Phase II Data in Alzheimer's & Parkinson's Data

AD/PD 2022

FORWARD-LOOKING STATEMENTS

Statements in this presentation contain "forward-looking statements" that are subject to substantial risks and uncertainties. Forward-looking statements contained in this presentation may be identified by the use of words such as "anticipate," "expect," "believe," "will," "may," "should," "estimate," "project," "outlook," "forecast" or other similar words, and include, without limitation, statements regarding Annovis Bio, Inc.'s expectations regarding projected timelines of clinical trials, and expectations regarding current or future clinical trials. Forward-looking statements are based on Annovis Bio, Inc.'s current expectations and are subject to inherent uncertainties, risks and assumptions that are difficult to predict. Further, certain forward-looking statements are based on assumptions as to future events that may not prove to be accurate, including that clinical trials may be delayed; that the data reported herein is from a Phase 2a study and subsequent clinical trials must be conducted; and that any anticipated meeting with or presentation to the FDA may be delayed. These and other risks and uncertainties are described more fully in the section titled "Risk Factors" in the Annual Report on Form 10-K for the year ended December 31, 2021, and other reports filed with the Securities and Exchange Commission. Forward-looking statements contained in this presentation are made as of this date, and Annovis Bio, Inc. undertakes no duty to update such information except as required under applicable law.

WHAT IS BUNTANETAP?

- Buntanetap (aka Buntanetap and Posiphen) is a translational inhibitor of neurotoxic aggregating proteins (TINAPs)
- Lowering levels of neurotoxic proteins leads to improved axonal transport and nerve cell life
- That results in improvement in several neurodegenerative diseases, as in Alzheimer's and Parkinson's disease

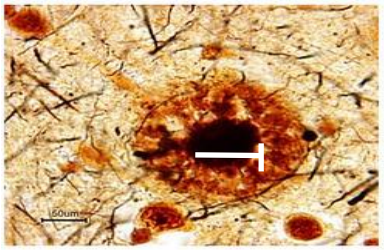
ANNOVIS' NEW APPROACH TO ATTACK AD AND PD

Chronic and acute brain insults lead to high levels of neurotoxic proteins, inflammation and neurodegeneration

Amyloid β

Alzheimer's - Parkinson's

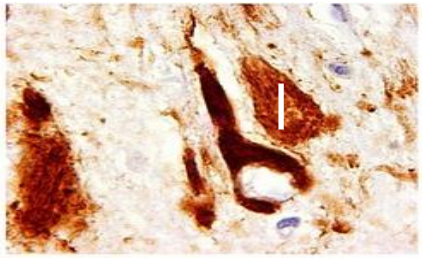
Aβ Targeting Compounds



Tau

Tauopathies - Alzheimer's

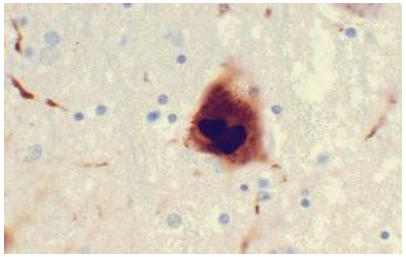
Tau Targeting Compounds



aSynuclein

Parkinson's - Alzheimer's

aSYN Targeting Compounds

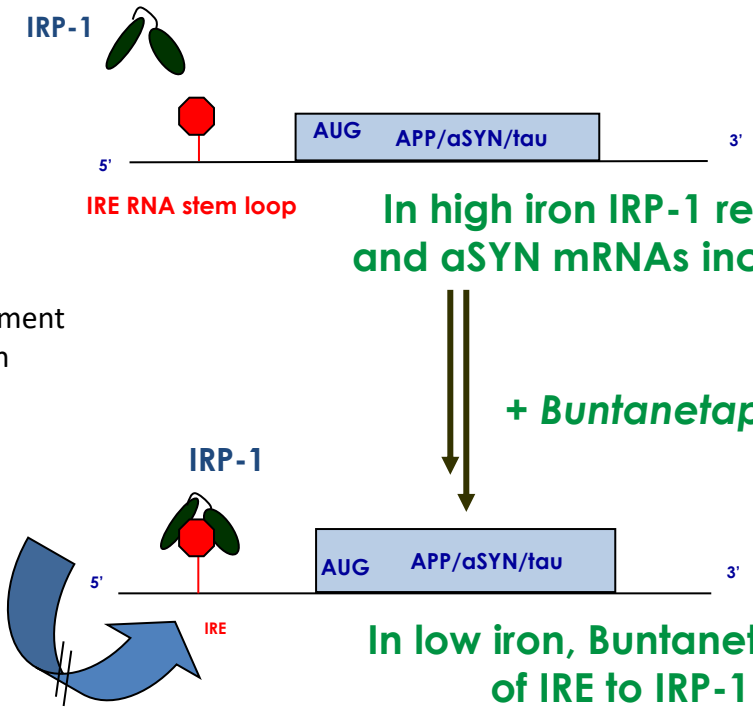


Attacking one neurotoxic protein results in minimal effect

Buntanetap is the only drug to attack multiple neurotoxic proteins simultaneously

MECHANISM OF ACTION

Buntanetap potentiates the binding of IRE to IRP1



IRE – iron responsive element
IRP – iron binding protein

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

REVERSAL OF TOXIC CASCADE

LOWER LEVELS OF NEUROTOXIC PROTEINS

IMPROVED AXONAL TRANSPORT

LOWER INFLAMMATION

LOWER NERVE CELL DEATH

IMPROVED COGNITION AND MOTOR FUNCTION

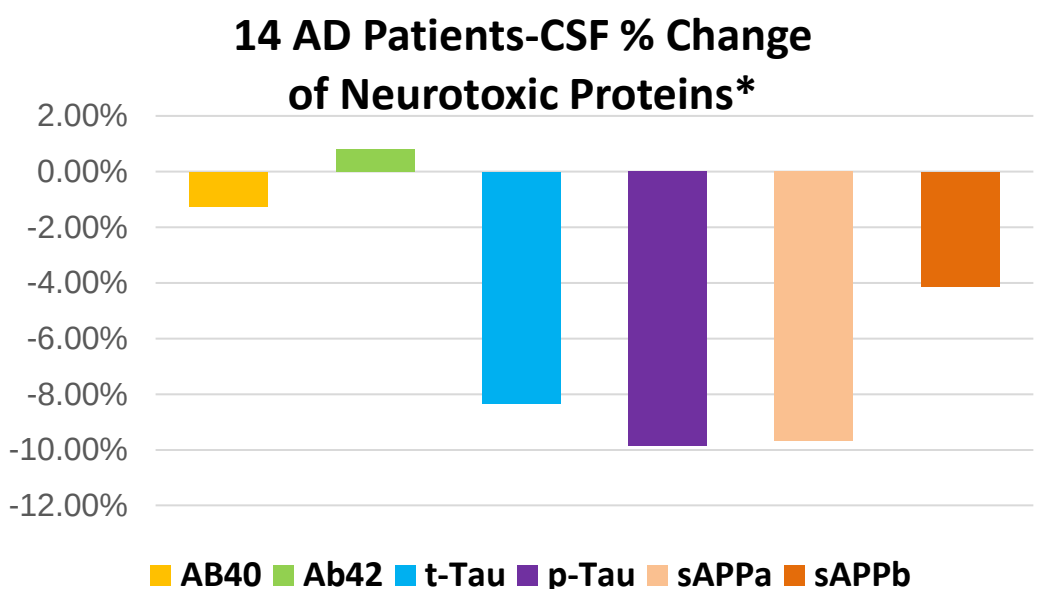
BUNTANETAP MET ALL PRIMARY, SECONDARY & EXPLORATORY ENDPOINTS

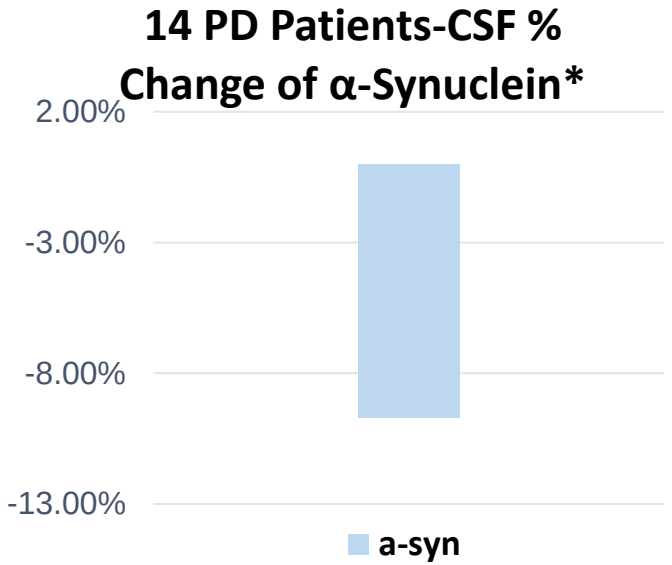
- **Primary Endpoint** – SAFETY: Buntanetap is safe
- **Secondary Endpoint** – PHARMACOKINETICS: as expected from previous experiments
- **Exploratory Endpoints**:
  - BIOMARKERS: reduced as expected
  - COGNITION AND FUNCTION:
    Improved ADAS-Cog and WAIS in AD patients
    Improved UPDRS and WAIS in PD patients

TWO PHASE 2 CLINICAL TRIALS

	AD Trial	PD Trial
Therapeutic Area	Early to Moderate AD and PD	
Phase	2	
Patients	14	54
Design	Double-Blind, Placebo-Controlled, Biomarker Study	
Dose	0 and 80 mg/day	0, 5, 10, 20, 40, 80 mg/day
Endpoints	Safety, PK	
Exploratory	Biomarkers, Efficacy	

REDUCED NEUROTOXIC PROTEINS IN BOTH AD AND PD PATIENTS

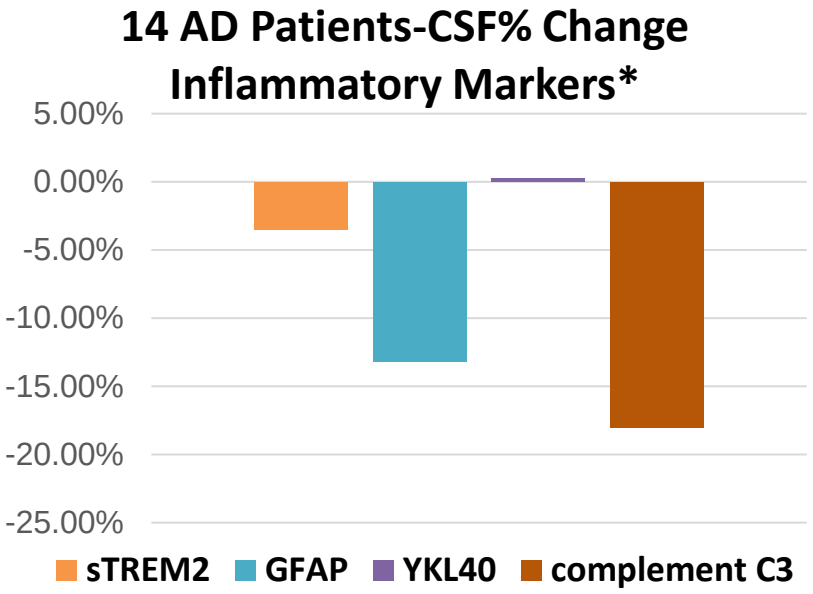


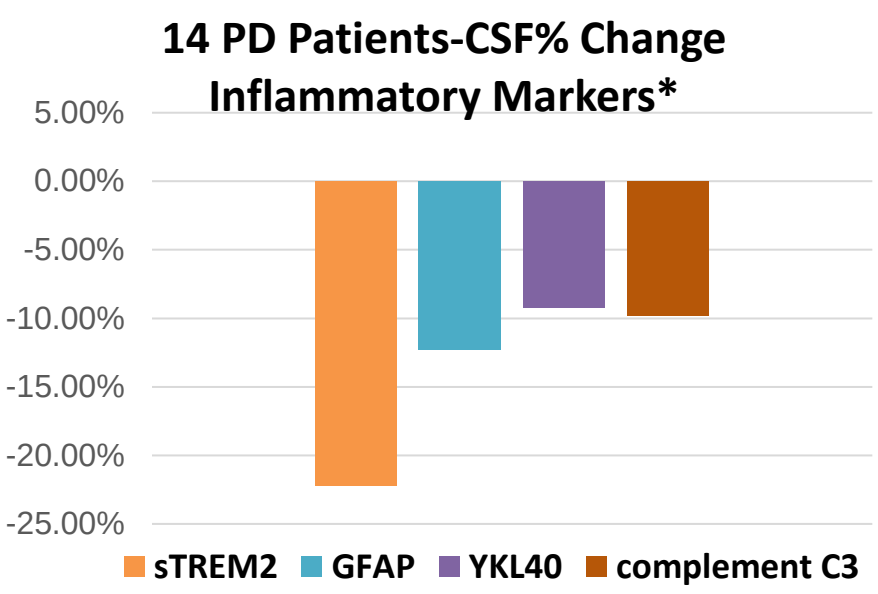


APP (and its downstream products), and p-Tau are the neurotoxic proteins involved in AD, while a-Synuclein is the neurotoxic culprit of PD. The reduction compares well to the reduction seen in animals at full efficacy.

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

REDUCED INFLAMMATION IN BOTH AD AND PD PATIENTS

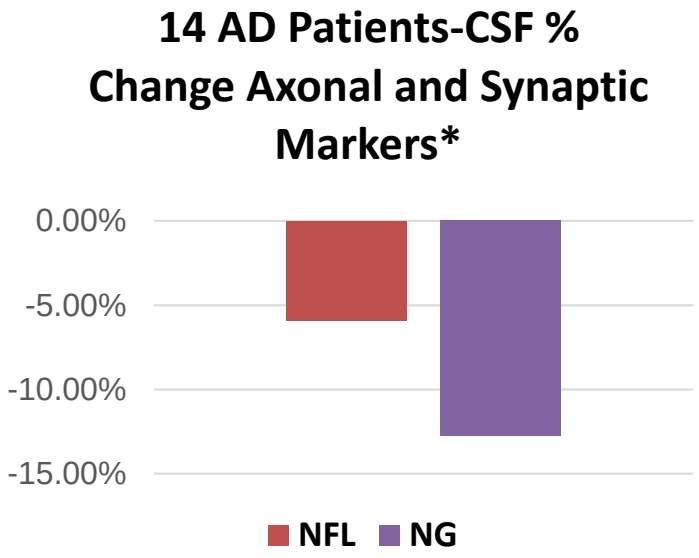


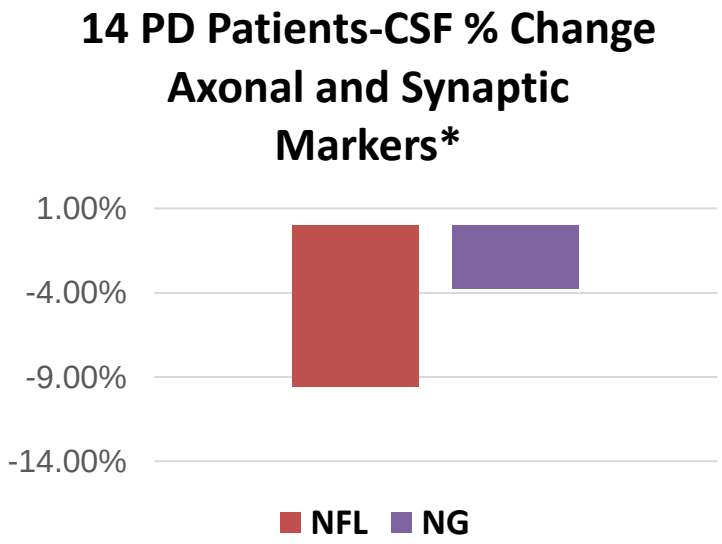


Inflammatory markers are lowered in AD and in PD patients, showing a normalization of inflammation in both neurodegenerative disorders.

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

REDUCED AXONAL AND SYNAPTIC DYSFUNCTIONS IN BOTH AD AND PD PATIENTS

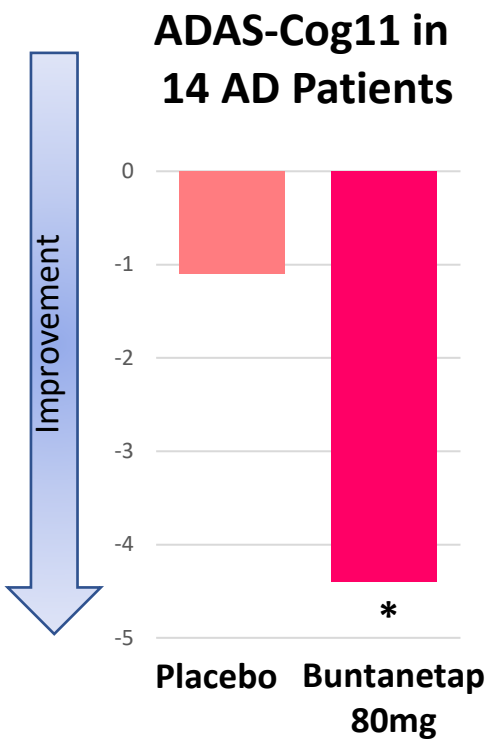




Neuronal and synaptic markers are lowered in AD and in PD patients, showing that the nerve cells are healthier.

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

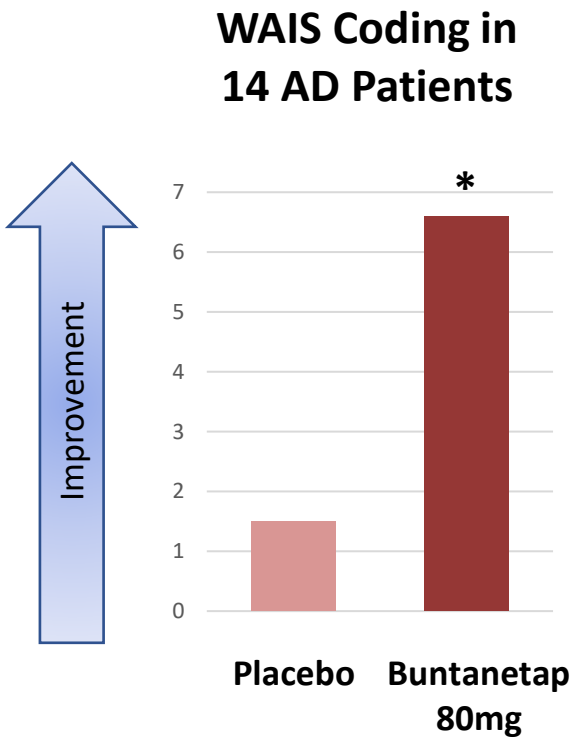
IMPROVED COGNITION IN AD PATIENTS – ADAS-Cog11



From baseline to 25 days in the Buntanetap-treated group, ADAS-Cog11 improves by 4.4 points, a statistically significant improvement of 30% ($p<0.05$). Compared to placebo at 25 days the treated group is 3.3 points better, an improvement of 22%.

* $P<0.05$

IMPROVED CODING SPEED IN AD PATIENTS - WAIS

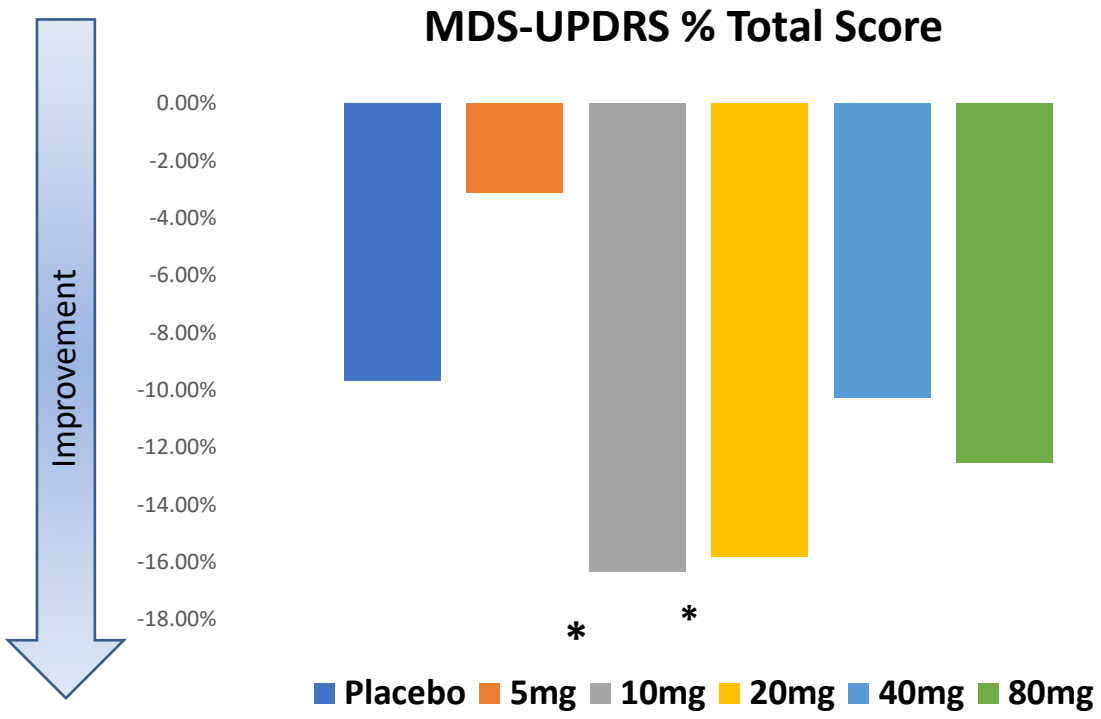


The WAIS coding test measures speed in movement and thinking. Treated AD patients show a 6.6 point statistically significant 23% improvement from baseline and a 4.9 point, 16% improvement from placebo.

* P<0.05

IMPROVED FUNCTION IN PD PATIENTS MDS-UPDRS TEST

Data from 54 PD Patients

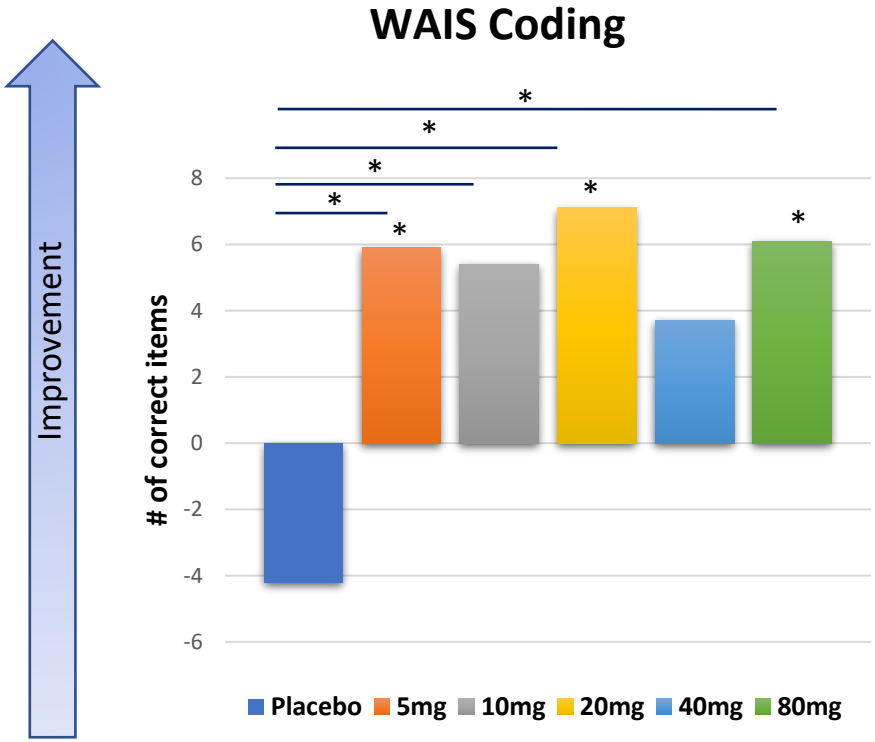


The MDS-UPDRS test showed the most improvements at 10 and 20 mg once per day

*p<0.05

IMPROVED SPEED AND ACCURACY IN PD PATIENTS WAIS CODING TEST

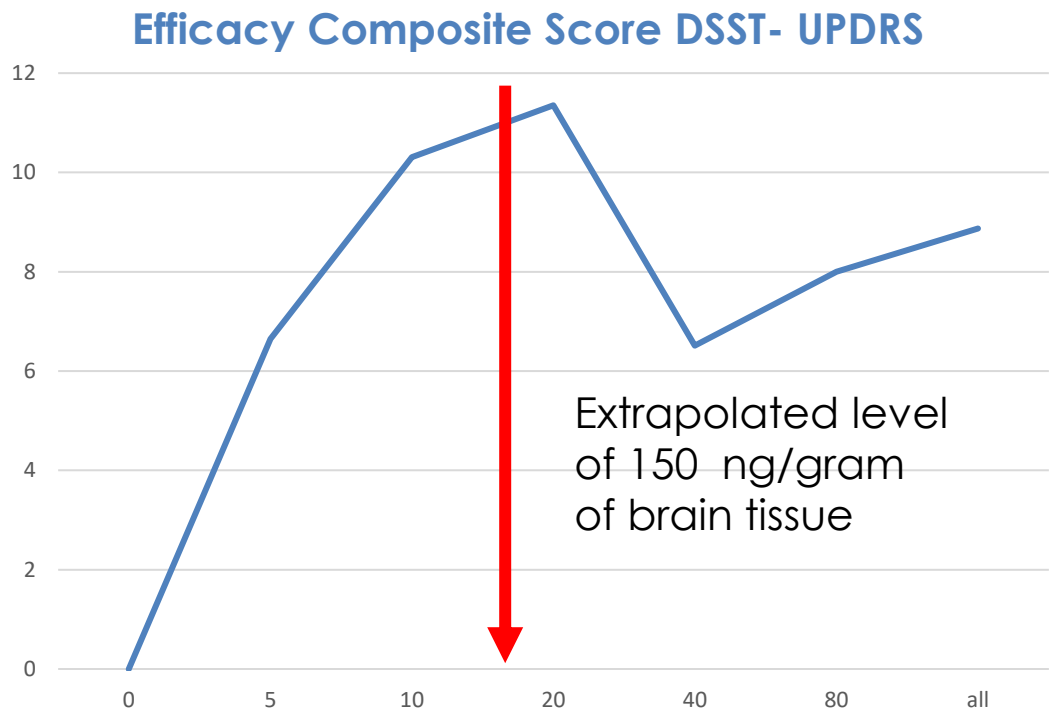
Data from 54 PD Patients



Across the dose response the WAIS coding test showed improvements in speed of movement and coordination

* $p<0.05$
**$p<0.01$

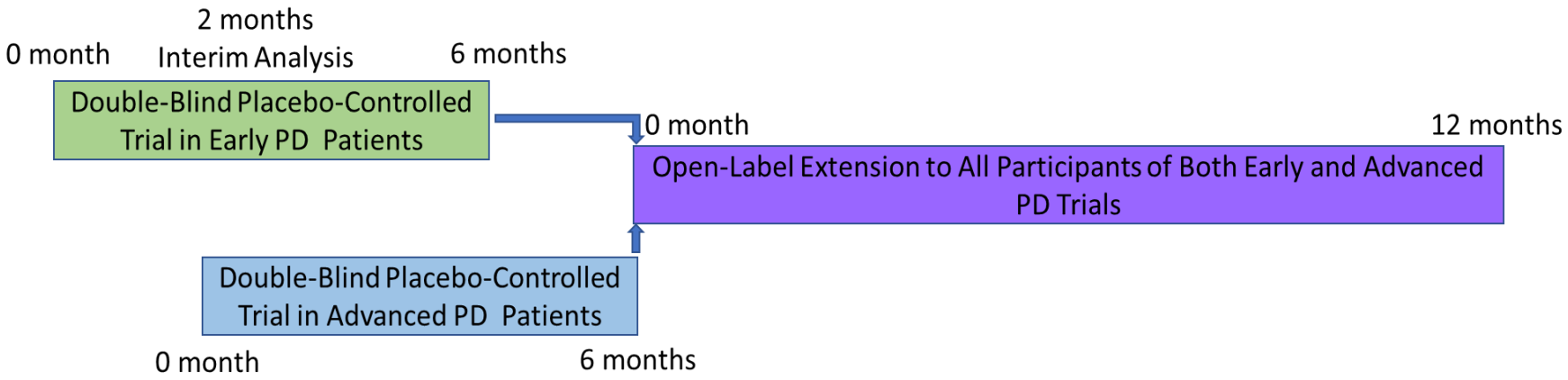
DOSE-RESPONSE AND OPTIMUM DOSES



Administered dose to PD patients ranging from 0 to 80 mg QD

In the MDS-UPDRS and WAIS test the most efficacious doses are 10 and 20 mg QD. These doses result in brain levels of Buntanetap that were found in mice and rats to lead to optimal efficacy.

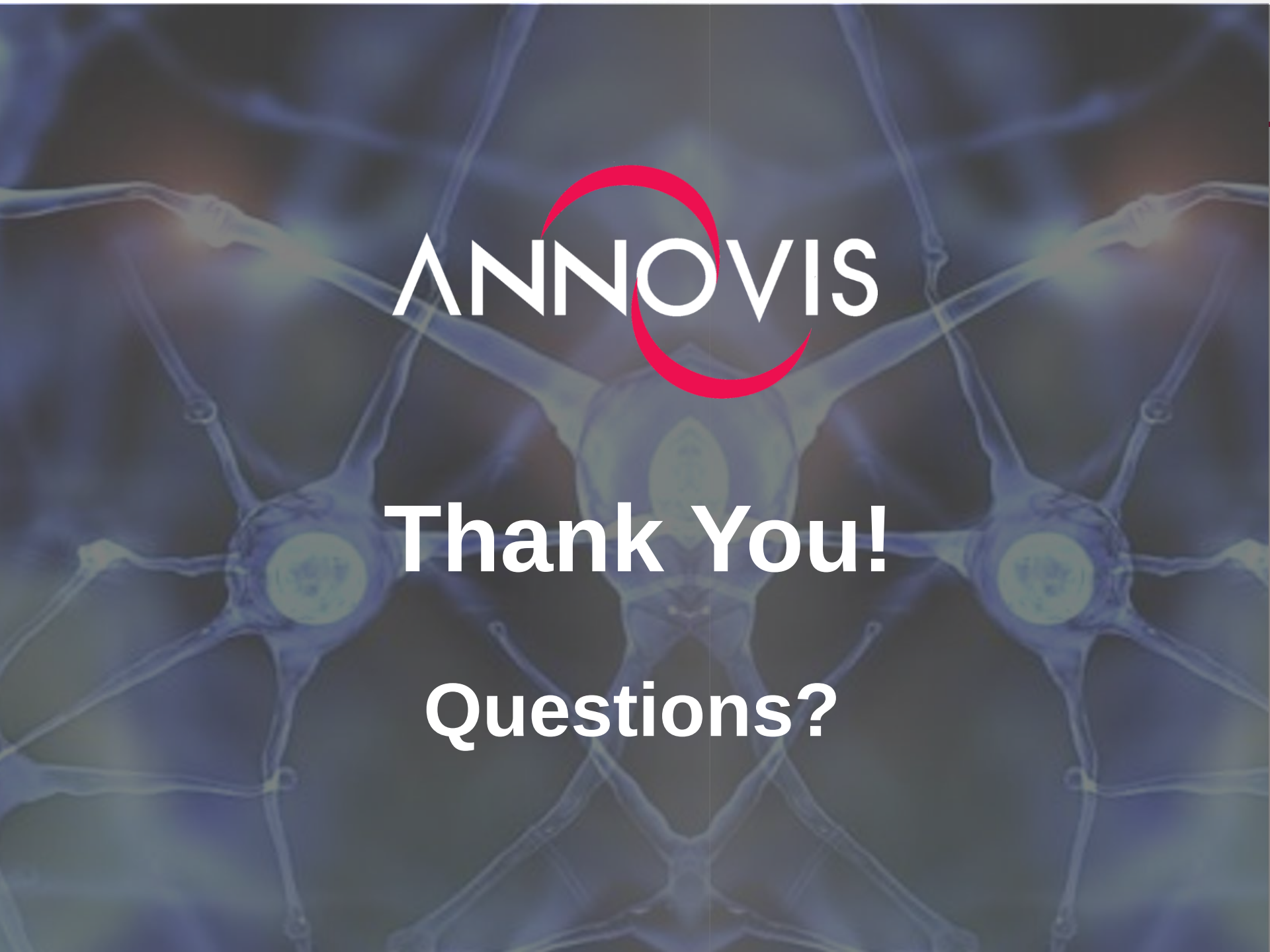
DEVELOPMENT OF BUNTANETAP FOR EARLY AND ADVANCED PD



The FDA approved initiation of phase 3 studies for early and advanced PD. We plan to follow the two 6-month studies with a 12-month open label extension for both early and advanced PD patients

SUMMARY AND NEXT STEPS

- Annovis has a novel approach to stop AD and PD
- Buntanetap shows improvements in Phase 2a clinical trials:
  - Cognition in AD patients
  - Motor function in PD patients
  - WAIS coding in AD and PD patients
- This is 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
- The FDA has green lighted the continued development of Buntanetap into phase 3 for early and advanced PD


ANNOVIS
Thank You!
Questions?