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
Alzheimer’s disease
- is the most common form of dementia of the elderly
- gets progressively worse and there is no remission
- is the 6th leading cause of death in the USA
- affecting more than 5 million Americans / 30 million worldwide
- is the only cause of death among the top 10 in America that cannot be prevented, cured or even slowed.
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.

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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

<table>
<thead>
<tr>
<th>Pre-clinical stage</th>
<th>Mild Cognitive Impairment due to Alzheimer’s</th>
<th>Dementia due to Alzheimer’s</th>
</tr>
</thead>
<tbody>
<tr>
<td>No clinical symptoms</td>
<td>Cognitive decline greater than expected.</td>
<td>Significant impairment of a daily function.</td>
</tr>
<tr>
<td>Can begin 20 years in advance of clinical symptoms</td>
<td>Affects 15 percent to 20 percent; age 65 or</td>
<td>30% of MCI Pts progress to dementia w/in 5 yrs.</td>
</tr>
<tr>
<td>Emerging imaging and molecular diagnostics</td>
<td>Emerging imaging and molecular diagnostics</td>
<td>Emerging imaging and molecular diagnostics</td>
</tr>
<tr>
<td><strong>Diagnostics</strong></td>
<td><strong>Therapeutics</strong></td>
<td><strong>Therapeutics</strong></td>
</tr>
<tr>
<td>Very few drugs in the pipeline.</td>
<td>Current approved drugs only treat and slow symptoms.</td>
<td>No approved treatments to stop or reverse progression.</td>
</tr>
<tr>
<td>Need for screening diagnostics.</td>
<td></td>
<td>Current aim of next gen therapies</td>
</tr>
<tr>
<td>Requires long-term trials</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
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.
Leptin regulates feeding behavior, metabolic activity and cognition.
DRUGS SUCCESSFULLY REPOSITIONED

<table>
<thead>
<tr>
<th>DRUG</th>
<th>ORIGINAL INDICATION</th>
<th>NEW INDICATION</th>
</tr>
</thead>
<tbody>
<tr>
<td>Amphotericin B</td>
<td>Fungal infections</td>
<td>Leishmaniasis</td>
</tr>
<tr>
<td>Aspirin</td>
<td>Inflammation, pain</td>
<td>Antiplatelet</td>
</tr>
<tr>
<td>Bromocriptine</td>
<td>Parkinson’s disease</td>
<td>Diabetes mellitus</td>
</tr>
<tr>
<td>Finasteride</td>
<td>Prostate hyperplasia</td>
<td>Hair loss</td>
</tr>
<tr>
<td>Gemcitabine</td>
<td>Viral infections</td>
<td>Cancer</td>
</tr>
<tr>
<td>Methotrexate</td>
<td>Cancer</td>
<td>Cancer</td>
</tr>
<tr>
<td>Minoxidil</td>
<td>Hypertension</td>
<td>Psoriasis, rheumatoid arthritis</td>
</tr>
<tr>
<td>Raloxifene</td>
<td>Cancer</td>
<td>Hair loss</td>
</tr>
<tr>
<td>Thalidomide</td>
<td>Morning Sickness</td>
<td>Osteoporosis</td>
</tr>
<tr>
<td>Sildenafil</td>
<td>Angina</td>
<td>Leprosy, multiple myeloma</td>
</tr>
</tbody>
</table>

Drug discovery: 10,000 Compounds
Pre-clinical: 250 Compounds
Clinical Trials: 5 Compounds
FDA Review: 1 Approved Drug
## REPOSITIONING LEPTIN CLEAR PATH

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

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

Amyloid Plaques

Neurofibrillary Tangles

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

Leptin treatment lowers extracellular Aβ in cell cultures

Leptin

<table>
<thead>
<tr>
<th>Leptin (ng/ml)</th>
<th>0</th>
<th>25</th>
<th>100</th>
<th>400</th>
</tr>
</thead>
<tbody>
<tr>
<td>Leptin (μg/ml)</td>
<td>1.6</td>
<td>10</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

IC₅₀ = 750 ng/ml (46.9 nM)
STUDIES: LEPTIN IMPROVES MEMORY IN AD ANIMAL MODELS

Animal studies: Behavioral (CRND8)
STUDIES: DIRECT EVIDENCE FOR A CAUSATION

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

  (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

- Surrogate biomarkers, accelerated approval (FDA preliminary interactions about our approach)
- 12y Market Exclusivity from BLA approval
**DRUG DEVELOPMENT PATH FOR MEMTIN: KEY MILESTONES**

<table>
<thead>
<tr>
<th>Precedent Licensing Agreements (Alzheimer's Disease)</th>
<th>Pre-clinical Mean Deal Size: $313 M</th>
<th>Phase I &amp; II Mean Deal Size: $527 M</th>
</tr>
</thead>
<tbody>
<tr>
<td>2008 - 2015</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**Timeline**

<table>
<thead>
<tr>
<th>Pre-clinical</th>
<th>Phase Ib Phase IIa</th>
<th>Phase II/III</th>
</tr>
</thead>
<tbody>
<tr>
<td>Year 1</td>
<td>Year 2</td>
<td>Year 3-4</td>
</tr>
</tbody>
</table>

**Company's Memtin Treatment**

- Cloning MCB, Stability, Formulation Manufacturing
- IND-enabling / Filing
- 1st and 2nd Clinical Trials
- 3rd Clinical Trial

**Funding/Exit options**

- Funding to Date: $4.5 Million (Founders' Capital & Grants)
- Series A: $10 Million
- Series B: $15 Million
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
aMGIs 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

US Population By Age, July 1st 2013

Source: US Census Bureau | William Sweet CFP® | www.williamsweet.com
Wins and losses demonstrate that the Aβ hypothesis is not that simple.

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

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

Source: Clarivate Analytics Cortellis
### 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)
• 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:

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President & CEO

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