Memtin™ – a patented hormone replacement therapy for slowing cognitive decline in Alzheimer's disease

"Our flagship"

Nikolaos Tezapsidis, President & CEO

September 2017

2017 ALZHEIMER'S DISEASE FACTS AND FIGURES

ALZHEIMER'S DISEASE IS THE
6TH LEADING CAUSE
OF DEATH IN THE UNITED STATES

MORE THAN **15 MILLION AMERICANS** provide unpaid care for people with Alzheimer's or other dementias

IN 2016 these caregivers provided an estimated **18.2 BILLION HOURS** of care valued at over **$230 BILLION**

In 2017, Alzheimer's and other dementias will cost the nation $259 billion
By 2050, these costs could rise as high as
$1.1 TRILLION

MORE THAN 5 MILLION AMERICANS ARE LIVING WITH ALZHEIMER'S
BY 2050, THIS NUMBER COULD RISE AS HIGH AS 16 MILLION

EVERY 66 SECONDS
someone in the United States develops the disease

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

IT KILLS MORE THAN
breast cancer and prostate cancer
COMBINED

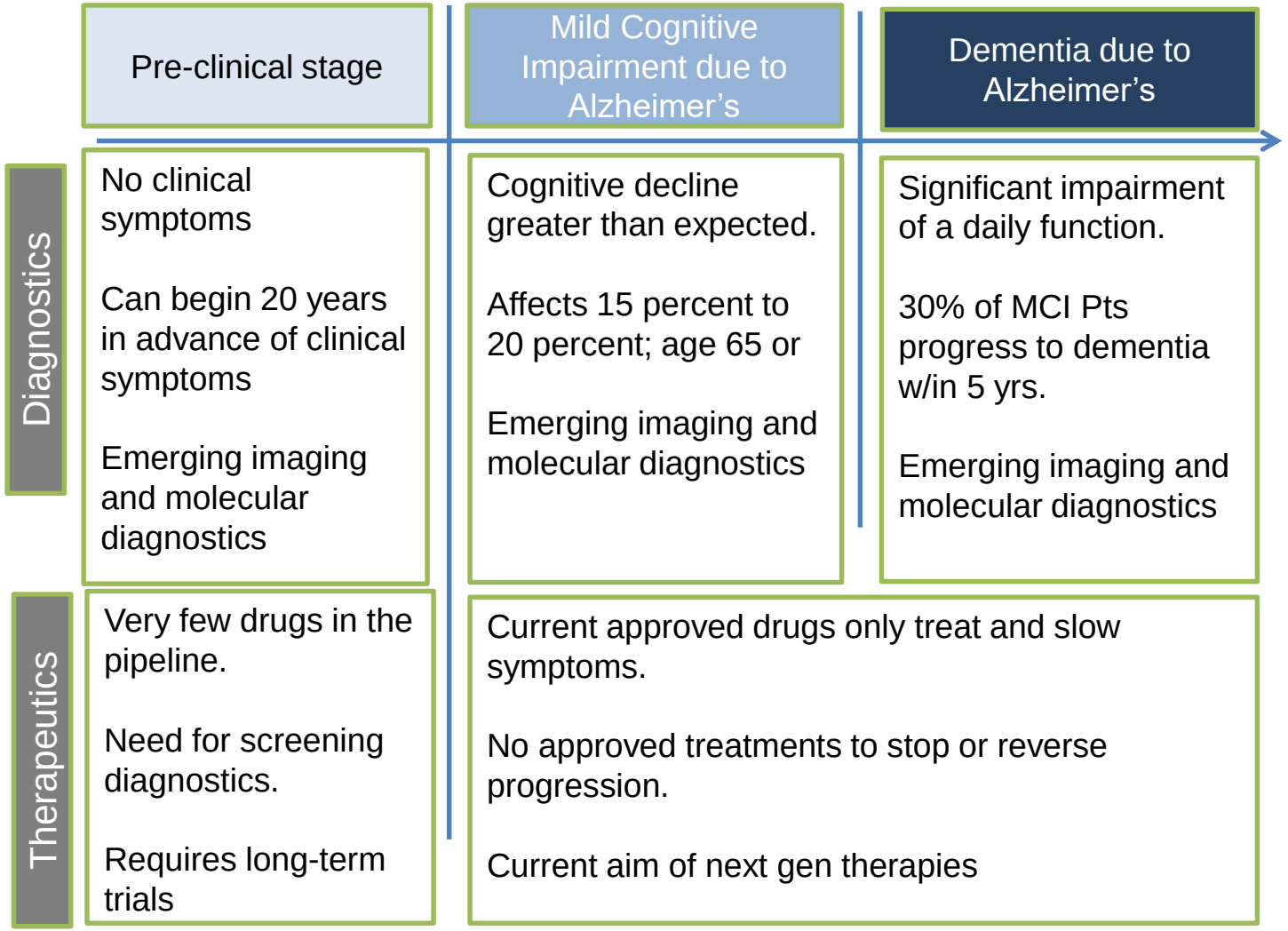
Since 2000, deaths from heart disease have decreased by 14%

while deaths from Alzheimer's disease have increased by 89%

alzheimer's association

THE BRAINS BEHIND SAVING YOURS.

The Alzheimer's Disease challenge requires a combination of Dx and Rx



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

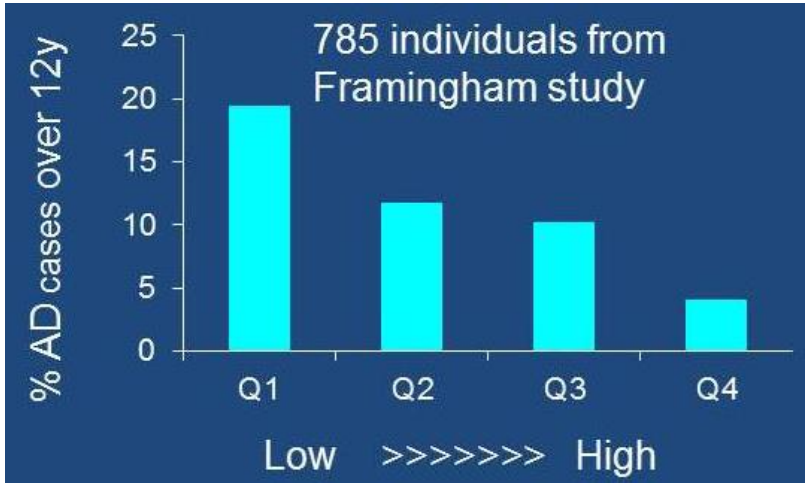
→ **Leptin as Replacement Therapy**

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.

STUDIES: SERUM LEPTIN LEVELS IN ELDERLY AND PROGNOSIS

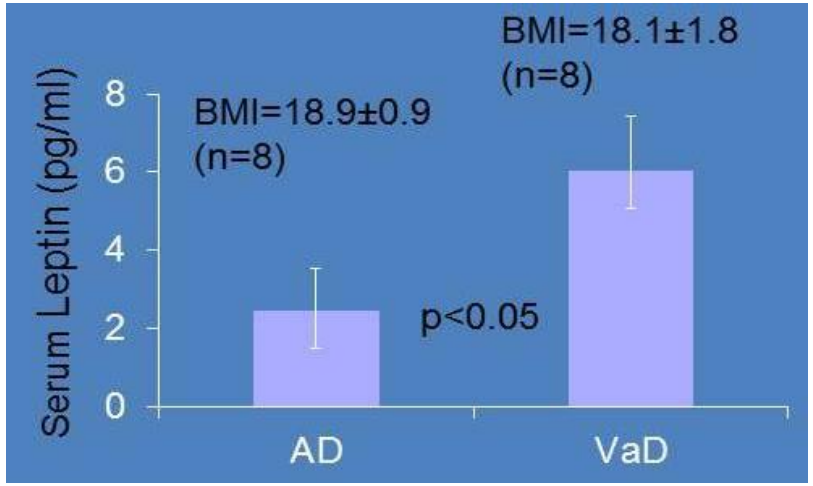
In elderly, higher serum Leptin is associated with a lower risk for Alzheimer's disease and dementia

Lieb *et al, JAMA, 2009*



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

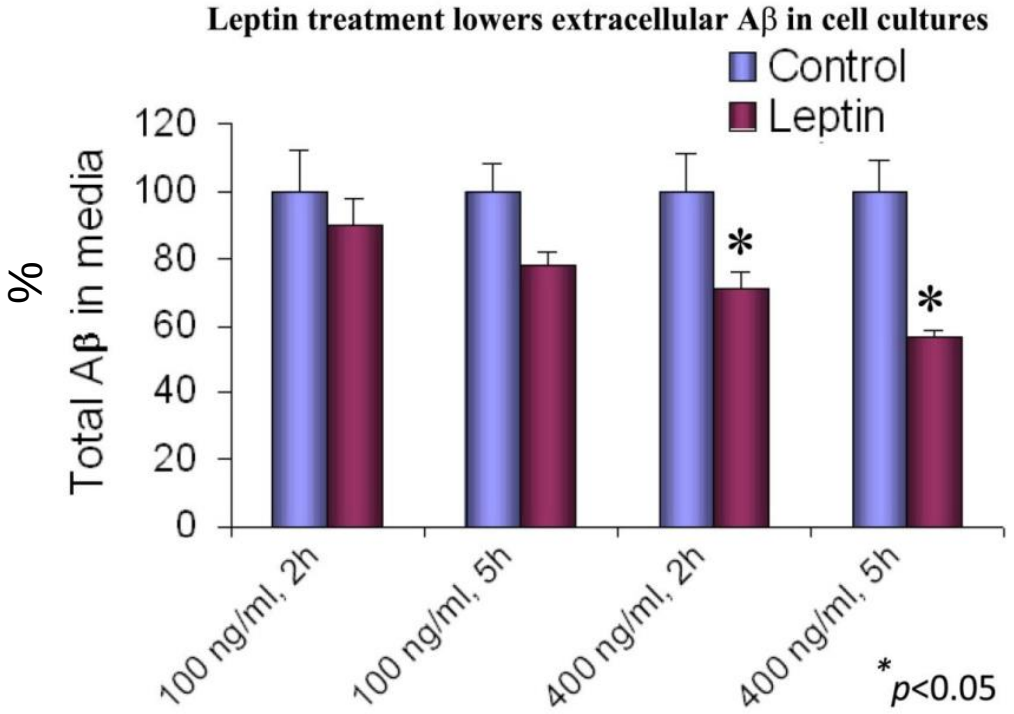
Power *et al, Dementia, 2001*



STUDIES: LEPTIN TARGETS AMYLOID BETA AND TAU PROTEIN

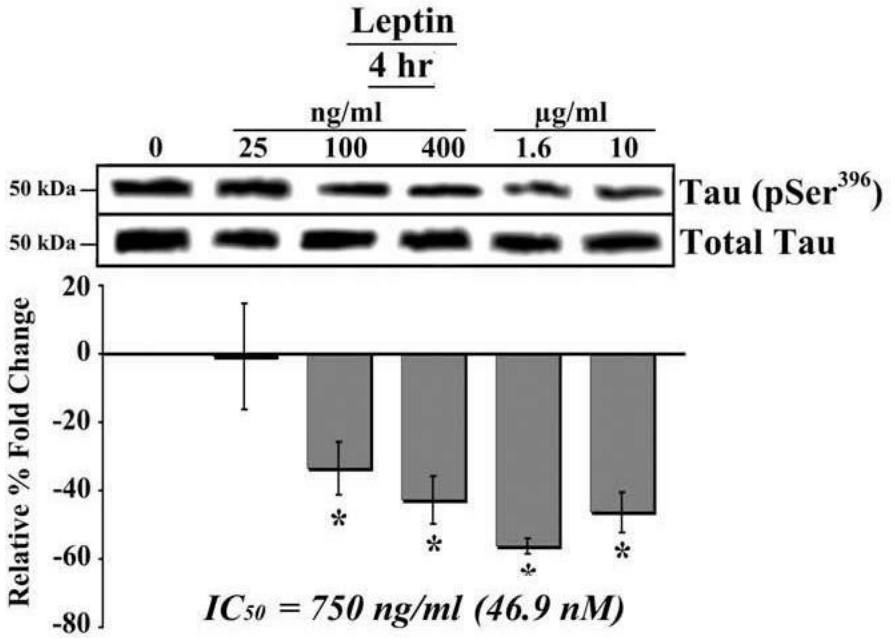
Amyloid Plaques

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



Neurofibrillary Tangles

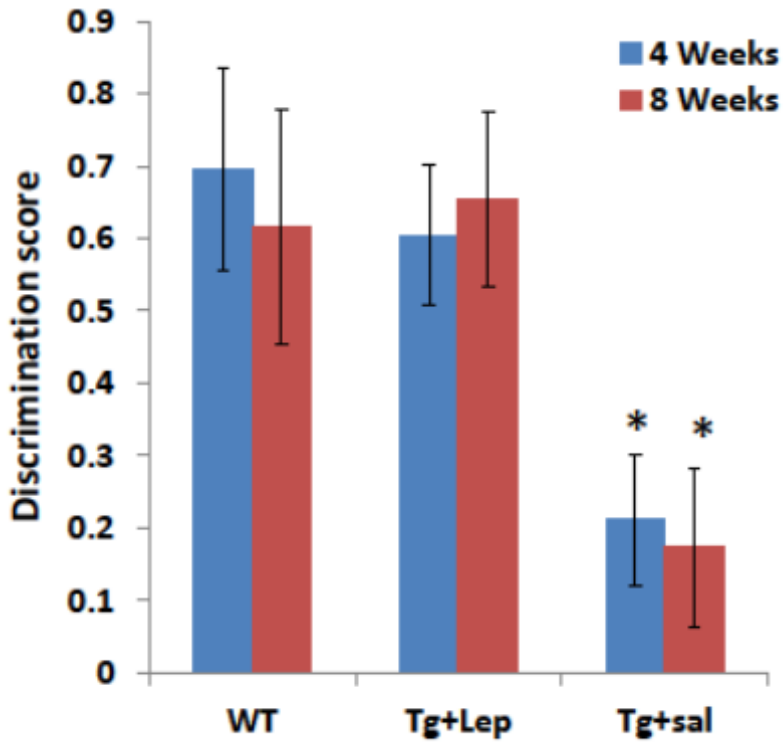
- Reduction of phosphorylation of tau protein in vitro and in vivo
- Phosphorylation of tau protein precedes the formation of neurofibrillary tangles



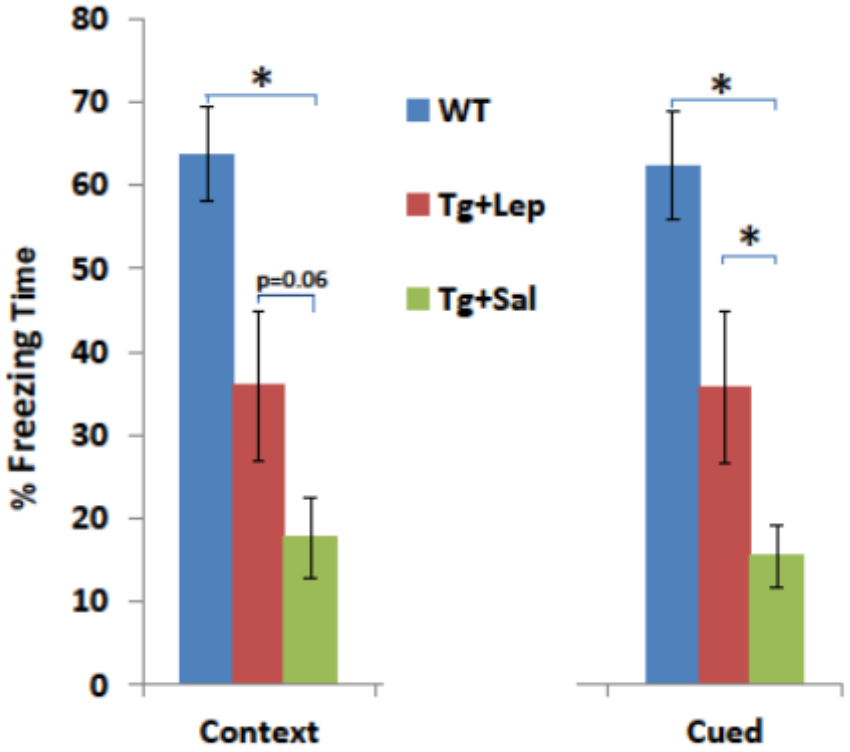
STUDIES: LEPTIN IMPROVES MEMORY IN AD ANIMAL MODELS

Animal studies: Behavioral (CRND8)

Novel Object Recognition, 4 & 8 wks



Fear Conditioning, 8 wks

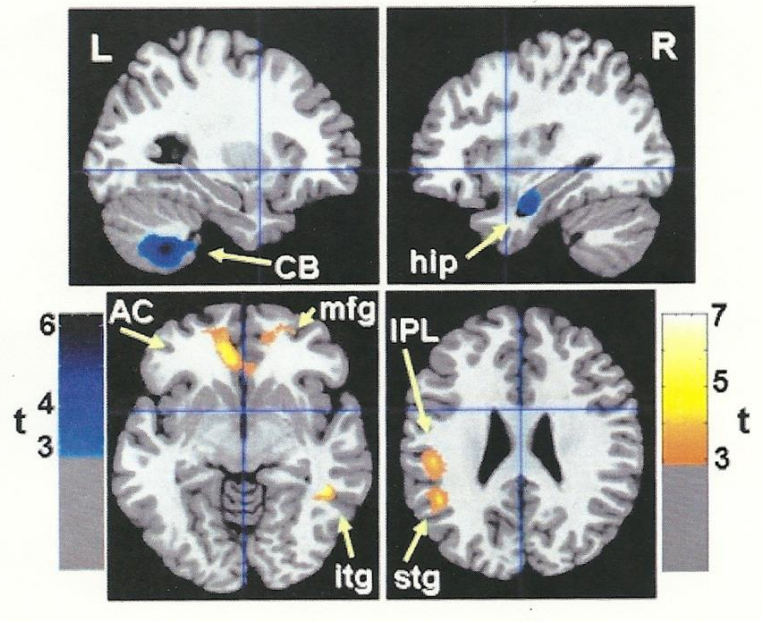


STUDIES: DIRECT EVIDENCE FOR A CAUSATION

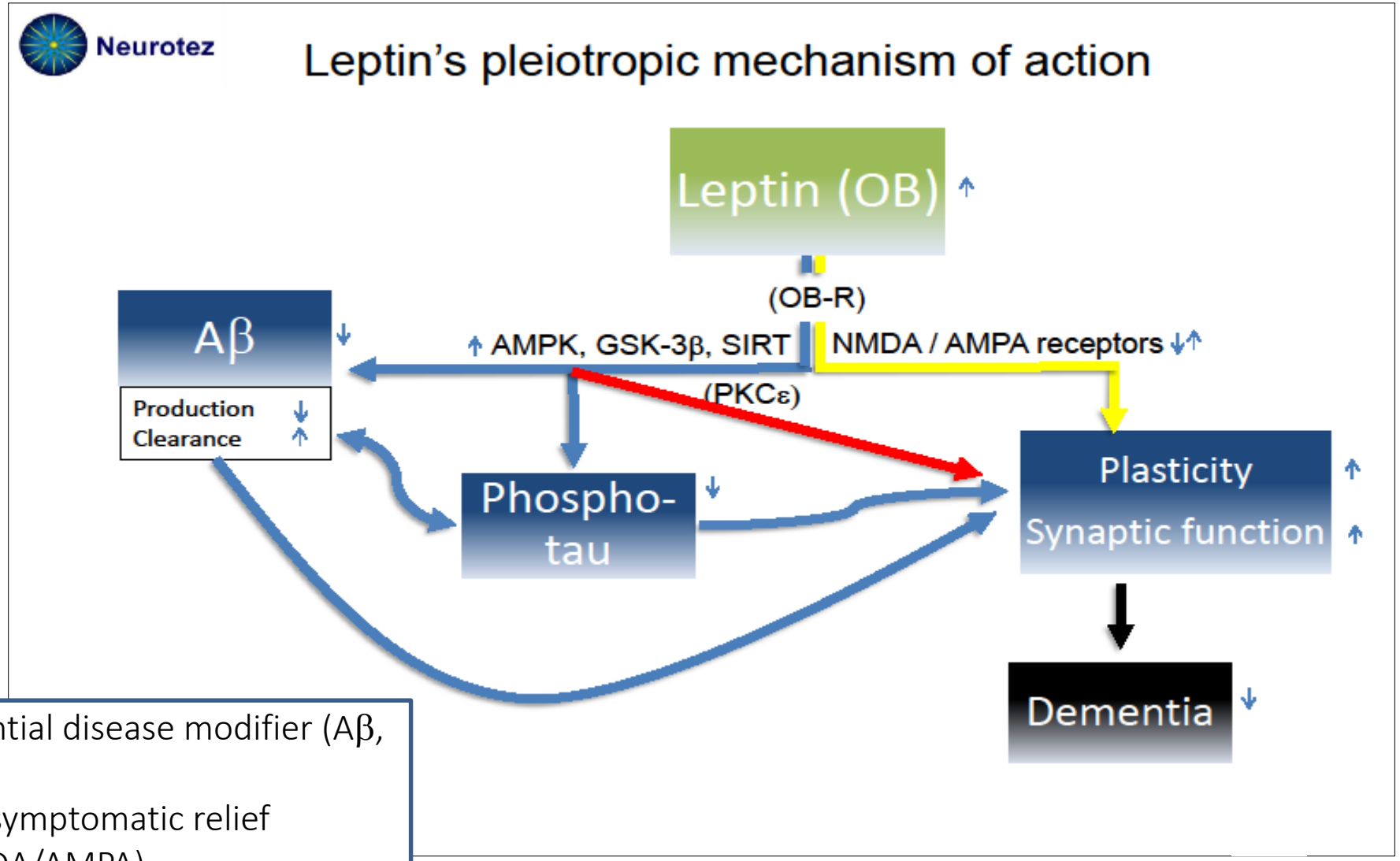
Cognitive benefits in humans: treating leptin deficiency in adults and young"

- **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)



MECHANISM OF ACTION



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

NOVEL, DIFFERENTIATING

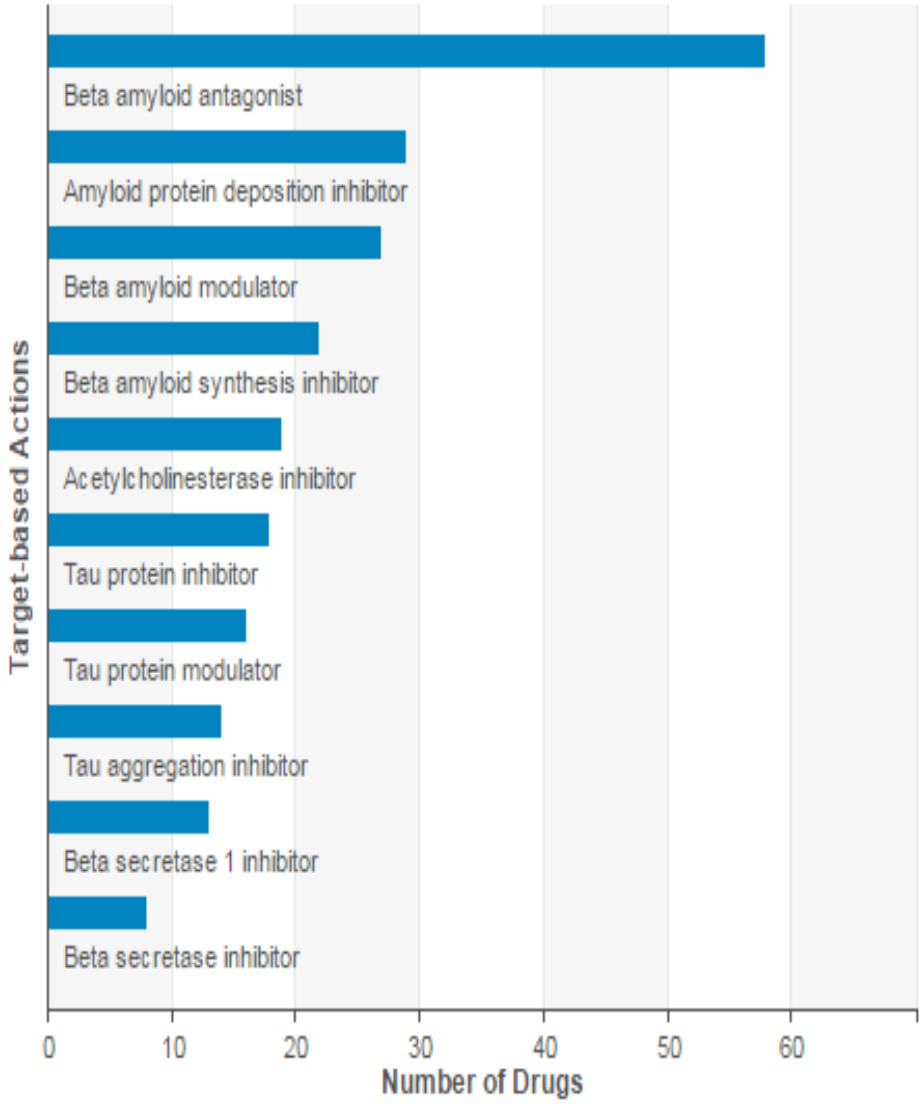
MEMTIN™ –

- 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)

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

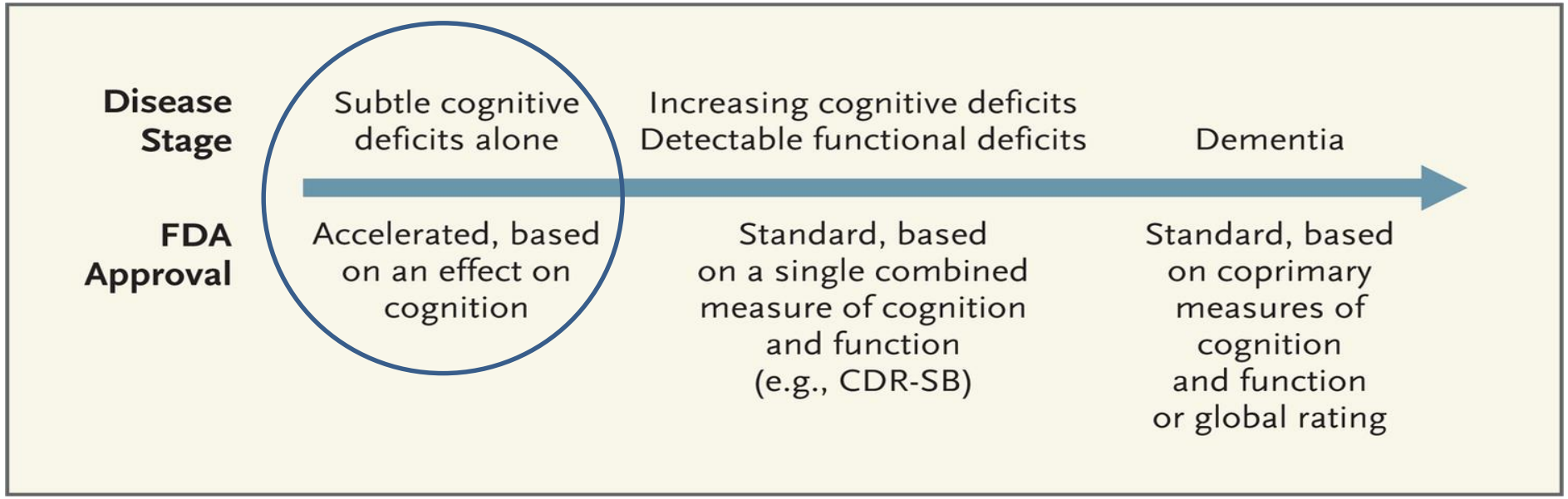
Aβ Disappointments

- **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

POTENTIAL REGULATORY PATHWAYS



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

The NEW ENGLAND JOURNAL of MEDICINE

- Surrogate biomarkers, cond. approval
- 12y Market Exclusivity from BLA approval

(R Katz, previous FDA Director of Neurology Products, was enthusiastic about our approach)

EXPERIENCED MGT TEAM

- **Nikolaos Tezapsidis, Ph.D.,** *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, Ph.D.,** *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, Ph.D.,** *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,** *VP 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

BOD & ADVISORS

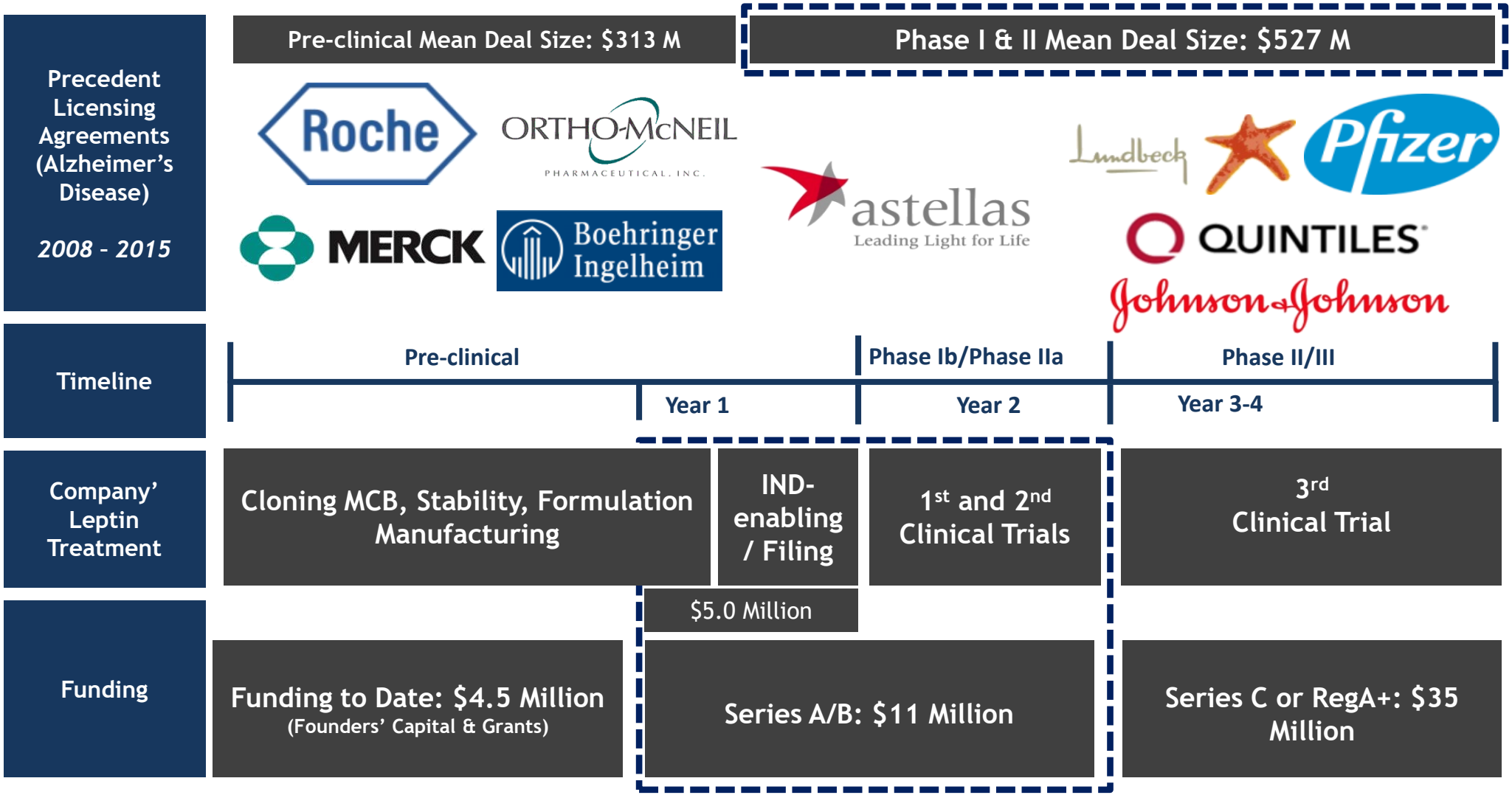
Directors

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

DRUG DEVELOPMENT PATH:
KEY MILESTONES



	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

FINANCING

- RAISED: $4.5million
  - NIH
  - NJEDA
  - IRS
  - Founders, Small private investors

- Series A, $5 million
- MILESTONES (12-18months):
  - Drug Manufacturing
  - IND-enabling studies
  - IND application
- SERIES B, $6 million
- MILESTONES (12-18months):
  - Phase I (SAD, MAD)
  - Phase II

AD 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