



Corporate Presentation

Development path to NDA:

- Alzheimer's disease
- Parkinson's disease

NYSE:ANVS

January 2026

FORWARD-LOOKING STATEMENTS

Forward Looking Statements and Other Important Cautions -- This presentation contains "forward-looking" statements within the meaning of Section 27A of the Securities Act of 1933, as amended, and Section 21E of the Securities Exchange Act of 1934, as amended. These statements include, but are not limited to, the Company's plans related to clinical trials and financial condition. Forward-looking statements are based on current expectations and assumptions and are subject to risks and uncertainties that could cause actual results to differ materially from those projected. Such risks and uncertainties include, but are not limited to, those related to patient enrollment, the effectiveness of buntanetap, and the timing, effectiveness, and anticipated results of the Company's clinical trials evaluating the efficacy, safety, and tolerability of buntanetap. Additional risk factors are detailed in the Company's periodic filings with the SEC, including those listed in the "Risk Factors" section of the Company's Annual Report on Form 10-K and Quarterly Reports on Form 10-Q. All forward-looking statements in this presentation are based on information available to the Company as of the date of this presentation. The Company expressly disclaims any obligation to update or revise its forward-looking statements, whether as a result of new information, future events, or otherwise, except as required by law.

Company highlights

Drug candidate



Our lead asset *buntanetap* is the only drug that improves cognition in AD and cognition and motor function in PD patients

Late-stage opportunity



We successfully completed:
Phase 2/3 trial in early AD
Phase 3 trial in early PD
Ongoing:
Pivotal Phase 3
in early AD

Unique MOA



Buntanetap is RNA-targeting small molecule that inhibits the overproduction of multiple neurotoxic proteins associated with AD and PD

Growing market



7M
AD patients
in the US

1.2M
PD patients
in the US

Intellectual property (IP)



Long duration IP estate that extends beyond 2046

Capital-efficient approach



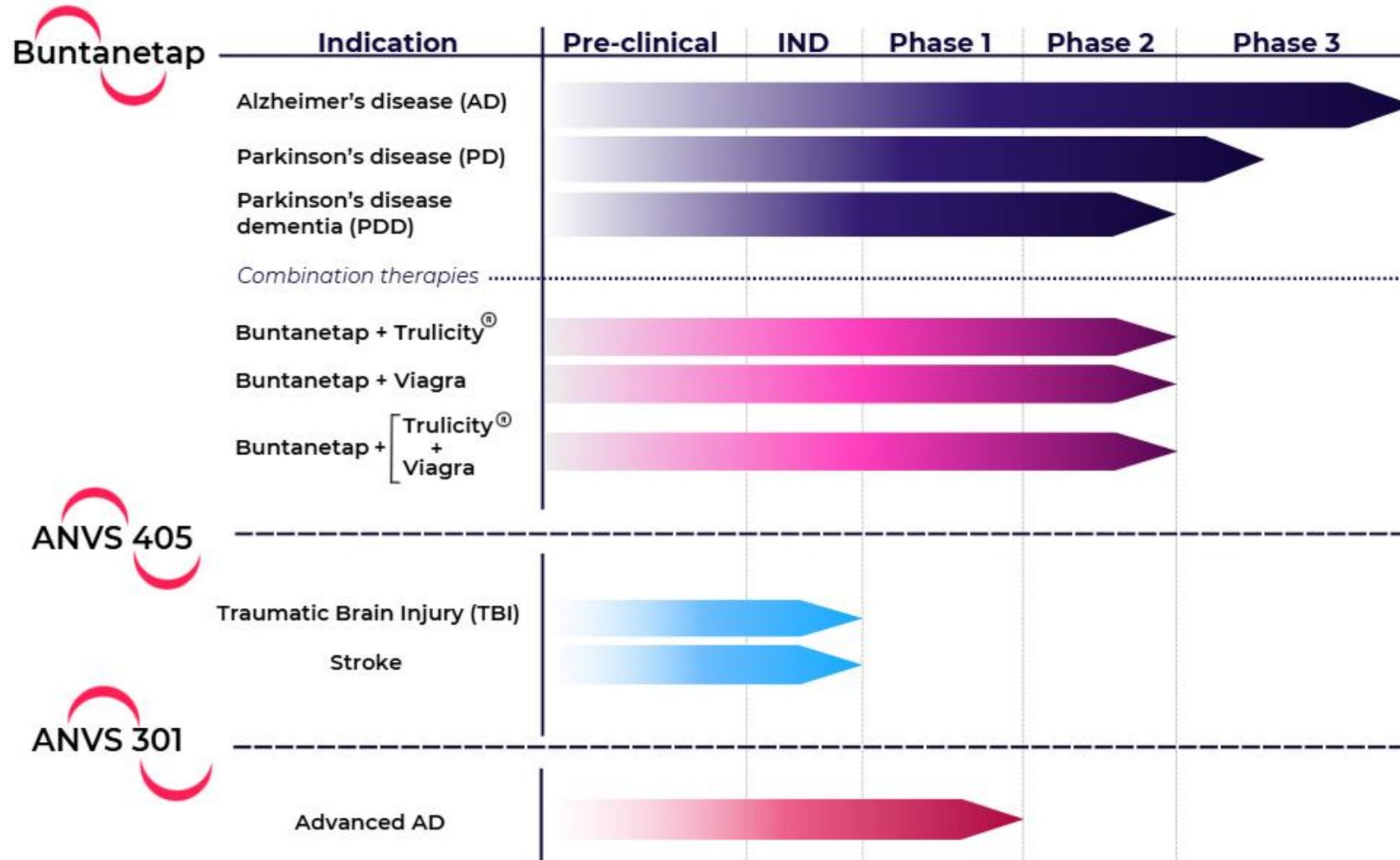
Current shares outstanding 26.5m.

Cash balance* \$19.5m., debt \$0

Raised \$35m. in 2025

*as of 12/10/25

Pipeline



Summary of clinical studies

Healthy volunteers

Phase 1	2 safety studies	N=120
	Food effect study	N=24
	Form A/B	N=24

Alzheimer's disease

Phase 1/2	2 studies	N=22
Phase 2	1 study	N=17
Phase 2/3	1 study	N=346
Pivotal Phase 3	1 study	N=760 (ongoing)

Parkinson's disease

Phase 2	1 study	N=58
Phase 3	1 study	N=523

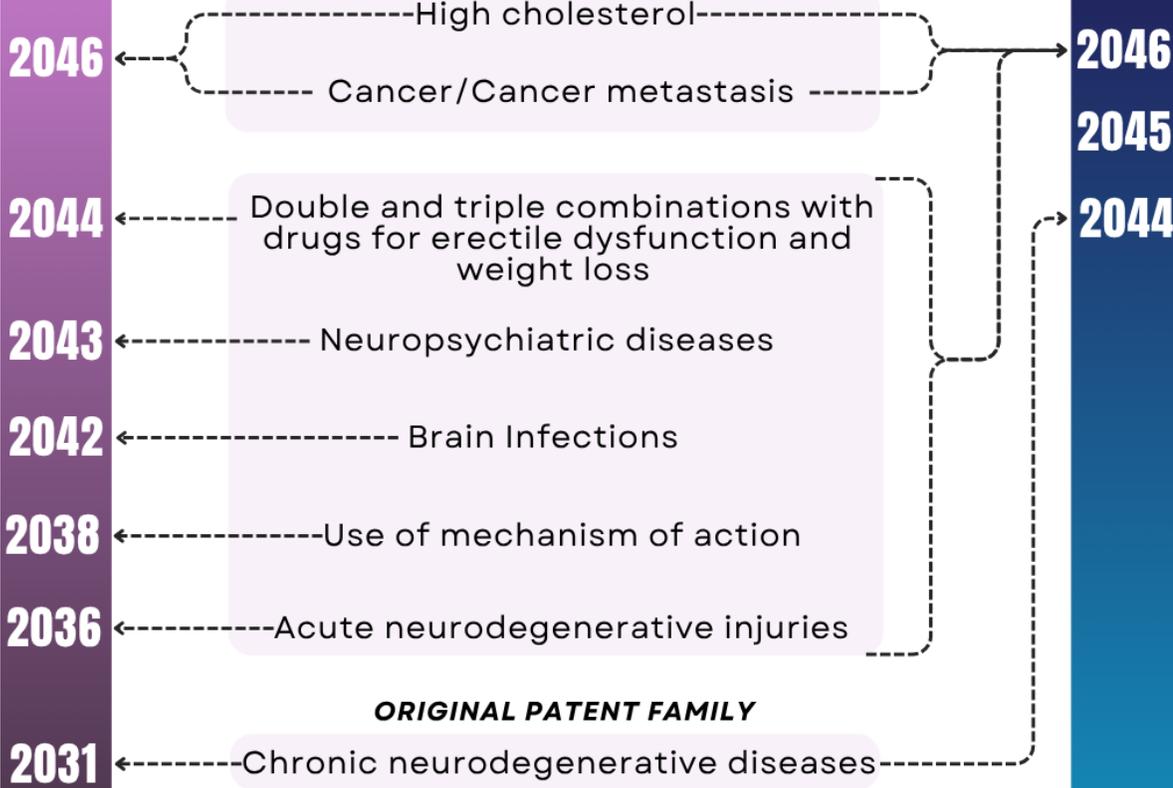
Over 1,200 people treated with buntanetap

Patent portfolio

**OLD
SEMI-CRYSTALLINE
FORM**

**NEW
CRYSTALLINE
FORM**

**EXTENSION AND
COMBINATION PATENTS**



Senior management team



Maria Maccellini, PhD
Founder, President, CEO



Mark Guerin
CFO



Cheng Fang, PhD
SVP, Research & Development



Eve Damiano, MS, RAC
SVP, Regulatory Operations



Melissa Gaines
SVP, Clinical Operations



Mike Christie, PhD
VP, Process Chemistry



Sarah MacCallum
Senior Clinical Director



Alexander Morin, PhD
Director, Strategic Communications

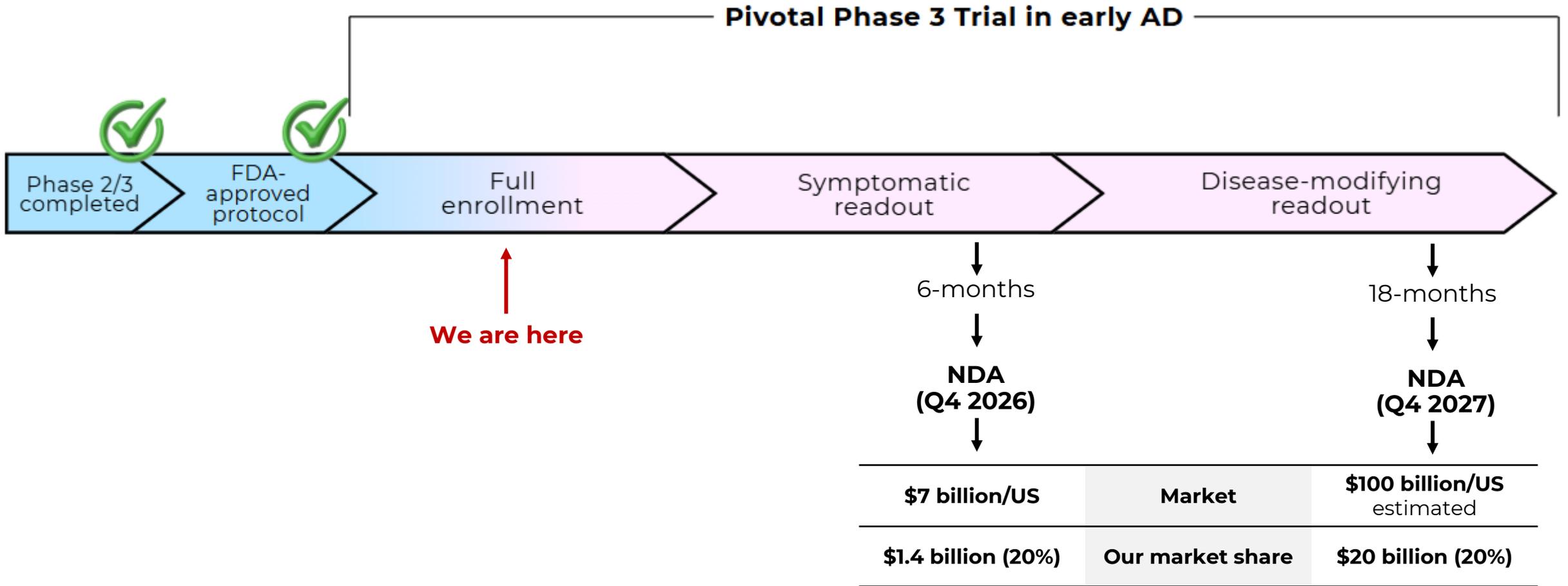


Hui Liu
Director, Biostatistics

Alzheimer's disease

The background of the slide features a stylized neural network. It consists of several interconnected nodes, each represented by a central yellow circle with a blue outline. These nodes are connected by thin, light blue lines that form a complex web across the entire page. The overall color scheme is a deep blue, with the yellow nodes providing a focal point.

Milestones toward approval for Alzheimer's disease



FDA-cleared pivotal Phase 3 study (ANVS-25001): A randomized, double-blind, placebo-controlled, multicenter study of buntanetap in participants with early Alzheimer's disease

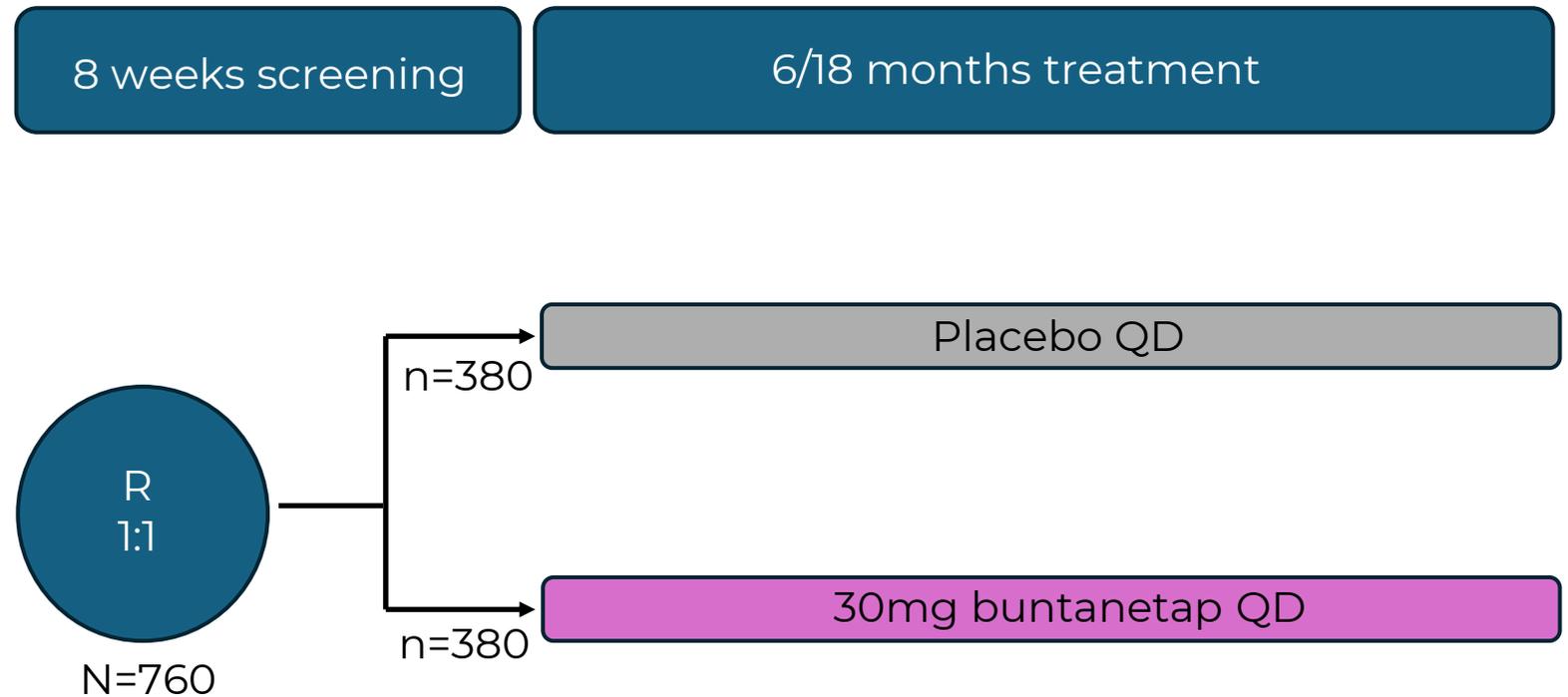
Key inclusion criteria:

- Diagnosis AD according to NIA and NIA-AA criteria (2024)
- pTau217 level positive for AD
- Age 55 to 85
- MMSE 21-28

Key clinical outcomes:

Primary endpoints:

- ADAS-Cog 13
- ADCS-iADL
- vMRI



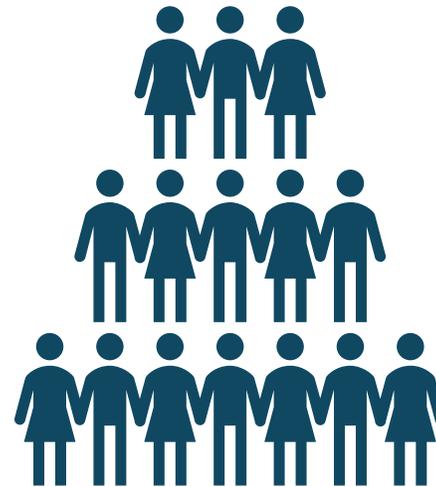
Progress of pivotal Phase 3 trial in early AD

Approaching completion of enrollment

83 clinical sites in the U.S.

760 total patients

40% complete



Completed Phase 2/3 study (ANVS22002):

A randomized, double-blind, placebo-controlled, dose-ranging, multicenter study in mild to moderate Alzheimer's disease

Key inclusion criteria:

- Diagnosis of probable AD according to NIA and NIA-AA criteria (2011)
- Age 55 to 85
- MMSE 14-24

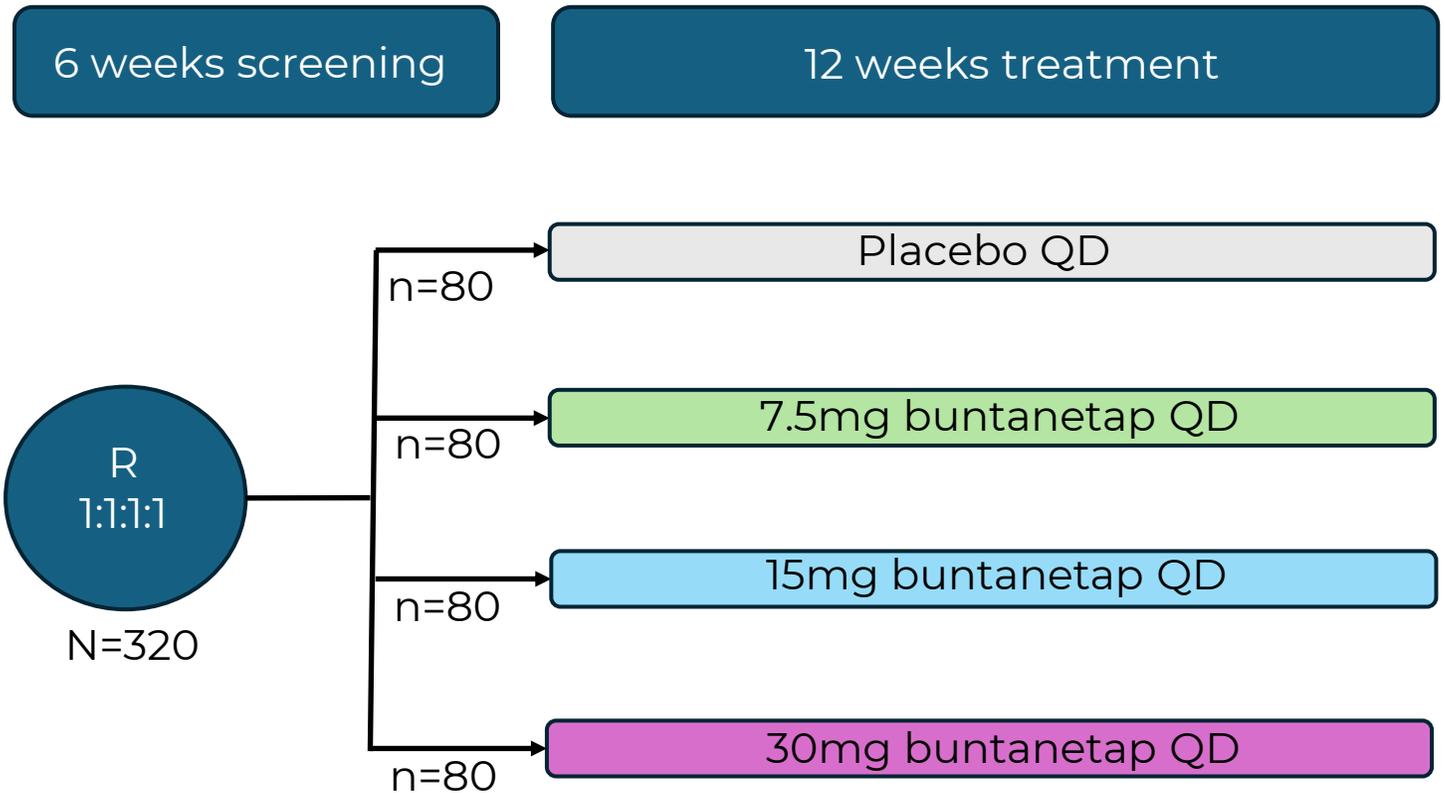
Key clinical outcome:

Primary endpoints:

- ADAS-Cog 11
- CGIC

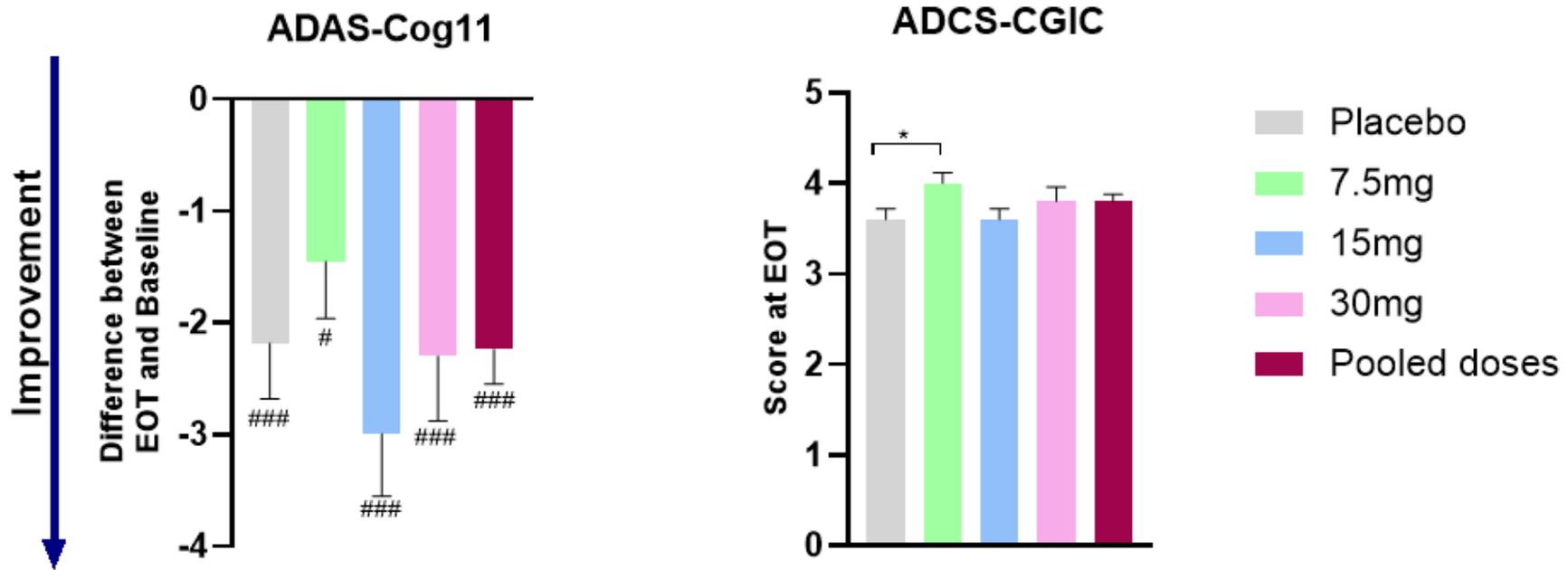
Key secondary endpoint:

- ADCS-ADL



Primary endpoints were not met in all enrolled patients

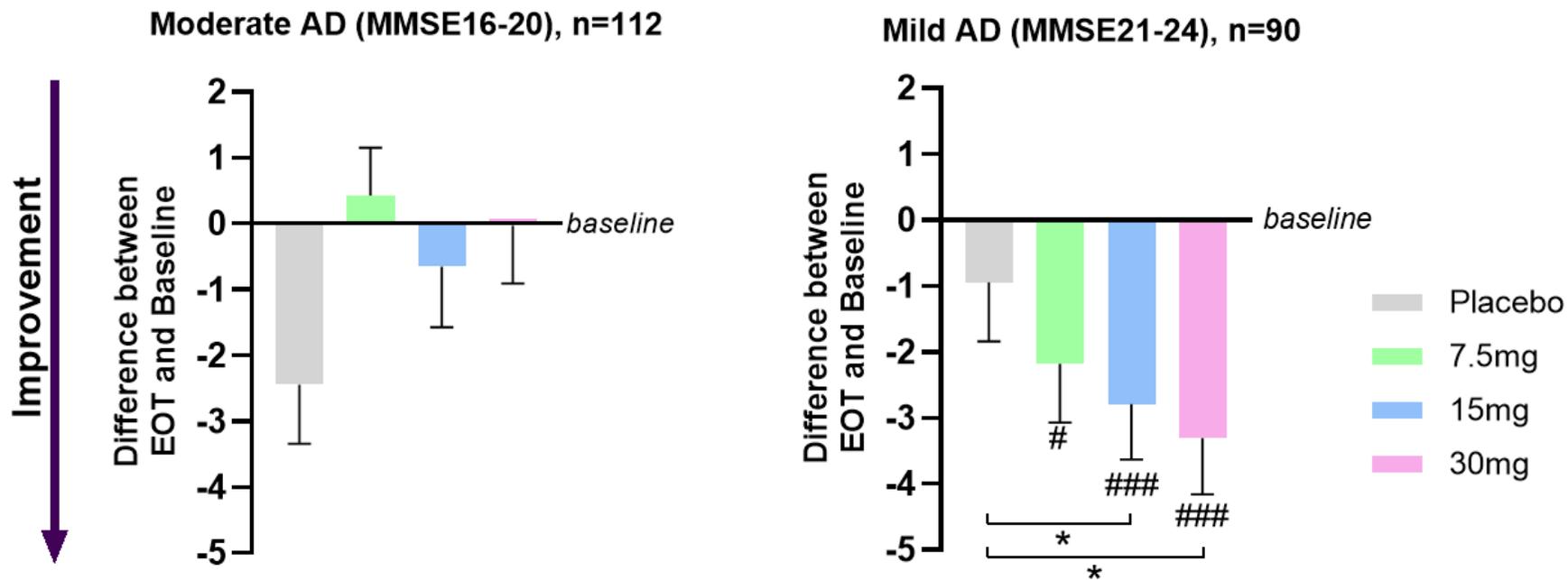
Entire enrolled population, n=351



* compared to placebo, # compared to baseline: #/* p<0.05; ## p<0.01; ### p<0.001

Buntanetap improves cognition in biomarker-positive patients with mild AD

ADAS-Cog11 (pTau217/t-Tau $\geq 4.2\%$)

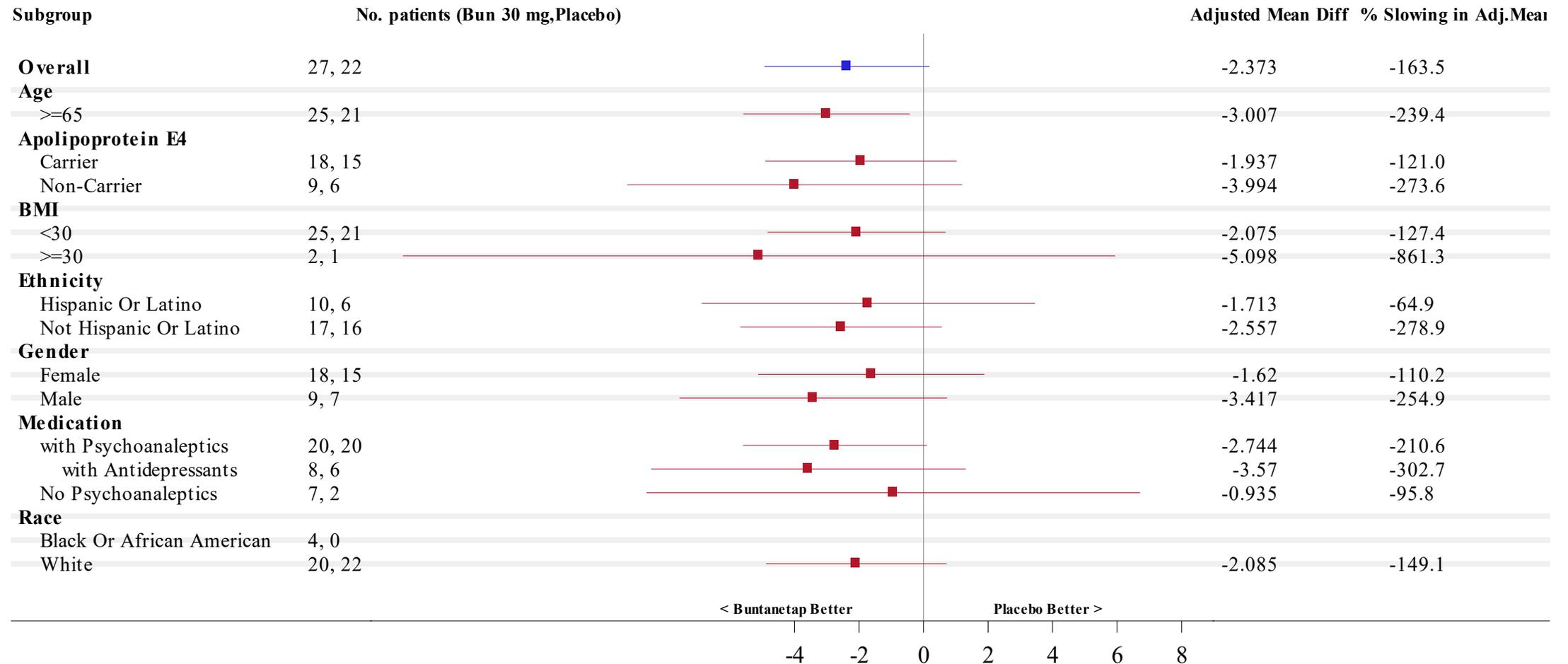


From the ITT population:

- AD patients were selected by pTau217 inclusion/exclusion.
- Mild and moderate AD were determined by MMSE selection.

* compared to placebo, # compared to baseline: #/* p<0.05; ### p<0.001

Forest plot shows consistency and robustness of efficacy



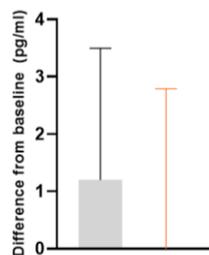
Biomarker data support the **target and pathway engagement**

Mild AD population (MMSE 21-24)

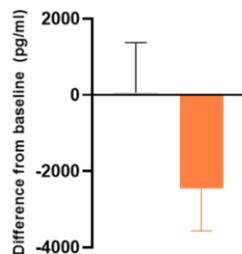
■ Placebo ■ Buntanetap (30mg)

Neurotoxic proteins

Total Tau (MMSE 21-24, N=45)

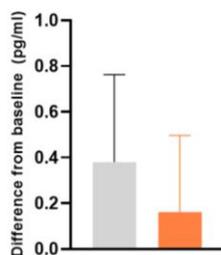


TDP43 (MMSE 21-24, N=43)

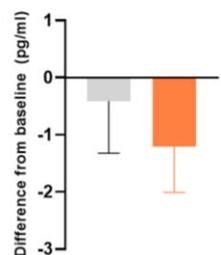


Inflammation

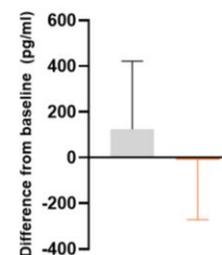
IL5 (MMSE 21-24, N=45)



IL6 (MMSE 21-24, N=45)

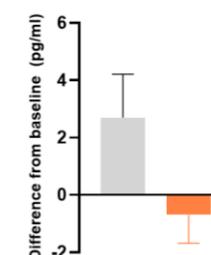


S100A12 (MMSE 21-24, N=49)

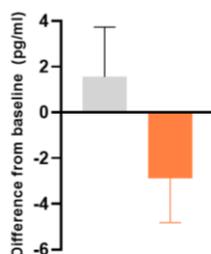


Neuronal damage

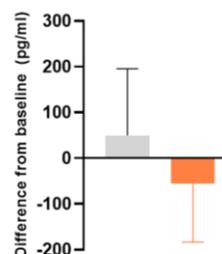
NFL (MMSE 21-24, N=45)



IFN- γ (MMSE 21-24, N=49)



IGF1R (MMSE 21-24, N=49)



Buntanetap shows strong safety profile in APOE4 carriers and non-carriers in ITT AD population

	Placebo	7.5mg Buntanetap	15mg Buntanetap	30mg Buntanetap	All Doses
APOE Carriers (N=159)	38	45	38	38	121
# TEAEs	13 (34.2%)	22 (48.9%)	17 (44.7%)	12 (31.6%)	51 (42%)
# TEAEs Related to Study Drug	1 (2.6%)	8 (17.8%)	6 (15.8%)	3 (7.9%)	17 (14%)
# Serious TEAEs	3 (7.9%)	0	0	1 (2.6%)	1 (2.5%)
# Serious TEAEs Related to Study Drug	0	0	0	0	0
APOE Non-Carriers (N=159)	41	34	43	41	118
# TEAEs	9 (22.0%)	4 (11.8%)	11 (25.6%)	17 (41.5%)	32 (27.1%)
# TEAEs Related to Study Drug	1 (2.9%)	1 (2.9%)	2 (4.7%)	3 (7.3%)	6 (5.1%)
# Serious TEAEs	0	0	0	2 (4.9%)	2 (1.7%)
# Serious TEAEs Related to Study Drug	0	0	0	0	0

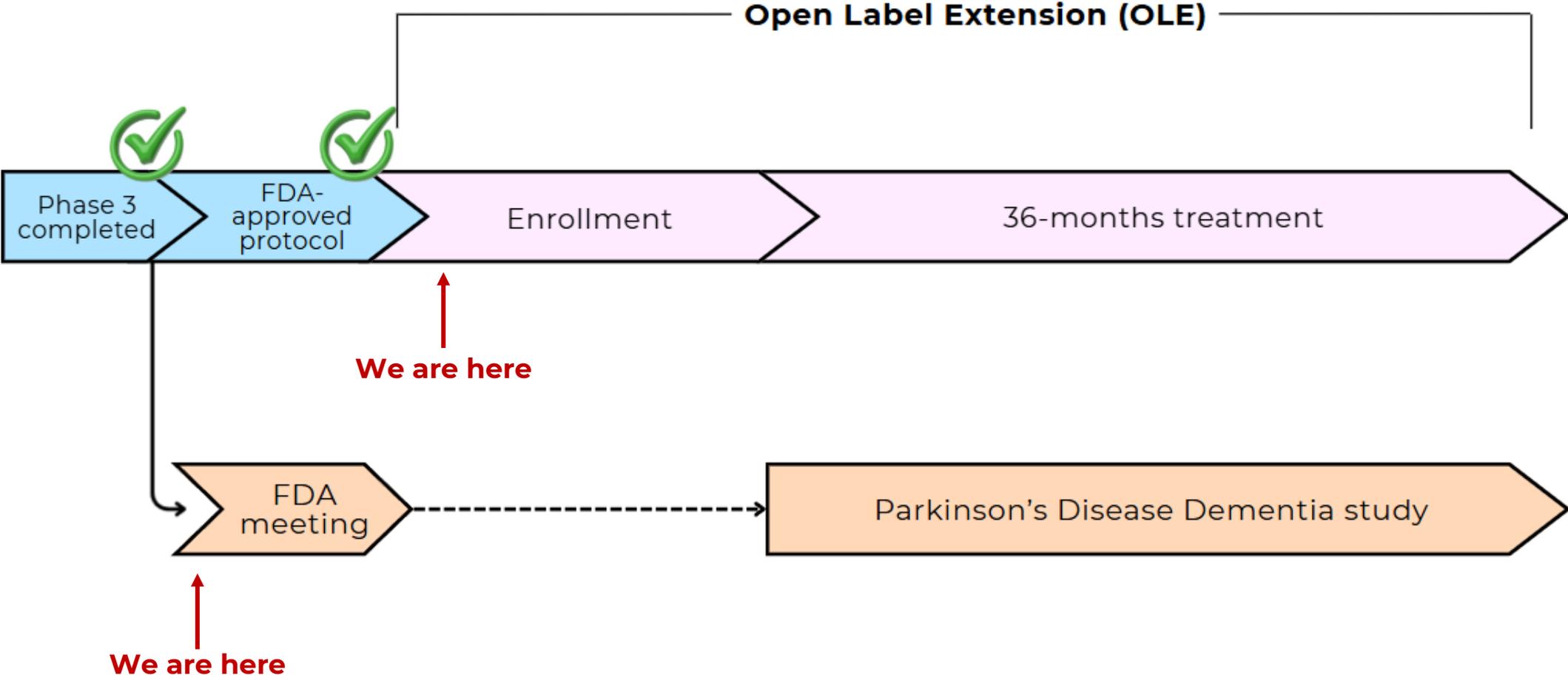
AE = Adverse Event

TEAE = Treatment Related Adverse Event

Parkinson's disease

A microscopic image of neurons, showing several cell bodies with prominent nuclei and extensive, branching dendrites and axons, set against a blue background. The neurons are arranged in a somewhat regular pattern, with some overlapping. The overall appearance is that of a neural network.

Upcoming milestones for Parkinson's program



FDA-approved PD Open Label Extension (OLE) study design

Key Inclusion Criteria:

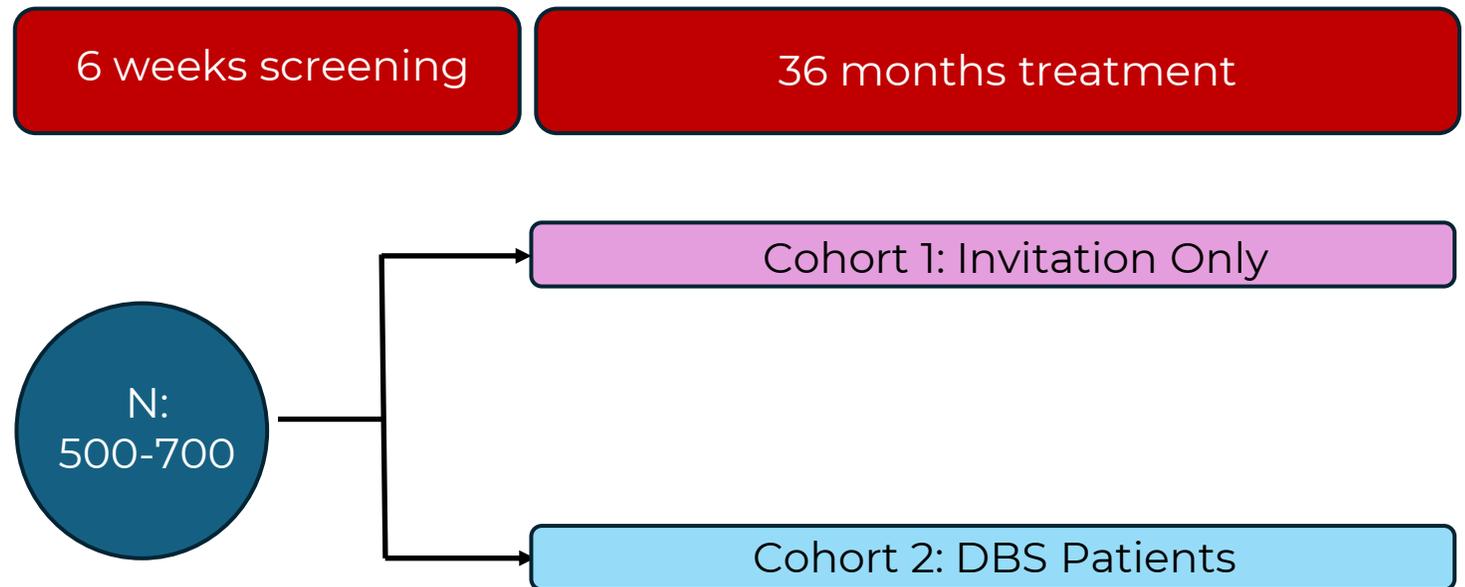
- Adults aged up to 85 years
- Hoehn and Yahr stage 1-3
- MMSE 21-30 at screening

Cohort 1:

Diagnosis of idiopathic PD and participated in a prior PD clinical trial with buntanetap.

Cohort 2:

Diagnosis of idiopathic PD and who has been receiving DBS treatment in either the subthalamic nucleus or the globus pallidus internus for at least 12 months after a successful DBS surgery that achieved the goal.



Completed Phase 3 study (ANVS22001):

A randomized, double-blind, placebo-controlled, dose-ranging, multicenter study in early Parkinson's disease

Key inclusion criteria:

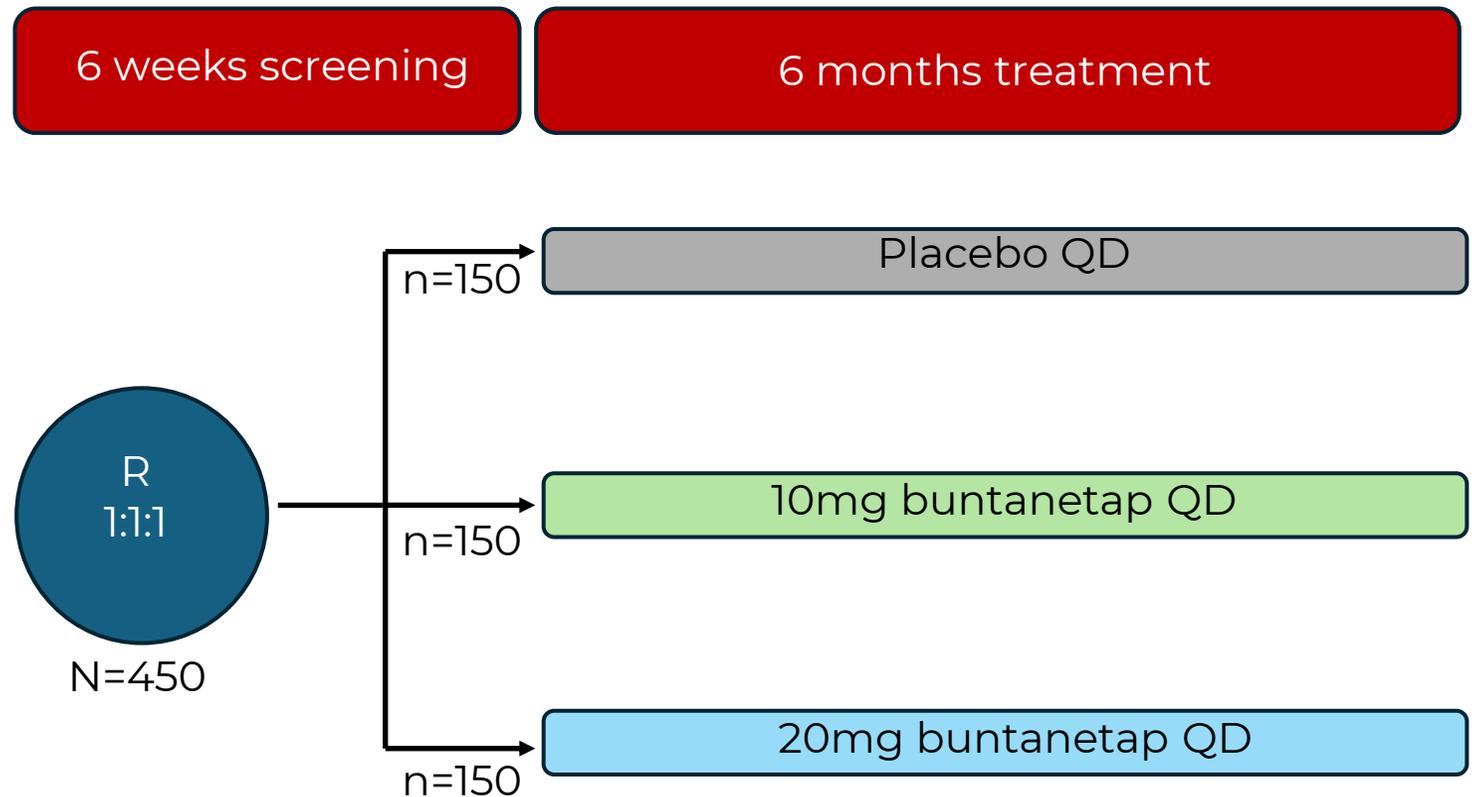
- Diagnosis of idiopathic PD (*Postuma, 2015*)
- H&Y score =1, 2 or 3 during ON-state & OFF-state <2hrs per day.
- 40 – 85 years

Primary endpoints:

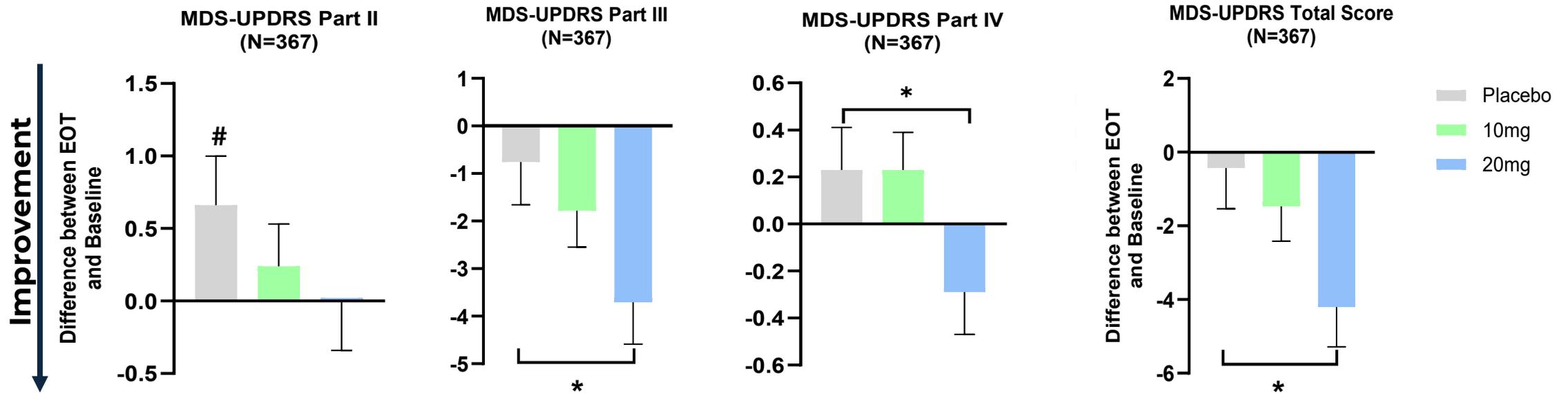
- MDS-UPDRS Part II (OFF state)

Secondary endpoints:

- MDS-UPDRS Part II+III (OFF state)
- MDS-UPDRS Part III (OFF state)

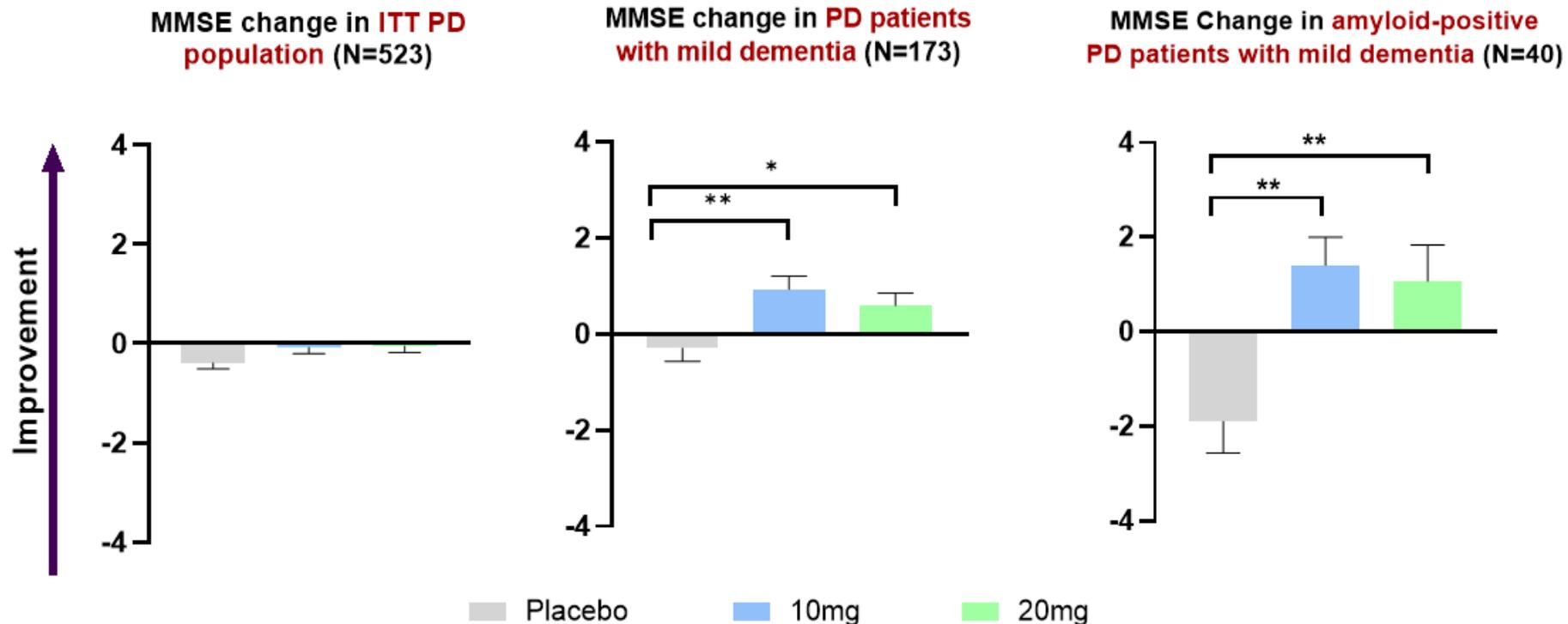


The study met its endpoints in the **per-protocol population**



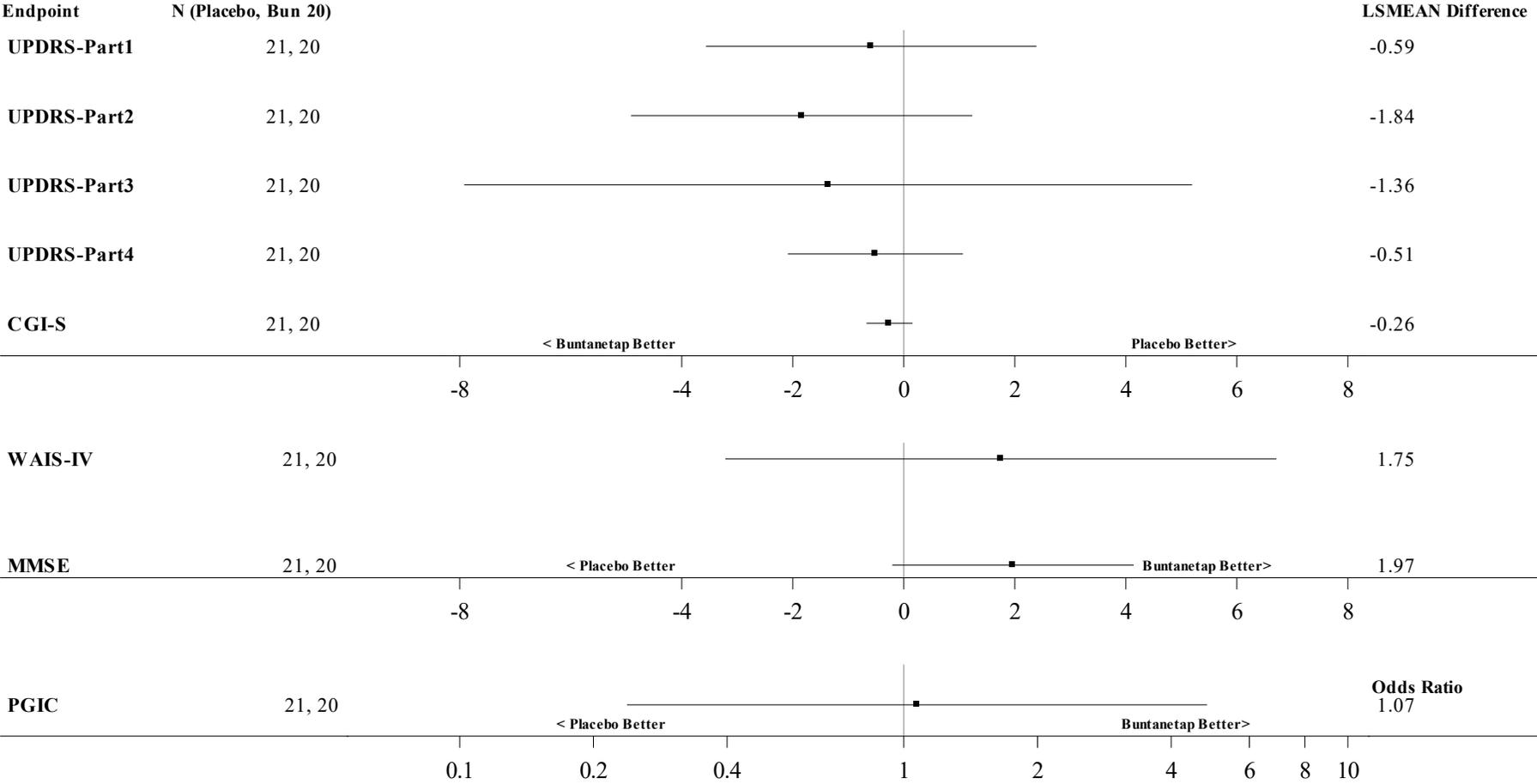
* compared to placebo, # compared to baseline: #/* p<0.05

The study met its cognition endpoint in the **ITT**, **cognitively impaired**, and **cognitively impaired with amyloid pathology Parkinson's patients**



* compared to placebo: * p<0.05; **p<0.01

Forest plot shows **consistency and robustness** of efficacy in PD patients with MMSE 20-26



Buntanetap shows strong safety profile in ITT PD population

	Placebo	10 mg Buntanetap	20mg Buntanetap	All Doses
	176	174	173	774
# Subjects with any AEs	91 (51.7%)	98 (56.3%)	108 (62.4%)	297 (56.8%)
# Subjects with TEAEs	86 (48.9%)	96 (55.2%)	105 (60.7%)	287 (54.9%)
# Subjects with Serious TEAEs	5 (2.8%)	4 (2.3%)	11 (6.4%)	20 (3.8%)
# Subjects with TEAEs Related to Study Drug	28 (15.9%)	28 (16.3%)	26 (15.9%)	82 (15.7%)
# Subjects with Serious TEAEs Related to Study Drug	0	0	0	0

AE = Adverse Event

TEAE = Treatment Related Adverse Event

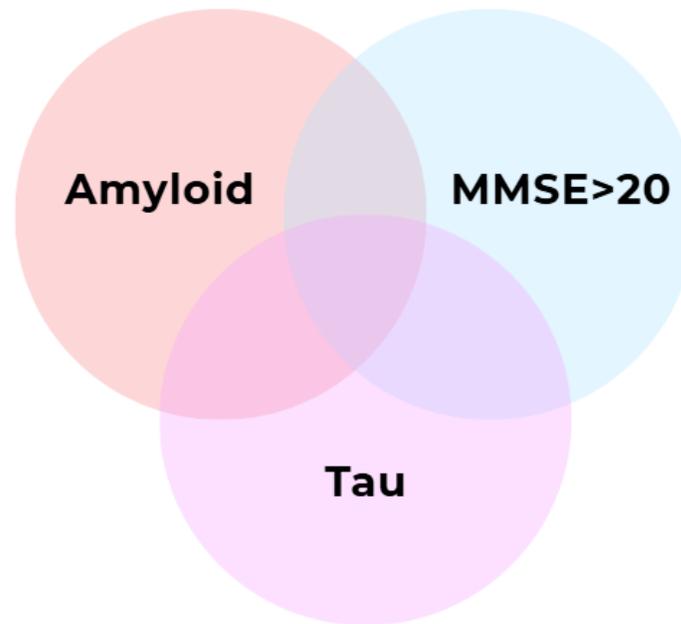
Summary: buntanetap and cognition

The background of the slide features a stylized neural network. It consists of several interconnected nodes, each represented by a central yellow circle with a blue outline. These nodes are linked by thin, light blue lines that form a complex web across the entire page. The overall color scheme is a deep blue, with the yellow and light blue providing contrast for the network structure.

Buntanetap shows a unified and reproducible pattern in improving cognition across AD and PD

Buntanetap demonstrates the most pronounced cognitive benefit in patients with mild dementia (MMSE >20) and biomarker-confirmed presence of amyloid and tau.

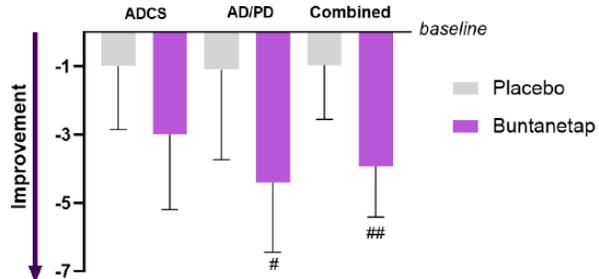
Unified treatment pattern



Buntanetap shows a fast improvement of cognition across four studies in Alzheimer's and Parkinson's patients

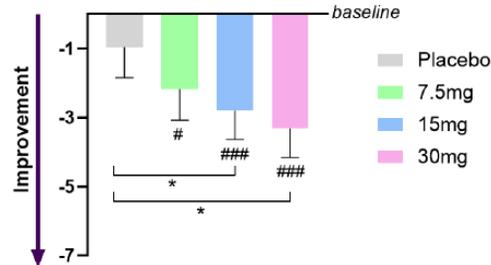
Phase 1/2 studies

ADAS-Cog11 in early AD and PD patients (N=26)



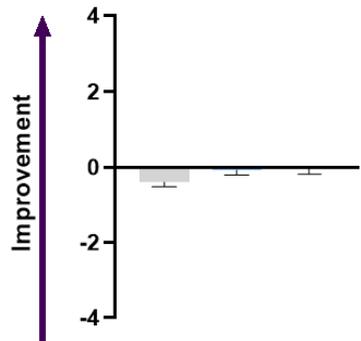
Phase 2/3 study

ADAS-Cog11 in amyloid-positive mild AD patients (N=90)

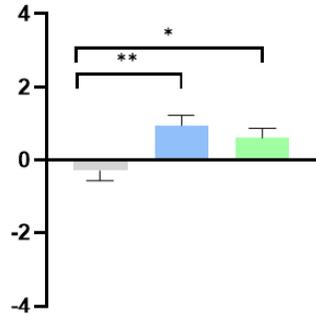


Phase 3 study

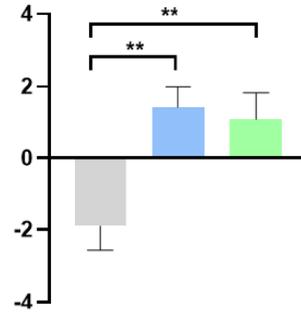
MMSE change in ITT PD population (N=523)



MMSE change in PD patients with mild dementia (N=173)



MMSE Change in amyloid-positive PD patients with mild dementia (N=40)



Placebo 10mg 20mg

Phase 1/2 studies in early AD and PD

1 month of treatment

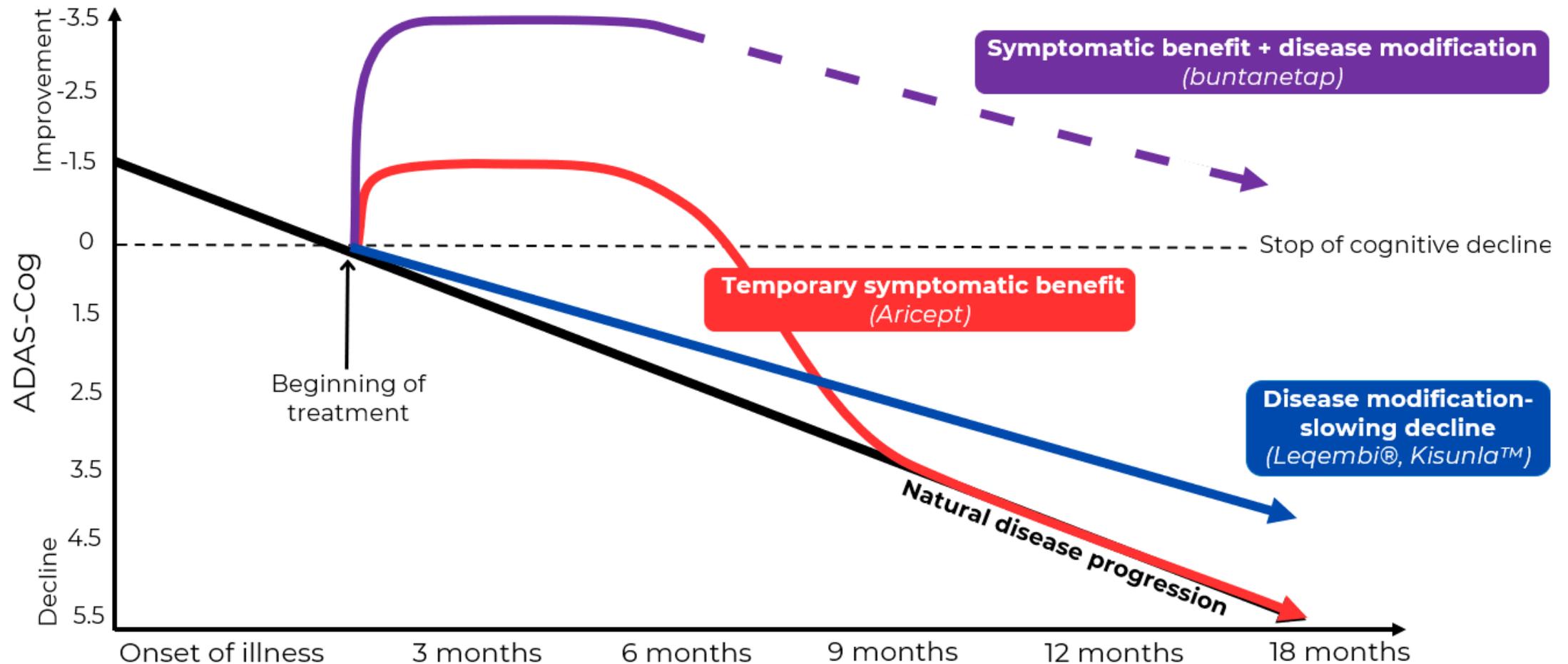
Phase 2/3 study in early AD

3 months of treatment

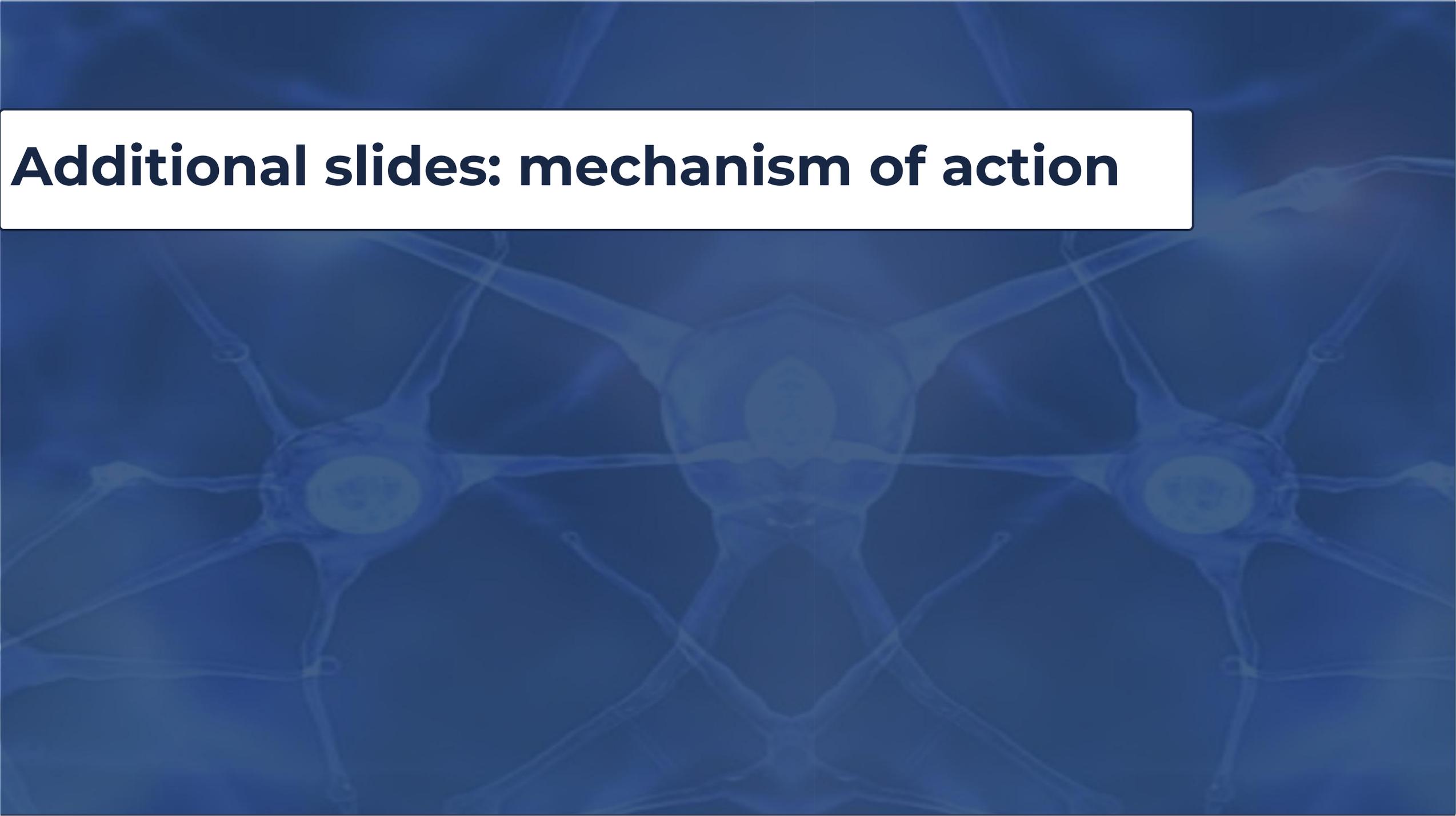
Phase 3 study in early PD

6 months of treatment

Disease modification vs symptomatic benefit in the treatment of Alzheimer's disease



Additional slides: mechanism of action

The background of the slide features a stylized, blue-tinted illustration of a neural network. It shows several interconnected neurons with prominent cell bodies (soma) and a dense web of axons and dendrites extending across the frame. The overall aesthetic is scientific and modern, with a monochromatic blue color scheme.

Annovis' new approach to attack AD and PD

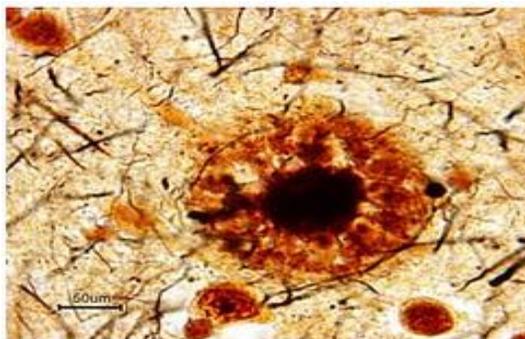
Chronic and acute brain insults lead to high iron levels, resulting in overexpression of neurotoxic proteins, impaired axonal transport, inflammation and neurodegeneration. Attacking one neurotoxic protein results in minimal effect.

Buntanetap targets RNA and inhibits the production of multiple neurotoxic proteins simultaneously.



Amyloid β

Alzheimer's - Parkinson's



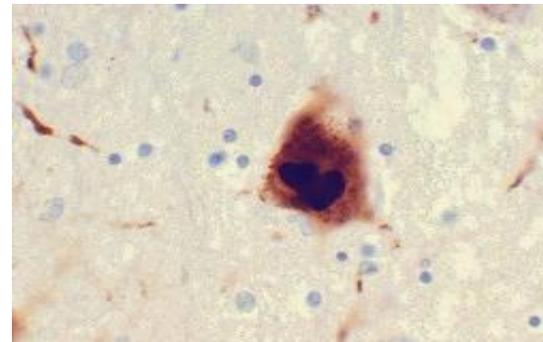
Tau

Tauopathies - AD, PD, FTD, CTE



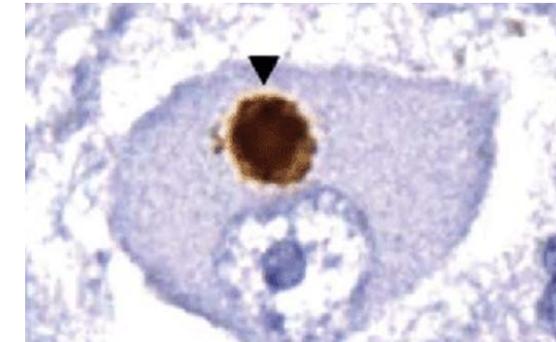
aSynuclein

Parkinson's - Alzheimer's



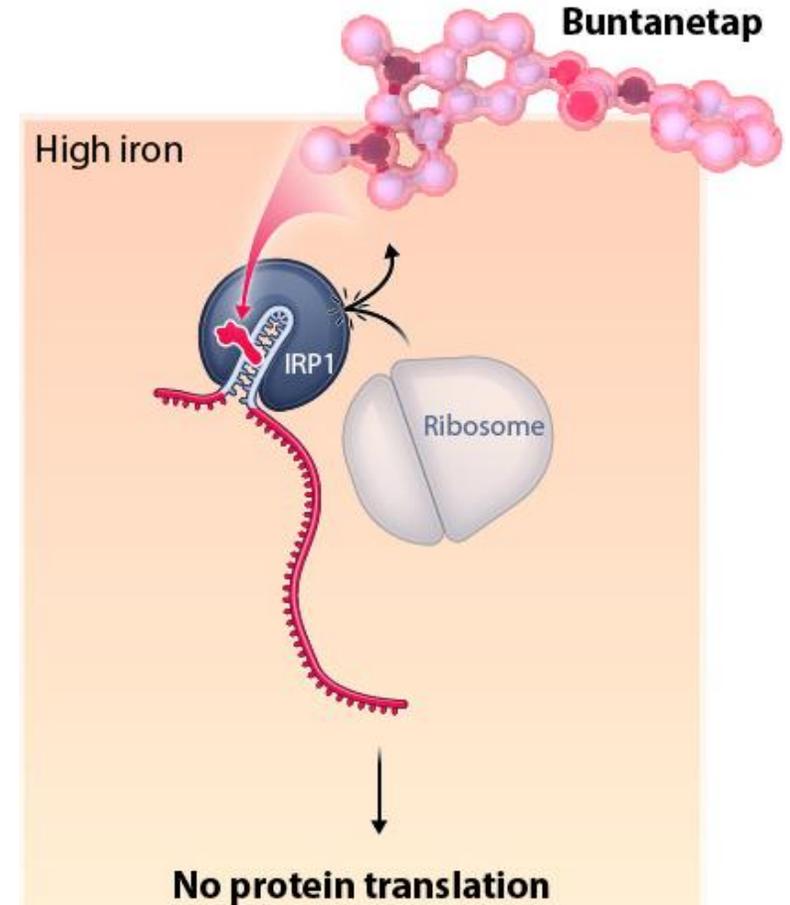
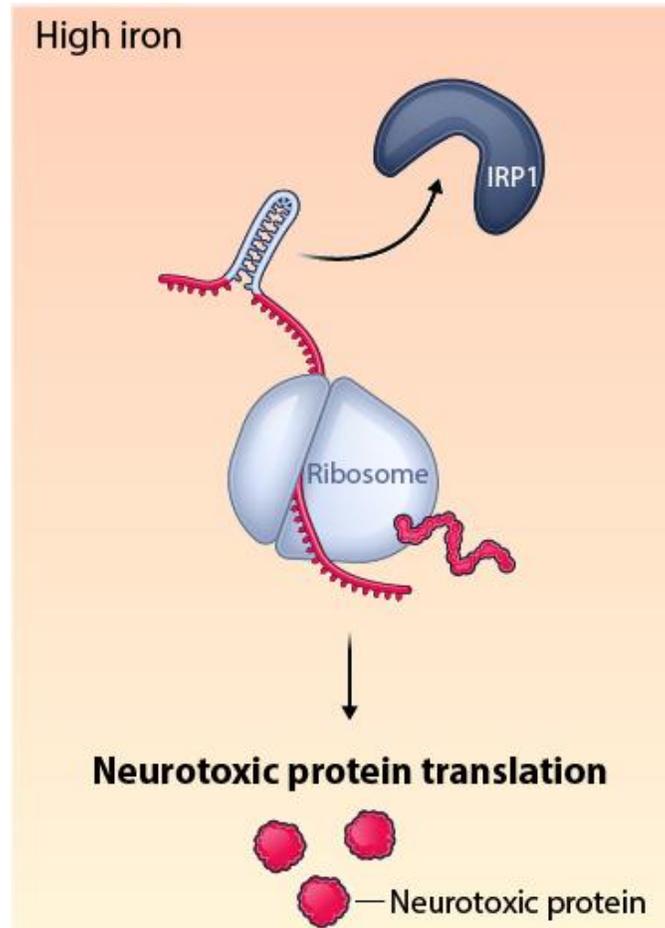
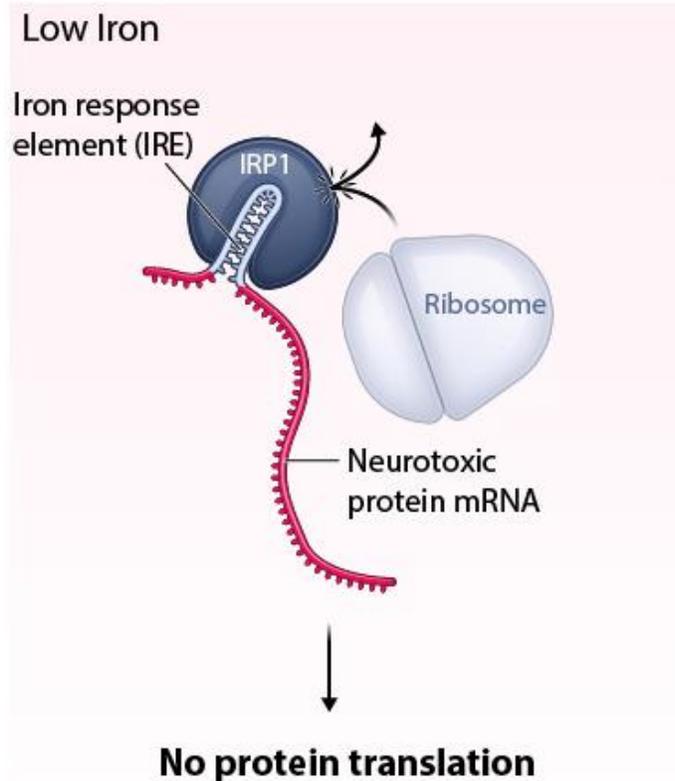
TDP43

ALS, AD, PD, FTD, CTE

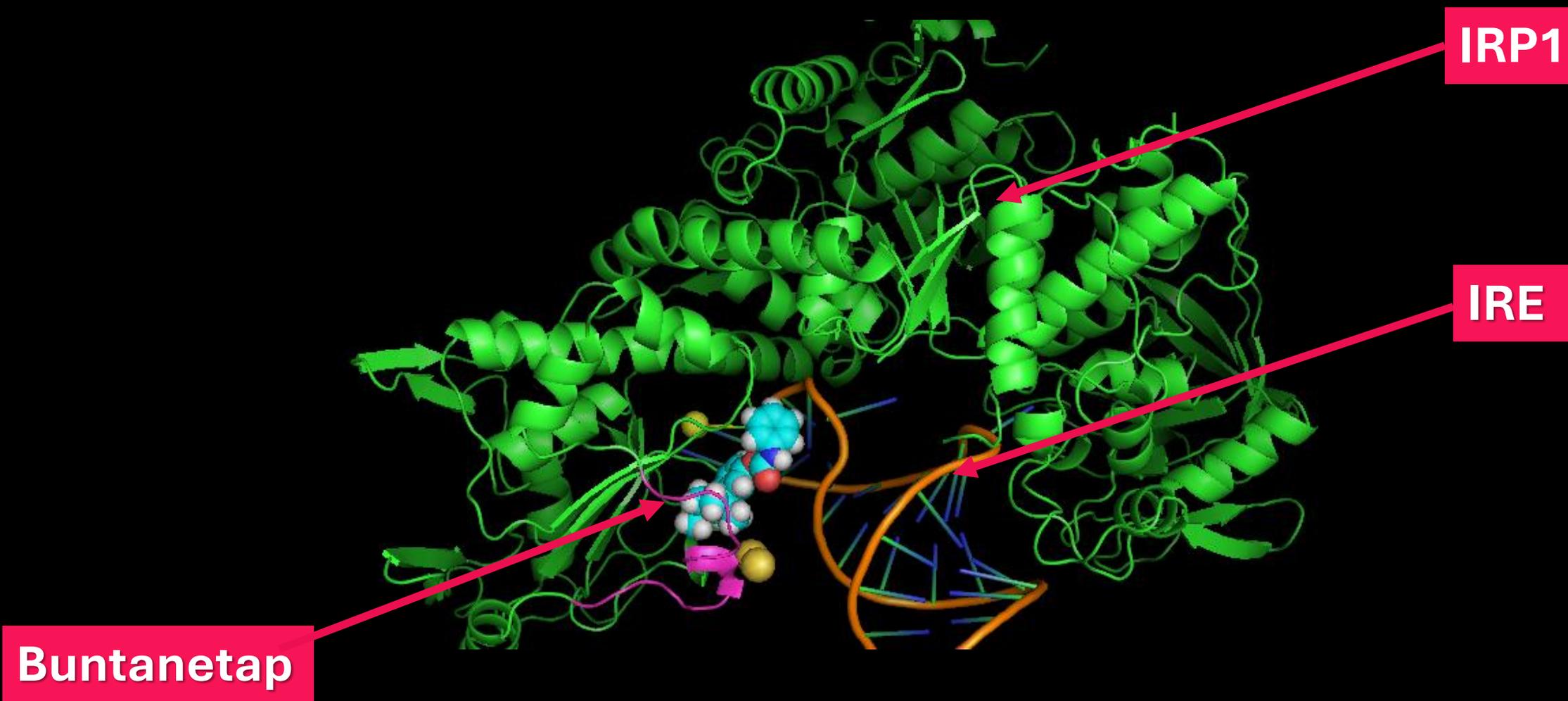


Buntanetap: RNA-targeting small molecule

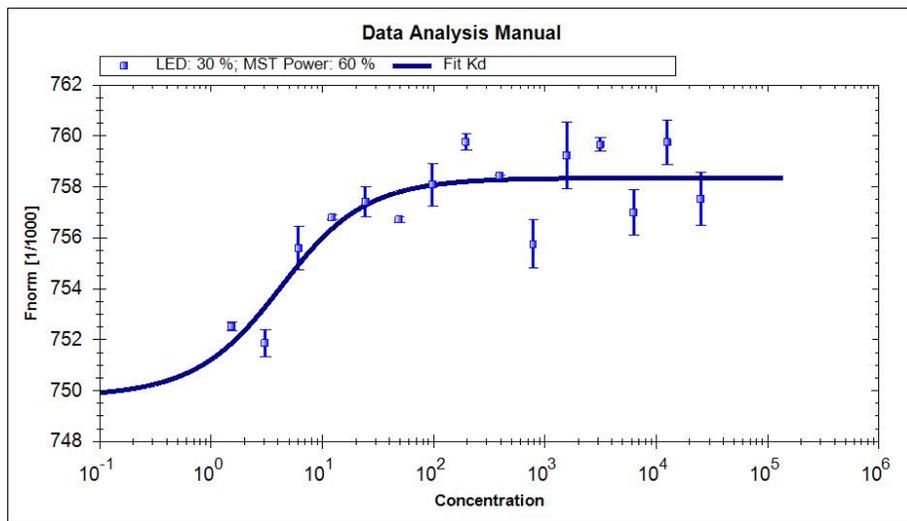
Mechanism of action



Molecular Model of how buntanetap locks IRP1 in the mRNA binding position



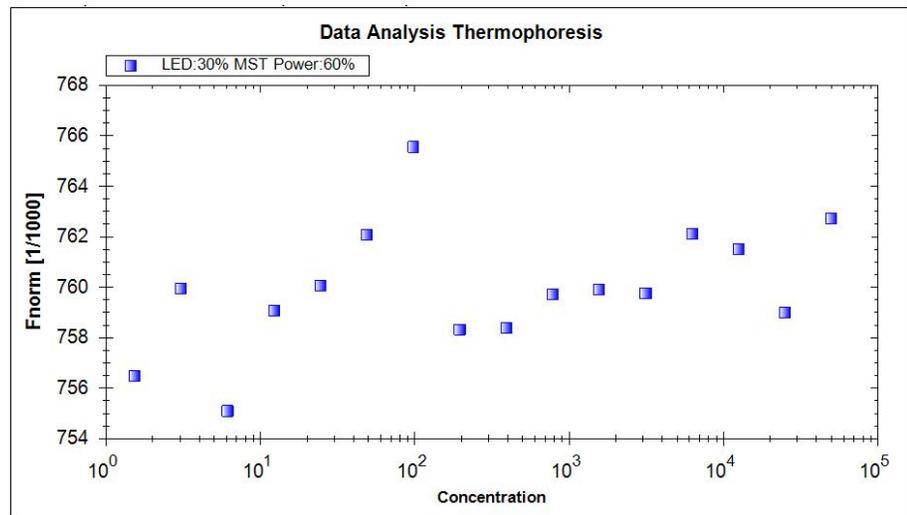
IRE-IRP1 binding is specific for mRNAs coding for neurotoxic proteins



APP IRE/IRP1/Buntanetap
Kd 3.2 nM

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

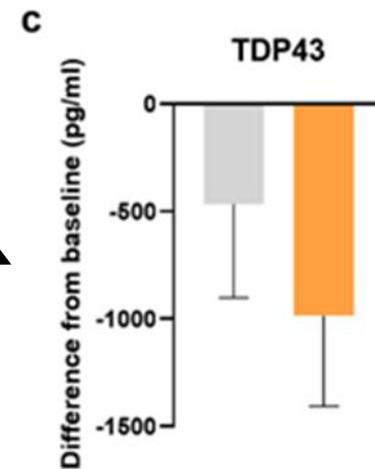
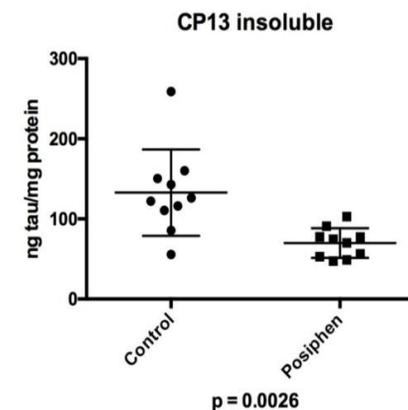
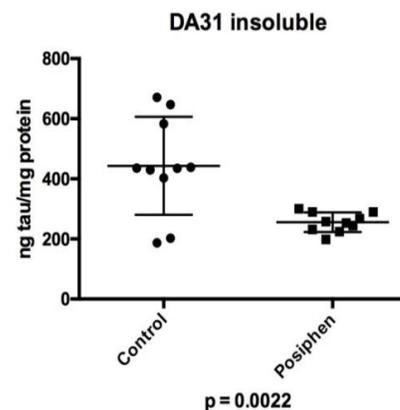
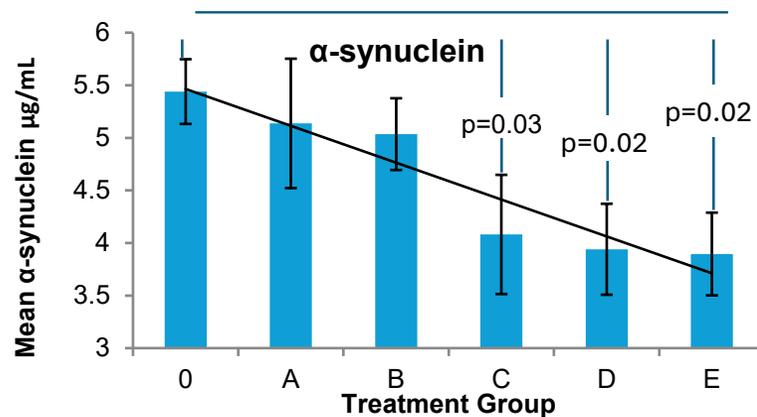
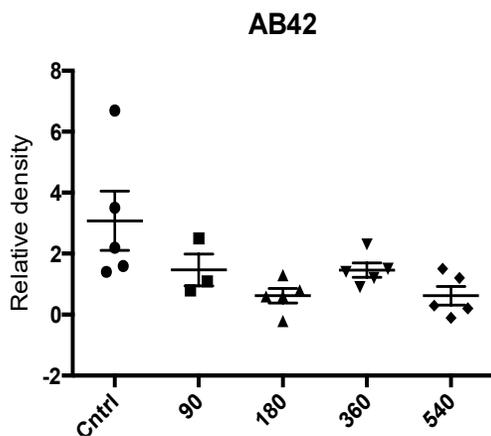
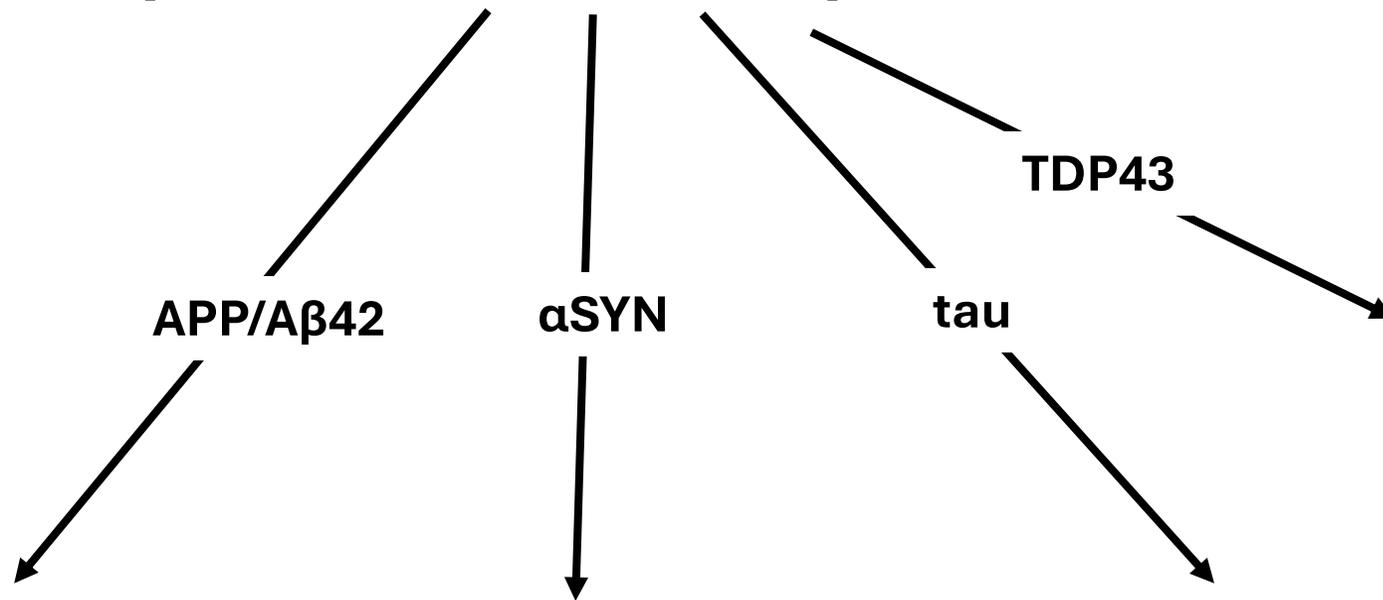
Buntanetap binds specifically to the **APP IRE**, but not to the ferritin IRE



Ferritin IRE/IRP1/Buntanetap
No Kd

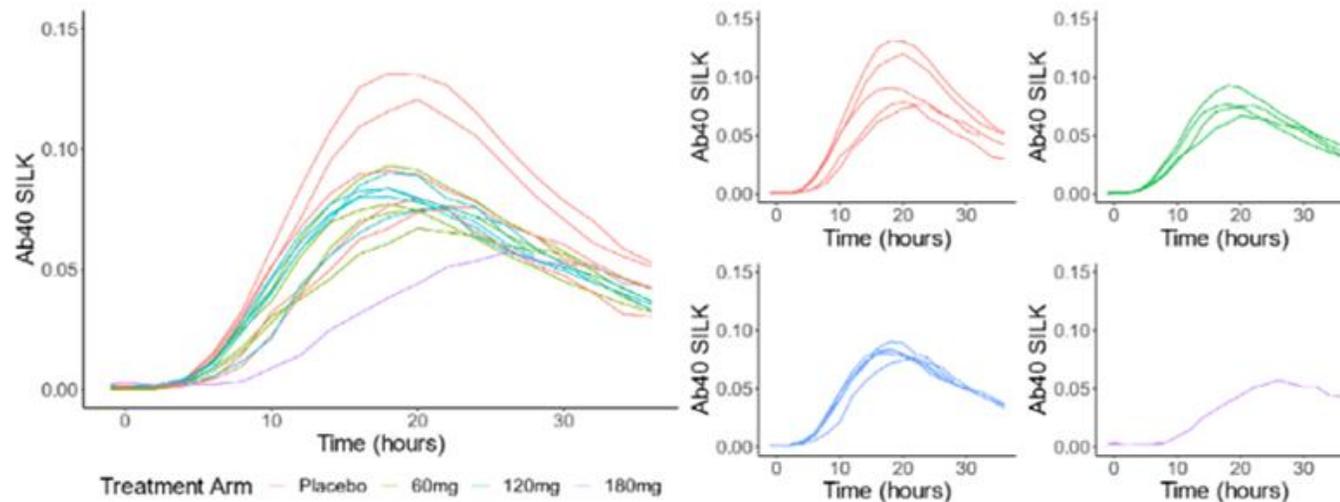
Buntanetap lowers neurotoxic proteins in mouse brain

Marker	(%) Drop	p-values
APP	39.8	0.008
CTF β	46.8	0.0024
CTF α	48.5	0.0031
A β 42	68	0.0008



Target engagement: APP, A β 42, A β 40, and A β 38 synthesis

SILK Evaluation of A β 40 in CSF

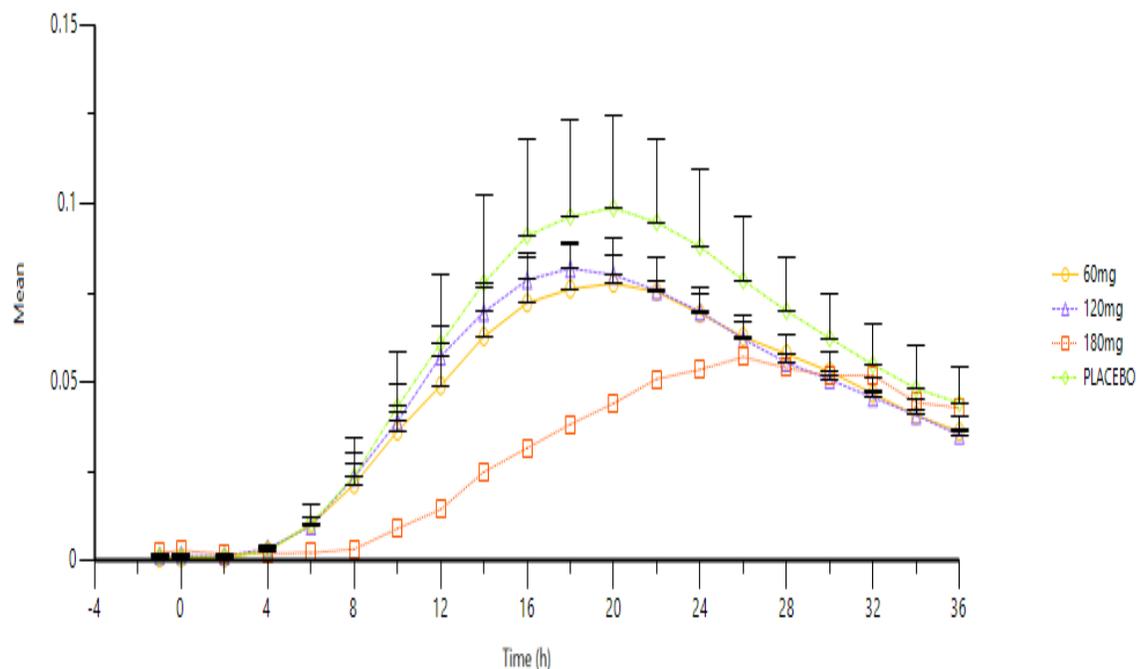


The Discover study was conducted through collaboration with ADCS and was designed to understand buntanetap's effect on synthesis of neurotoxic aggregating proteins – APP, using Stable Isotope Labeling Kinetic (SILK) analysis.

For SILK, lumbar and venous catheters were placed in AD patients and $^{13}\text{C}_6$ -leucine infused for 9 hours with dosing of placebo or buntanetap according to their dose arm (placebo, 60mg once, 60mg twice or 60mg three times per day for 21 days). CSF and venous blood were collected every two hours over a 36-hour period. Pharmacokinetics of the drug and its metabolites were assessed in plasma and CSF.

APP, A β 40, and A β 42 synthesis was measured by LC-MS differentiation of heavy $^{13}\text{C}_6$ -leucine labelled APP versus light ^{12}C -leucine normal APP, A β 40, and A β 42.

Target engagement: buntanetap inhibits translation of A β

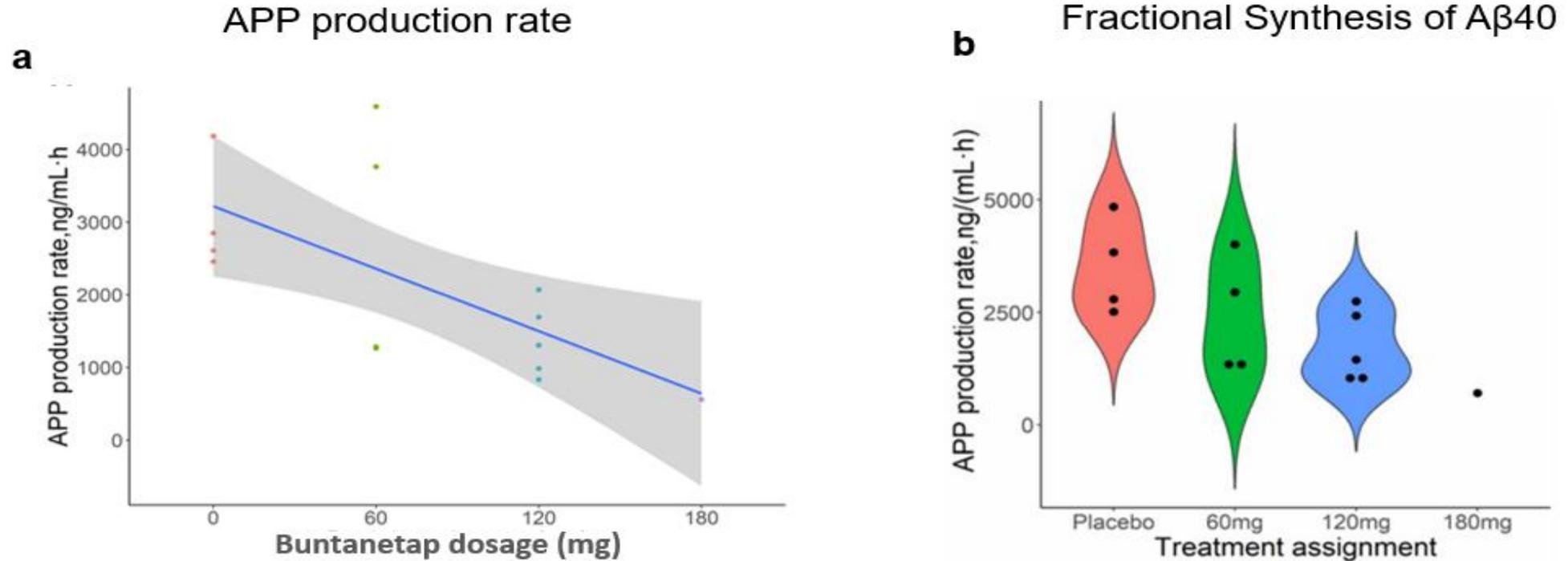


Buntanetap showed a dose-dependent lowering of A β 40 production as seen by a delayed start, lower synthesis rate, lower C_{max}, and smaller Area Under the Curve (AUC) of produced A β 40.

Buntanetap statistically significantly reduced AUC (A β 38 p=0.039, A β 40 p=0.045), C_{max} of A β 38 and A β 40 (A β 38 p=0.04, A β 40 p=0.036), proving that buntanetap is a translational inhibitor of APP synthesis.

Treatment mg	Start h	Slope	C _{max}	T _{max} h	AUC
0	0.2	0.0065	0.1	14	1.971
60	0.5	0.0059	0.08	18.8	1.631
120	1.1	0.0053	0.07	19.5	1.529
180	6.2	0.0028	0.05	26	1.033

Target engagement: buntanetap reduces APP production rate



The APP production rate (calculated by ADCS; Galasko & Elbert) showed a statistically significant decrease in APP synthesis rate with increasing dose of buntanetap (859 ng/mL·h decrease per 60 mg buntanetap ($p=0.012$). These results prove that buntanetap lowers the rate of APP synthesis.

Buntanetap improves axonal transport

“Axonal transport disruption is linked to human neurological conditions.”

- Nature Review, September 2019

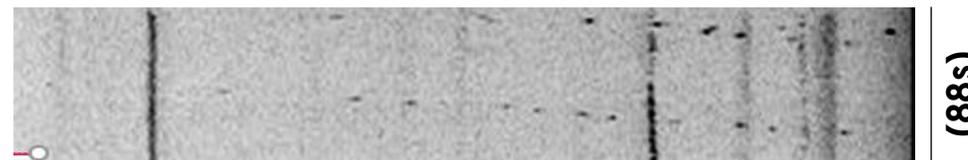
Axonal transport is responsible for:

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

— Retrograde (0.5 frame/sec) —→

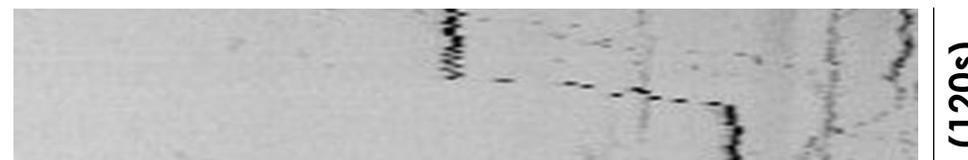
Normal Transport

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

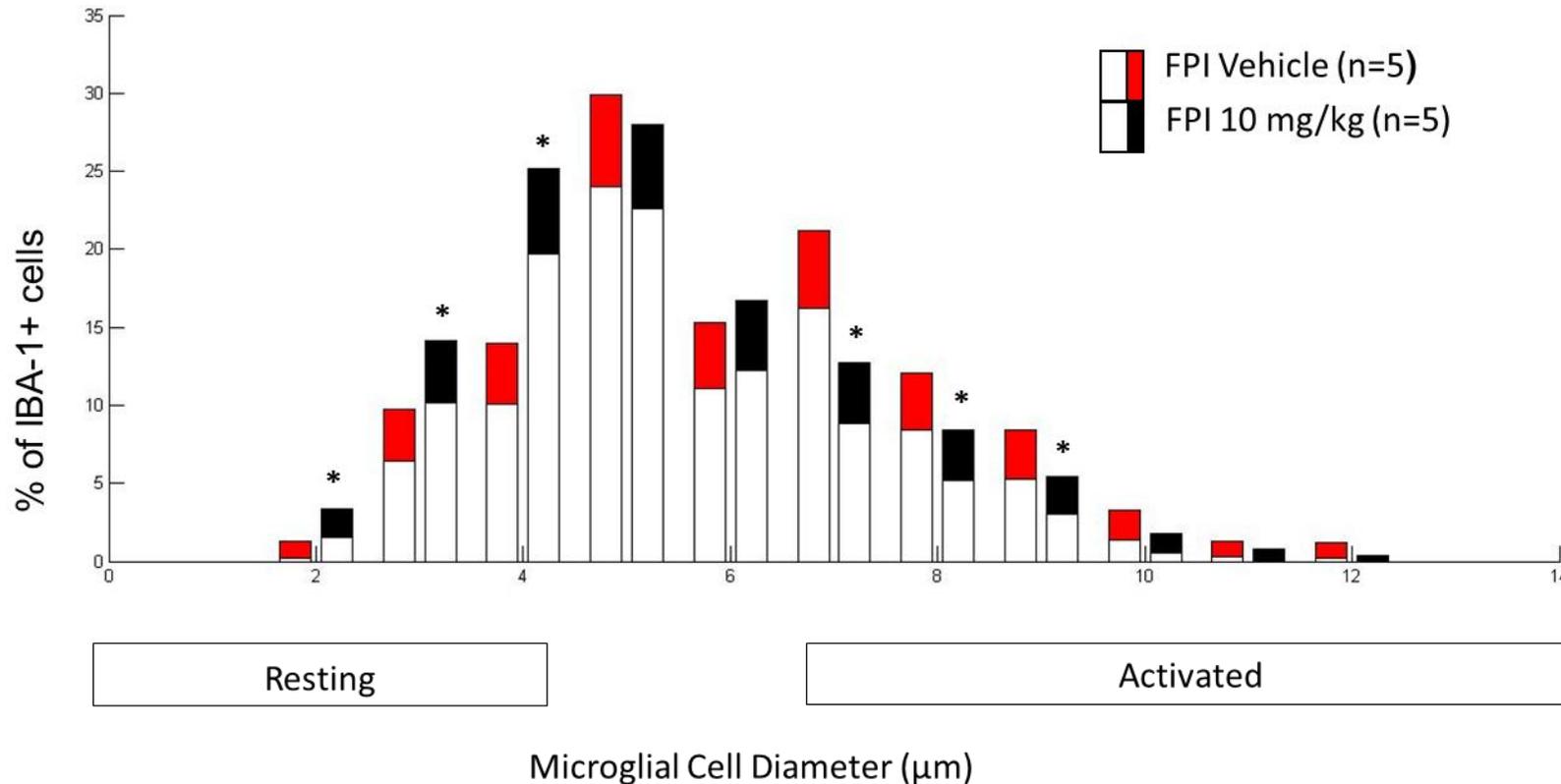
The **Flow and Speed** of axonal transport is improved.



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

Buntanetap decreases inflammation (microglia activation)

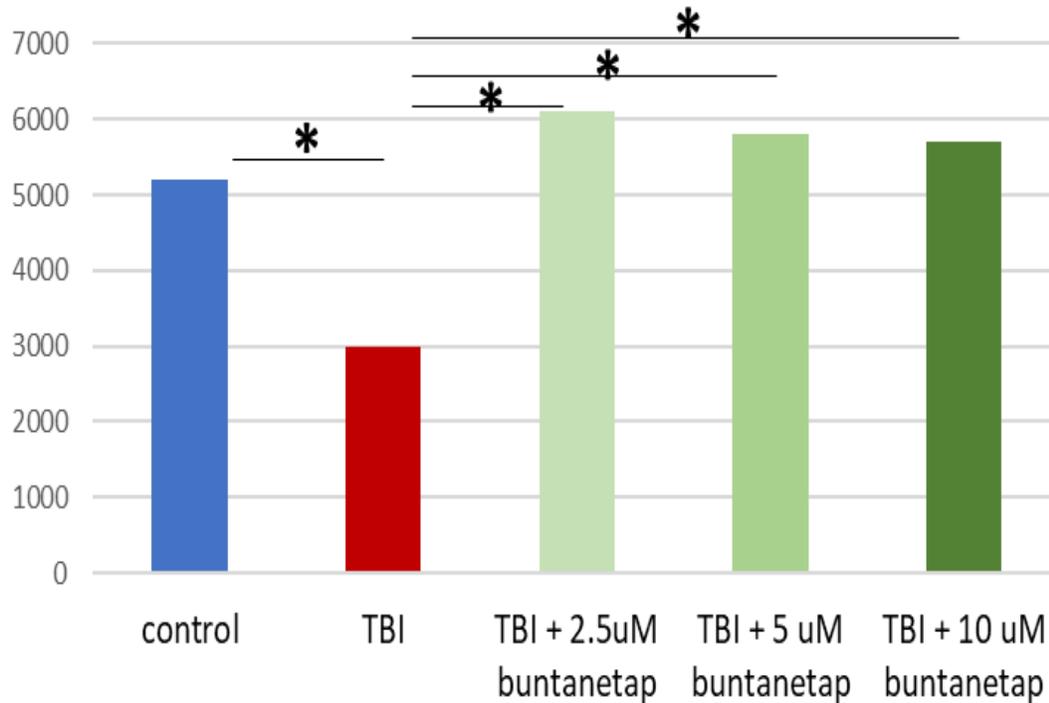
Data (Mean + 95% CI) analyzed with Bootstrapping method, *p<0.05



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

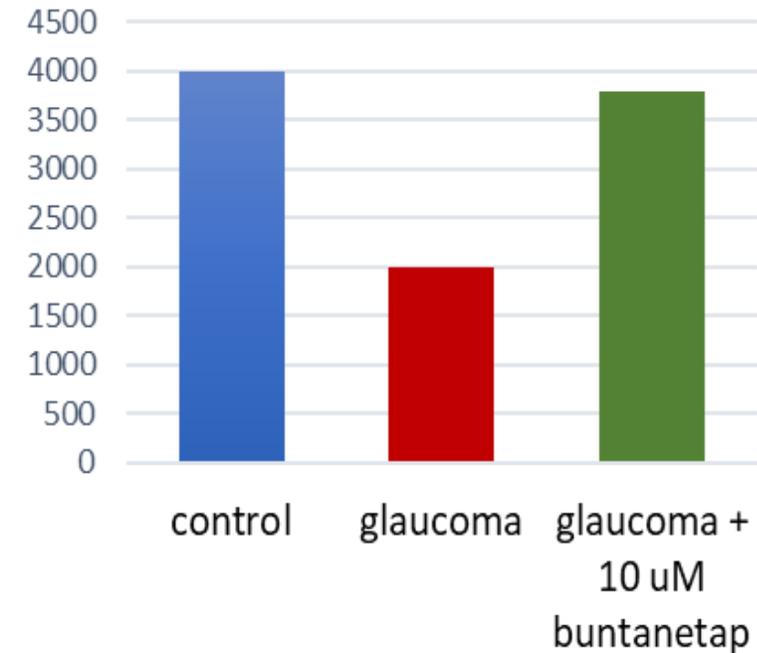
Buntanetap protects nerve cells from dying

Alive cells in TBI brain



Buntanetap protects nerve cells from dying in mice with Traumatic Brain Injury (TBI)

Alive cells in glaucoma retina



Buntanetap protects nerve cells from dying in the eye of rats with glaucoma

Summary of studies in animal models

Evaluated function	Test	Animal model
Memory & Learning	<ul style="list-style-type: none">• Mazes	<ul style="list-style-type: none">• APP/PS1 Alzheimer's mice• Trisomic Down Syndrome mice• Stroke mice• Traumatic Brain Injury rats
Movement	<ul style="list-style-type: none">• Colonic motility• Grip strength	<ul style="list-style-type: none">• aSYN Parkinson's mice• Tau Frontotemporal Dementia mice
Vision	<ul style="list-style-type: none">• Sight	<ul style="list-style-type: none">• Glaucoma rats
Infections	<ul style="list-style-type: none">• Cell death	<ul style="list-style-type: none">• <i>P. Gingivalis</i> mice• COVID mice



ANNNOVIS

The logo features the word "ANNNOVIS" in a white, bold, sans-serif font. A red graphic element, consisting of two curved lines that form a partial circle, is positioned behind the letters "NO". The background is a dark blue with a faint, repeating pattern of interconnected lines and nodes, resembling a network or a molecular structure.