for efficacy)

AGB101 Phase 2 Trial Design

- Randomized double blind within subject crossover
- Enrollment criteria: diagnosis of aMCI (ADNI-1 criteria)
- Trial size: 54 aMCI patients completed the study
- Initial aMCI Cohort 1 (250 mg)
- Additional dose ranging: Cohort 2 (125 mg); Cohort 3 (500 mg)
- Measures: fMRI, memory task performance



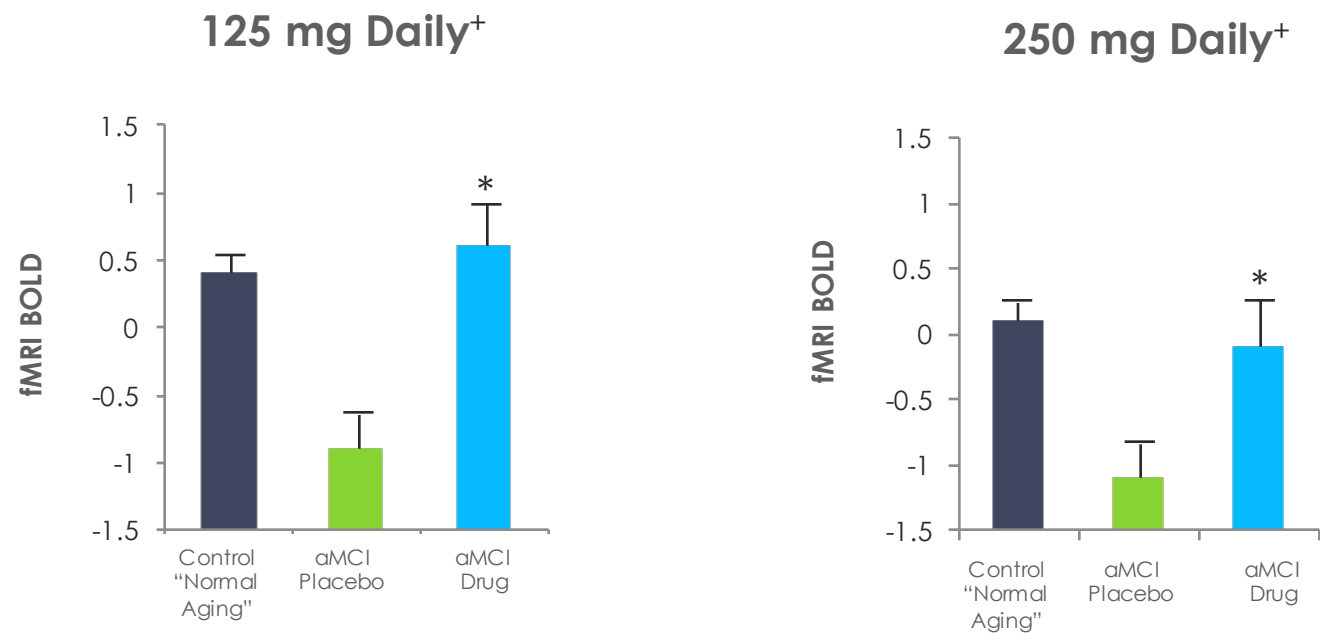
AGB101 Reduces Hippocampal Overactivity in aMCI Patients to Range of Normal Aging



- Low dose efficacy: 125 mg and 250 mg daily significantly reduced hippocampal overactivity
- 500 mg daily failed to reduce hippocampal overactivity

⁺ The dosing schedule for the Phase 2 clinical trial was twice daily (BID); patients underwent a three choice memory task to assess pattern separation and completion process while simultaneously undergoing a fMRI that measured activity in the hippocampus and the entorhinal cortex.

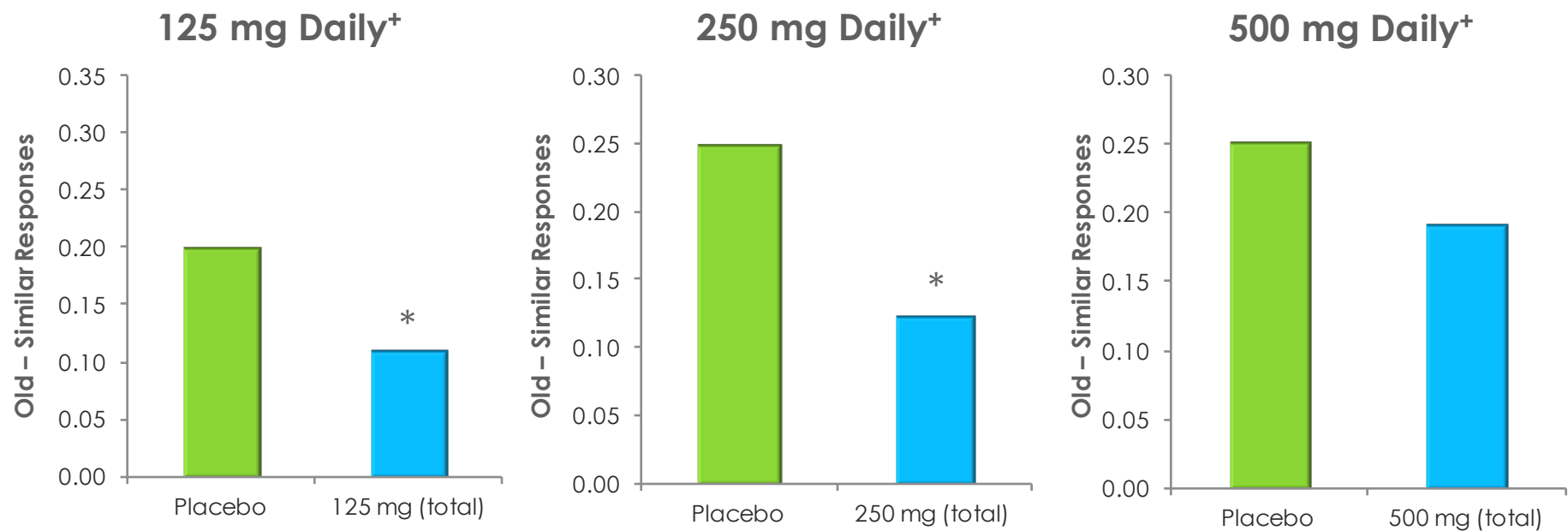
AGB101 Restores Entorhinal Cortex Function in aMCI Patients to Range of Normal Aging



- Low dose efficacy: 125 mg and 250 mg daily rescued entorhinal cortex activation

⁺ The dosing schedule for the Phase 2 clinical trial was twice daily (BID).

AGB101 Restores Pattern Separation in aMCI Patients to Range of Normal Aging



- Low dose efficacy: 125 mg and 250 mg daily restored pattern separation
- 500 mg daily failed to restore pattern separation

+ The dosing schedule for the Phase 2 clinical trial was twice daily (BID).

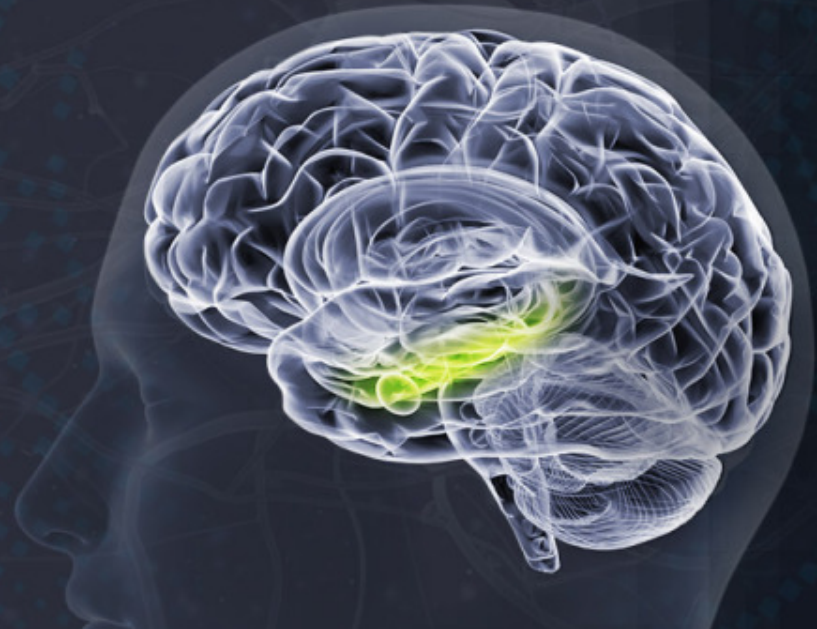
Safety and Tolerability of AGB101

- Phase 2 efficacy study AEs comparable between placebo and AGB101 (up to 500 mg daily)
- **FDA Comments on Safety Profile**
 - No additional nonclinical studies needed
 - Single study safety database sufficient

Study Conclusions – 220 mg

- Exposures of 220-mg dose maintained in efficacious range throughout the day – consistent with preferred range goals
- Formulation appropriate for once-daily dosing
- Food did not alter the pharmacokinetic profile

Formulation Suitable for Phase 3



AGB101 Phase 3 Trial

HOPE4MCI

HOPE4MCI is a landmark public-private partnership supported by:



AGENE BIO™



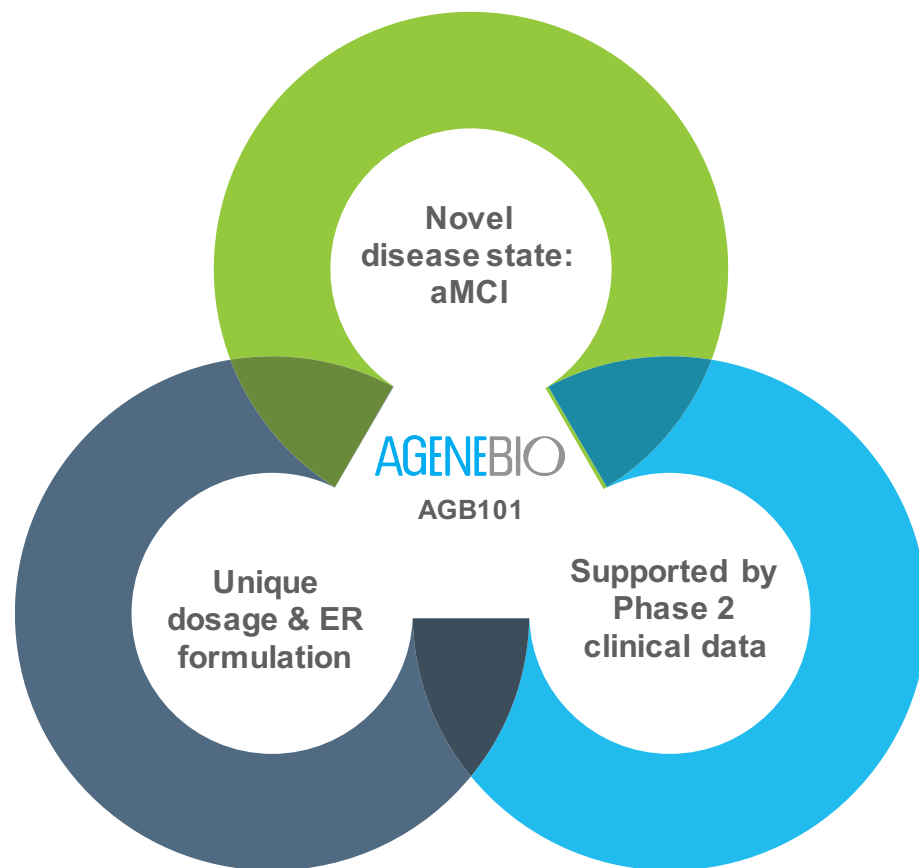
AGB101 Phase 3 Trial Design

- Enrollment criteria well defined and consistent with earlier clinical studies
 - Diagnosis of aMCI
 - Logical memory impairment (Wechsler LM)
 - Positive PET scan with florbetapir F18 injection (Amyvid™ beta-amyloid scan)
- Subjects: patients randomized to AGB101 (220 mg of levetiracetam) or placebo (once-daily dosing)
- Treatment duration: 18 months
- Trial size: 880 (440 per arm)
- Retention should not be affected by drug-related adverse events



Efficacy	Endpoints/ Outcomes Measures
Primary Efficacy Clinical	Change in Clinical Dementia Rating - Sum of Boxes (CDR-SB)
Key Secondary Biomarker	Neuronal injury as measured by change in entorhinal cortex atrophy using structural MRI
Additional Secondary Outcomes Clinical	FAQ (functional), MMSE (cognitive), BPS-O (neuropsychological)

Strong Intellectual Property: Broad Application Protection and Coverage



U.S. patent 8,604,075

- Issued December 2013 (expiry October 2029)
- Using low-dose levetiracetam to treat age-related cognitive impairment and to delay progression to Alzheimer's dementia
- Supported by clinical data and protects effective dose for AGB101
- Extensive examination considering prior art and clinical data

Additional patent applications include:

- Combinations including acetylcholinesterase inhibitors (e.g., donepezil), memantine and antipsychotics
- Extended-release formulation
- Indications: age-related cognitive impairment (e.g., aMCI, AAMI, ARCD), dementia, Alzheimer's disease, PTSD, schizophrenia, bipolar disorder, amyotrophic lateral sclerosis, cancer-therapy-related cognitive impairment, mental retardation, Parkinson's disease, autism, compulsive behavior and substance addiction

AGB101 Summary

- **Restores balance to key brain network in aMCI**
 - Hippocampal/entorhinal cortical network imbalance drives brain atrophy
 - AGB101 has demonstrated very clear target engagement
- **Phase 3 ready risk-mitigated development program**
 - Successful translation from animal models to Phase 2 clinical data
 - Safety profile already established at >12 times the AGB101 dose
 - Clear regulatory pathway now exists in high-need disease state
 - Strong intellectual property – supported by clinical data
 - Generic substitution not an issue

Novel Program in Late Discovery Stage: Multiple Potential Indications with Unmet Need

Late Discovery Stage Ready for Clinical Development

Rapid translational potential to human clinical trials

- Phase 1 receptor occupancy study
- Phase 2 fMRI study

IND ready 2017

- Compounds identified with strong PAM activity, high receptor selectivity and behavioral efficacy
- Next steps: Lead identification and IND-enabling toxicology

Strong intellectual property

- Issued US patent claim on use of GABA_A $\alpha 5$ agonists to treat cognitive impairment
 - NCE patent for pyridazine series allowed July 2015
- Pending worldwide application claims on novel GABA_A $\alpha 5$ agonists (NCEs)

Applicability to Multiple Cognition-Related Indications with No Current Therapeutic Options

MCI

Selective GABA_A $\alpha 5$ positive allosteric modulators improve cognitive function in aged rats with memory impairment

Ming Teng Koh^{a,*}, Sharon Rosenzweig-Lipson^b, Michela Gallagher^{a,b}

^aDepartment of Psychological and Brain Sciences, Johns Hopkins University, Ames Hall, 3400 North Charles Street, Baltimore, MD 21218, USA
^bAgeneBio, Inc., 17711 North Meridian Street, Suite 520, Carmel, IN 46032, USA

Schizophrenia cognitive impairment (CIAS)

Neuropsychopharmacology (2011), 1–9
© 2011 American College of Neuropsychopharmacology. All rights reserved. 0893-1330/11
www.neuropsychopharmacology.org

A Novel $\alpha 5$ GABA_AR-Positive Allosteric Modulator Reverses Hyperactivation of the Dopamine System in the MAM Model of Schizophrenia

Kathryn M Gill^{a,*}, Daniel J Lodge^{a,b}, James H Cook^a, Shansim Aras^a and Anthony A Grace^a
^aDepartments of Neuroscience, Psychiatry, and Psychology, University of Pittsburgh, Pittsburgh, PA, USA; ^bDepartment of Chemistry, University of Wisconsin–Milwaukee, Milwaukee, WI, USA

Autism



Contents lists available at SciVerse ScienceDirect

Neuropharmacology

journal homepage: www.elsevier.com/locate/neuropharm



The brain GABA-benzodiazepine receptor alpha-5 subtype in autism spectrum disorder: A pilot [¹¹C]Ro15-4513 positron emission tomography study

Maria Andreina Mendez^{a,b}, Jamie Horder^{a,*}, Jim Myers^c, Suzanne Coghlan^a, Paul Stokes^b, David Erritzoe^b, Oliver Howes^d, Anne Lingford-Hughes^b, Declan Murphy^a, David Nutt^b

Company Summary

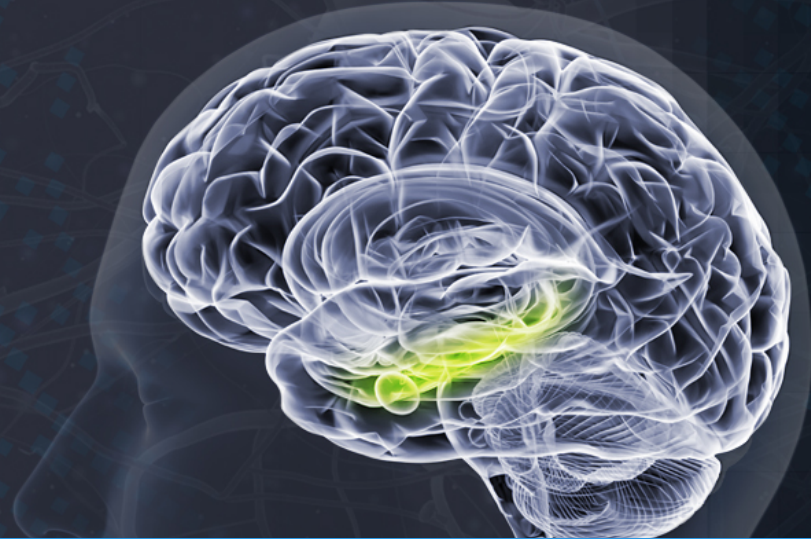
- Unparalleled science with right team in place
- Clear clinical and regulatory pathway to FDA approval
- Key patents issued for all pipeline assets
- Substantial multi-billion dollar commercial opportunities

AGB101

Potentially the first therapeutic for aMCI and the first to delay progression to Alzheimer's dementia

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