



## **Corporate Overview**

**Dr. Charles S. Ryan**  
Chief Executive Officer

**July 2019**

 **Nasdaq NTRP**

Certain statements in this presentation, particularly those pertaining to our strategy, constitute forward-looking statements. Such statements are based upon the current beliefs and expectations of management and are subject to significant risks and uncertainties. Actual results may differ materially from those set forth in the forward-looking statements.

Any statements that are not statements of historical fact (including statements containing the words “believes,” “plans,” “anticipates,” “expects,” “estimates” and similar expressions) should also be considered to be forward-looking statements. There are a number of important factors that could cause actual results or events to differ materially from those indicated by such forward-looking statements. These factors are contained in Neurotrope Inc.’s filings with the SEC, including Neurotrope’s Annual Report on Form 10-K for the year ended December 31, 2017, We encourage all viewers of this presentation to review the aforementioned filings. All statements contained in this presentation are made only as of the date of this presentation, and we do not undertake any obligation to publicly update any forward looking statements.

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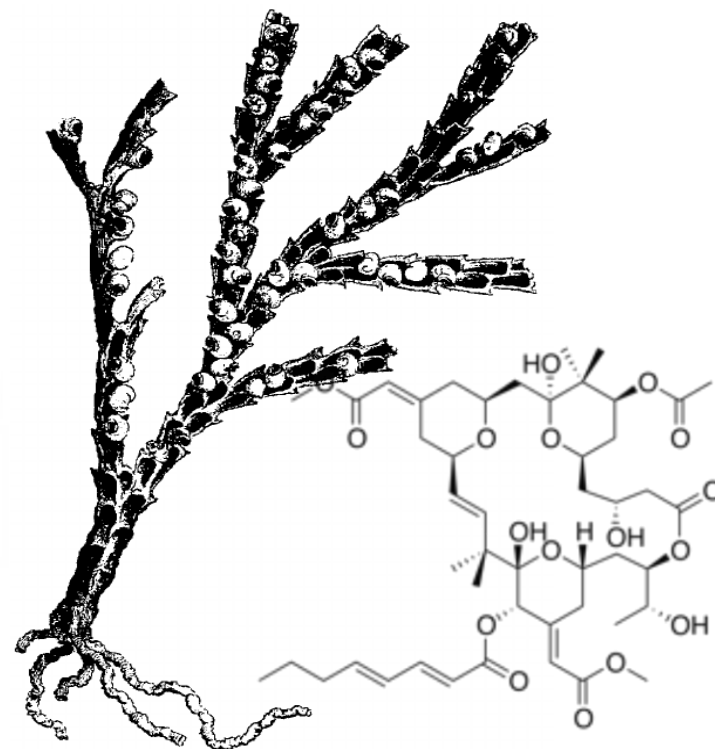
The full text of Neurotrope’s SEC filings can be found at the SEC’s website (<http://www.sec.gov>)

**Neurotrope is a biopharmaceutical company, focused on the development of a product platform for the treatment of Alzheimer's disease (AD).**

- **Our lead product candidate is bryostatin, a natural product isolated from a marine invertebrate organism, a bryozoan called *Bugula neritina*. The company also develops bryostatin for other neurodegenerative or cognitive diseases and dysfunctions, such as Fragile X.**

**Neurotrope is discovering restorative therapeutics for patients with life-altering neurodegenerative diseases and developmental disorders**

**Neurotrope has the exclusive license from Stanford University for the IP of synthetic bryostatin for our field of use**



## ✓ **Reversing Alzheimer's Disease by Treating its Cause**

Neurotrope's is developing the only drug to treat the progression and underlying disease of Alzheimer's disease, by helping the brain repair and rebuild synaptic networks. Neurotrope's Bryostatin is a naturally occurring molecule that penetrates the blood-brain barrier to activate the creation of new synapses, potentially reversing the disease.



## ✓ **Conducting Confirmatory Phase 2 Study to Treat Advanced Alzheimer's**

Results from Neurotrope's exploratory Phase 2 study of Bryostatin in 150 patients for the treatment of moderate to severe Alzheimer's disease was published in the *Journal of Alzheimer's Disease*, showing potential in the most challenging-to-treat and underserved patient population. The study reported 94% of the patients treated with bryostatin in the absence of memantine showed improvement in their Severe Impairment Battery (SIB) score. Based on these results, Neurotrope is conducting a double blind, placebo controlled confirmatory Phase 2 study of Bryostatin, administering 20µg of bryostatin or placebo to 100 patients with moderate to severe Alzheimer's. These patients are not on memantine therapy. Data is expected in the second half of 2019.

## ✓ **Phase 1 Trial with Nemours Hospital for Treatment of Fragile X Syndrome**

Neurotrope is developing a Phase 1 trial of Bryostatin in the treatment of Fragile X Syndrome, a genetic disorder, in conjunction with a premier children's hospital, Nemours / Alfred I. duPont Hospital for Children. The U.S. FDA has given Orphan Drug designation to Bryostatin for this disease, which causes mental disability in 135,000 Americans. Current drugs only treat symptoms. Bryostatin has exhibited the strongest long-term, pre-clinical evidence for a disease modifying therapy for Fragile X.

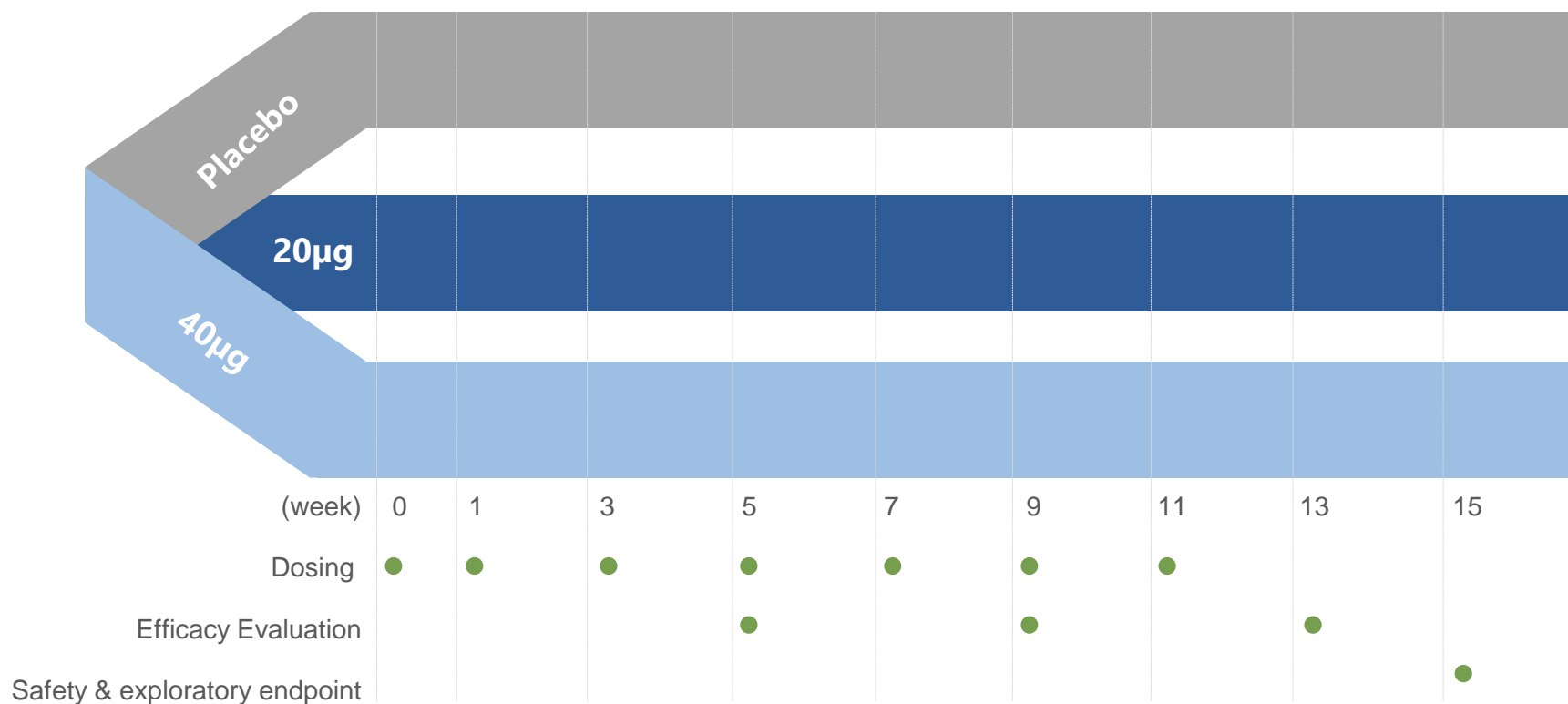
## ✓ **Bryostatin to Treat Numerous Neurodegenerative Diseases**

Bryostatin activates brain synaptic growth factors BDNF, NGF, IGF-1 and others. It simultaneously inhibits the build-up of amyloid plaques and tau tangles. Preclinical studies have shown that treatment with Bryostatin prevented synaptic loss in the brains of animals. The National Cancer Institute has tested Bryostatin in over 1,500 patients and found it to be safe and well tolerated. Bryostatin's ability to repair, rebuild, and protect synapses makes it a leading candidate to treat many neurological diseases in addition to Alzheimer's.

## **Treatment of Alzheimer's Will be \$10 Billion Global Market by 2021**

The market for treating Alzheimer's is now \$5 billion globally and expected to grow to \$10 billion by 2021 driven by an aging population. 5.7 million Americans are living with Alzheimer's today and the number is expected to grow to 14 million by 2050. It is the 6<sup>th</sup> leading cause of death in the U.S. with direct medical costs of \$20 billion per year.

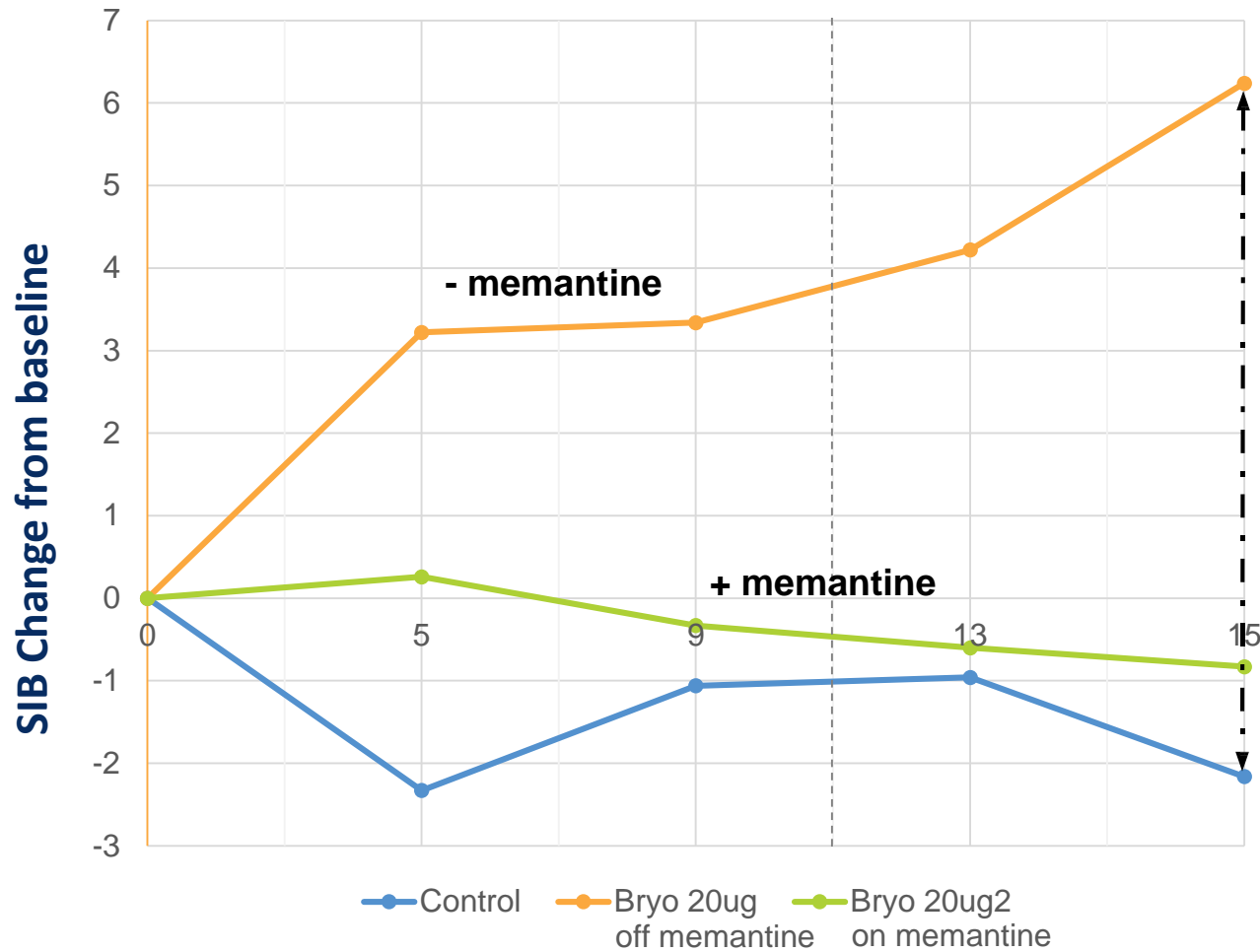
# DOUBLE-BLIND, RANDOMIZED (1:1:1), CONTROLLED, EXPLORATORY PHASE 2 TRIAL IN MODERATE TO SEVERE ALZHEIMER'S DISEASE



## 150 Patients with moderate to severe AD (MMSE 4-15)

- **Primary Endpoints:** Safety; change from baseline in Severe Impairment Battery (SIB) at 13 weeks (nine subscales include attention, language, orientation, memory, praxis, visuospatial ability, construction, social skills, orienting head to name)
- **Secondary Endpoints:** SIB at weeks 5 and 9; change from baseline in Alzheimer Disease Cooperative Study Activities of Daily Living Inventory-Severe Impairment Version (ADCS-ADL-SEV); Change from baseline in MMSE-2; change from baseline in Neuropsychiatric Inventory (NPI). Clinical Global Impression of Improvement (CGI-I)
- **Pre-specified exploratory analysis:** memantine vs. non-memantine (background therapy)

# SIB BY VISIT: 30 DAYS POST DOSING IN COMPLETERS (CAS) ON AND OFF MEMANTINE

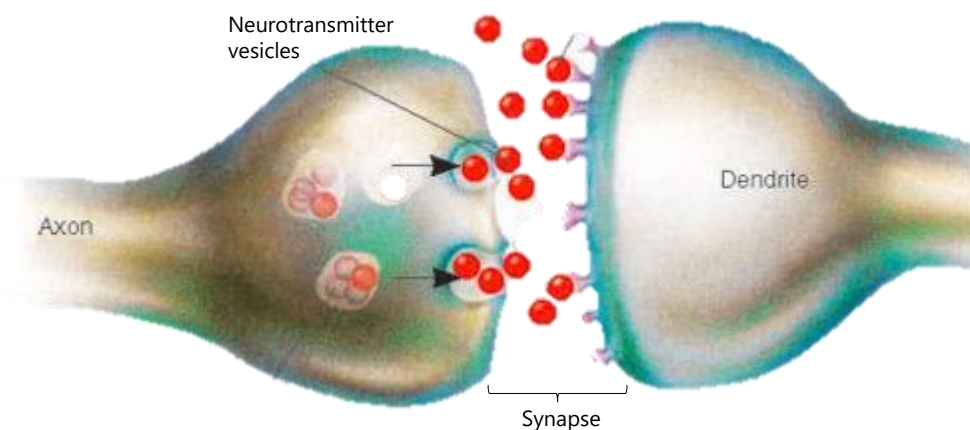


$$\Delta = 8.4$$

Week 15 data show increased treatment effect due to:

- a) improving efficacy signal
- b) sustained decline of control groups

- **Synapses are tiny connectors** that permit a neuron (or nerve cell) to pass an electrical or chemical signal to another neuron. Millions of synapses form networks in the brain.
- When abundant and working correctly, **synapses allow neurons to communicate with each other effectively**. This means our nervous system is performing well and with sharp cognitive functioning (i.e. reasoning, attention, memory, and language).
- **Fewer or defective synapses means less connectivity in the brain**, a weaker nervous system, and ultimately impaired cognition.<sup>1</sup>



**This synaptic loss is the major pathologic correlate of Alzheimer's and other dementias, and has been shown to occur in very early stages of such diseases.<sup>2</sup>**

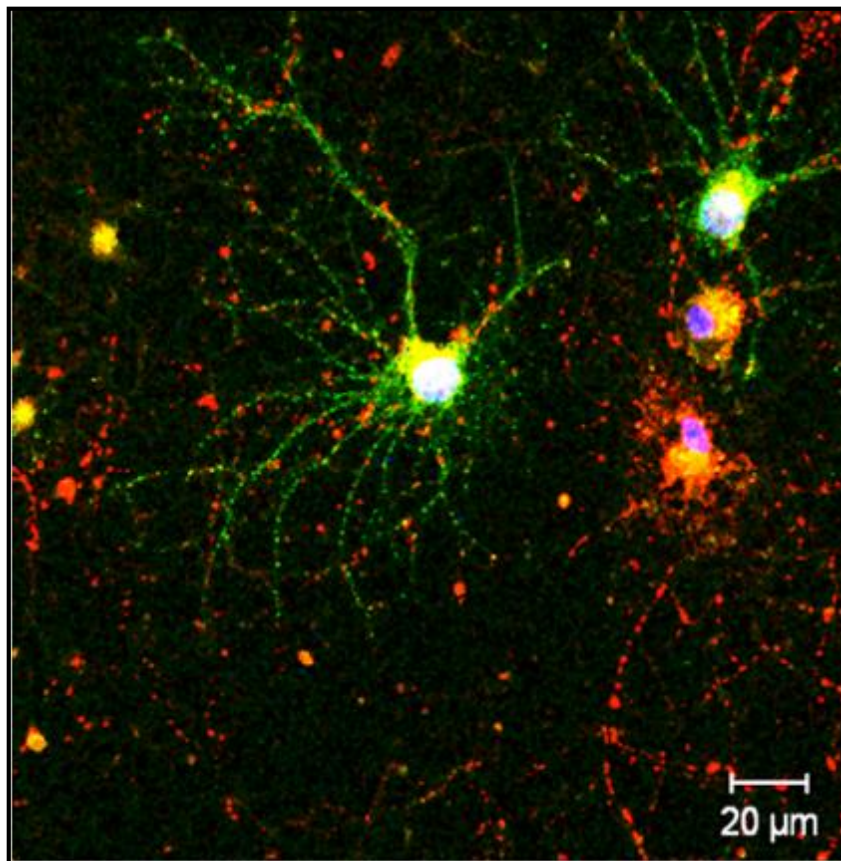
1 Terry RD, Masliah E, Salmon DP, et al. Synapse Loss is the Major Correlate of Cognitive Impairment Ann Neurol. 1991 Oct; 30 (4): 572-80.

2 Scheff SW, Price DA. Alzheimer's disease-related alterations in synaptic density: neocortex and hippocampus. J Alzheimers Dis. 2006;9 (3 Suppl): 101-15.

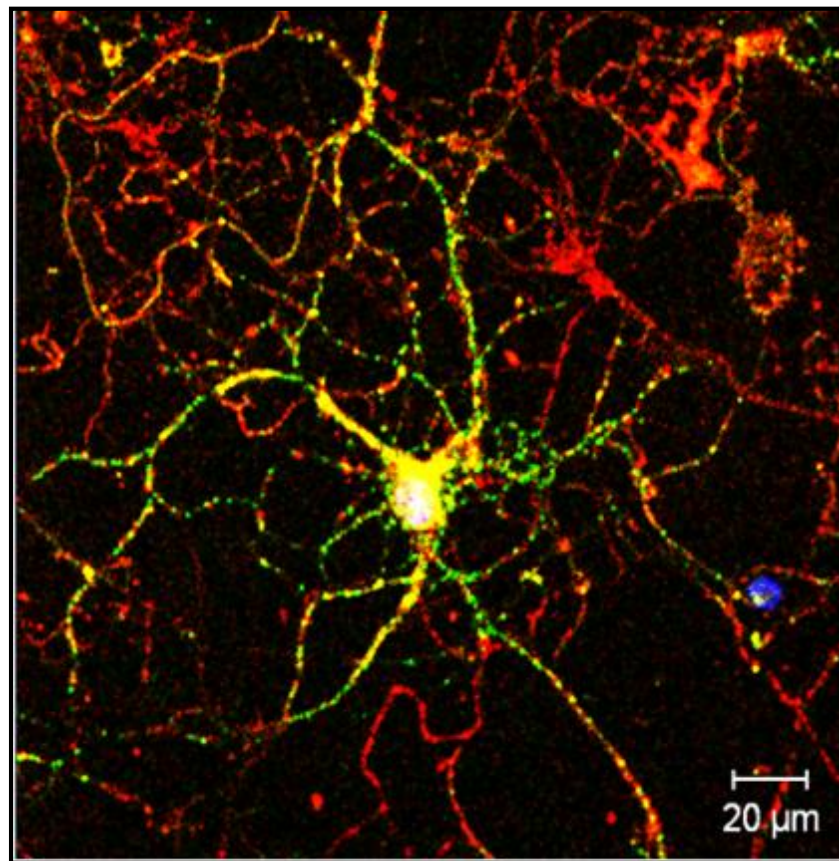
## Confocal microscopic images of hippocampal neuronal networks in rats

- Presynaptic staining (Synaptophysin)
- Postsynaptic staining ( PSD-95)
- Merged

*Synaptic Networks degenerate with A $\beta$  oligomers*



*Bryostatin protects synaptic networks against A $\beta$  oligomers and promotes growth*

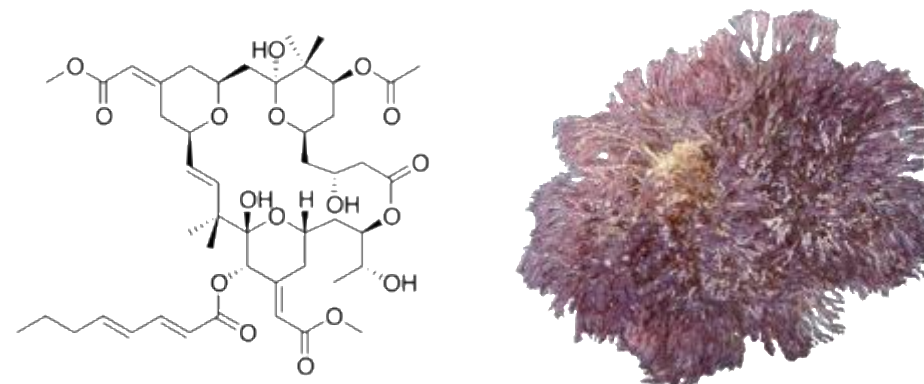


Source: Sen A et al. J Biol Chem. 2012;287(19):15947-15958. Sen A et al. J Biol Chem. 2016; 291(32):16462-16467.

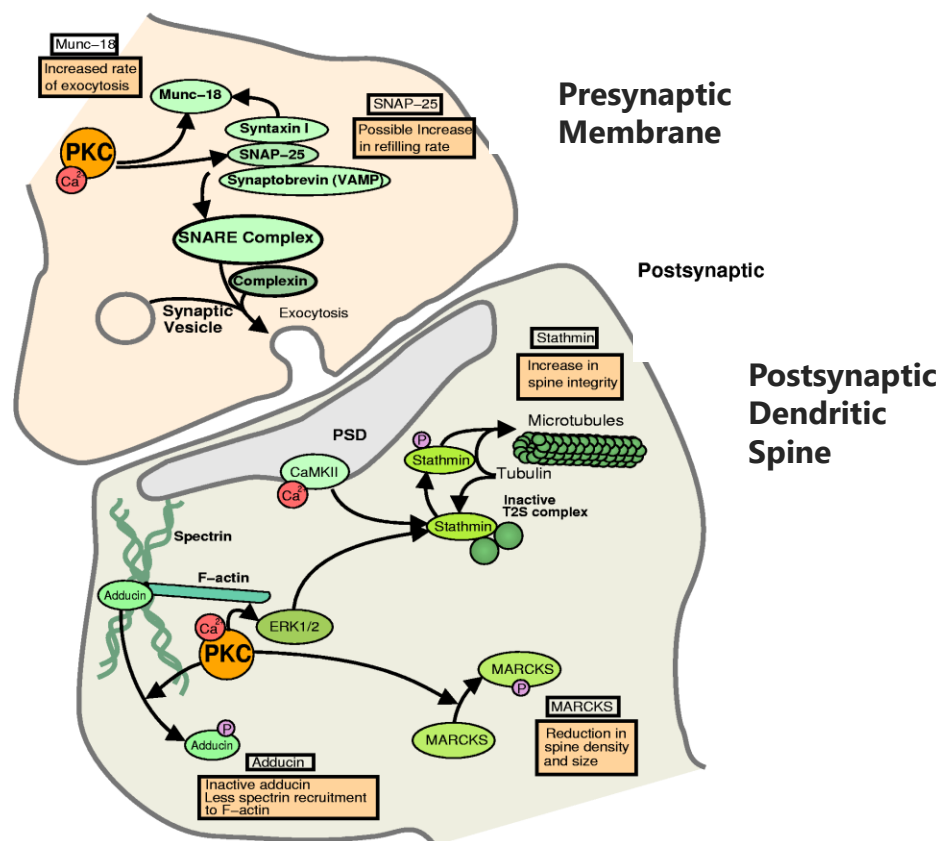


# BRYOSTATIN-1, LEAD COMPOUND AND THE PROTEIN KINASE C (PKC) PATHWAY

- Purified from marine bryozoan *Bugula neritina*
- BBB penetrant, potent activator of PKC $\alpha$ ,  $\epsilon$
- Studied through Ph2 as an anti-tumor agent
- Synthetic replica licensed from Stanford University



## Regulation of Synaptic Function in Memory by Protein Phosphorylation

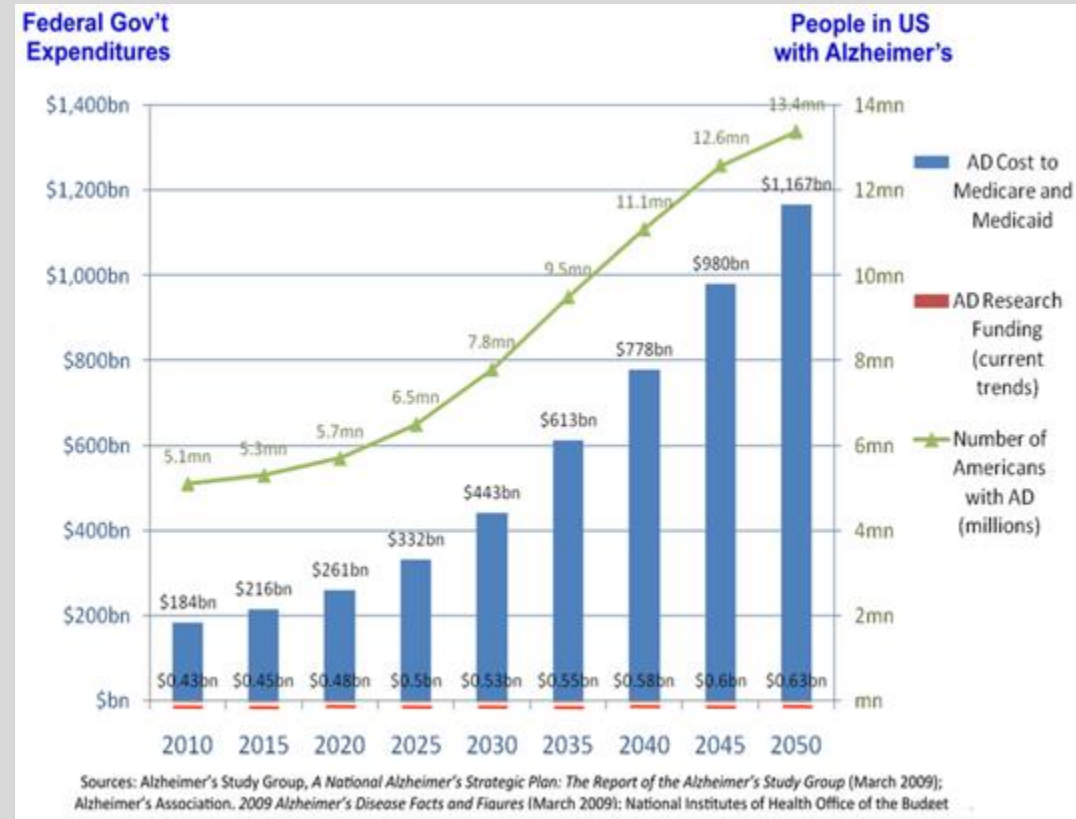


## Multi-modal PKC $\alpha$ , $\epsilon$ pathway: Bryostatin

- Prevents Amyloid Plaques (extra neuronal)
- Prevents Neurofibrillary tangles (intraneuronal)
- Promotes synaptogenesis
- Prevents neuronal death
- Enhances molecular cascades of memory
- Degrades A Beta Oligomers
- Promotes maturation of synapses
- Restores cognitive Function

- **Synaptic loss is a major pathologic correlate of neurodegenerative disease and cause of cognitive dysfunction**
- **Bryostatin has been found to restore synaptic loss and prevent neuronal death**
- **Bryostatin protects synapses against toxic A $\beta$  oligomers**
- **Initial Phase 2 clinical trial demonstrated increased cognitive function in advanced Alzheimer's patients**

- Number of patients with Alzheimer's disease (AD) is predicted to increase exponentially during the next few decades<sup>1</sup>
- Current therapies for AD are based on two main strategies that offer very limited benefit
  - Cholinergic treatments (Donepezil, Galantamine)
  - Antiglutamatergic treatment (Memantine)
  - Despite limited efficacy, these current therapies have achieved blockbuster status (>\$1B in sales)
- Single targeted therapies to date do not treat the underlying disease or its pathogenesis



1. Selkoe, D.J. Preventing Alzheimer's disease. Science 2012, 337, 1488–1492.



**Dr. Charles Ryan**

Chief Executive Officer & Board Director  
Extensive experience in the Pharmaceutical industry



**Dr. Daniel Alkon**

President and Chief Scientific Officer  
Leading authority on Molecular Memory Mechanisms,  
and Bryostatin



**Dr. Michael Ciraolo**

Chief Operating Officer and General counsel  
Former Executive at Ovid and Forest Laboratories, Inc



**Elaine Grenier**

Executive Director, Clinical Operations  
She has more than 25 years of experience in the  
pharmaceutical industry



**Dr. Alan Tuchman**

Acting Chief Medical Officer  
Clinical Professor of Neurology at NY Medical College



**Dr. Martin Farlow**

Professor Emeritus, Department of Neurology  
Co-Director of the Alzheimer's Disease Center  
Indiana University



**Dr. Marwan Sabbagh**

Director of the Cleveland Clinic Lou Ruvo Center for  
Brain Health



**Dr. Paul Coleman**

Associate at the (UA) McKnight Brain Institute  
Professor at UA BioDesign Institute



**Dr. Daniel Hanley**

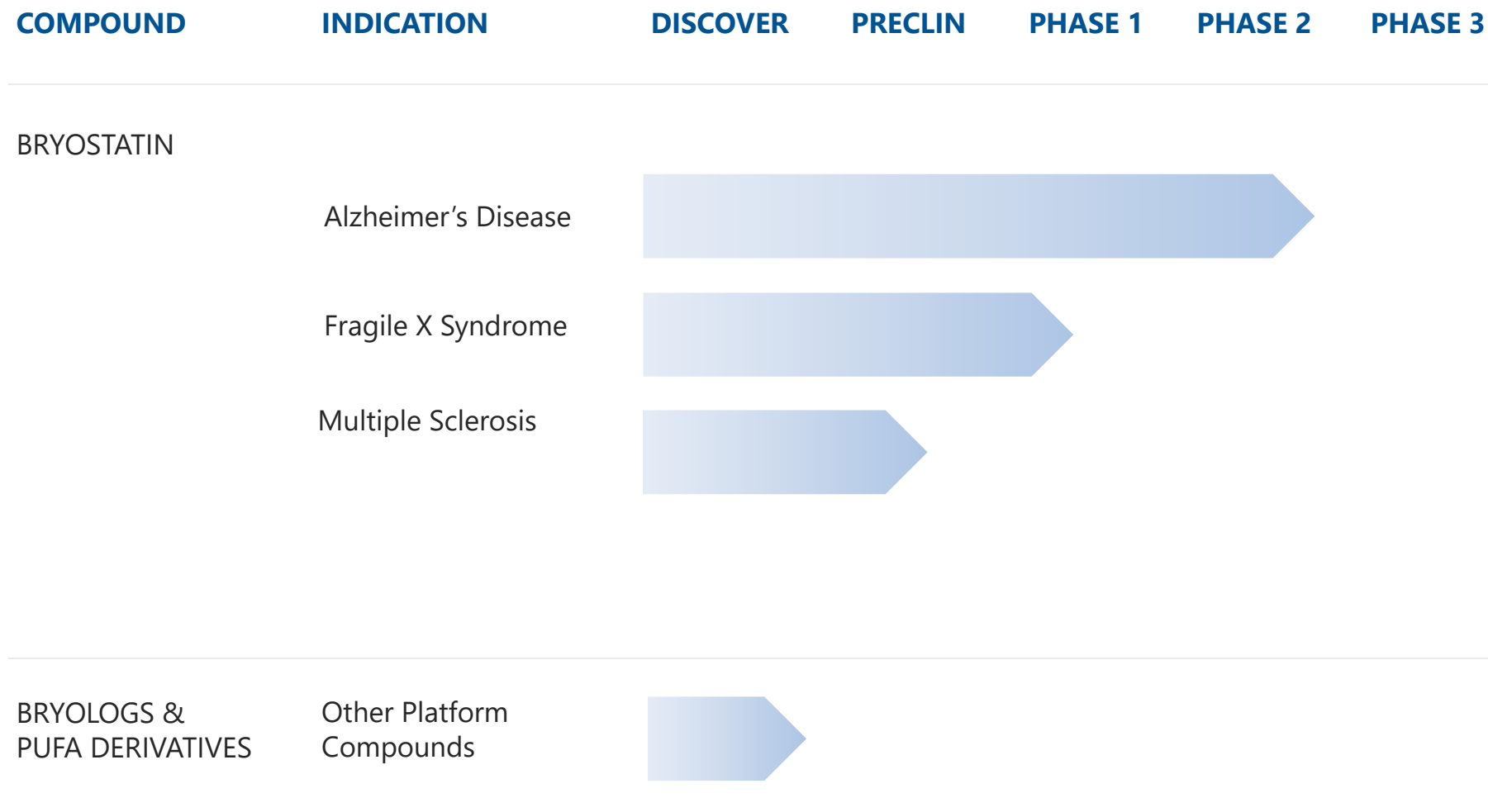
Professor of Neurology & Director of the  
Neurosurgery and Anesthesia/Critical Care Medicine  
Johns Hopkins University



**Dr. Lee-Jen Wei**

Professor of Biostatistics  
Harvard University

# A PLATFORM APPROACH - NEURORESTORATION IN ALZHEIMER'S AND MULTIPLE NEURODEGENERATIVE DISORDERS



Neurotrope	
Ticker Symbol: (Nasdaq)	NTRP
Share Price (05/30/19)	\$7.20
Common Stock outstanding	12.9 million
Market Capitalization	\$93 million
Warrants and options outstanding: Warrants outstanding – Weighted average price = \$9.72 Options outstanding – Weighted average price = \$18.07	10.2 million 1.5 million
Q3 2018 Cash Balance plus Dec. 2018 net capital raise	\$30 million



- **Targeting Diseases with High Unmet Medical Needs and Large Potential Markets: Alzheimer's Disease and Other Central Nervous System Disorders**
- **Compelling Data For Lead Product Candidate: Prior Phase 2 Results for Bryostatin Demonstrated Increased Cognitive Function in Advanced Alzheimer's Patients**
- **Validated Mechanism of Action: Bryostatin Has Been Found To Prevent Neuronal Death by Restoring Synaptic Loss, a Major Correlate of Neurodegenerative Disease and Cognitive Dysfunction**
- **Key Catalyst Approaching: Additional Phase 2 Trial Results for Bryostatin Anticipated Mid-2019**
- **Resources to Drive Value: Approximately \$30M in Cash and Equivalents, Highly Experienced Leadership Team, World Class Scientific Advisors**

## FOR MORE INFORMATION



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