ANNOVIS

- People Focused, Purpose Driven, Passion Powered -

Attacks Neurodegeneration, Alzheimer's and Parkinson's Diseases by Improving the Information Highway of the Nerve Cell

Symbol: ANVS (NYSE)

February 2024

FORWARD-LOOKING STATEMENTS

Forward Looking Statements and Other Important Cautions -- This presentation contains forward-looking statements within the meaning of the Private Securities Litigation Reform Act of 1995. These forward-looking statements relate to all information other than historical matters, such as expectations or forecasts of future events. Forward-looking statements may be identified by the use of words such as "forecast," "intend," "seek," "target," "anticipate," "believe," "expect," "estimate," "plan," "outlook," and "project" and other similar expressions that predict or indicate future events or trends or that are not statements of historical matters. Forward-looking statements with respect to the operations, strategies, prospects and other aspects of the business of Annovis Bio are based on current expectations that are subject to known and unknown risks and uncertainties, which could cause actual results or outcomes to differ materially from expectations expressed or implied by such forward-looking statements. These risks and uncertainties include but are not limited to: that clinical trials may be delayed; that the data reported herein is from a Phase 2a study and subsequent clinical trials are being conducted; and that any anticipated results from clinical trials may be delayed. These and other risks and uncertainties are described more fully in the section titled "Risk Factors" in Annovis Bio's Annual Report on Form 10-K for the year ended December 31, 2022, and other periodic reports filed with the Securities and Exchange Commission. You are cautioned not to place undue reliance upon any forward-looking statements, which speak only as of the date made. Although it may voluntarily do so, from time to time, Annovis Bio undertakes no commitment to update or revise the forward-looking statements contained in this presentation, whether as a result of new information, future events or otherwise, except as required under applicable law.

COMPANY HIGHLIGHTS

Therapeutic focus/approach: treatment of Alzheimer's disease (AD) and Parkinson's disease (PD) as neurodegenerative, axonal transport diseases

Buntanetap (lead asset): only drug to improve cognition in AD ***AND*** motor function in PD patients

Unique MoA: restores health of nerve cells and improves function by inhibiting production of multiple neurotoxic proteins associated with AD/PD

Late-stage opportunities: Phase 3 trial in early PD patients and Phase 2/3 trial in moderate AD will read out in first half of 2024

INVESTMENT HIGHLIGHTS

Targeting growing indications

- Parkinson's Disease – 1.2 million patients in US
- Alzheimer's Disease – 6 million patients in US

Long Duration IP Estate
IP extends well into 2040's

- Buntanetap – Multiple Chronic neurodegenerative diseases
- ANVS405 – Multiple acute brain and nerve injuries

Multiple Catalysts

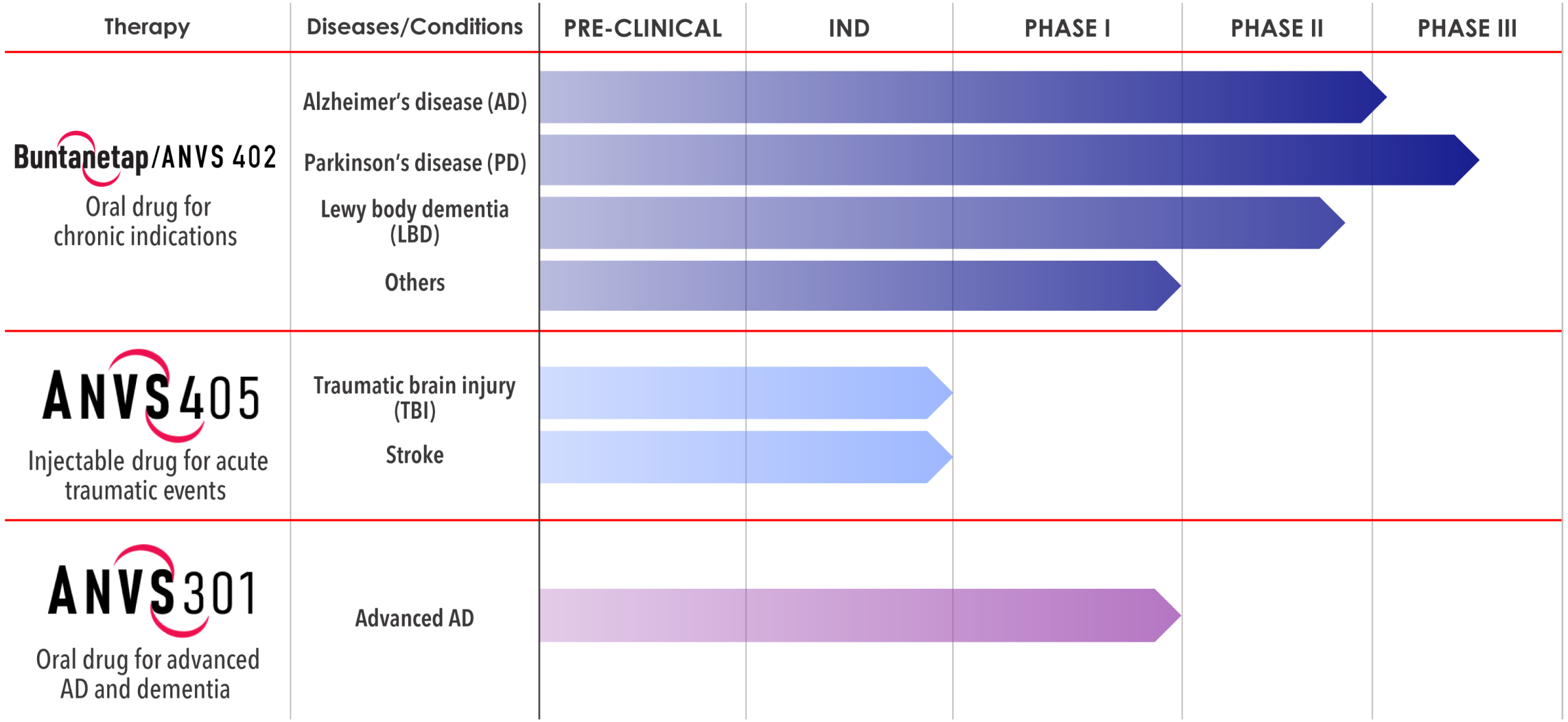
Key clinical and regulatory milestones

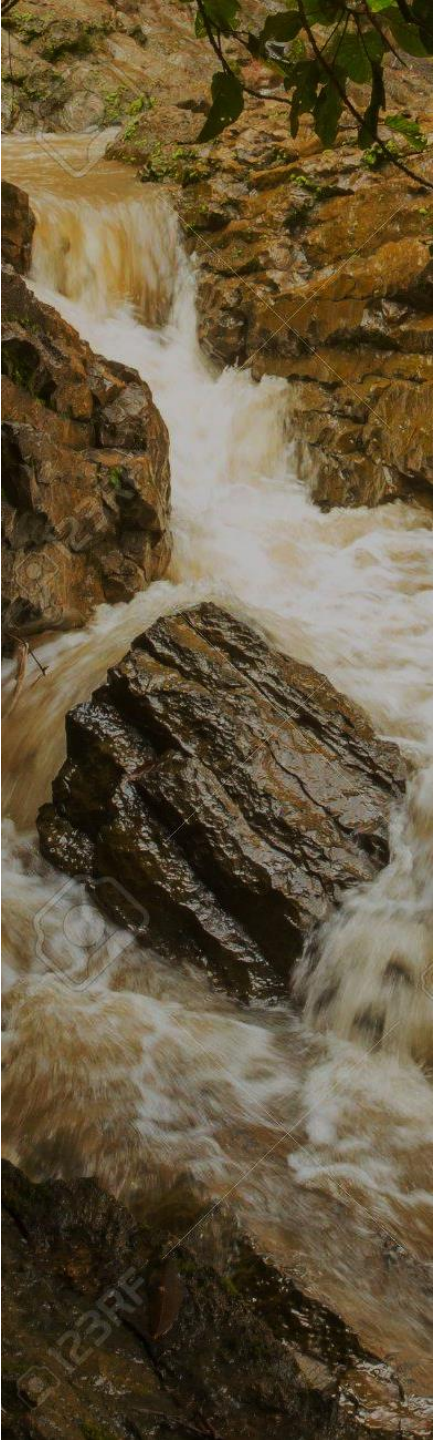
- PD – phase 3, blinded, interim analysis received
- AD – first patient dosed in phase 2/3 trial Feb. 2023

Capital-efficient approach

- On 9/30/23
  Cash balance $ 6.4 mil.
  Debt $ 0
- November 2023
  Raised $10 mil.

PIPELINE


Therapy
Diseases/Conditions
PRE-CLINICAL
IND
PHASE I
PHASE II
PHASE III
Buntanetap/ANVS 402
Oral drug for chronic indications
Alzheimer's disease (AD)
Parkinson's disease (PD)
Lewy body dementia (LBD)
Others
ANVS405
Injectable drug for acute traumatic events
Traumatic brain injury (TBI)
Stroke
ANVS301
Oral drug for advanced AD and dementia
Advanced AD



NEUROTOXIC PROTEINS IMPAIR AXONAL TRANSPORT AND **CAUSE A TOXIC CASCADE**

HIGH LEVELS OF NEUROTOXIC PROTEINS

IMPAIRED AXONAL TRANSPORT

SLOWER SYNAPTIC TRANSMISSION

INFLAMMATION

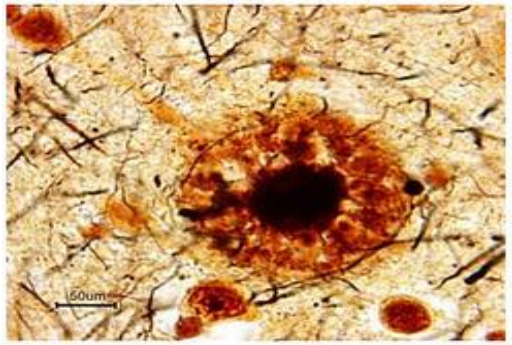
DEATH OF NERVE CELLS

LOSS OF COGNITIVE AND MOTOR FUNCTION

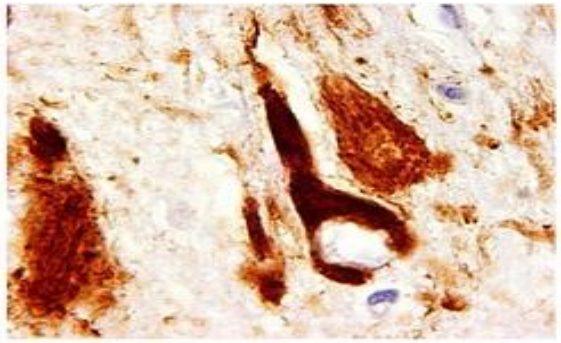
ANNOVIS' NEW APPROACH TO ATTACK AD AND PD

Chronic and acute brain insults lead to high iron levels, resulting in overexpression of neurotoxic proteins, impaired axonal transport, inflammation and neurodegeneration

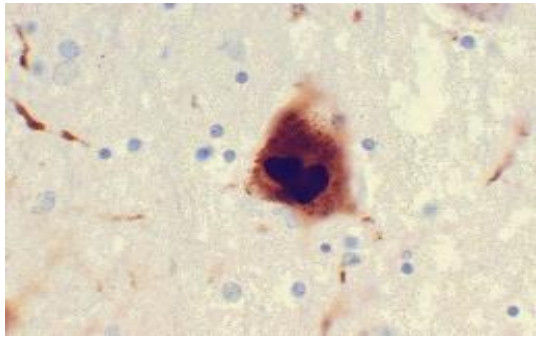
Amyloid β
Alzheimer's - Parkinson's



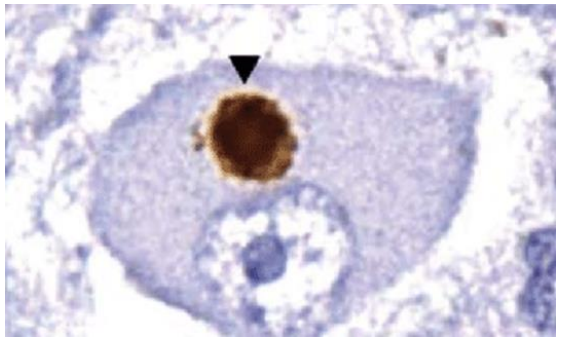
Tau
Tauopathies - AD, PD, FTD, CTE



αSynuclein
Parkinson's - Alzheimer's



TDP43
ALS, AD, PD, FTD, CTE



Attacking one neurotoxic protein results in minimal effect

Buntanetap inhibits the production of multiple neurotoxic proteins simultaneously

NEURODEGENERATION IS AN AXONAL TRANSPORT DISEASE

"Axonal transport disruption is linked to human neurological conditions."

- Nature Review, September 2019

Axonal transport is responsible for:

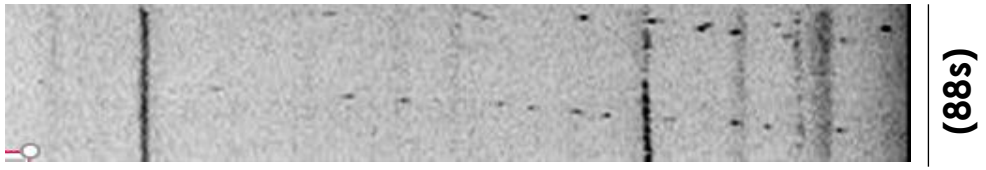
- Neurotransmitters GABA (anxiety), ACh (cognition), dopamine (movement), serotonin (mood)
- Neurotrophic factors NGF, BDNF
- All communication within and between nerve cells

Chen XQ et al. *Alzheimer's & Dementia; 08-2020*

Retrograde (0.5 frame/sec)

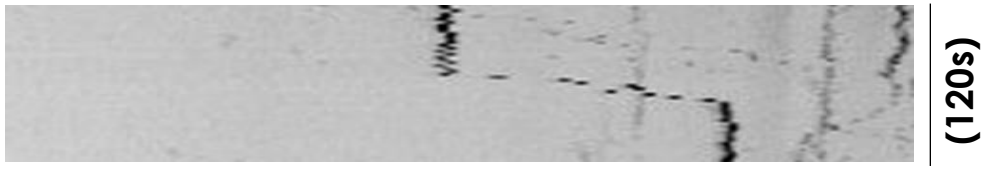
Normal Transport

The ***Normal Flow and Speed*** of vesicles carrying BDNF across the axon.



Abnormal Transport

Shows the ***Blockage and Slowing*** of BDNF across the axon. Black areas demonstrate where transport is slowed due to high levels of neurotoxic proteins.



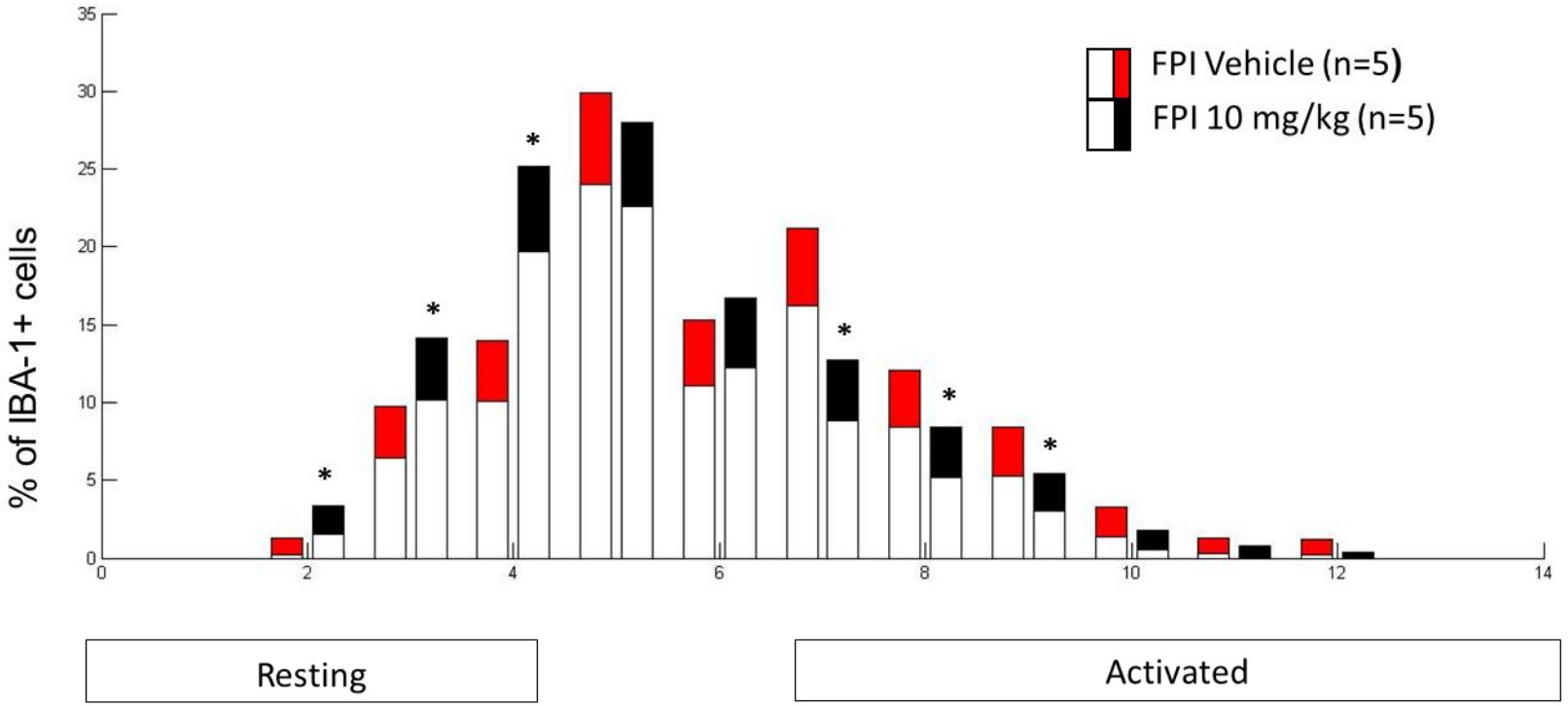
TREATED WITH BUNTANETAP

The ***Flow and Speed*** of axonal transport is improved.

APP, Ab42, C99 – Mobley, UCSD; aSYN – Isacson, Harvard; Lee, U.Penn;
Tau – U. Muenich & Zuerich; Htt – Mobley, UCSD; TDP43 – Taylor, Northwestern

INHIBITS MICROGLIA ACTIVATION IN RAT BRAIN

Data (Mean + 95% CI) analyzed with Bootstrapping method, *p<0.05



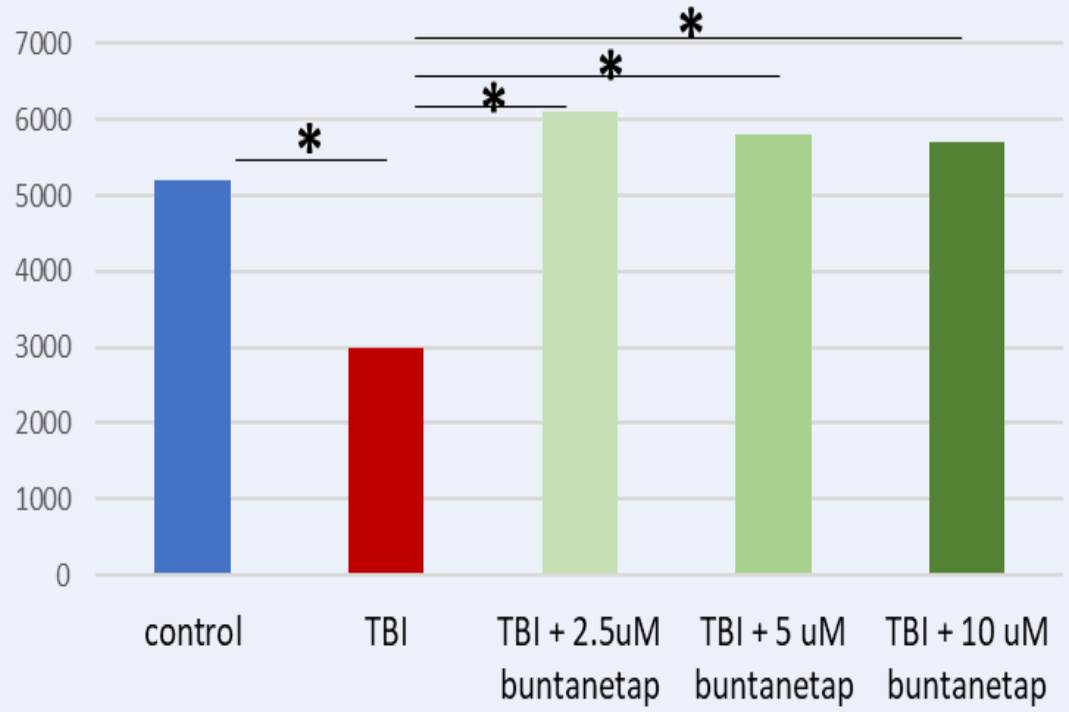
Microglial Cell Diameter (µm)

ANVS401 increases the number of resting microglia and reduces the number of activated microglia – it reduces inflammation

* $p < 0.05$

UCLA, Marie-Francoise Chesselet and David Hovda's lab

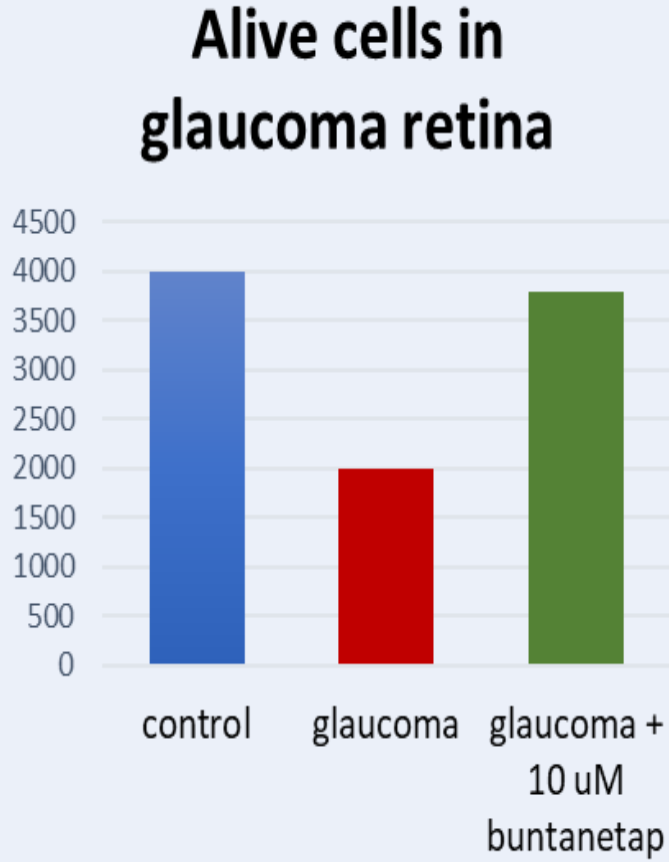
NEURODEGENERATION MEANS **DEAD NERVE CELLS**



Buntanetap protects nerve cells from dying in the brain of traumatic brain injury rats

* $p < 0.05$

Hatami A. et al: Buntanetap improves dopaminergic neuropathology and working memory in a rat model of traumatic brain injury; in preparation -UCLA



And it protects nerve cells from dying in the eye in glaucoma rats

Sundstrom J. et al. Hershey Medical Center

BUNTANETAP IMPROVES AXONAL TRANSPORT AND **IMPEDES THE TOXIC CASCADE**

BY LOWERING LEVELS OF NEUROTOXIC PROTEINS

IMPROVED AXONAL TRANSPORT

INCREASED SYNAPTIC TRANSMISSION

LOWER INFLAMMATION

HEALTHY NERVE CELLS

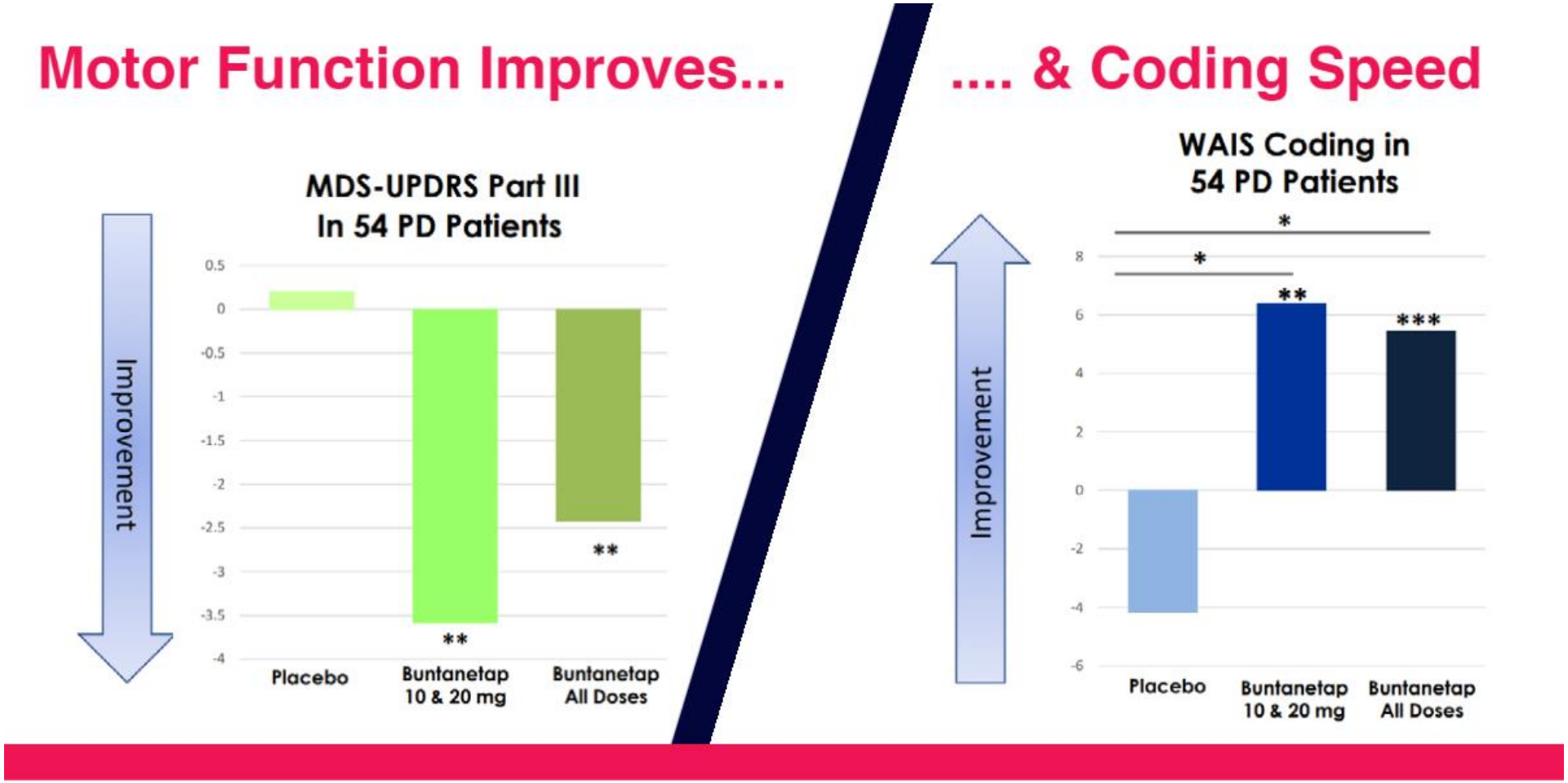
IMPROVED COGNITIVE AND MOTOR FUNCTION

STUDIES IN EIGHT ANIMAL AND HUMAN MODELS

FUNCTION	TEST	ANIMAL MODEL
Memory & learning - 4 models	Mazes	APP/PS1 Alzheimer mice Trisomic Down Syndrome mice Stroke mice Traumatic brain injury rats
Movement – 2 models	Colonic motility, grip strength	Alpha-synuclein Parkinson's mice Tau frontotemporal dementia mice
Vision	Sight	Glaucoma rats
Infections	Cell death	P. Gingivalis mice Covid mice

BUNTANETAP PHASE 2 POSITIVE DATA IN PARKINSON'S DISEASE

SIGNIFICANT IMPROVEMENTS IN BOTH MOTOR FUNCTION AND CODING SPEED



* p < 0.05
** p < 0.01
*** p < 0.001

Fang et al: Buntanetap Proves Promising in Both Alzheimer's and Parkinson's Patients; J Prevention Alzheimer Disease 10-2022

FULLY ENROLLED PHASE 3 CLINICAL TRIAL IN **EARLY PD PATIENTS**

Therapeutic Area	Early PD
Phase	3
Sites	43 US + 24 EU = 67
Patients	3 X 174 = 523 = 471
Dose	placebo, 10 and 20 mg/day
Start/End	August 2022/December 2023
Design	Double-Blind, Placebo-Controlled Efficacy
Endpoints	MDS-UPDRS 2
Other	Total MDS-UPDRS 3 and total, PGIC, CGIS, WAIS, Biomarkers

NCT04524351 at ClinicalTrials.gov.

PD INTERIM EFFICACY AND SAFETY ANALYSIS
30% OF PATIENTS AT 2 MONTHS

Interim analysis for the two primary endpoints:

MDS-UPDRS 2 + 3 → **Promising**

Interim analysis for safety by DSMB

no drug-related SAEs
each AE: < 2%
very low dropout rate: 6%
enrolled well ahead of timeline: 9 months for 523 patients

→ **Well-tolerated**

Continue as planned

DEVELOPMENT OF BUNTANETAP FOR **EARLY AND ADVANCED PD**

Interim Analysis

Symptomatic Studies

Early PD Patients – 6 m

Naïve PD Patients – 6 m

Advanced PD Patients – 6 m

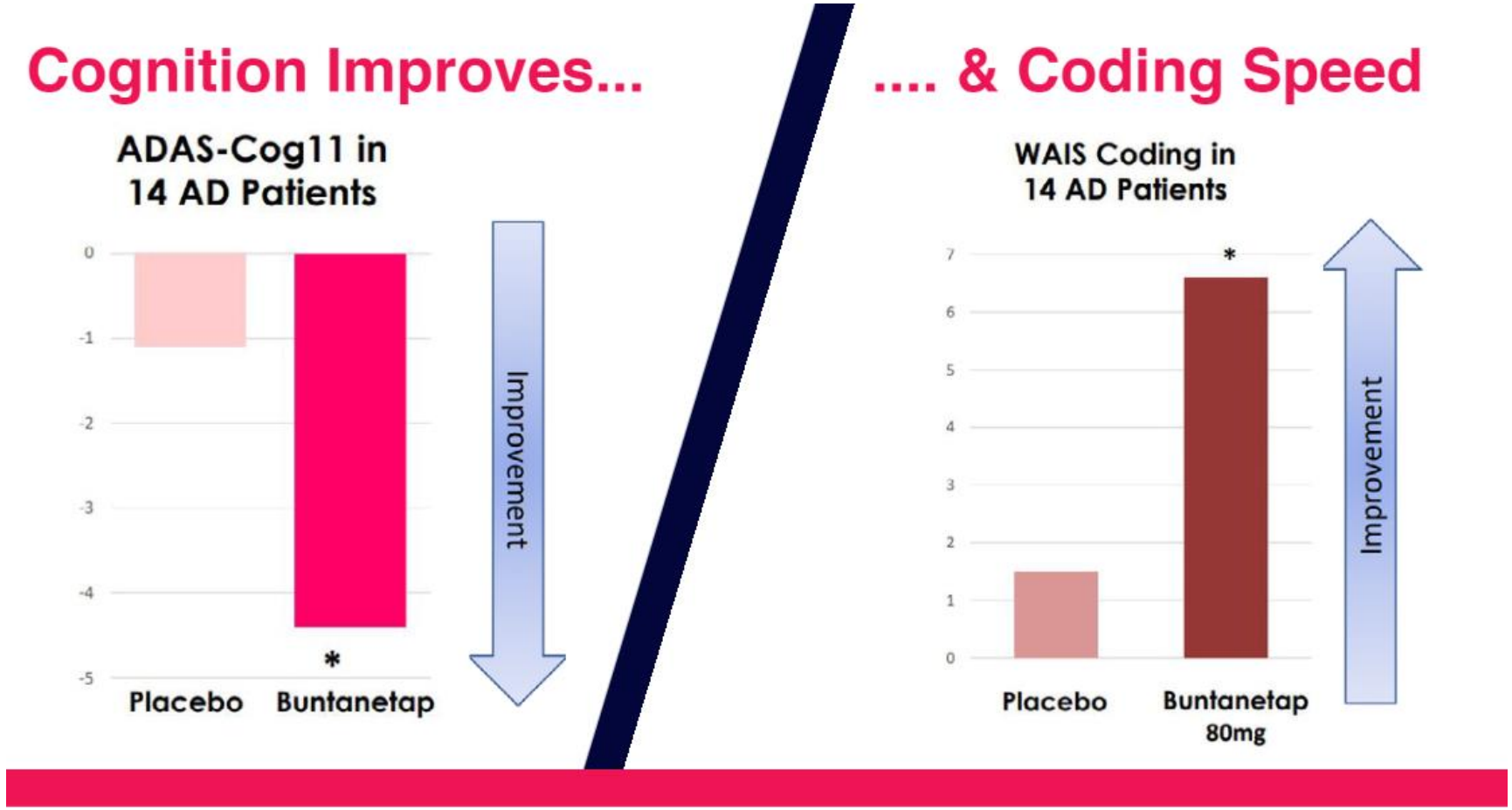
Disease-modifying Study

Long chronic study in early PD - 18 m

Open Label Study for all treated PD Patients

BUNTANETAP PHASE 2 POSITIVE DATA IN ALZHEIMER'S DISEASE

SIGNIFICANT IMPROVEMENTS IN BOTH COGNITIVE FUNCTION AND CODING SPEED

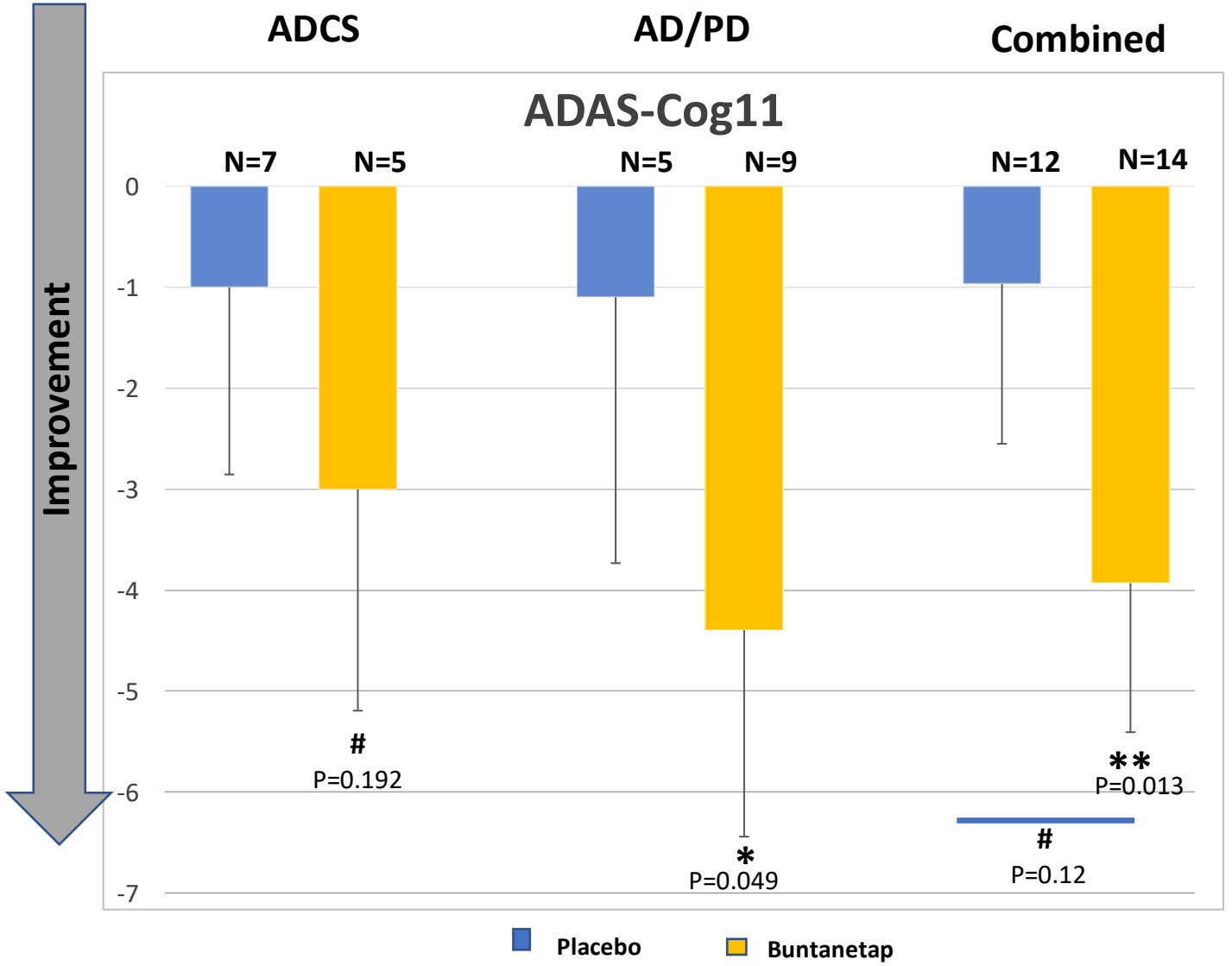


* $p < 0.05$

Fang et al: Buntanetap Proves Promising in Both Alzheimer's and Parkinson's Patients; J Prevention Alzheimer Disease 10-2022

ADCS EFFICACY AND COMBINATION

ADAS-Cog IN TWO SMALL STUDIES – ADCS AND AD/PD



Buntanetap shows improvement of -3 and -4.4 points from baseline and of -2.9 points from placebo in two small exploratory studies in ADAScog 11 after one month of treatment. The data is either statistically significant or shows a strong trend

strong trend
* P = 0.05
** p = 0.01

ONGOING PHASE 2/3 CLINICAL TRIAL IN **AD PATIENTS**

Therapeutic Area	Moderate AD
Phase	2/3
Sites	64 US
Patients	4 X 88 = 353
Dose	placebo, 7.5, 15 and 30 mg/day
Start/End	February 2023/February 2024
Design	Double-Blind, Placebo-Controlled Efficacy
Endpoints	ADAScog 11, ADCS-CGIC
Other	WAIS, Biomarkers

AD INTERIM EFFICACY AND SAFETY ANALYSIS 30% OF PATIENTS AT 6 WEEKS

Interim analysis for the two co-primary endpoints:

ADAScog 11, ADCS-CGIC → **Promising**

Interim analysis for safety by DSMB

no drug-related SAEs
each AE: < 5%
very low dropout rate: 4.7%
enrolled as planned: 9 months for 353 patients

→ **Well-tolerated**

Continue as planned

DEVELOPMENT OF BUNTANETAP
FOR EARLY AND ADVANCED AD

Interim Analysis

Symptomatic Study

Moderate AD – 3 m

Disease-modifying Study

Long chronic study in early AD – 18 m

Basket study for advanced disease 1 month

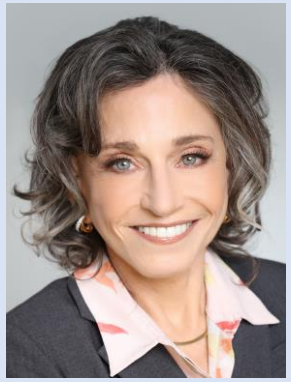
Advanced AD – 6 m

Open label study for all AD patients

CORPORATE PATENT ESTATE

Patent/Application	Subject Matter	Status	Expiry
Provisional	Novel composition of matter for ANVS402	Pending	**2044**
Provisional	3 Combination Applications	Pending	**2044/5**
PCT	Neuropsychiatric Indications	Pending	**2044**
PCT	Other Diseases	Pending	**2043**
PCT	Brain infections	Pending	**2042**
PCT	Use of mechanism of action	One patent granted	**2038**
PCT	Acute neurodegenerative injuries	Multiple patents granted	**2036**
PCT	Chronic neurodegenerative diseases	Multiple patents granted	**2031**

SENIOR MANAGEMENT TEAM



Maria Maccecchini, PhD
Founder, President & CEO

Andrew Walsh
VP, Finance

Michael Christie
VP, Process Chemistry

Eve Damiano, MS, RAC
SVP, Regulatory

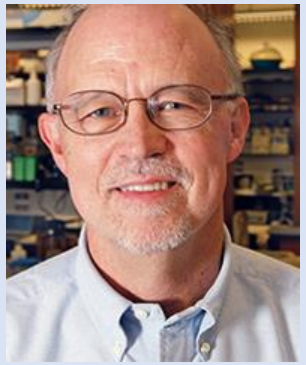
Henry Hagopian, MBA
Chief Financial Officer

Cheng Fang, PhD
SVP, R & D

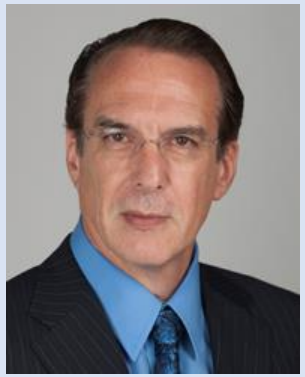
Melissa Gaines,
VP, Clinical Operations

David Prohaska
VP, Tox & Pharmocol

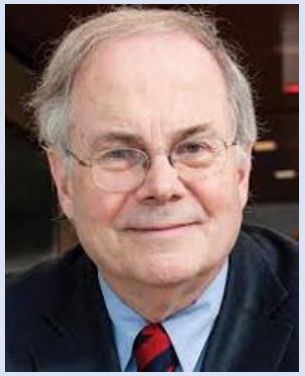
SCIENTIFIC ADVISORY BOARD



Sidney Strickland, PhD, Chairman
Vice President and Dean for Educational Affairs and Research Professor, Patricia and John Rosenwald Laboratory of Neurobiology and Genetics at Rockefeller University. Dr. Strickland's laboratory investigates how dysfunction of the circulatory system contributes to Alzheimer's and other neurodegenerative disorders. He will serve as the Chairman of Annovis Bio's SAB.



Jeffrey Cummings, MD
Dr. Cummings completed Neurology residency and a Fellowship in Behavioral Neurology at Boston University, Massachusetts. US training was followed by a Research Fellowship in Neuropathology and Neuropsychiatry at the National Hospital for Nervous Diseases, London, England. Dr. Cummings was formerly Professor of Neurology and Psychiatry, Director of Alzheimer's Disease Research and Director of the Center for Neurotherapeutics at UCLA. He was Director of the Cleveland Clinic Lou Ruvo Center for Brain Health in Las Vegas, Cleveland and Florida.



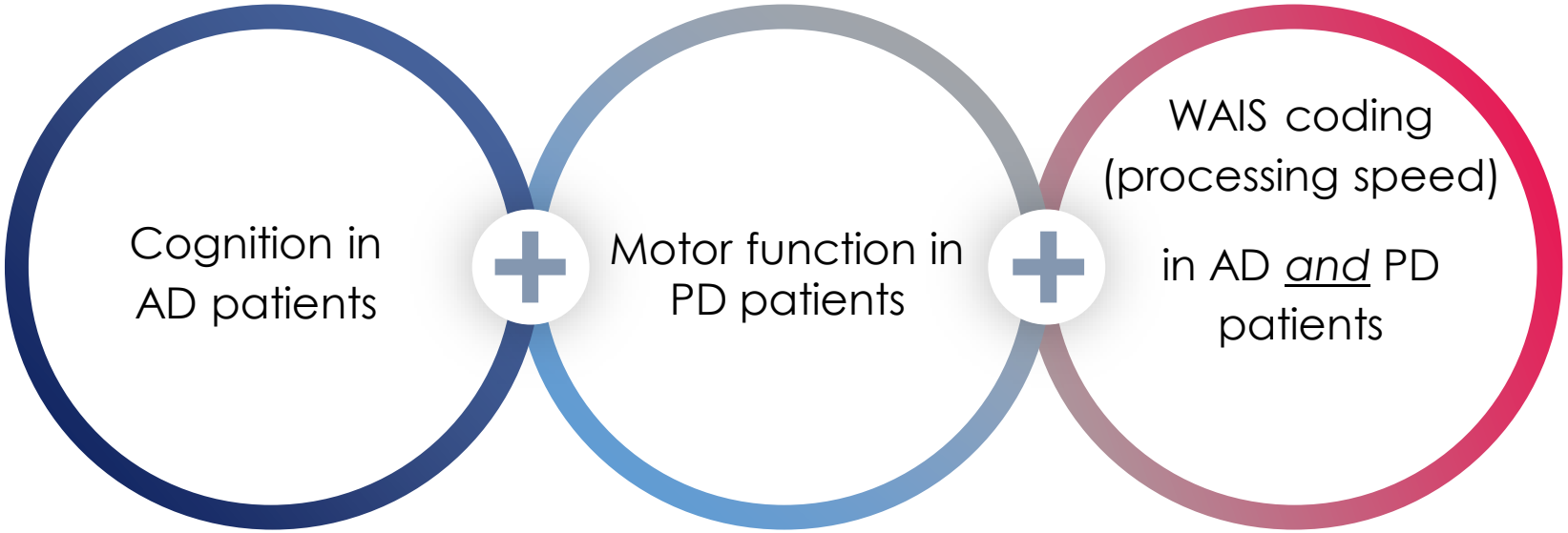
Gregory Petsko, PhD
Dr. Petsko is a member of the National Academy of Sciences, the National Academy of Medicine, the American Academy of Arts and Sciences and the American Philosophical Society. His research interests are directed towards understanding the biochemical bases of neurological diseases like Alzheimer's, Parkinson's, and ALS discovering treatments (especially by using structure-based drug design), that could therapeutically affect those biochemical targets, and seeing any resulting drug candidates tested in humans. He has also made key contributions to the field of protein crystallography.

KEY TAKEAWAYS

Annovis has a novel approach to address **AD *and* PD**

The first double-blind, placebo-controlled study that shows improvements in **AD** patients as measured by **ADAS-Cog** *and* in **PD** patients as measured by **UPDRS**

Buntanetap shows improvements in **Phase 2a** clinical trials:



We started our phase 3 study for early PD, and our phase 2/3 in moderate AD

ANNOVIS

Improves **THE FLOW** of Axonal Transport in Alzheimer's Disease and Neurodegeneration

Symbol: **ANVS** (NYSE)

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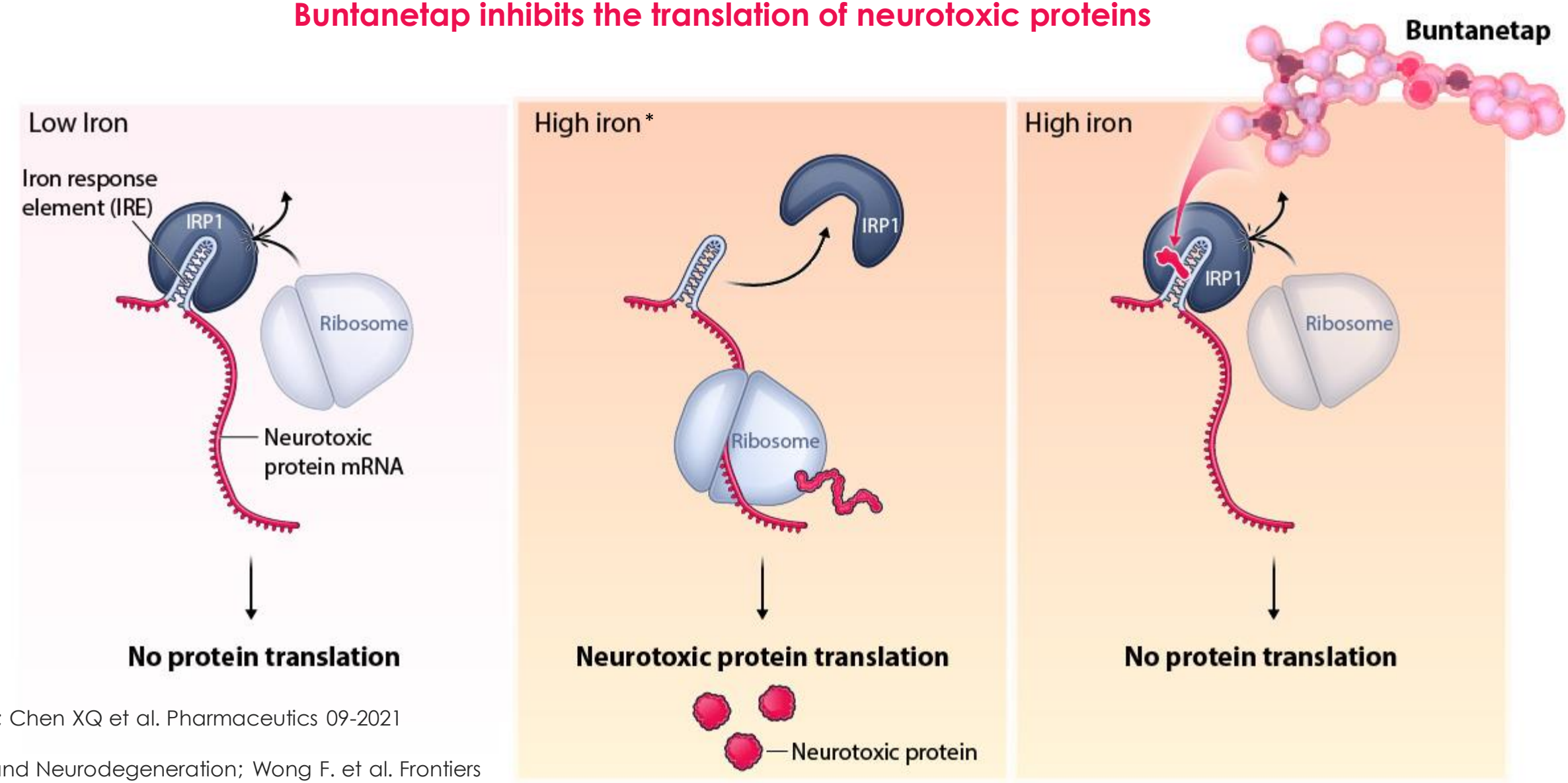
Appendix

MECHANISM OF ACTION

Buntanetap inhibits the translation of neurotoxic proteins

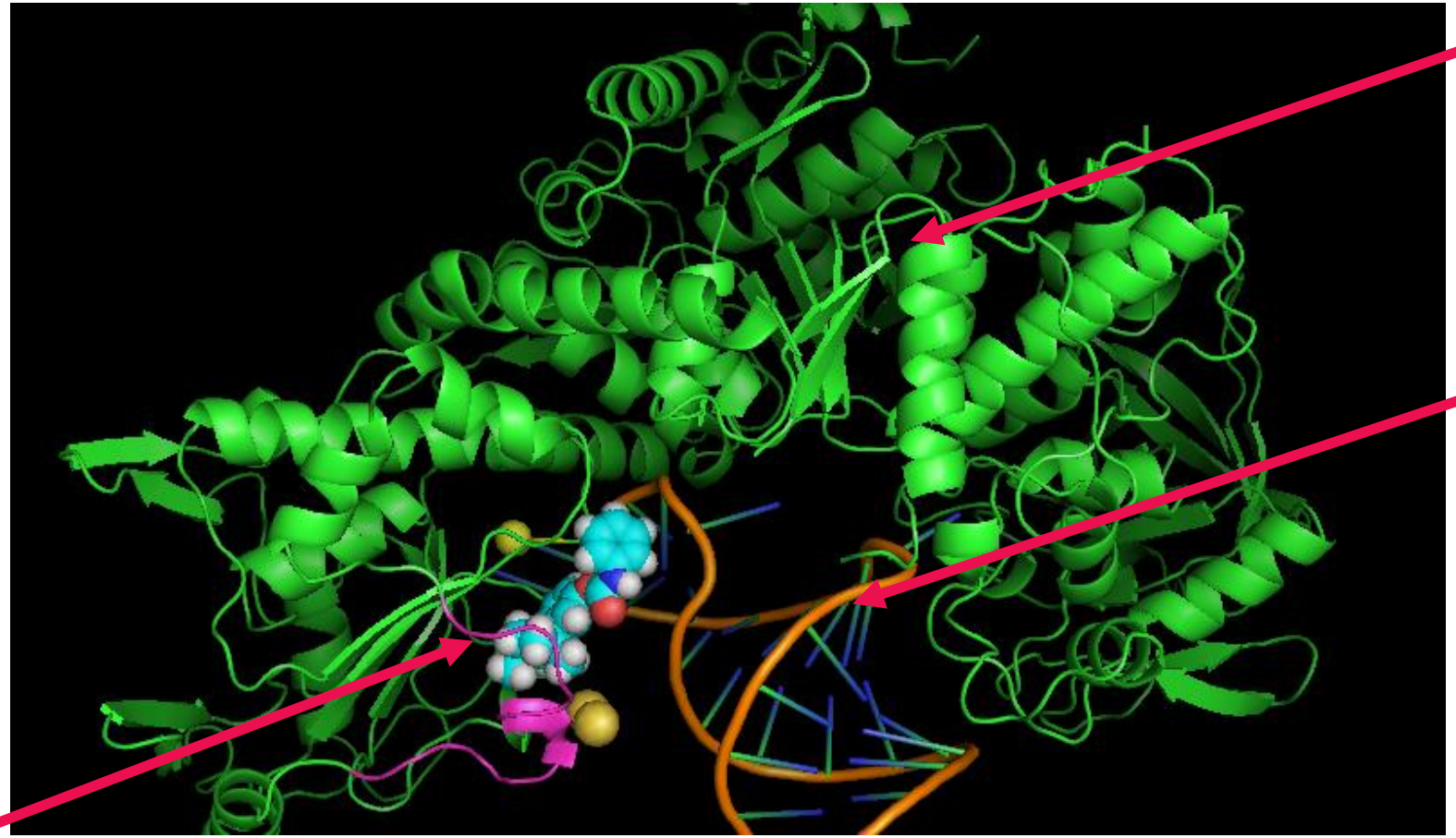


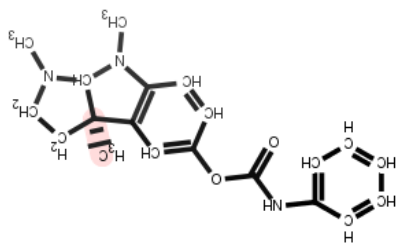
MOA; Chen XQ et al. Pharmaceutics 09-2021

Iron and Neurodegeneration; Wong F. et al. Frontiers Aging Neuroscience; 03-2022

MECHANISM OF ACTION

Molecular Model of how Buntanetap locks IRP1 in the mRNA Binding Position

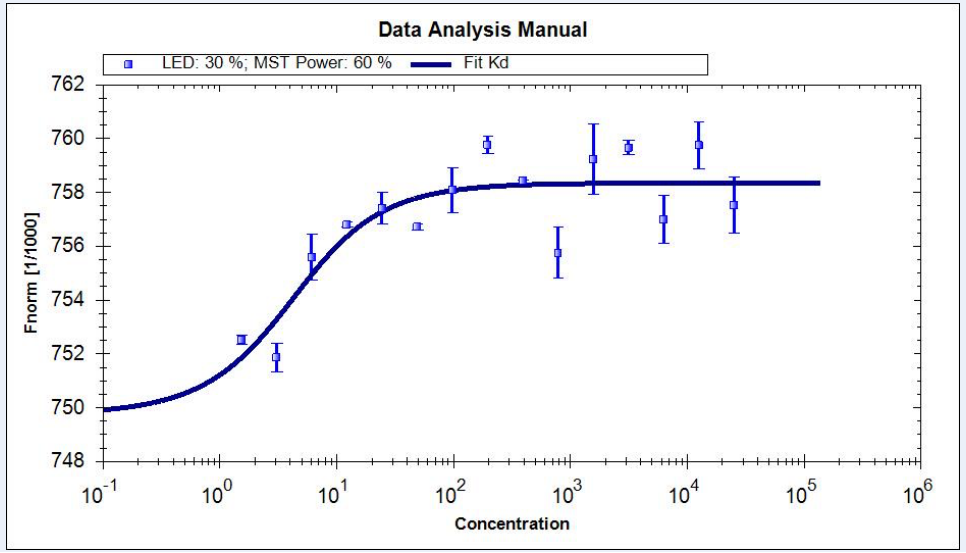




Buntanetap

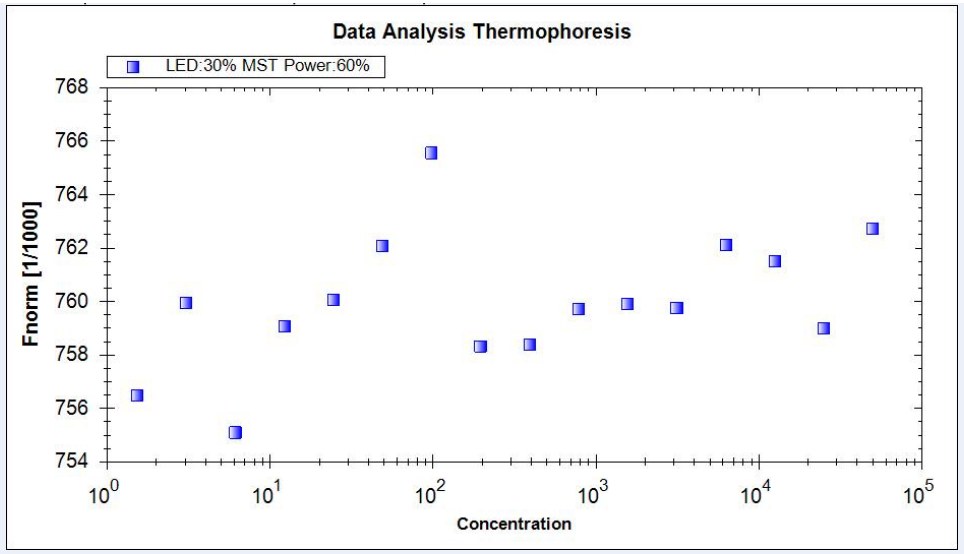
Eric Baldwin, NCI

IRE to IRP1 BINDING IS **SPECIFIC FOR** mRNAs CODING FOR **NEUROTOXIC PROTEINS**



APP IRE/IRP1/Buntanetap
Kd 3.2 nM

Fitting for Kd Formular	Fitted Value
Fitted Parameter	
Dissociation Constant	3.22+/-0.464
Fluo.Conc	2
Bound	758.35
Unbound	749.76
Amplitude	8.59

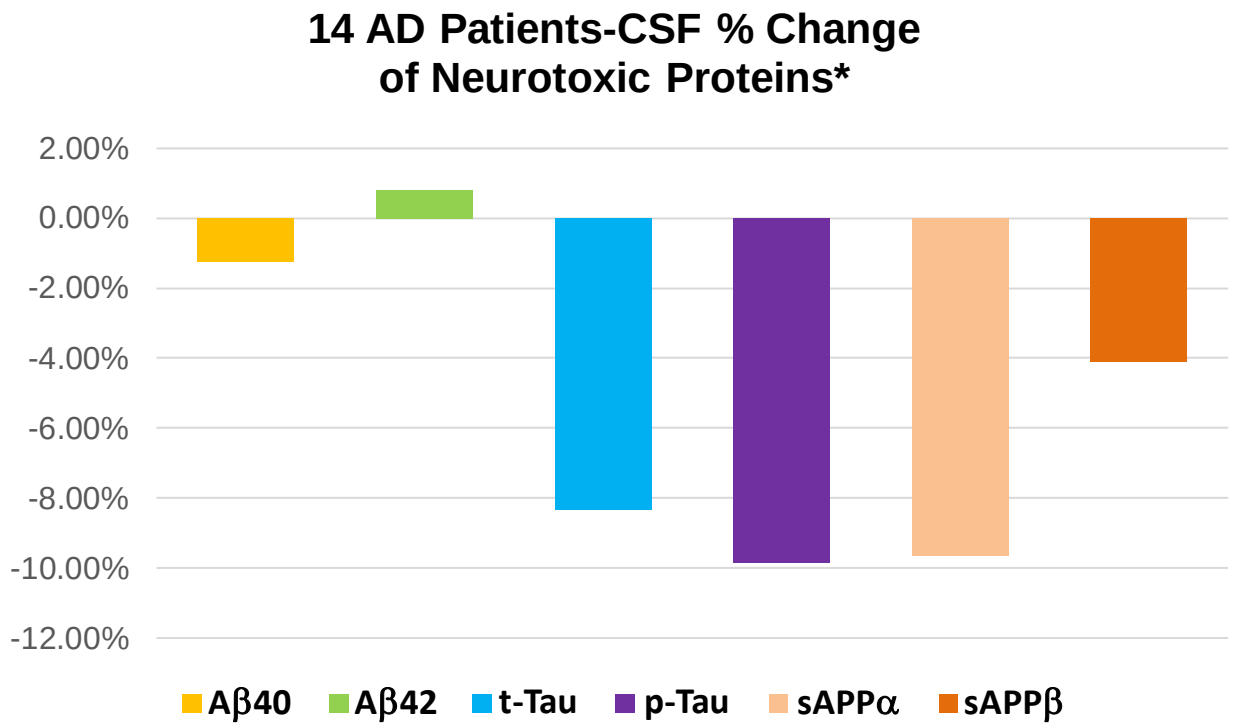


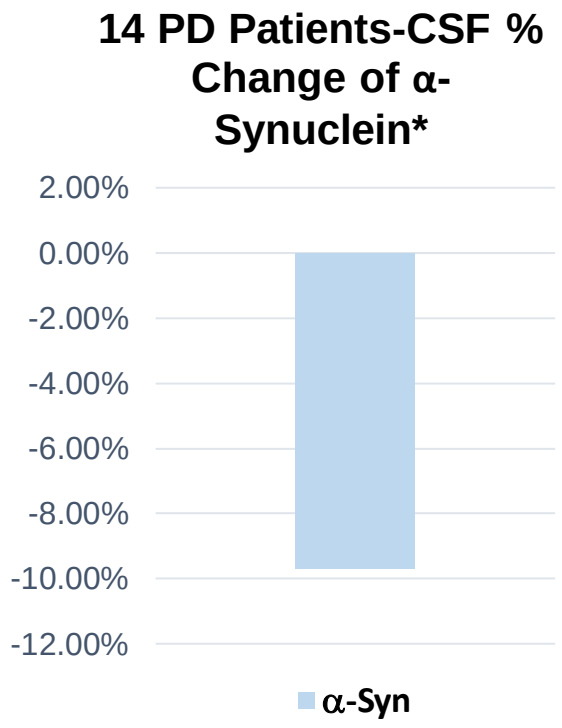
Ferritin IRE/IRP1/Buntanetap
No Kd

Buntanetap binds specifically to the APP IRE, but not to the ferritin IRE

Chen XQ et al, *Pharmaceutics* **2021**, *13*(12), 2109

REDUCED NEUROTOXIC PROTEINS IN BOTH AD AND PD PATIENTS



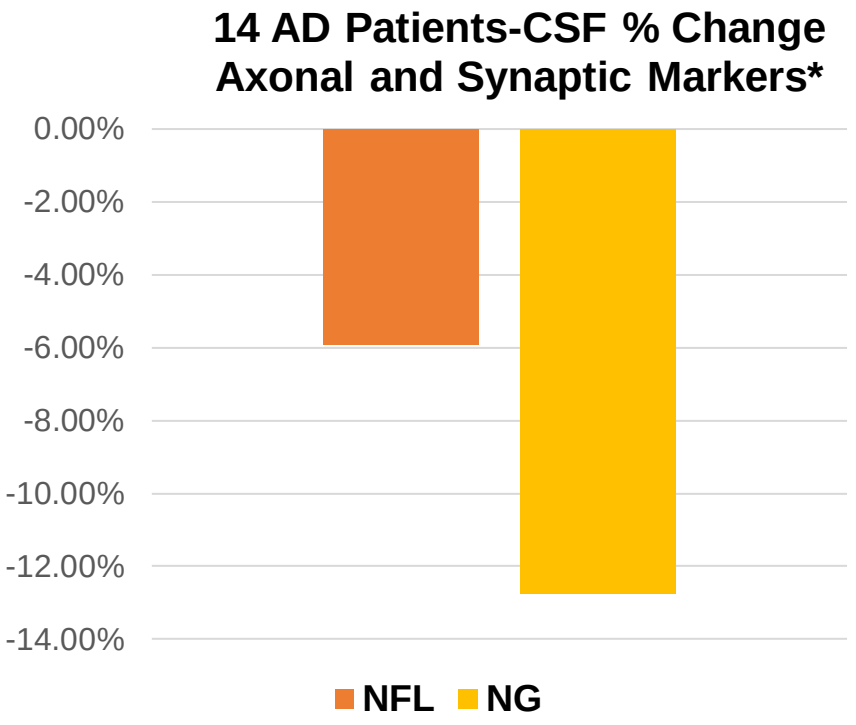


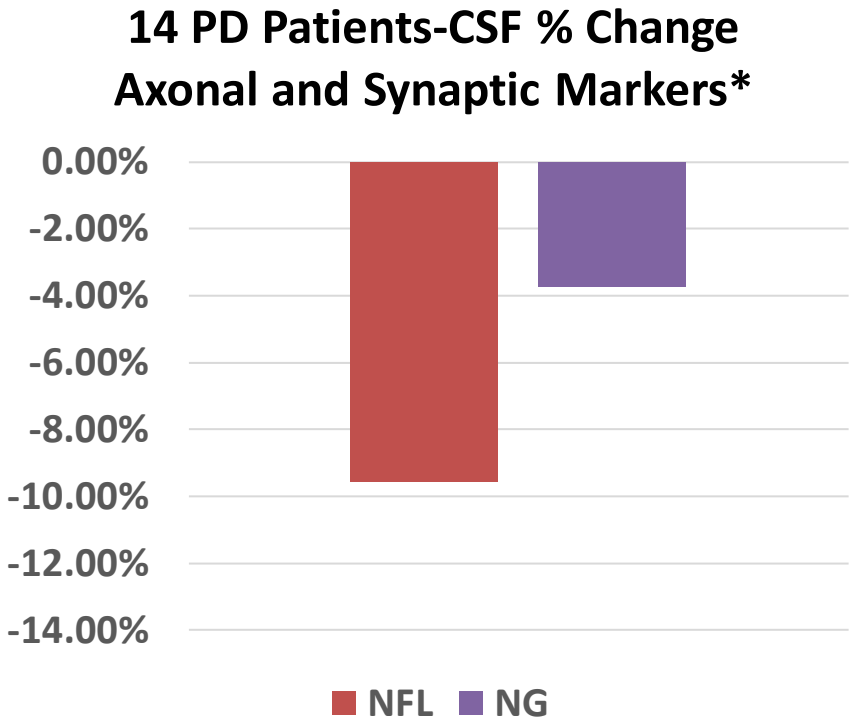
APP (and its downstream products), and p-Tau are the neurotoxic proteins involved in AD, while α-Synuclein is the neurotoxic culprit of PD. The reduction compares well to the reduction seen in animals at full efficacy.

*All values are in comparison to placebo based on all data points

ANNOVIS

REDUCED AXONAL AND SYNAPTIC DYSFUNCTIONS IN BOTH AD AND PD PATIENTS

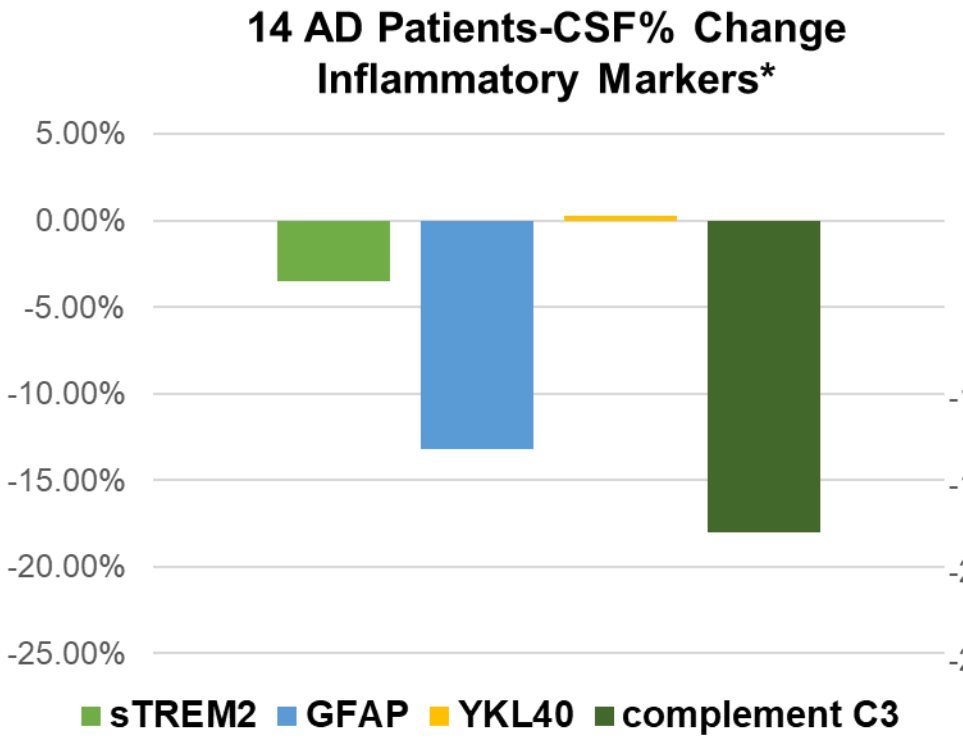


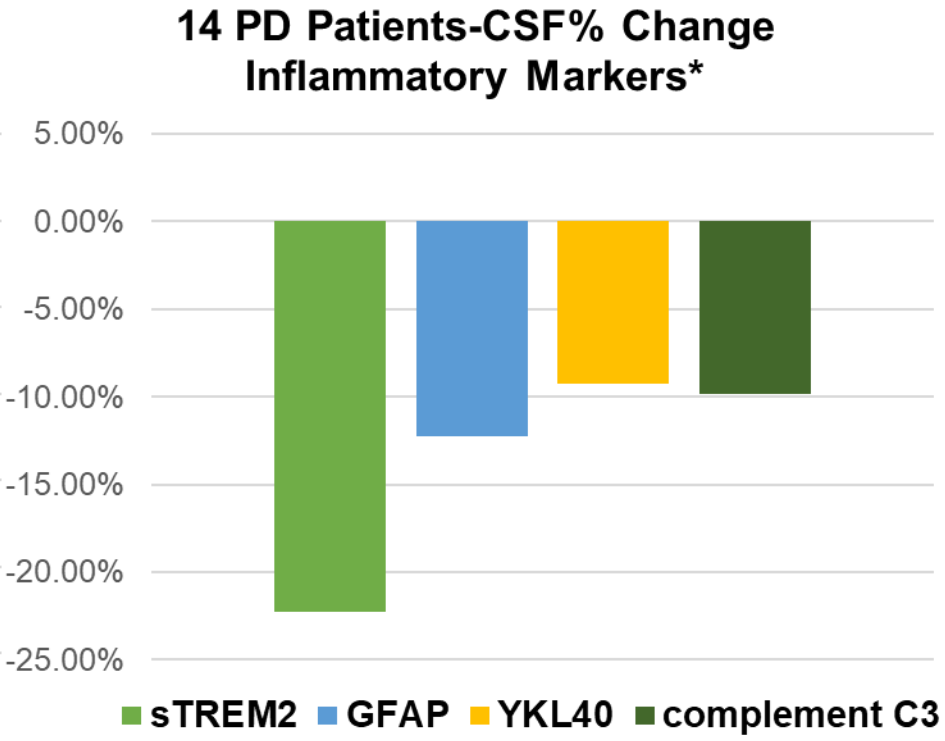


Neuronal and synaptic markers are lowered in AD and in PD patients, showing that the nerve cells are potentially healthier.

*All values are in comparison to placebo based on all data points.

REDUCED INFLAMMATION IN BOTH AD AND PD PATIENTS





Inflammatory markers are lowered in AD and in PD patients, showing a normalization of inflammation in both neurodegenerative disorders.

*All values are in comparison to placebo based on all data points