AGENEBIO™

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

November 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

Board of Directors (non-management)

Pat LePore, Chairman	Floyd Bloom, MD	Charles Clarvit	Ronald Nordmann
Former Chairman & CEO, of Par Pharmaceuticals	Founder and Director of Alkermes, former Editor-In-Chief of *SCIENCE*	Former CEO of Vinci Partners US, former Co-Head of BlackRock Alternative Advisors, Johns Hopkins Trustee	Former Partner at Deerfield Management, PaineWebber Group, Johns Hopkins Trustee Emeritus

AGENEBIO

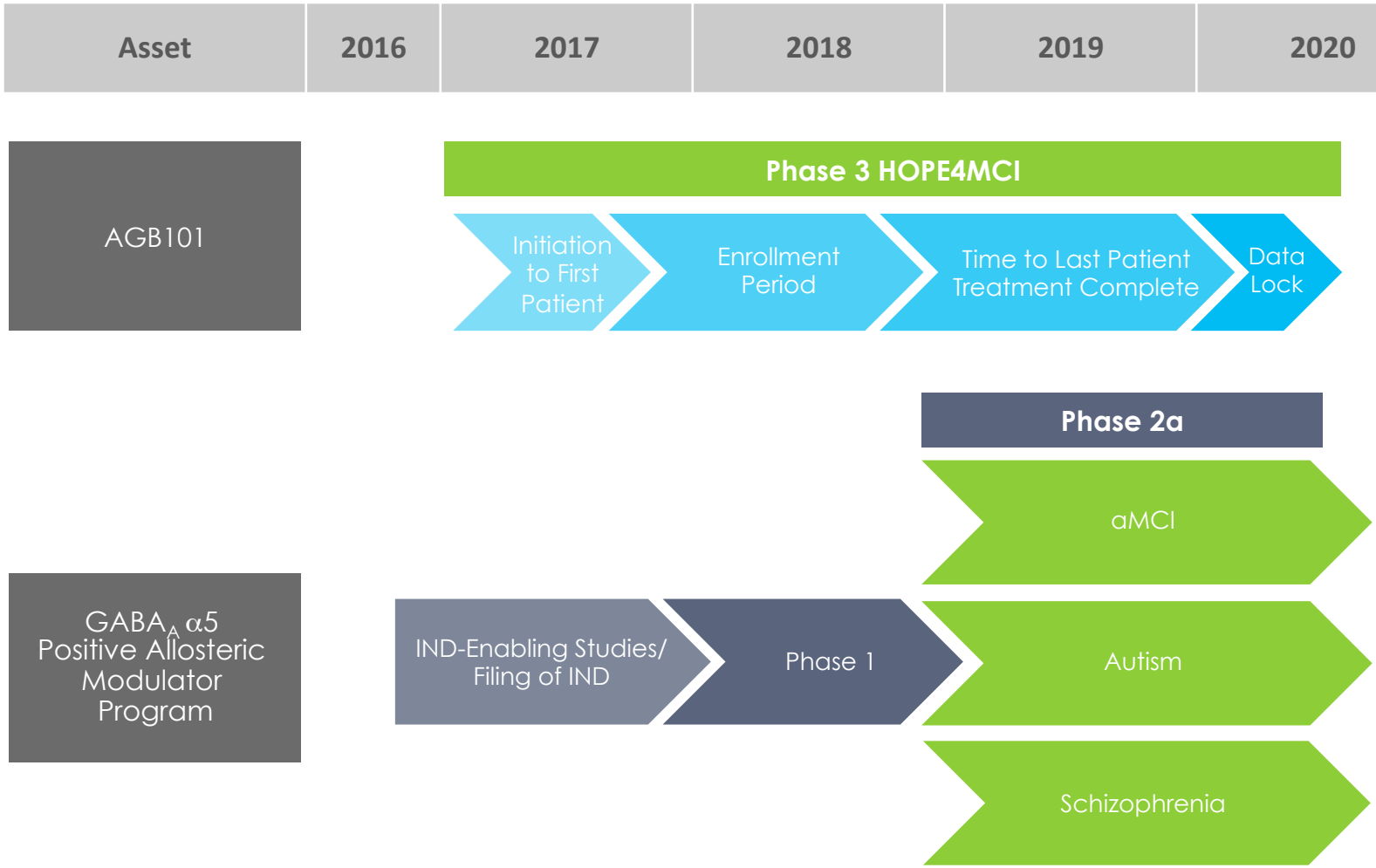
Novel Pipeline for Neurological and Psychiatric Diseases Addressing Significant Unmet Medical Needs

- Phase 3 ready program: AGB101
  - Targets large population with aMCI* due to Alzheimer's disease
    - No treatments exist for the more than 5 million patients
  - Positive Phase 2 trial results
    - First and only product candidate addressing brain network imbalance that leads to memory loss and brain atrophy
  - Novel, extended release once-a-day medication
  - Extensive intellectual property protection and coverage
- Late discovery stage new chemical entity program
  - $GABA_A$ $\alpha 5$ positive allosteric modulator program
  - Applicability to multiple cognition-related indications with no current options including Alzheimer's disease, schizophrenia, and autism
  - Ready to move in to human clinical trials by early 2018

AGENEBIO

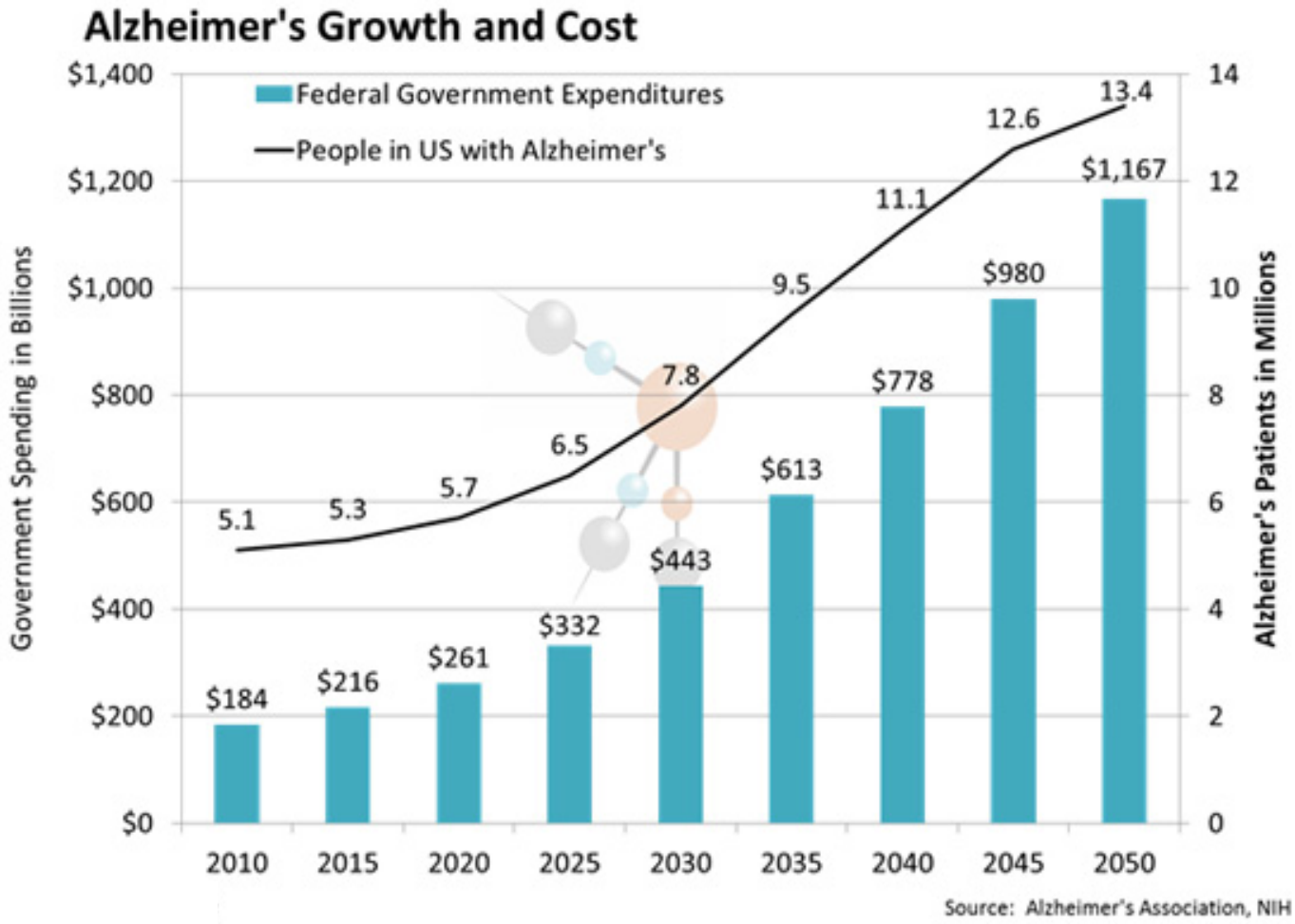
* aMCI – amnestic mild cognitive impairment

Company Development Milestones 2016 - 2020



AGENEBIO

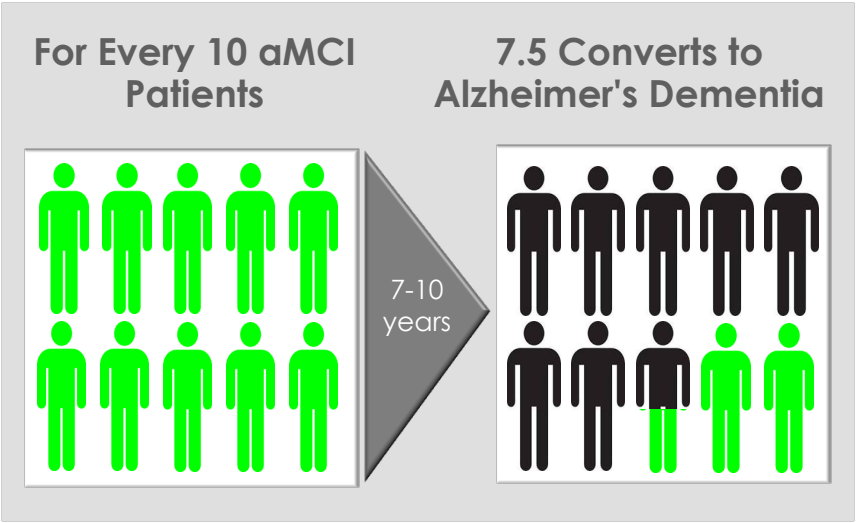
National Crisis: The Population with Alzheimer's and Government Expenditures will Increase at an Alarming Rate

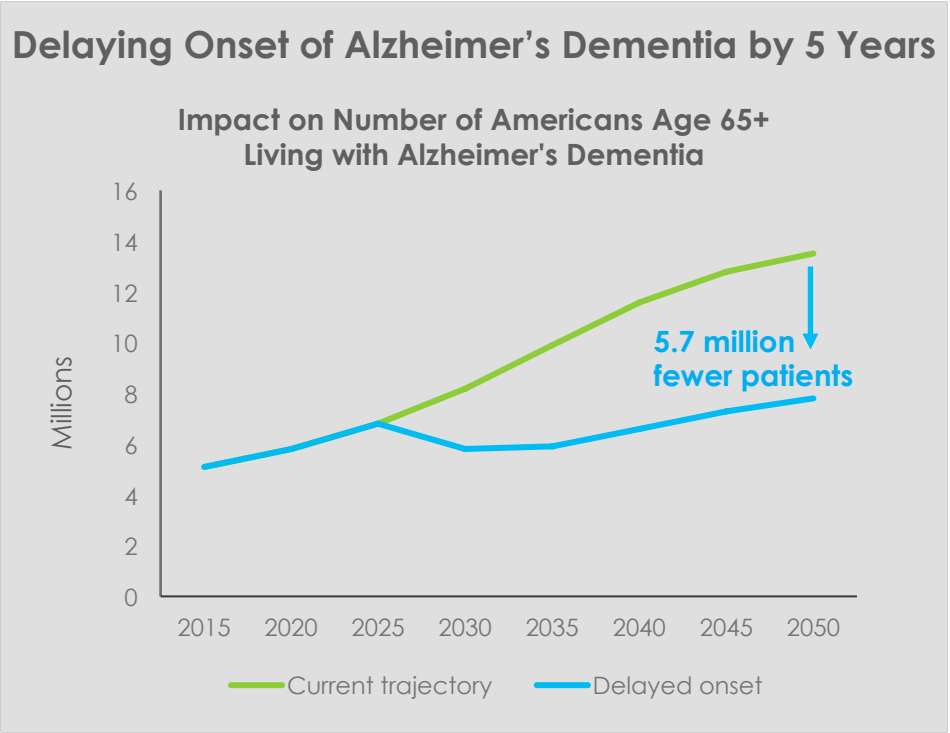


AGENEBIO

5 Million in US Currently with aMCI – will Double by 2050; a Majority Progress to Alzheimer's Dementia

- aMCI is the first symptomatic clinical condition between normal aging and Alzheimer's dementia characterized by impaired episodic memory
- There are no FDA approved treatments for aMCI and existing Alzheimer's products are ineffective for this population
  - Evidence points to early intervention (e.g. during aMCI stage) as best chance to alter progression and reduce Alzheimer's dementia prevalence



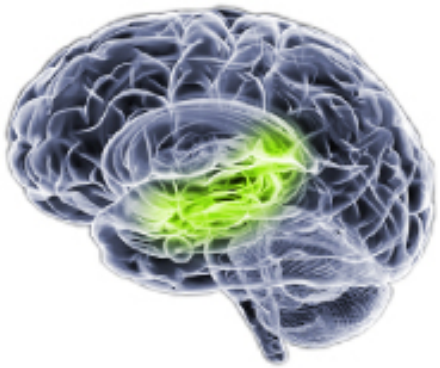


SOURCE: Alzheimer's Association

AGENEBIO

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?

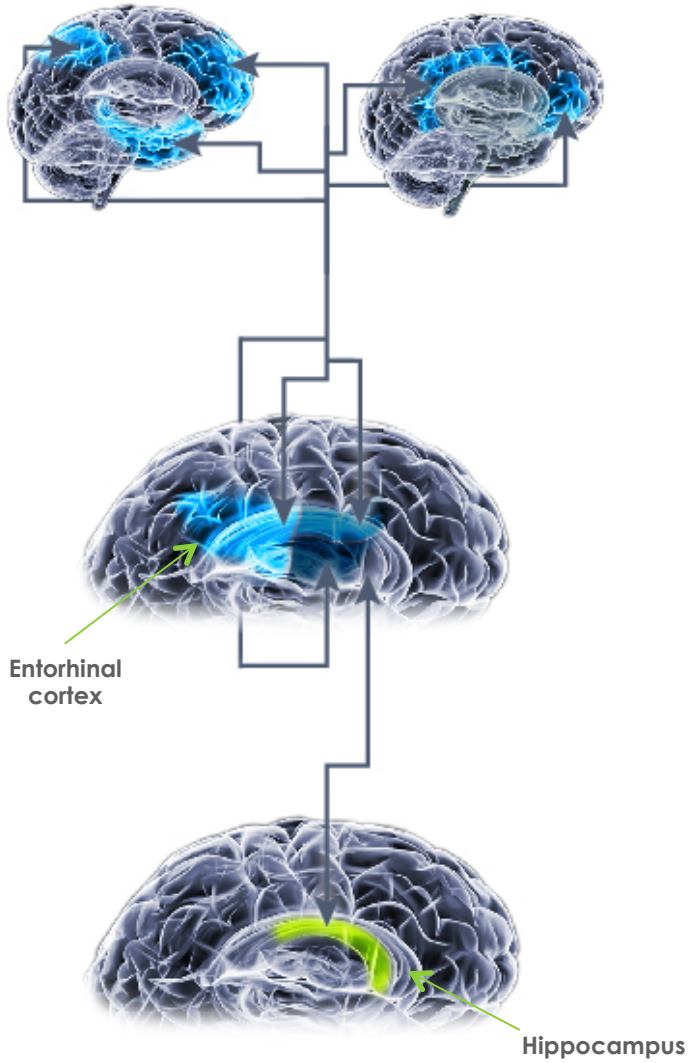
AGENEBIO

The Hippocampus Is Part of a Neural Network Critical for Episodic Memory

1. Experiences and events of your life are represented in large-scale networks in your brain.

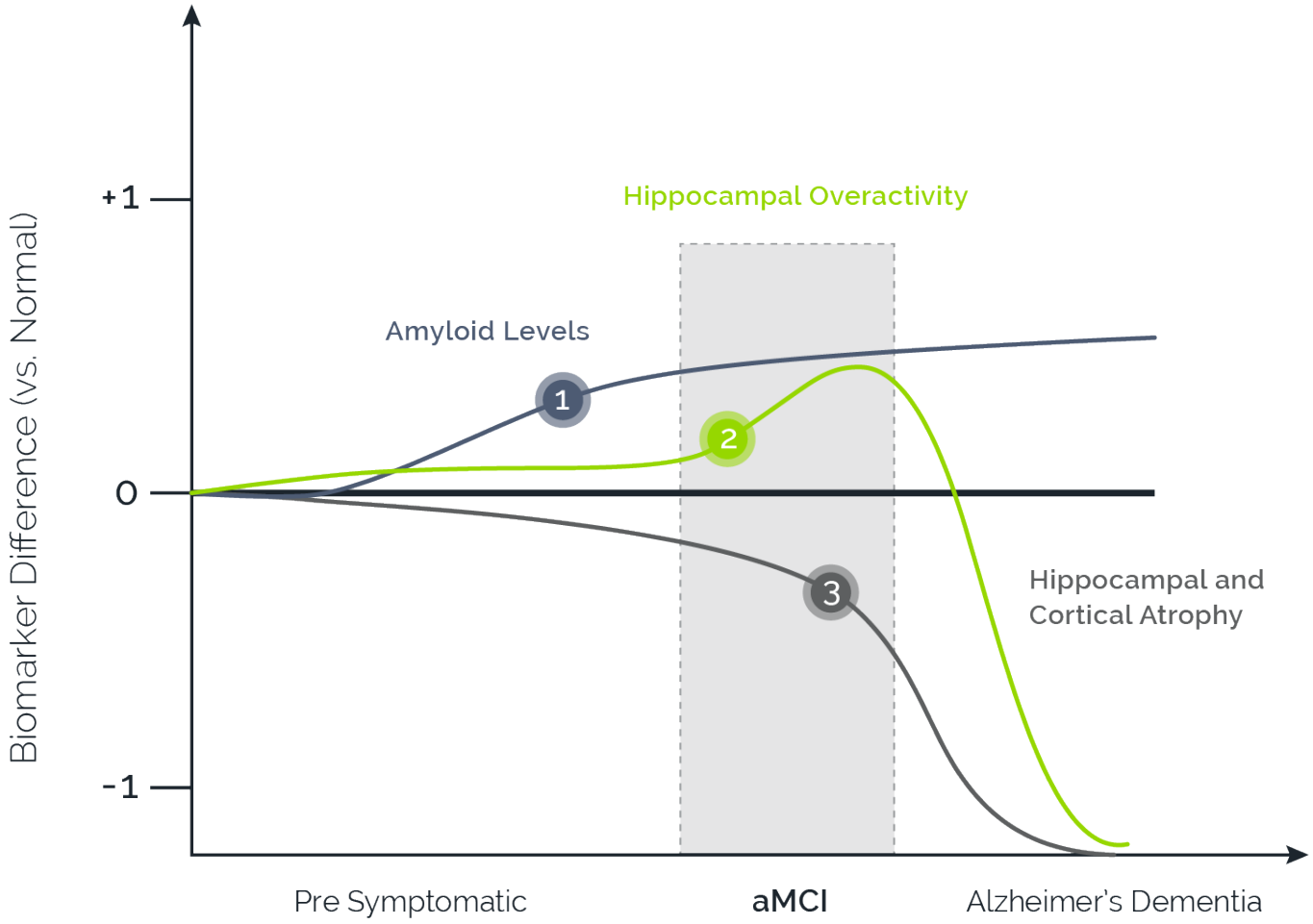
2. The **entorhinal cortex** is the conduit for the formation of episodic memories by the **hippocampus.**

3. Overactivity in the **hippocampus** disrupts its normal memory-making function and drives degeneration that spreads through large-scale networks, with the **entorhinal cortex** going first.



AGENEBIO

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



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

AGENEBIO

A Promising Solution to the Problem: AGB101 Mitigates Key Driver of Neurodegeneration in Alzheimer's

- Normalizes neuronal firing in the hippocampus
  - Restores a key brain network balance
  - Potential to delay or prevent neurodegeneration associated with Alzheimer's
  - Mechanistic target: SV2A inhibitor
- Positive Phase 2 clinical trial results for patients with aMCI
  - Restored hippocampal activity to pre-disease levels
  - Restored entorhinal cortex activity to pre-disease levels
  - Improved memory performance
- Excellent safety and tolerability profile
  - Demonstrated for decades at doses >12-fold higher than the AGB101 dose
  - No drug interactions - important as patients with Alzheimer's often are taking 4 to 6 prescription medications per day

AGENEBIO

Phase 2 Study & Novel Extended-Release Formulation

AGENEBIO

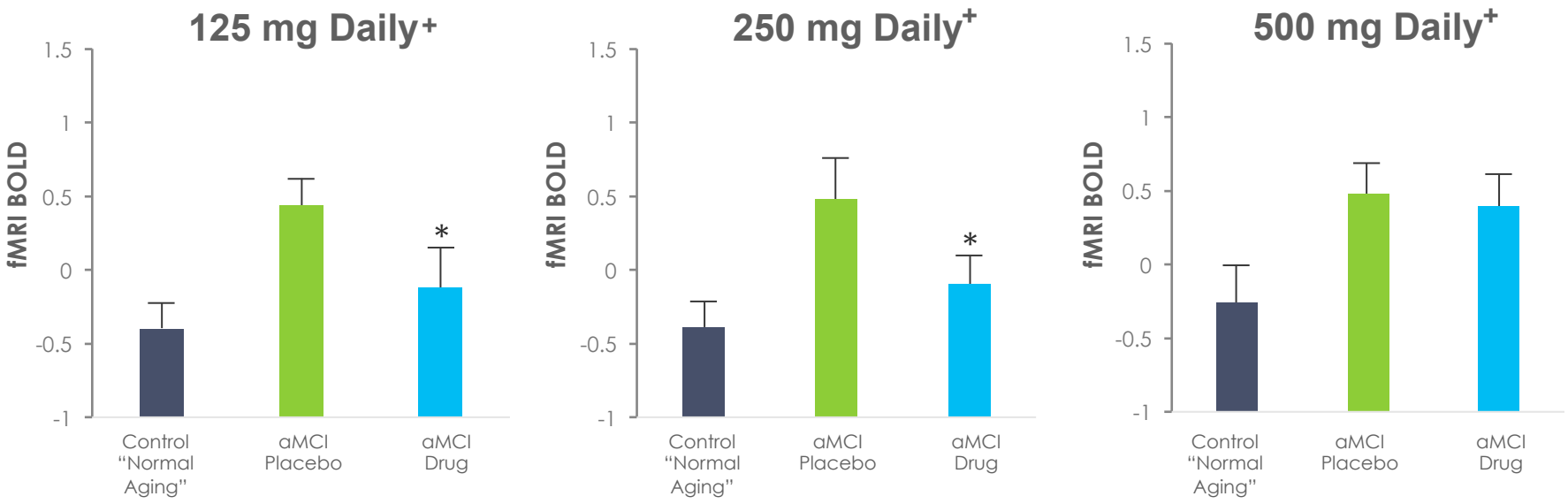
AGB101 Phase 2 Trial Design

- 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

AGENEBIO

PHASE 2

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

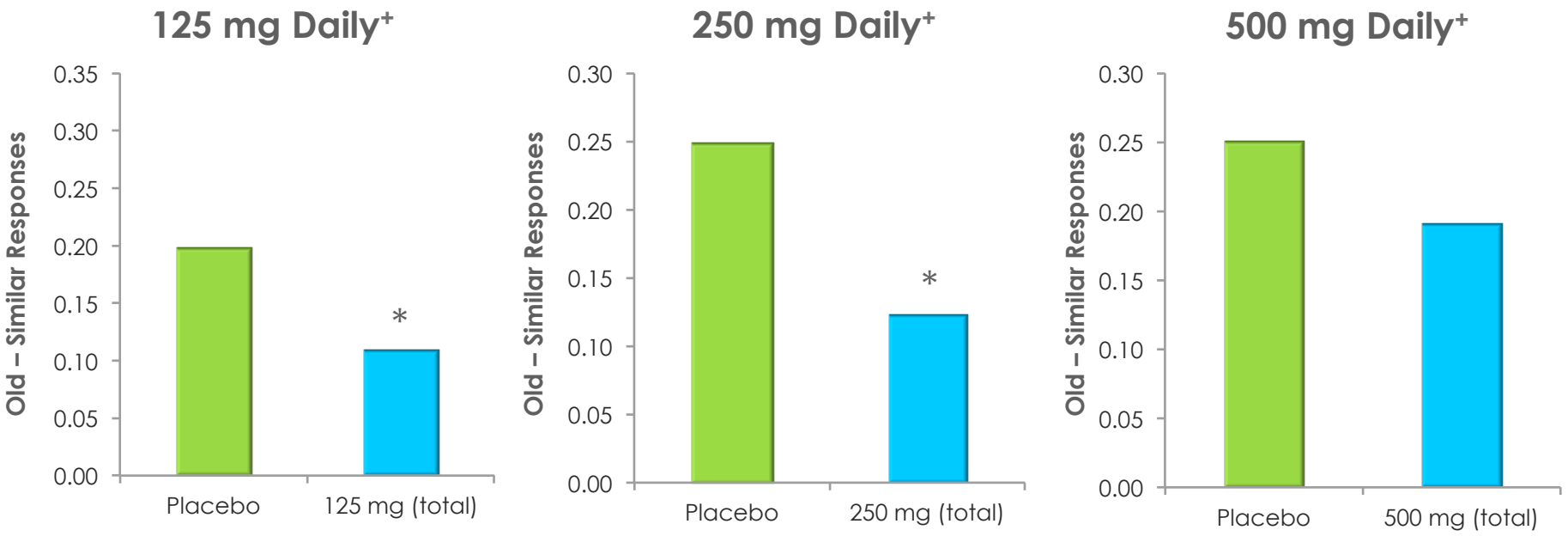
+ The dosing schedule for the Phase 2 clinical trial was twice daily (BID); patients underwent a three choice memory task to assess pattern separation and completion process while simultaneously undergoing a fMRI that measured activity in the hippocampus and the entorhinal cortex.

Bakker et al. 2012, 2015

AGENEBIO

PHASE 2

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).

Bakker et al. 2012, 2015

AGENEBIO

AGB101 Phase 3 Trial

HOPE4MCI

HOPE4MCI is a landmark public-private partnership supported by:

NIH National Institute on Aging

AGENEBIO™

Johns Hopkins University

AGB101 Phase 3 Trial is Designed and Ready

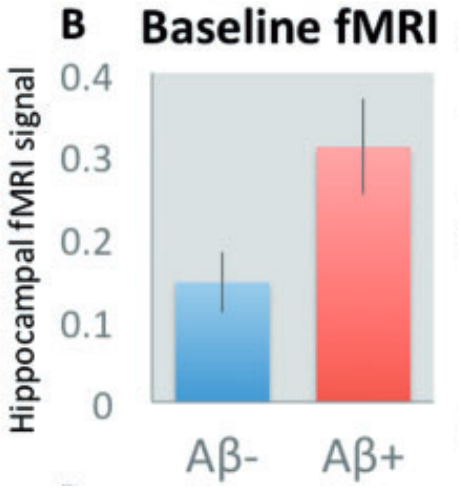
- Enrollment criteria well defined and consistent with earlier clinical studies
  - Diagnosis of aMCI
  - Logical memory impairment (Wechsler LM)
  - Positive PET scan with florbetapir F18 injection (Amyvid™ beta-amyloid scan)
- Subjects: patients randomized to AGB101 (220 mg of levetiracetam) or placebo (once-daily dosing)
- Treatment duration: 18 months
- Trial size: 830 (415 per arm)
- Retention should not be affected by drug-related adverse events

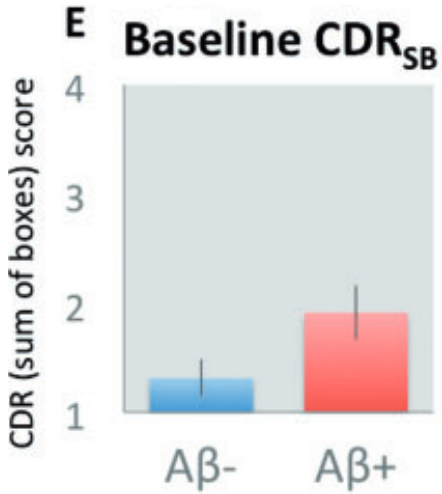
HOPE 4 MCI

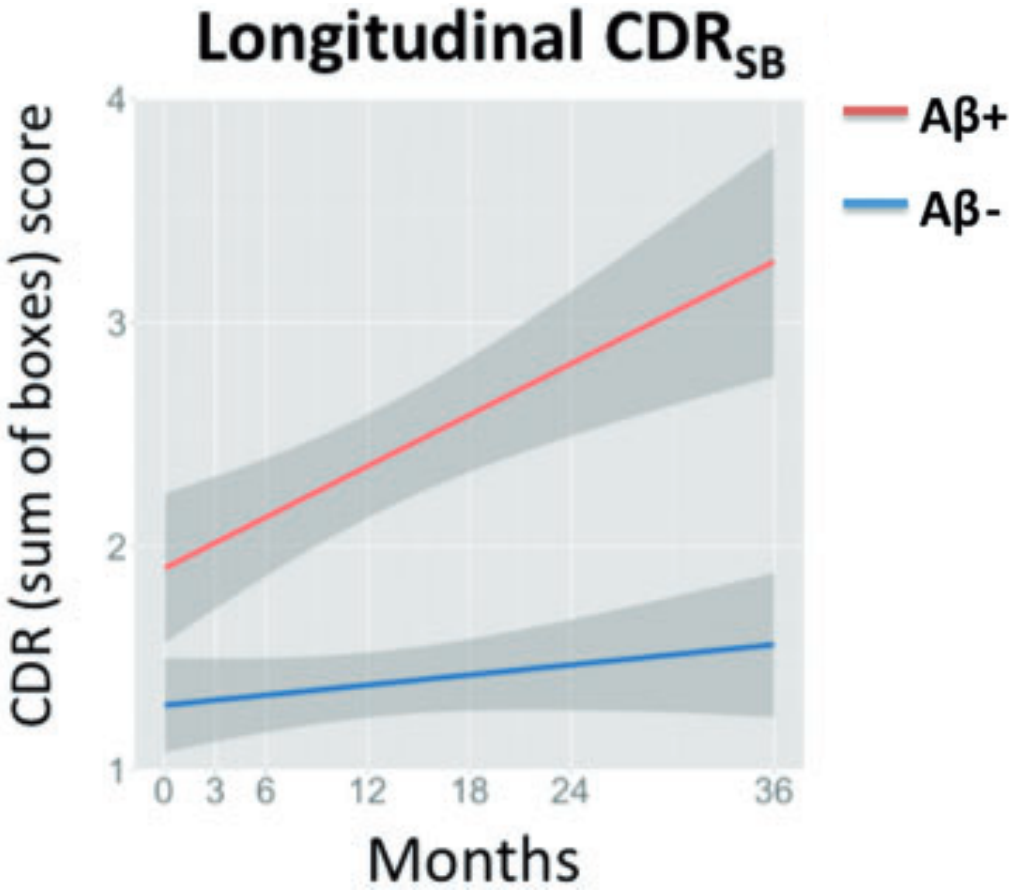
Efficacy	Endpoints/ Outcomes Measures
Primary Efficacy Clinical	Change in Clinical Dementia Rating - Sum of Boxes (CDR-SB)
Key Secondary Biomarker	Neuronal injury as measured by change in entorhinal cortex atrophy using structural MRI
Additional Secondary Outcomes Clinical	FAQ (functional), MMSE (cognitive),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

AGENEBIO

Amyloid (Aβ+) in aMCI: Hippocampal Overactivity, Increased CDR-SB, and CDR-SB Progression







Huijbers et al, 2015

AGENEBIO

Development History of Current Enrolling/Planned Phase 3 Programs for aMCI

Company & Candidate	Phase 1/1b/2 Studies	Biomarker Evidence	Evidence of Cognitive Benefit to Date	Phase 3 Primary Endpoint
AgeneBio AGB101	Phase 2 clinical trial (n= 54 aMCI patients diagnosed using CDR-SB). Measured hippocampal and entorhinal cortex activity, and memory performance	Hippocampal & Entorhinal Cortex fMRI Activity	Memory Performance Improvement	CDR-SB
Merck MK8931	Safety and pharmacodynamics in participants with mild to moderate AD treated for 7 days (n=32). No measurement of clinical benefit	CSF Amyloid	None (Never Tested)	
Eli Lilly/ AstraZeneca LY3314814 (AZD3293)	Multiple Phase 1 safety, PK, and pharmacokinetic studies in healthy volunteers.	CSF Amyloid	None (Never Tested)	
Biogen BIIB037	Phase 1B, 1 year trial (n=197). Demonstrated reduction in amyloid plaque in the brain; improvement in CDR-SB scores at the highest of 4 doses. ARIA-E was most common at the highest dose	Amyloid Plaque	CDR-SB score improvement	

AGENEBIO

Strong Intellectual Property: Broad Application Protection and Coverage

U.S. patent 8,604,075

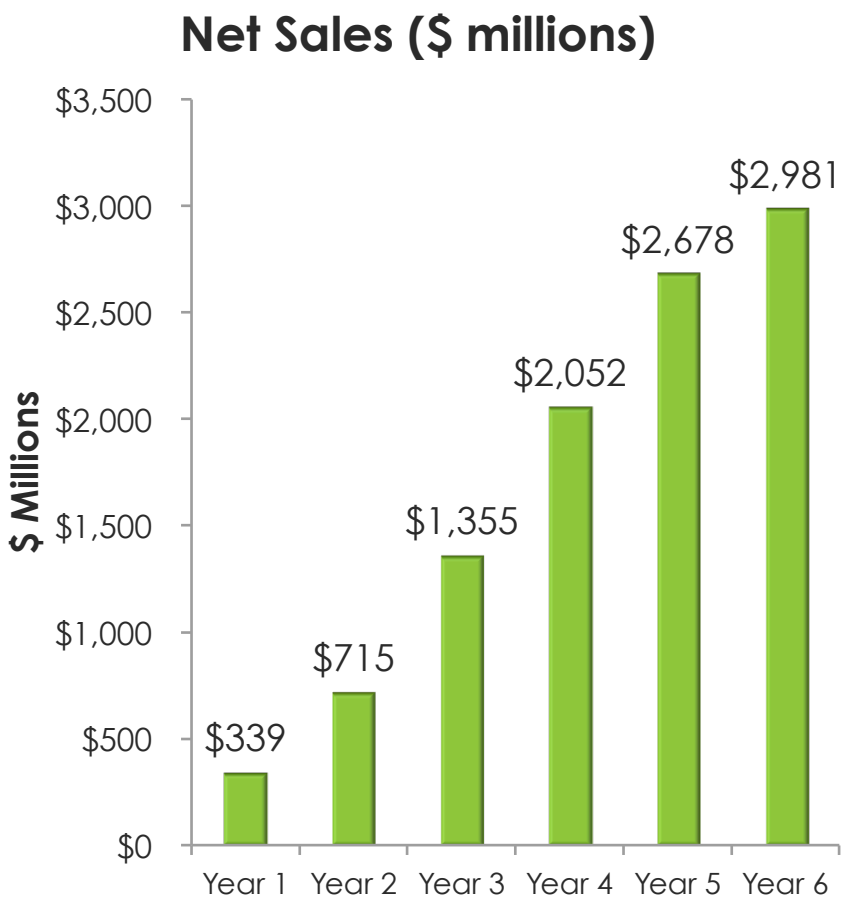
- Issued December 2013 (expiry October 2029)
- Using low-dose levetiracetam to treat age-related cognitive impairment and to delay progression to Alzheimer's dementia
- Supported by clinical data and protects effective dose for AGB101
- Extensive examination considering prior art and clinical data

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

AGENEBIO

AGB101 Net Sales Projections (US Only)



- 5.9 million Americans with aMCI in 2016 (4% y/y growth)
- Peak diagnosed & treated rate of 50%
- AGB101 captures 25% share of treated aMCI patients
  - 6 years to peak
- Compliance rate of 70%
- WAC pricing of $15 per tablet (2016 pricing)
  - 40% gross-to-net deductions
  - 2% annual price increase

AGENEBIO

AGB101 Phase 3 Program Provides Attractive Investment Risk-Reward Profile

- AGB101 Phase 3 trial a fraction of the cost associated with current Phase 3 Alzheimer's programs

Biogen Aducanumab	Axovant RVT-101	AgeneBio AGB101
• $2.5 billion – Phase 3 and manufacturing facility • In development for the treatment of aMCI / mild AD • Phase 3 enrolling	• $125 - $135 million Phase 3 development program • In development for treatment of mild-to-moderate AD • Phase 3 enrolling	• $58 million cost for HOPE4MCI Phase 3 trial • In development for the treatment of aMCI due to AD • Phase 3 ready

*The market for Alzheimer's Disease (AD) treatment will reach an estimated $13.3 billion by 2023.**

* Global Data research report

AGENEBIO

Market Valuations for Alzheimer Category Comps

Company	Market Cap*/ Valuation	Stage of Development	Target/Molecule(s)	Indication
Avanir (AVNR)	Acquired for $3.2 billion	Phase 3 Initiated	Dextromethorphan/ ultra low-dose quinidine	Agitation with Alzheimer's dementia
Axovant (AXON)	$1.34 billion	Phase 3 initiated	5-HT antagonist plus donepezil	Alzheimer's dementia
Chase Pharma (Private)	$125 million upfront ($1 billion total deal value)	Phase 3 ready	Donepezil plus solifenacin (re-purposed molecules)	Alzheimer's dementia
vTv Therapeutics (VTVT)	$182 million	Phase 3 initiated (previously failed Phase 2b)	Sigma 1 receptor agonist plus donepezil	Alzheimer's dementia
Anavex (AVXL)	$150 million	Phase 2a ongoing (not placebo controlled)	Phase 2a ongoing	Alzheimer's dementia

AGENEBIO

* Market cap as of November 29, 2016

Funding History for AgeneBio
Capital Efficient and Proven Ability to Obtain Grants

Funding Source	Amount
AgeneBio	
Equity (preferred stock)	$18.4 million
Alzheimer's Drug Discovery Foundation Convertible Note	$0.9 million
NIH U01 Grant (R-Lipson, AgeneBio) for $GABA_A$ α5 Program	$3.4 million
Gallagher/Johns Hopkins University (JHU) Grants	
NIH GO Grant (Gallagher, JHU)*	$1.3 million
NIA Basic Research Grant (Gallagher, JHU)**	$2.0 million
NIA R01 HOPE4MCI Trial (Gallagher, Albert, JHU)***	$7.5 million
TOTAL	**$33.5 million**

* NIH GO Grant was awarded to Johns Hopkins (Michela Gallagher). Supported the AGB101 Phase 2 trial.
** Long-standing basic research support by NIH to Johns Hopkins (Gallagher) advancing AgeneBio programs
*** NIH R01 award to Johns Hopkins (Gallagher, Albert) for AGB101 HOPE4MCI trial - public-private partnership

AGENEBIO

AgeneBio 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
- Favorable risk-benefit investment profile

AGB101	Potentially the first therapeutic for aMCI and the first to delay progression to Alzheimer's dementia

AGENEBIO

AGENEBIO™

November 2016