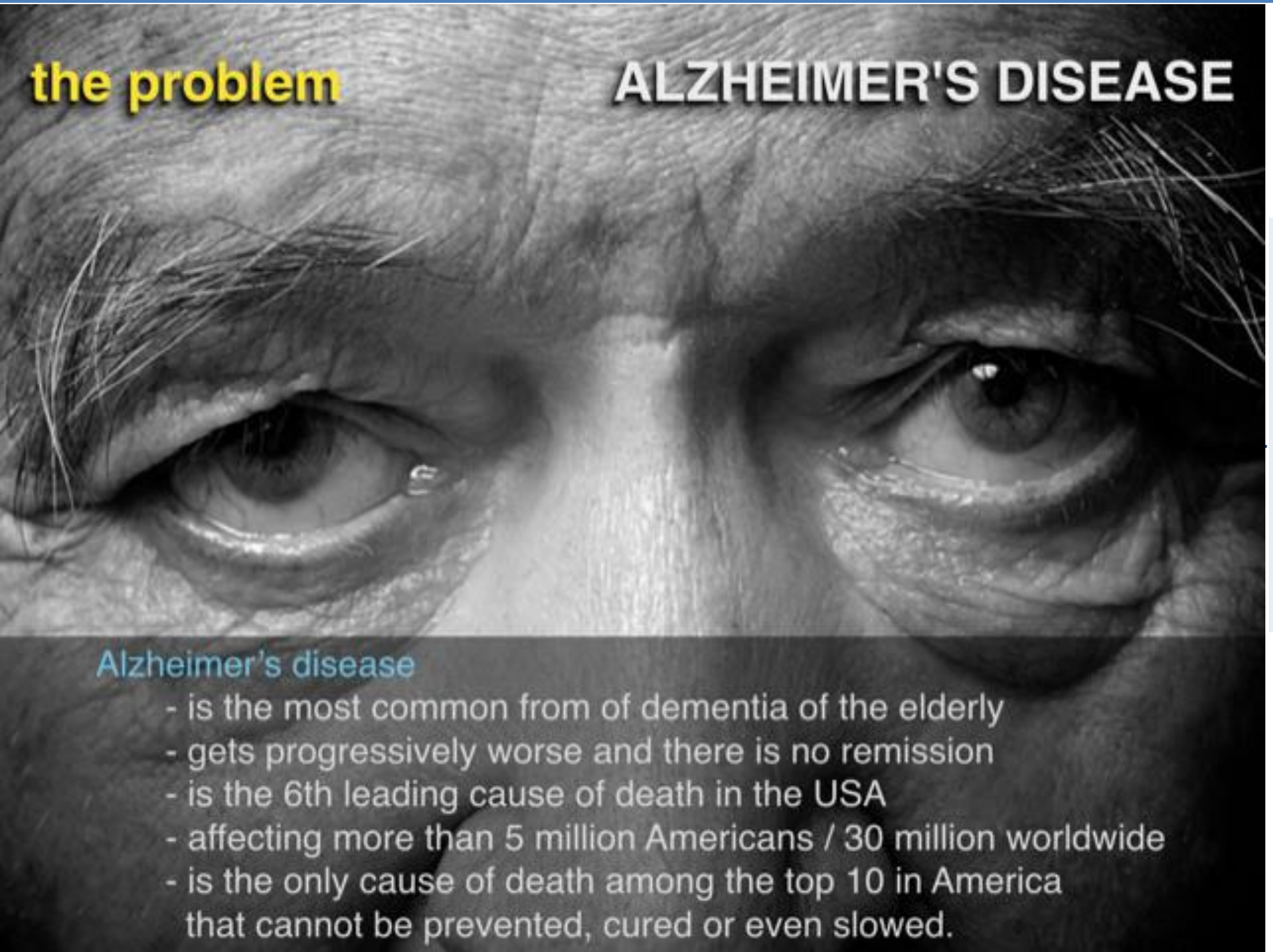
Memtin™ – our patented hormone replacement therapy for slowing cognitive decline in Alzheimer's disease and other dementias

"Our flagship"

Nikolaos Tezapsidis, President & CEO

August 5, 2019

Neurotez



$10 million
Financing Sought

Starting at $500,000

2019 ALZHEIMER'S DISEASE FACTS AND FIGURES

ALZHEIMER'S DISEASE IS THE

6TH leading cause of death in the United States

5.8 MILLION Americans are living with Alzheimer's

BY 2050, this number is projected to rise to nearly **14 MILLION**

82% of seniors say it's important to have their thinking or memory checked

BUT ONLY **16%** say they receive regular cognitive assessments

MORE THAN 16 MILLION AMERICANS provide unpaid care for people with Alzheimer's or other dementias

These caregivers provided an estimated **18.5 BILLION HOURS** valued at nearly **$234 BILLION**

IN 2019, Alzheimer's and other dementias will cost the nation **$290 BILLION**

BY 2050, these costs could rise as high as **$1.1 TRILLION**

EVERY 65 SECONDS someone in the United States develops the disease

Between 2000 and 2017 deaths from heart disease have decreased **9%**

while deaths from Alzheimer's disease have increased **145%**

1 IN 3 seniors dies with Alzheimer's or another dementia

It kills more than breast cancer and prostate cancer **COMBINED**

alzheimer's association®

DEMENTIA

A public health priority

World Health Organization

What are the symptoms?

- Difficulties with everyday tasks
- Confusion in familiar environments
- Difficulty with words and numbers
- Memory loss
- Changes in mood and behaviour

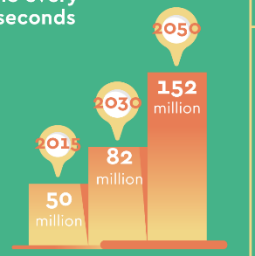
Who is affected?

Nearly 10 million new cases every year

One every 3 seconds

50 million people worldwide

Set to triple by 2050



Majority of people who will develop dementia will be in **low- and middle-income countries**

What is the cause?

Conditions that affect the brain, such as Alzheimer's disease, stroke or head injury

What does it cost?

2015 — **US$818 billion:** estimated costs to society in 2015

2030 — **US$2 trillion**

Families and friends provide most of the care

Carers experience physical, emotional and financial stress

The Global Action Plan on the Public Health Response to Dementia 2017 - 2025

Vision

A world in which dementia is prevented and people with dementia and their carers live well and receive the care and support they need to fulfil their potential with dignity, respect, autonomy and equality.

Goal

To improve the lives of people with dementia, their carers and families, while decreasing the impact of dementia on them as well as on communities and countries.

The seven action areas and targets

1 Dementia as a public health priority

By 2025, **75%** of countries have national policies, strategies, plans or frameworks for dementia

2 Dementia awareness and friendliness

By 2025, **100%** of countries have a functioning public-awareness campaign on dementia

By 2025, **50%** of countries have at least one dementia-friendly initiative

3 Dementia risk reduction

Risk reduction targets identified in the Global action plan for prevention and control of noncommunicable diseases 2013-2020 are achieved

4 Dementia diagnosis, treatment & care

By 2025, **50%** of people with dementia are diagnosed, in at least 50% of countries

5 Support for dementia carers

By 2025, **75%** of countries provide support and training for carers and families

6 Information systems for dementia

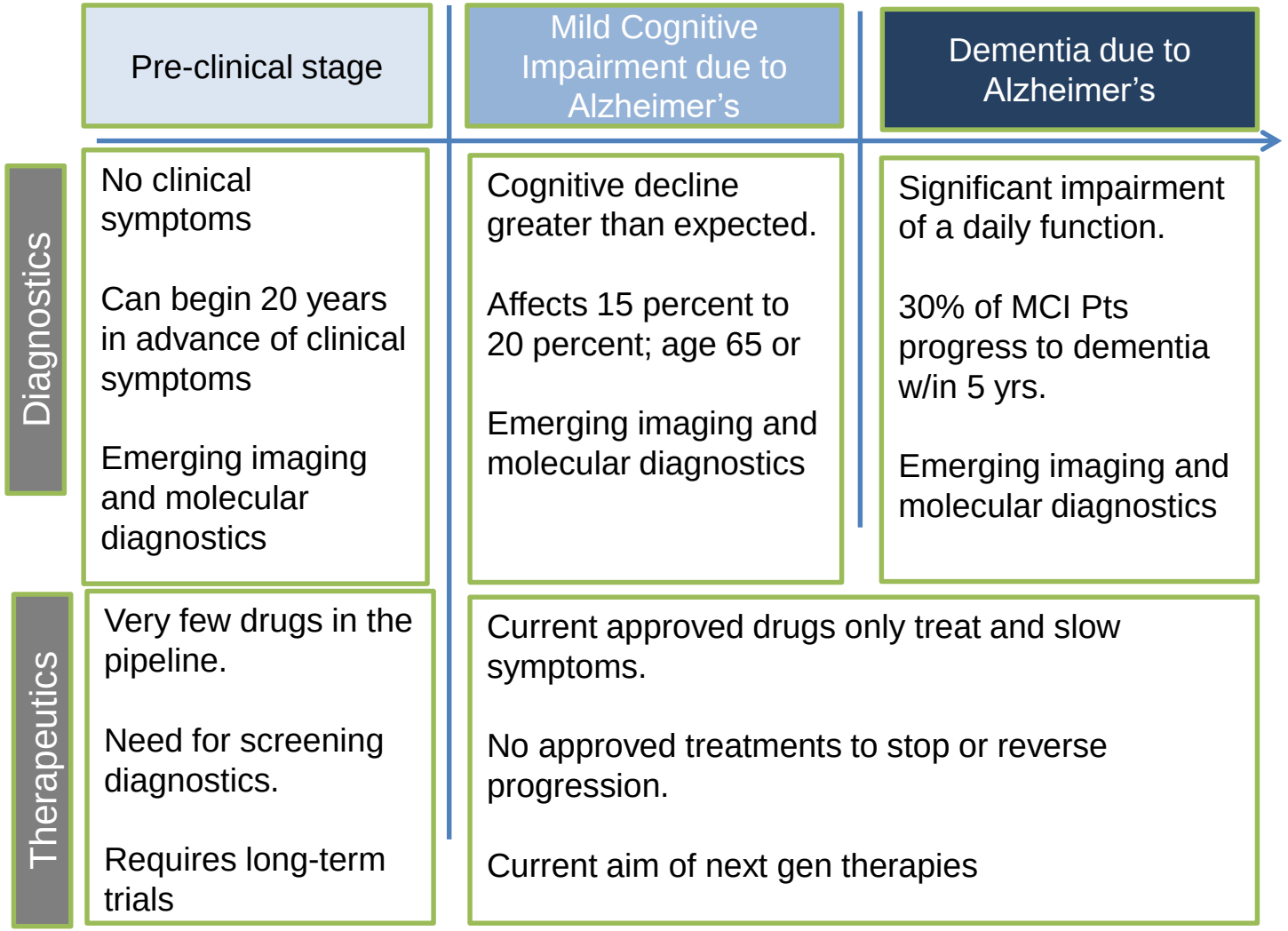
By 2025, **50%** of countries routinely collect data on core dementia indicators

7 Dementia research and innovation

Global research output on dementia doubles between 2017 and 2025

Alzheimer's disease accounts for 60 **percent** to 80 **percent of dementia** cases.

The Alzheimer's Disease challenge requires a combination of Diagnostics and Therapeutics



Clarivate Analytics

A VERY PROMISING SOLUTION

MEMTIN™ (Leptin) for Cognitive Decline

- Ten years of *in vitro* and *in vivo* pre-clinical studies (Neurotez)
- Retrospective (including one by Neurotez) and prospective human studies and a few anecdotal interventional human studies

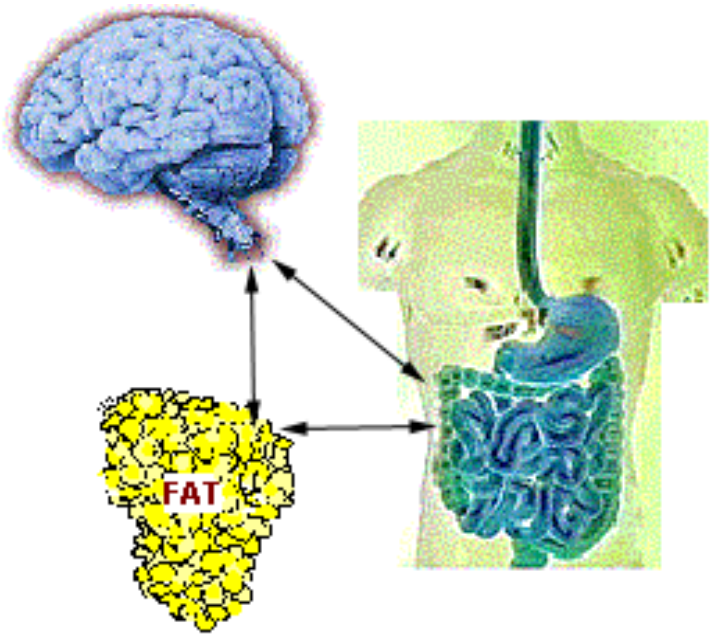
Support a role of Leptin in

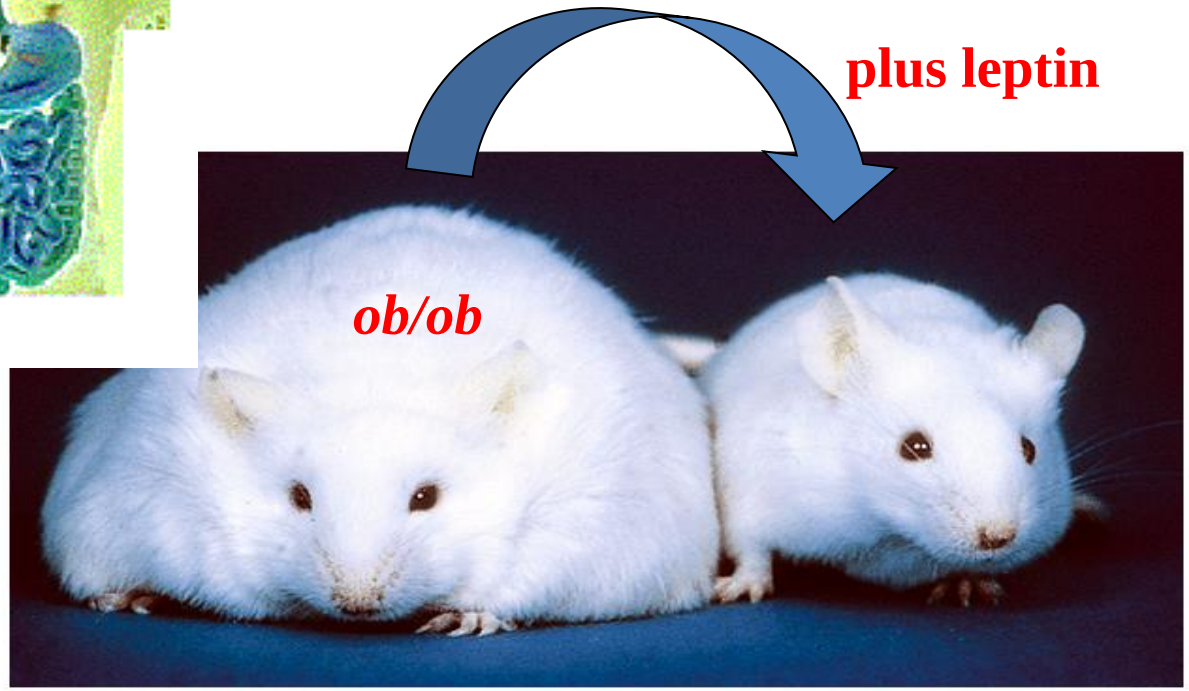
- Neuroprotection, Cognitive enhancement, Decreasing levels of phospho-tau/tau, Decreasing beta amyloid (Aβ)
- **and** is associated with lower risk for dementia in elderly

→ **Leptin as Replacement Therapy**

A relatively de-risked multi-functional preventative and therapeutic approach for cognitive decline due to Alzheimer's and optimally for early stage (prodromal AD) hypoleptinimics.

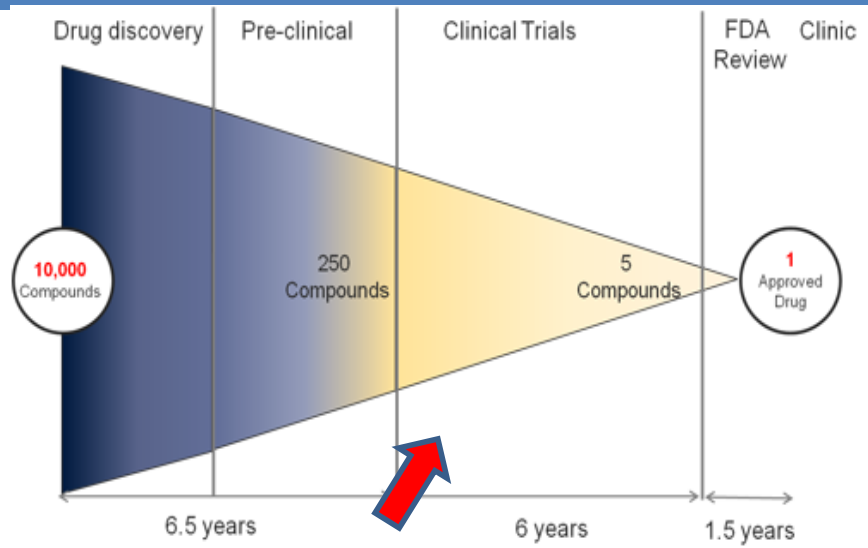
Linking Leptin to Alzheimer's Disease





Leptin regulates feeding behavior, metabolic activity and cognition

DRUGS SUCCESFULLY REPOSITIONED



DRUG	ORIGINAL INDICATION	NEW INDICATION
Amphotericin B	Fungal infections	Leishimaniasis
Aspirin	Inflammation, pain	Antiplatelet
Bromocriptine	Parkinson's disease	Diabetes mellitus
Finasteride	Prostate hyperplasia	Hair loss
Gemcitabine	Viral infections	Cancer
Methotrexate	Cancer	Psoriasis, rheumatoid arthritis
Minoxidil	Hypertension	Hair loss
Raloxifene	Cancer	Osteoporosis
Thalidomide	Morning Sickness	Leprosy, multiple myeloma
Sildenafil	Angina	Erectile dysfunction

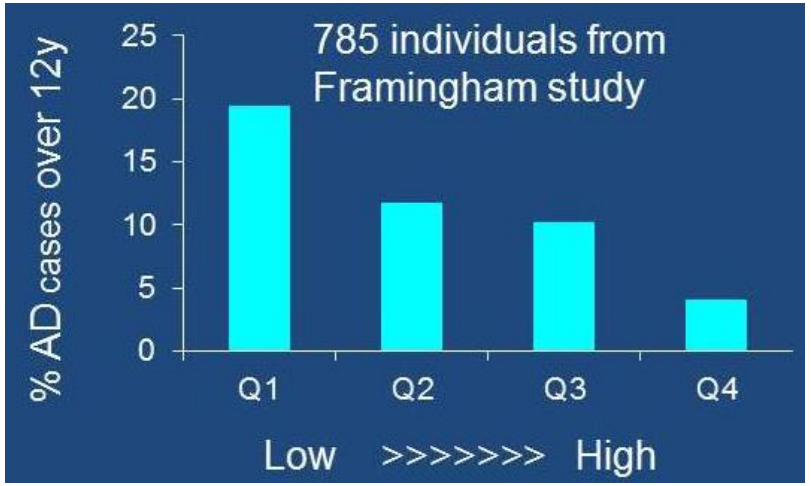
REPOSITIONING LEPTIN CLEAR PATH

Route and frequency of administration	Subcutaneous, once a day
Recommended starting dose for generalized lipodystrophy	0.06 mg/kg/day (if body weight ≤40 kg)
	2.5 mg/day (males >40 kg)
	5 mg/day (females >40 kg)
Maximum dose	0.13 mg/kg (if body weight ≤40 kg)
	10 mg/day (if body weight >40 kg)
Cmax	4.0–4.3 hours
Tmax	4 hours (range 2–8 hours)
Half-life	3.8–4.7 hours
Most common adverse reactions (≥10%)	Headache, hypoglycemia, decreased weight, and abdominal pain
Use in geriatric patients >65 years-old	Unclear; dose selection should be cautious, and start at the low end of the dosing range
Drug interactions	Potential to alter the formation of CYP450 enzymes

STUDIES: SERUM LEPTIN LEVELS IN ELDERLY AND PROGNOSIS

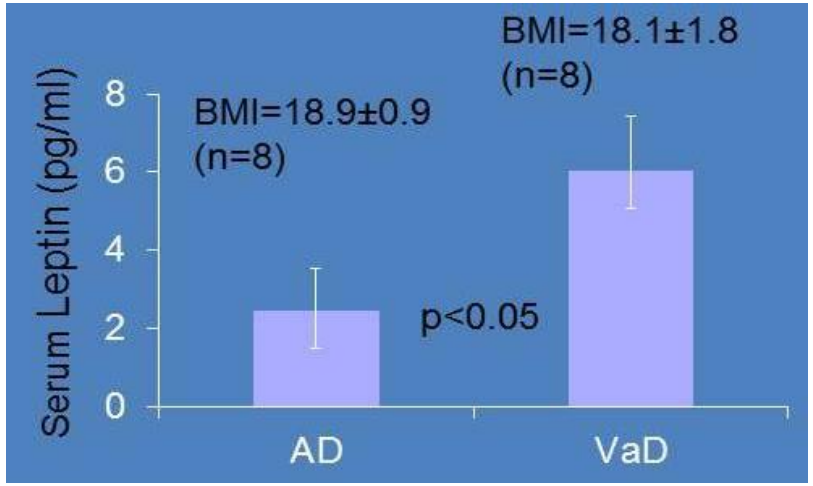
In elderly, higher serum Leptin is associated with a lower risk for Alzheimer's disease and dementia

Lieb *et al, JAMA, 2009*



For BMI<25, patients with AD have lower serum Leptin levels compared to patients with Vascular Dementia (VaD)

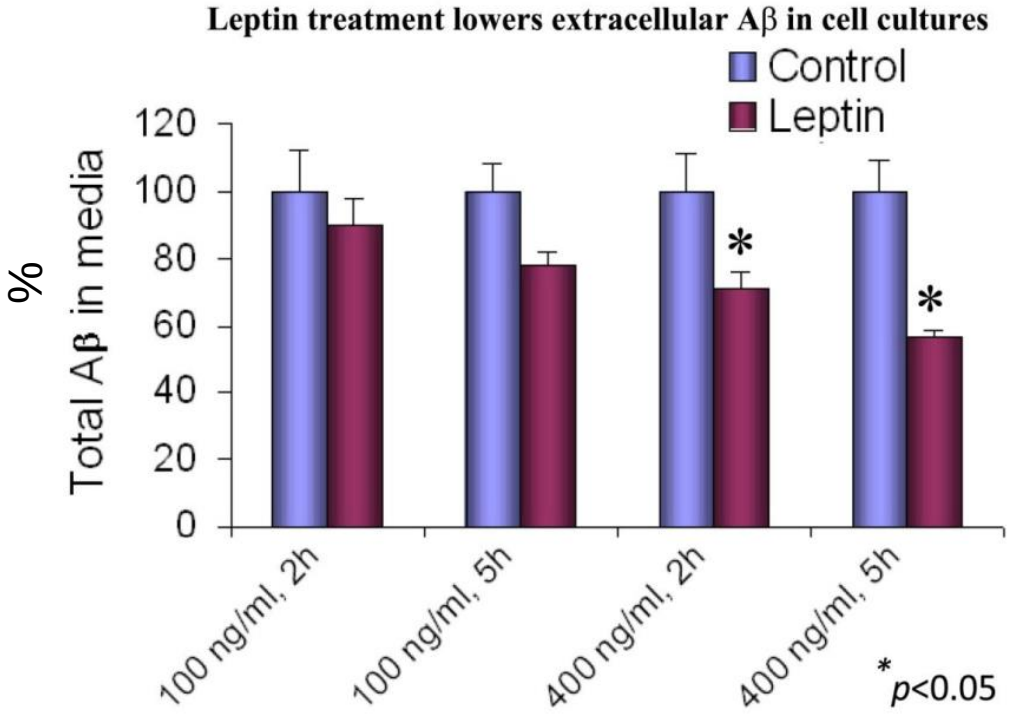
Power *et al, Dementia, 2001*



STUDIES: LEPTIN TARGETS AMYLOID BETA AND TAU PROTEIN

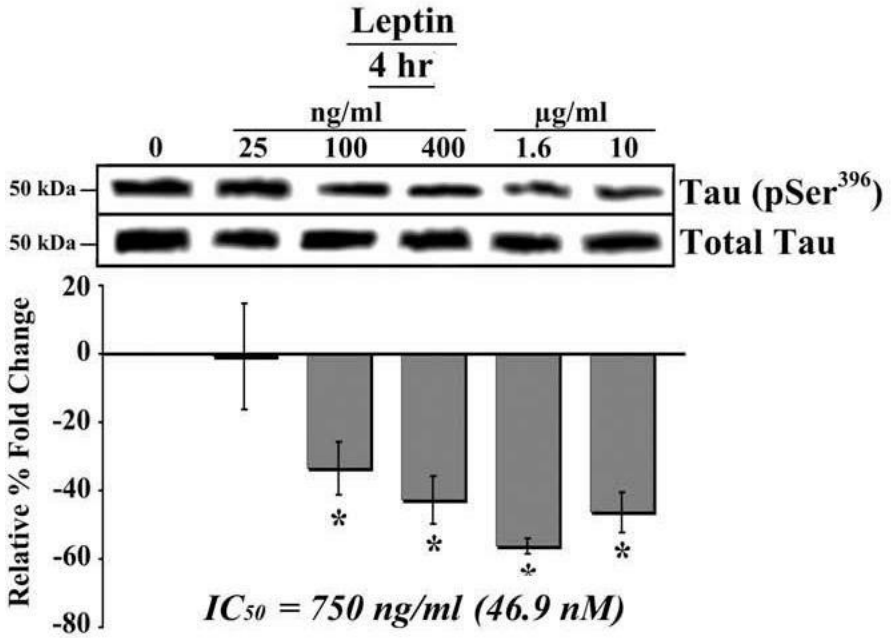
Amyloid Plaques

- Inhibition of amyloid beta (Aβ)
- Up-regulation of Aβ uptake
- Reduction of brain levels of Aβ
- Reduction of plaque density



Neurofibrillary Tangles

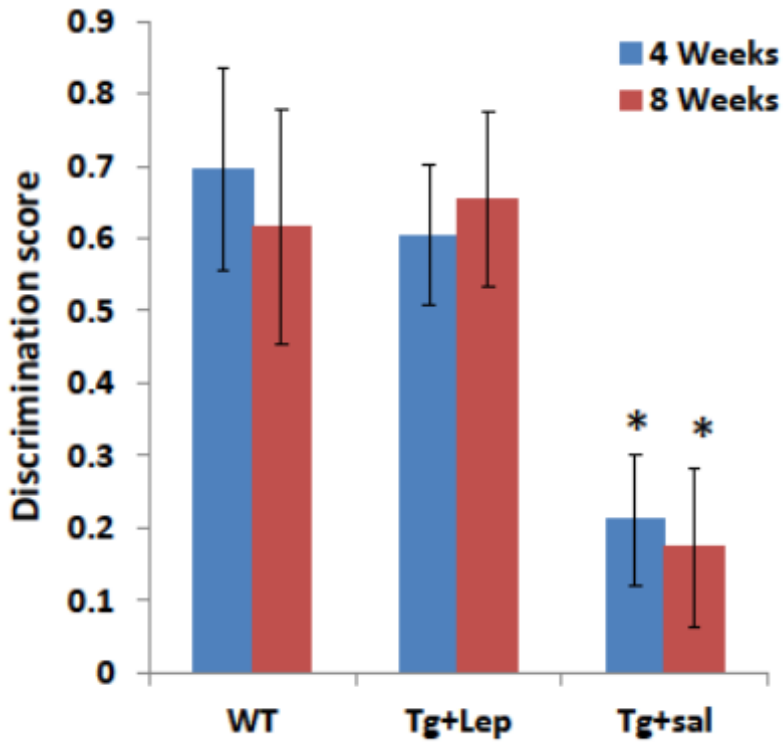
- Reduction of phosphorylation of tau protein in vitro and in vivo
- Phosphorylation of tau protein precedes the formation of neurofibrillary tangles



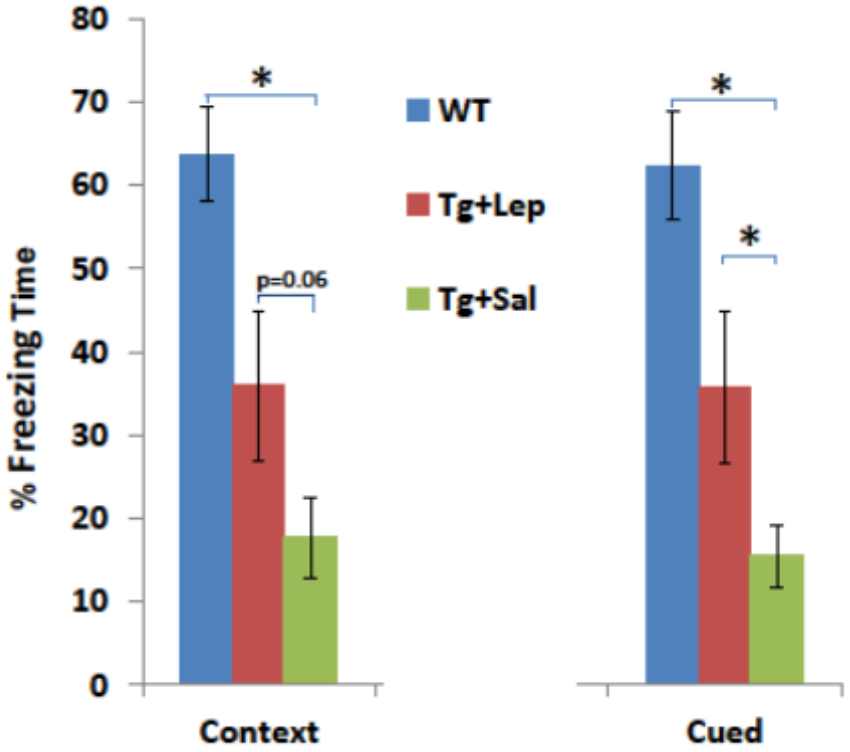
STUDIES: LEPTIN IMPROVES MEMORY IN AD ANIMAL MODELS

Animal studies: Behavioral (CRND8)

Novel Object Recognition, 4 & 8 wks



Fear Conditioning, 8 wks

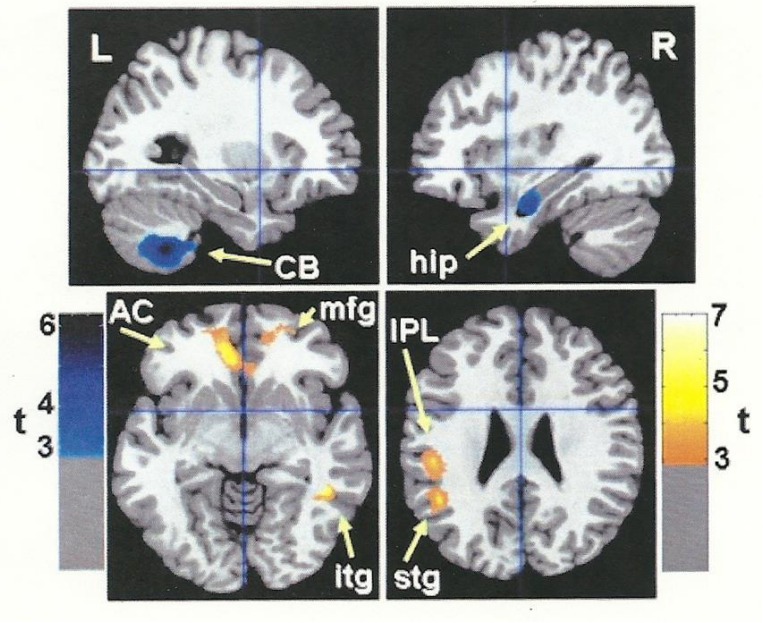


STUDIES: DIRECT EVIDENCE FOR A CAUSATION

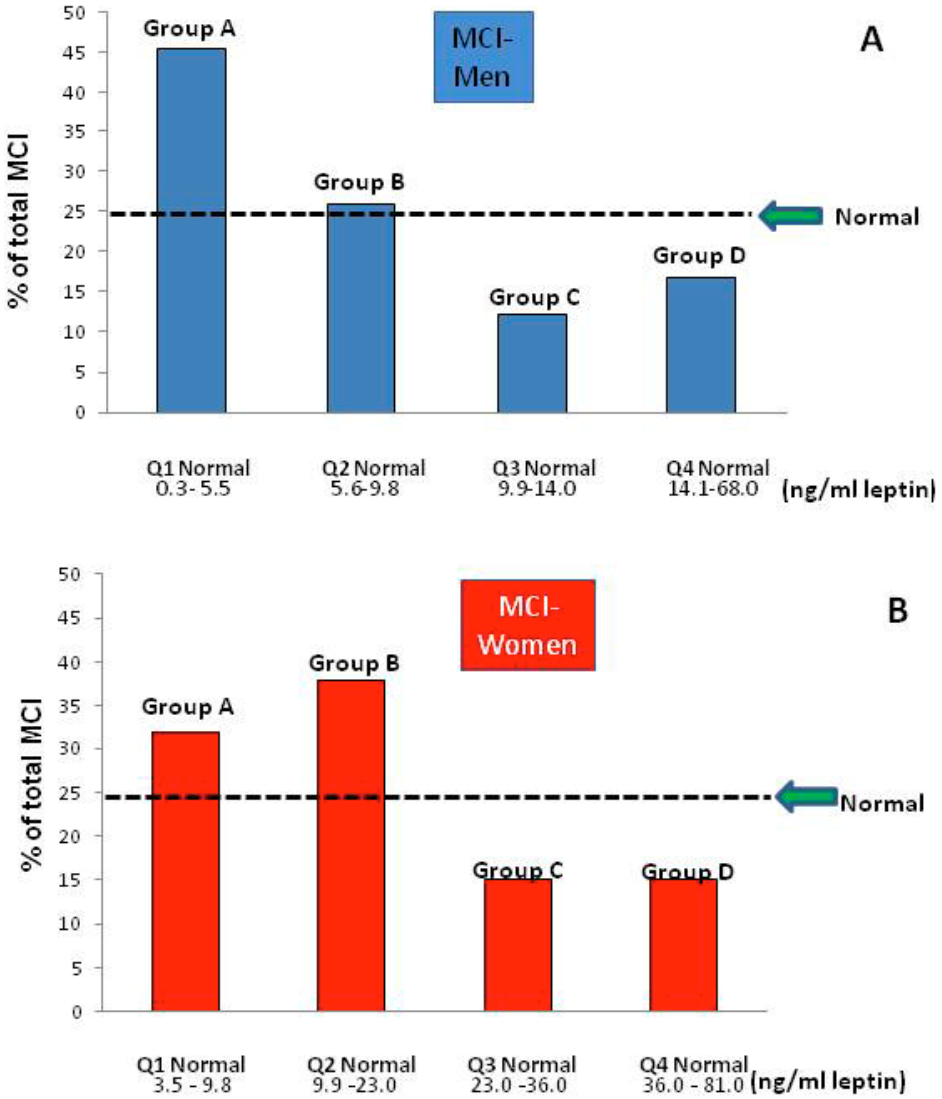
Cognitive benefits in humans: treating leptin deficiency in adults and young"

- **Behavioral changes after 2 wks Licinio et al (2004)**
- **Leptin Replacement increases Gray matter concentration in Leptin (-) adults Matochik et al (2005)**
- **Plasticity of Gray Matter changes following Leptin discontinuation / reinitiation in Leptin (-) adults London et al (2011)**
- **Leptin Replacement improves Cognitive Development in Leptin (-) young Paz-Filho et al (2008)**

(Licinio's interventional clinical studies)



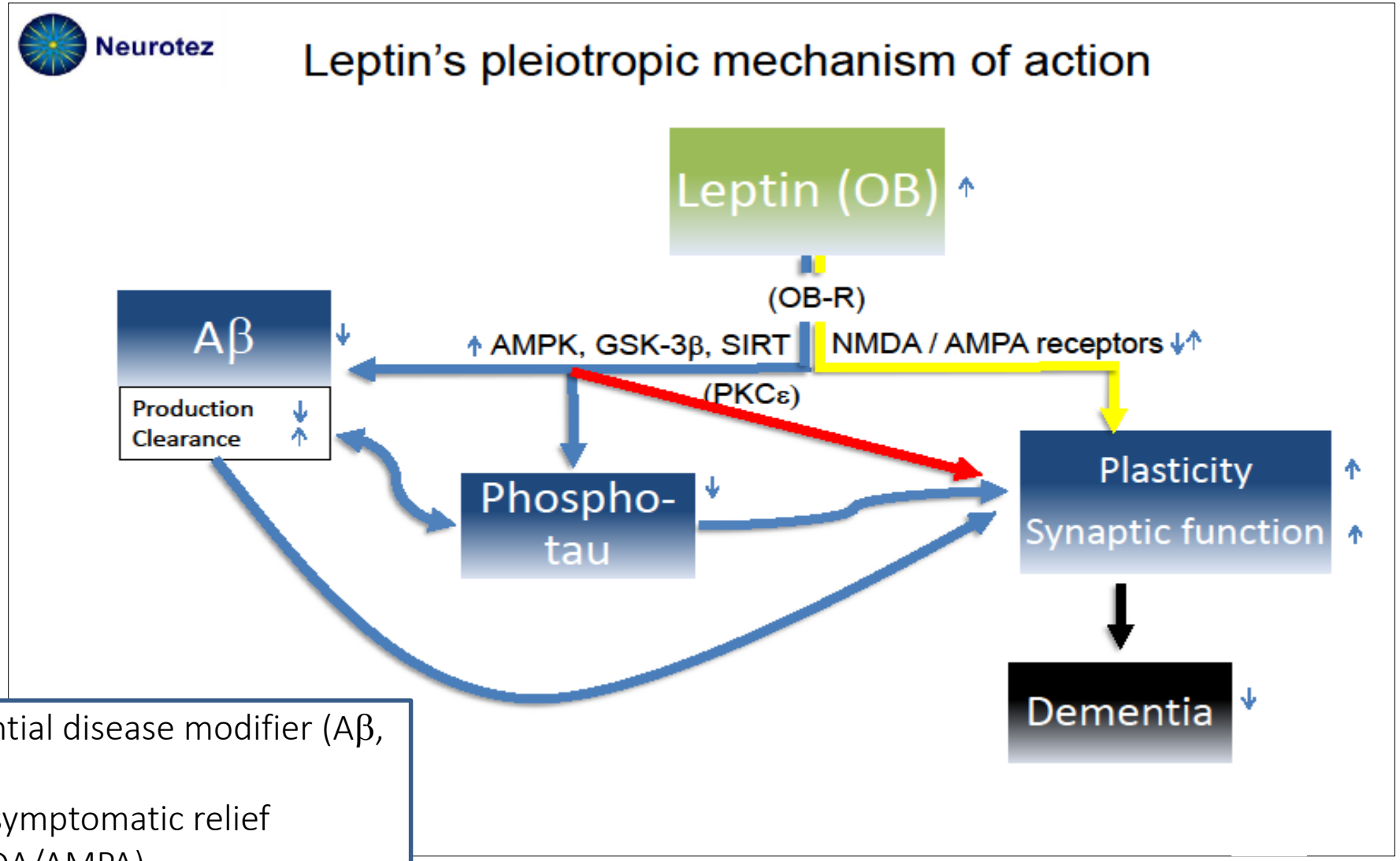
STUDIES: SERUM LEPTIN LEVELS IN MCI



Approximately 70% of MCI Subjects Have Plasma Leptin Values Lower than the Median Leptin Value of Normal Elderly.

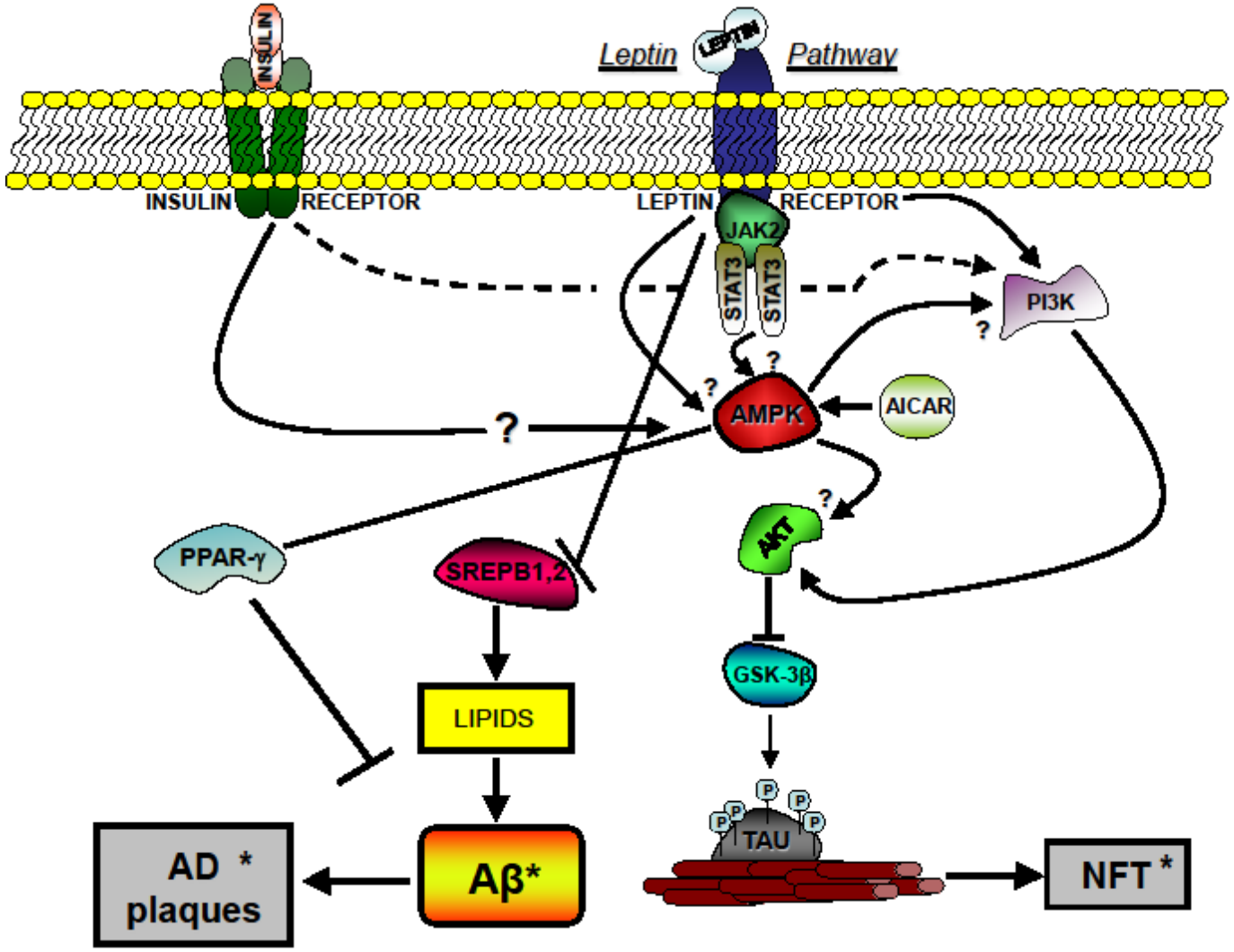
(Neurotez)

MECHANISM OF ACTION



- Potential disease modifier (Aβ, tau)
- And symptomatic relief (NMDA/AMPA)

Leptin shares pathways with insulin in neurons



NOVEL, DIFFERENTIATING

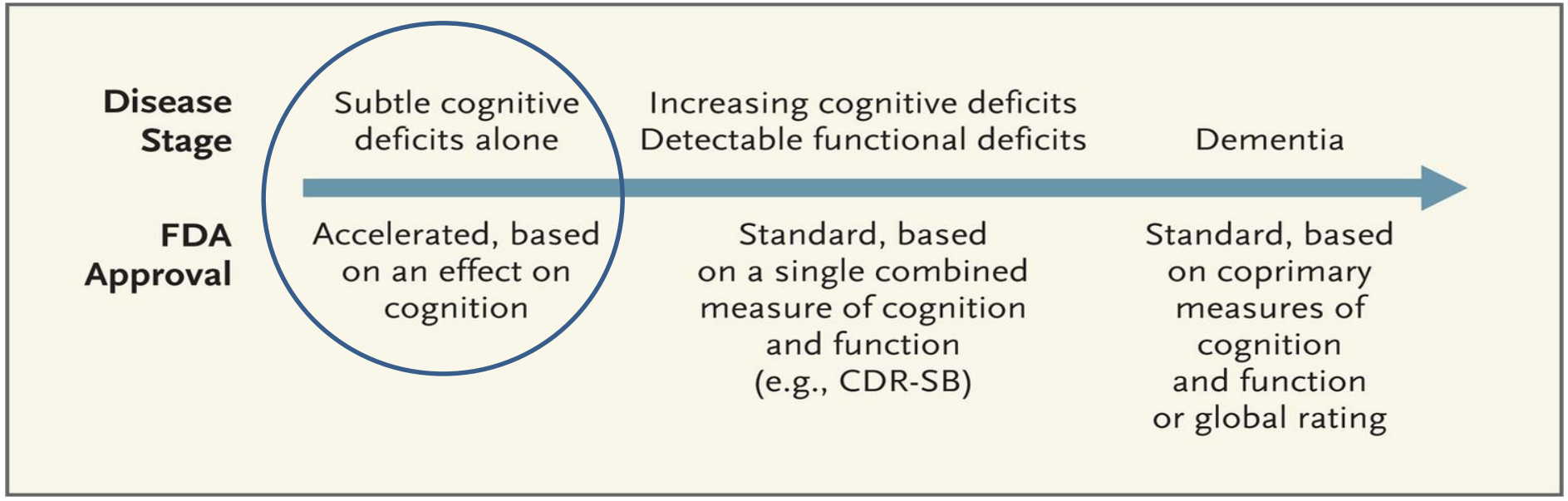
MEMTIN™ –

- Alzheimer's disease as diabetes of the brain or Type III diabetes
- A natural protein with procognitive properties at Low levels in Alzheimer's (AD) with known Safety Profile (Effectively Phase II ready)
- Ameliorates both Abeta and tau pathologies, upstream molecular target related to metabolism
- Clinical Strategy involving enrichment of patients, targeting patient group most likely to respond

PREVIOUS FAILURES-

- Antibodies directed against Abeta or tau are difficult to penetrate into the brain and are toxic at the high doses needed for efficacy
- Heterogeneity in patient groups and targeting late stage AD patients
- Wrong targets (Abeta and/or tau may be biomarkers, not culprits)

POTENTIAL REGULATORY PATHWAYS



Kozauer N, Katz R. N Engl J Med 2013;368:1169-1171.

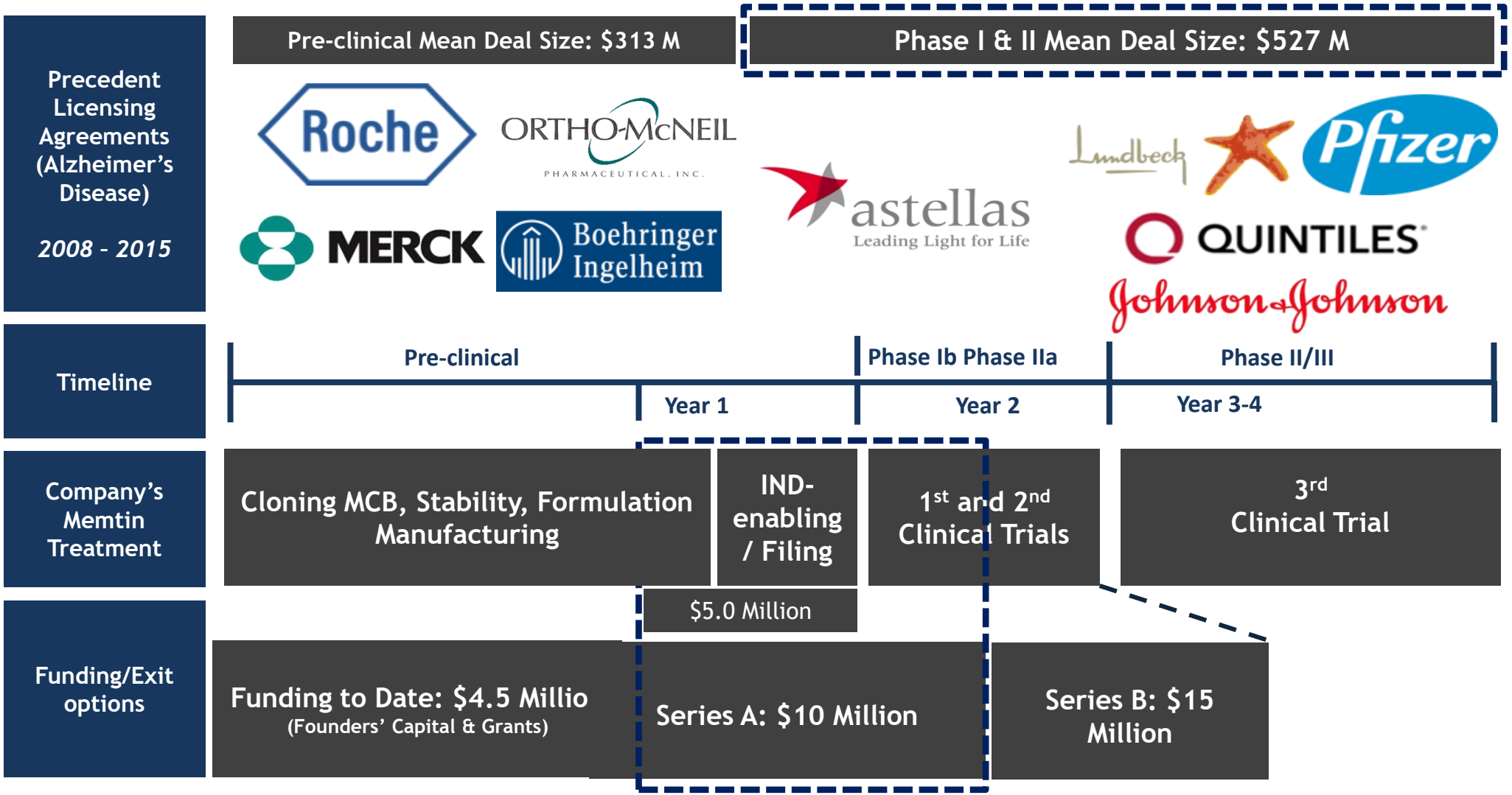
The NEW ENGLAND JOURNAL of MEDICINE

- Surrogate biomarkers, accelerated approval

(FDA preliminary interactions about our approach)

- 12y Market Exclusivity from BLA approval

DRUG DEVELOPMENT PATH FOR MEMTIN:
KEY MILESTONES



CLINICAL TRIALS:
PHASE 1 & 2

PHASE 1B

Participants
Enriched MCI/Early AD (MMSE>23) with high probability to convert to AD

Outcome Measures
- Leptin in CSF/plasma
- Markers in CSF/plasma: Aβ40/42, tau/p-tau
- FDG-PET and Amyvid-PET
- Metabolic markers
- Safety & tolerance
- Open-label 1-yr extension: preliminary efficacy data

PHASE 2

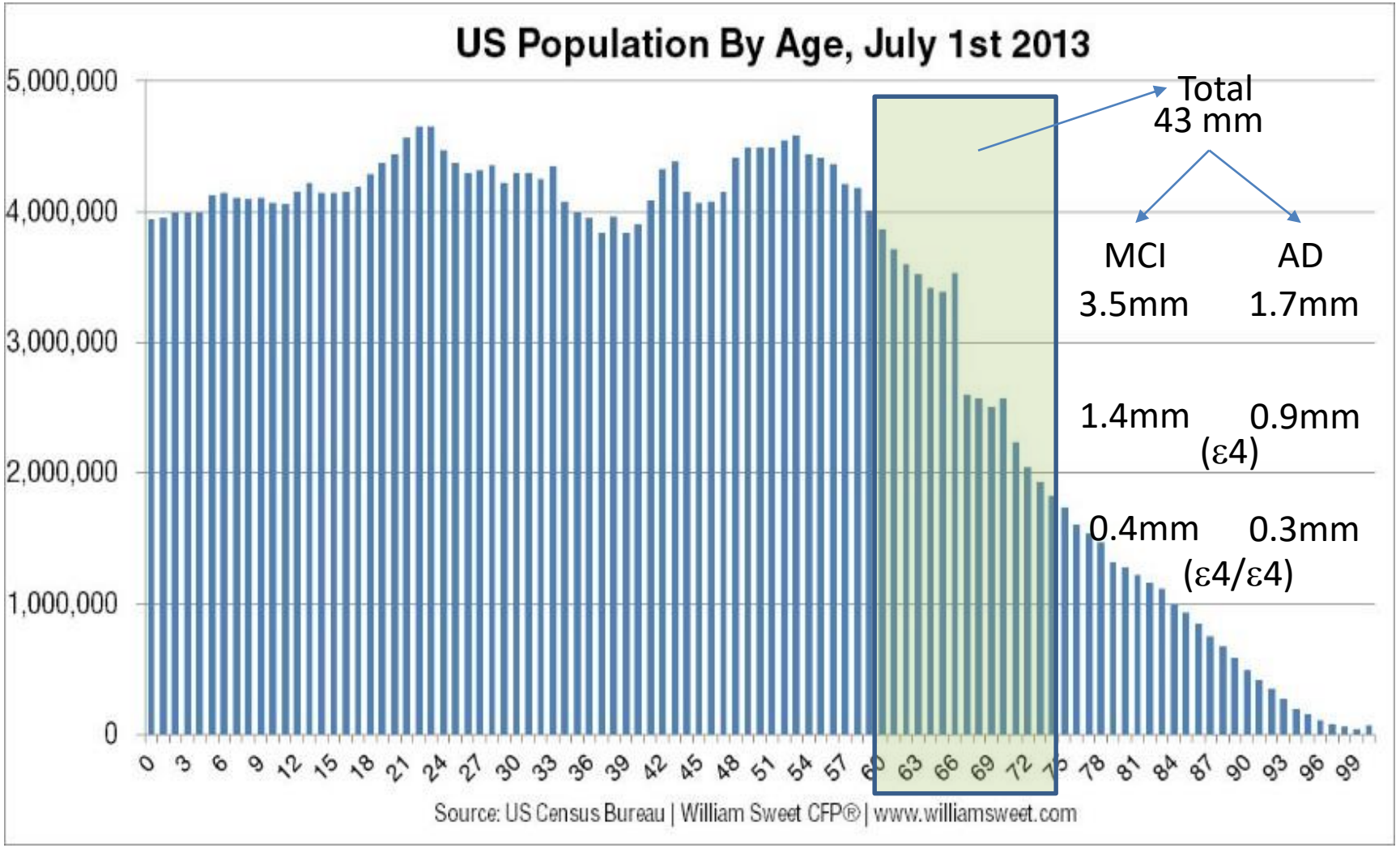
Biomarkers of exposure and cognitive enhancement (26-52 wks)

Participants
aMCIs or mild AD (MMSE>15)

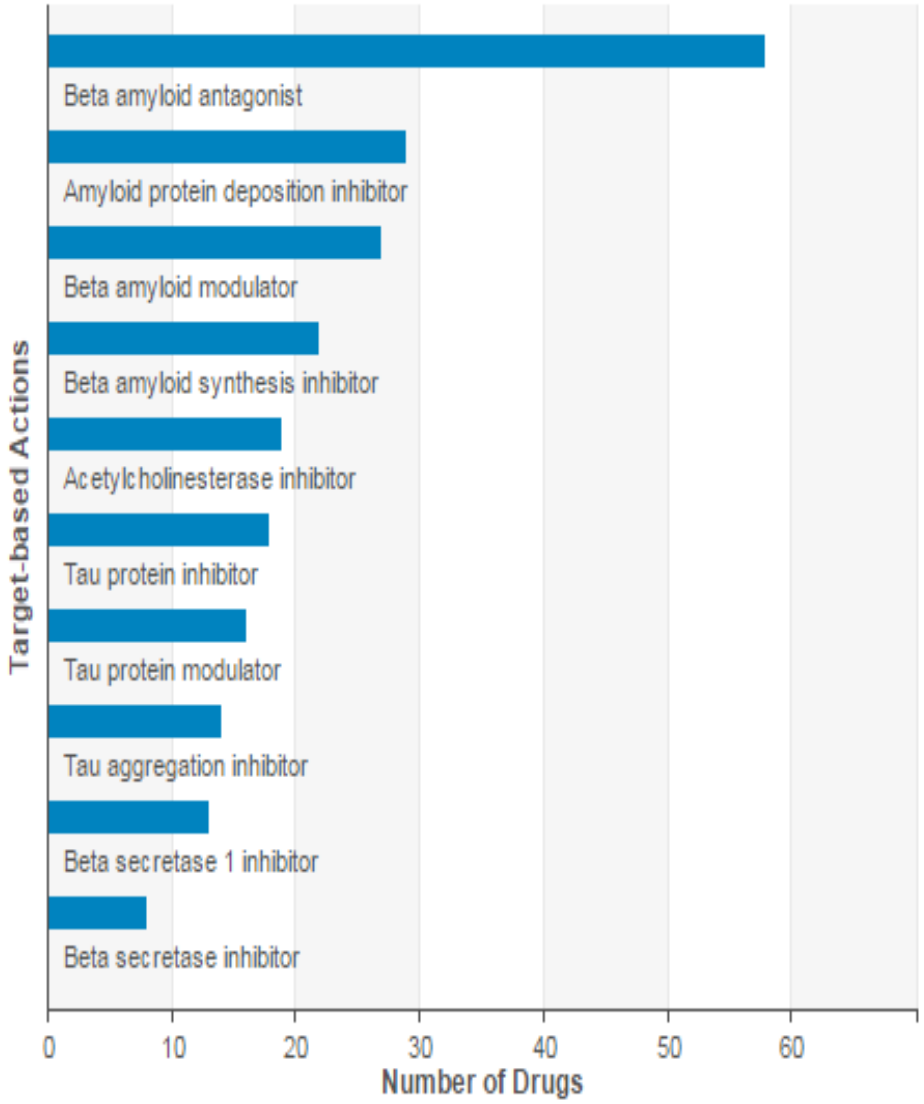
Outcome Measures
- Surrogate markers in CSF/plasma: Aβ40/42, tau/p-tau
- MRI
- Metabolic markers
- Cognition & function

Potentially accelerated approval mechanism under 21 CFR 601.41 for biologics

DEFINING A SUBSET OF MCI/AD FOR LEPTIN TREATMENT



Wins and losses demonstrate that the Aβ hypothesis is not that simple



Aβ on the fast-track

- **Lanabecestat** (AstraZeneca/Lilly): BACE1 inhibitor; Phase III
- **AMG-520** (Amgen/Novartis): BACE1 inhibitor; Phase II
- **Aducanumab** (Biogen): anti-Abeta; Phase III
- **Elenbecestat** (Eisai/Biogen): BACE1 inhib; Phase III
- **ELND-005** (Transition): Aβ aggregation inhib; Phase II/III

Aβ Disappointments

- **Verubecestat** (Merck): Phase II/III terminated in Feb 2017
- **Solanizumab** (Lilly): Failed Phase III in mild AD in 2016.
- **Bapinezumab** (Pfizer): Discontinued in Phase III
- **LY-2599666** (Lilly): Discontinued in Phase I
- **AN-1792** (Elan/Wyeth): Discontinued in 2002.
- **Affitope** (Affiris/GSK): Aβvaccine ; Phase I terminated in 2013.

Source: Clarivate Analytics Cortellis

Clarivate Analytics

	Total Size ($M)	Buyer	Seller	Year	Drug	Stage @ Sign/Today
A-BETA	$530/$130 upfront	Lilly	AZ via Astex	2014	Lanabecestat	PI/PIII
	$340/$25 upfront	Genentech	AC Immune	2006	Crenezumab	Discovery/PIII
	Not-specified	JnJ	Shionogi	2012	BACE inhibitor	Discovery/PIII
	$825	Otsuka	Lundbeck	2013	Lu-AF20513 vaccine plus others	Clinical
	Not-specified	JnJ	Cellzome	2008	Gamma-secretase mods.	Discovery
TAU	$638	Roche	reMYND	2010	ReS3-T and others	Discovery
	Not-specified	Mitsubishi	Sanofi	2005	SAR-502250	Discovery
	$509/$26 upfront	JnJ	AC Immune	2014	ACI-35; Tau vaccine	Phase I
	Not specified	Abbvie	C2N	2015	Anti-Tau mAb	Discovery/PII
OTHER	$31	JnJ	Orion	2013	A2C-adrenoreceptor	Phase II
	$289	Merck	Alectos	2010	MK-8719; N-acetyl glucose amidase mod.	Discovery/ PI Orphan

Major pharma: notable deals since 2005 have focused on Aβ and Tau

Source: Clarivate Analytics Cortellis

Clarivate Analytics

EXPERIENCED MANAGEMENT TEAM

- **Nikolaos Tezapsidis, PhD,** *Chairman, Chief Executive Officer & President* 18+ years experience in biomedical research; Two awards from the Alzheimer's Association Fellow of the Science and Engineering Council and the Wellcome Trust
- **Hamish McArthur, PhD,** *Manufacturing Chief Officer*, Executive with 33 years biologics experience within Pfizer, directly involved in numerous approved products .
- **J. Wesson Ashford, MD, PhD,** *Chief Medical Officer* Clinical Professor (affiliated), Department of Psychiatry & Behavioral Sciences, Stanford University, Scientific Advisory Board Member and Chair of the Memory Screening Advisory Committee of the Alzheimer's Foundation of America
- **George Perry, PhD,** *Chief Scientific Officer* Holder of the Semmes Foundation Endowed Chair in Neurobiology at the Univ of Texas at San Antonio Distinguished as one of the top Alzheimer's disease researchers with over 1,000 publications
- **Jukka Karjalainen, MD, PhD,** *Chief Operating Officer.* Experience in pharmaceuticals and medical devices and clinical drug development from Phase I to Phase IV
- **James Harris, MBA,** *Chief Financial Officer* 20+ years experience in startups, licensing and biosimilars.
- **Michael J. Hoy, MS,** *Consultant of Regulatory Affairs* 15+ years in the pharmaceutical industry; Served as a consultant with pharmaceutical companies of all sizes
- **Jane Johnston, PhD**, *VP of Operations* 18+ years of research in cellular neuroscience

BOARD OF DIRECTORS & ADVISORS

Directors

Nikolaos Tezapsidis, PhD (Chair)	Neurotez
J Wes Ashford, MD, PhD	Stanford U/ Neurotez
James Harris III, MBA	Healthcare Economics
Tom Humphries, MD	Bayer, retired
Bob Oliver, MBA	Recent CEO, Otsuka (US)
George Perry, PhD	Dean, U Texas, S. Antonio

Advisors

Julio Licinio, MD, FRANZCP	SVP and Dean at SUNY
Arthur Klausner, MBA	Director at Monopar Therapeutics
Steven Jacobsen, PhD	CEO at ALSP Inc
Daniel P. van Kammen, MD, PhD	CNS Pharma
Gil Block, MD	CMO at Neuraltus, Inc
Robert Winkler, MD	SVP at Taiho Oncology
Kent Iverson, BS	Pharmaceutical Advisors
Lex Van der Ploeg, PhD	CSO at Rhythm Pharma
Izabela Ochocka	BIMA Capital

FINANCING

- RAISED: $4.5million
  - National Institutes of Health
  - New Jersey Commission of Science and Technology
  - Internal Revenue Service
  - Founders, Small private investments

- This round: $10,000,000, starting with $500,000

- MILESTONES (12-18months):
  - Drug Manufacturing
  - IND-enabling studies
  - IND application

- MILESTONES (next 12-18months):
  - Phase I (Safety and biomarkers)
  - Phase II (Efficacy and biomarkers)

ALZHEIMER'S DISEASE MARKET FORECAST.

- *Goldman Sachs projects Alzheimer's disease modification drugs could top $**30 billion,** (**$12 billion** at peak)*

SUMMARY

- Repurposing MYALEPT, an approved drug, as **Memtin™**
- Drug is an endogenous protein naturally transported into the brain with receptors in the hippocampus (area affected by disease)
- Data from thousands of patients supporting an association of the drug to protection against Alzheimer's
- Data from preclinical studies demonstrating efficacy as a disease modification entity
- Perfectly positioned to allow early intervention and prevention therapy for those at risk (because of its safety profile)
- Novel use patents issued in US, Japan, China, Australia, S Africa and have pending in Europe, Canada and India, protection until 2029
- Drug as a biologic, will get 12 y of market exclusivity from approval in the US (similar provisions ex-US)
- Drug can be produced cost-effectively and in large batches in Ecoli
- Treatment will be combined with diagnostic tests (plasma leptin)/apoE4)
- Can be subject to accelerated approval, using protein as a surrogate marker as an endpoint, can cut clinical development costs by 10s of $millions and time by 3-4 years.

Contact:

Nikolaos Tezapsidis
President & CEO

Neurotez, Inc.
991 Highway 22, Suite 200A,
Bridgewater, NJ 08807, USA
Tel:+1-908-998-1340
Fax: +1-908-864-8957
ntezapsidis@neurotez.com