Corporate Presentation

Development path to NDA for

- Annovis
- Alzheimer's disease
- Parkinson's disease
- Mechanism of action

NYSE:ANVS

September 2025

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 patients

Phase 3 trial in early PD patients

Unique MOA

Buntanetap helps restore health of nerve cells by inhibiting production of multiple neurotoxic proteins associated with AD/PD

Growing market

6.9M
AD patients in the US

1.2M
PD patients in the US

Intellectual property (IP)

Long duration IP estate that extends into 2046

Capital-efficient approach

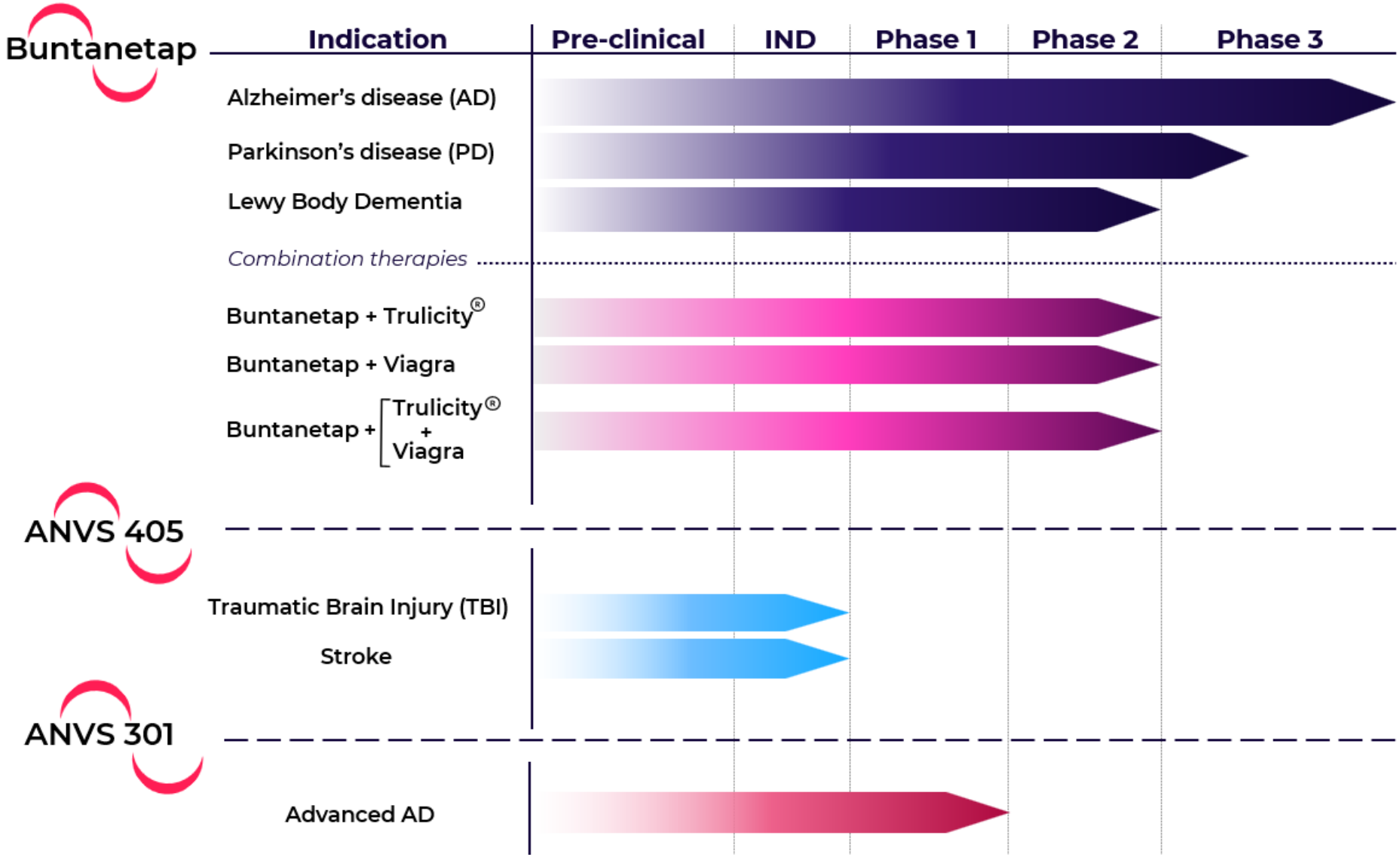
Current shares outstanding 19.5m.

Cash balance* $17.1m., debt $0

Closed $21m. public offering in Feb. 2025

**as of 6/30/25*

Pipeline


Buntanetap
Indication
Pre-clinical
IND
Phase 1
Phase 2
Phase 3
Alzheimer's disease (AD)
Parkinson's disease (PD)
Lewy Body Dementia
Combination therapies
Buntanetap + Trulicity®
Buntanetap + Viagra
Buntanetap + Trulicity® + Viagra
ANVS 405
Traumatic Brain Injury (TBI)
Stroke
ANVS 301
Advanced AD

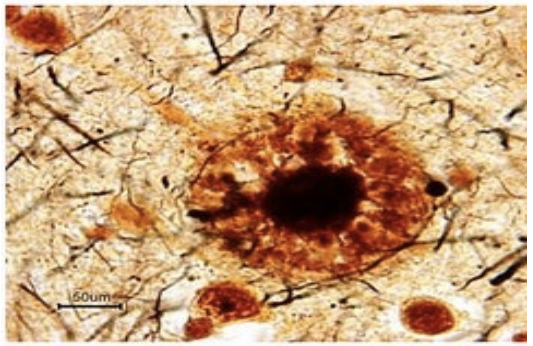
Multiple neurotoxic proteins are implicated in Alzheimer's disease

Adapted from R. Peterson, Neurology 2018

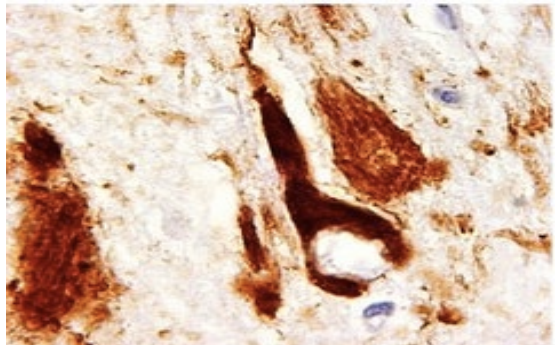
Annovis' new approach to attack AD and PD

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



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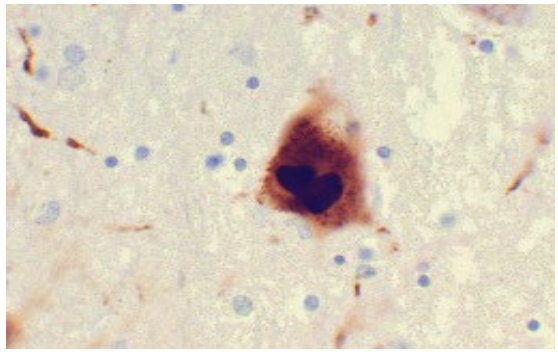
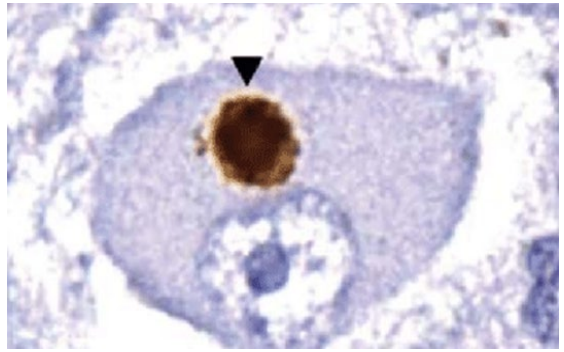
Parkinson's - Alzheimer's



TDP43
ALS, AD, PD, FTD, CTE

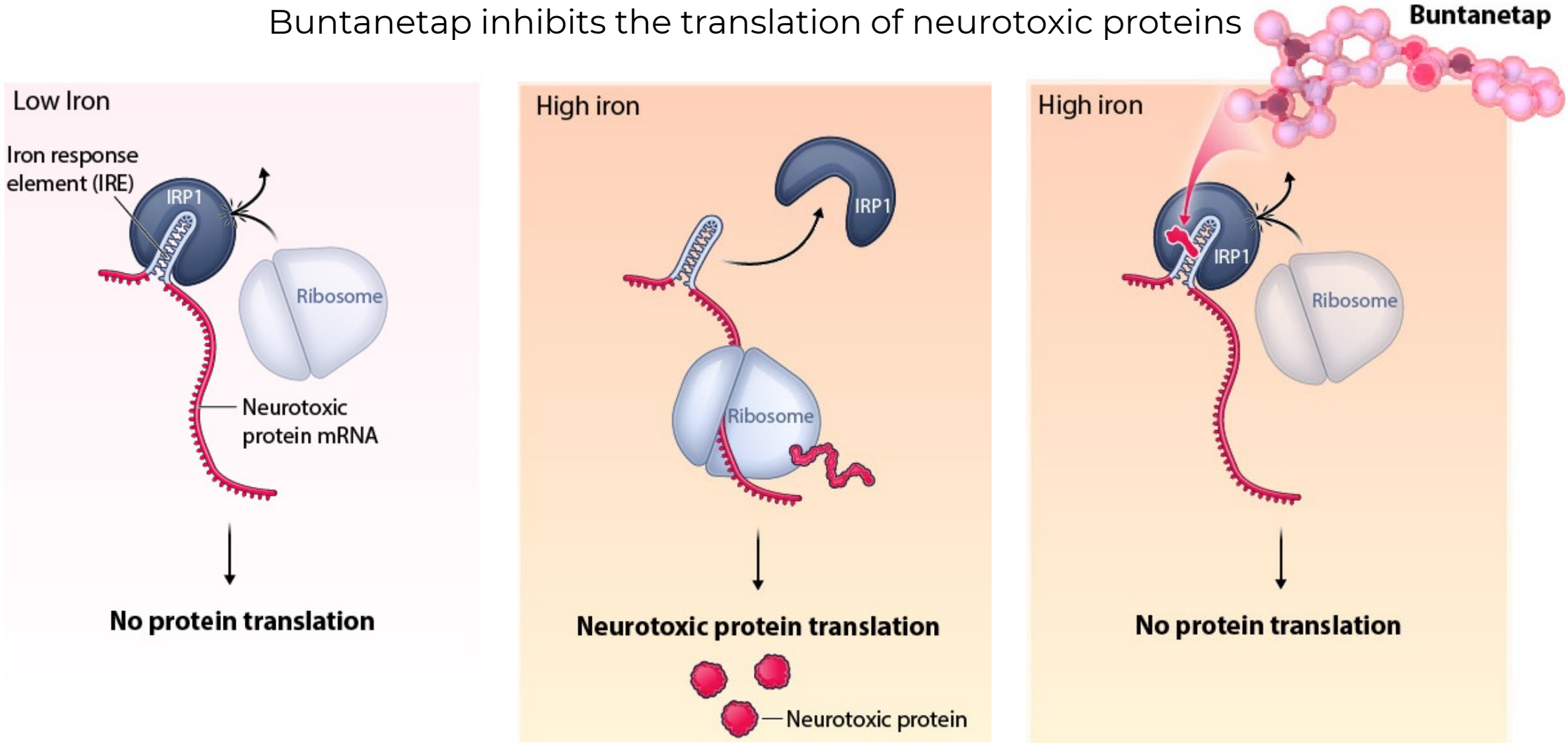


Attacking one neurotoxic protein results in minimal effect.

Buntanetap inhibits the production of multiple neurotoxic proteins simultaneously.

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

Summary of clinical studies

Healthy volunteers

Phase 1:

- 2 safety studies (n=120)
- Food effect study (n=24)
- Bridge study
  - ➢ Form A/Form 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 (*ongoing*)

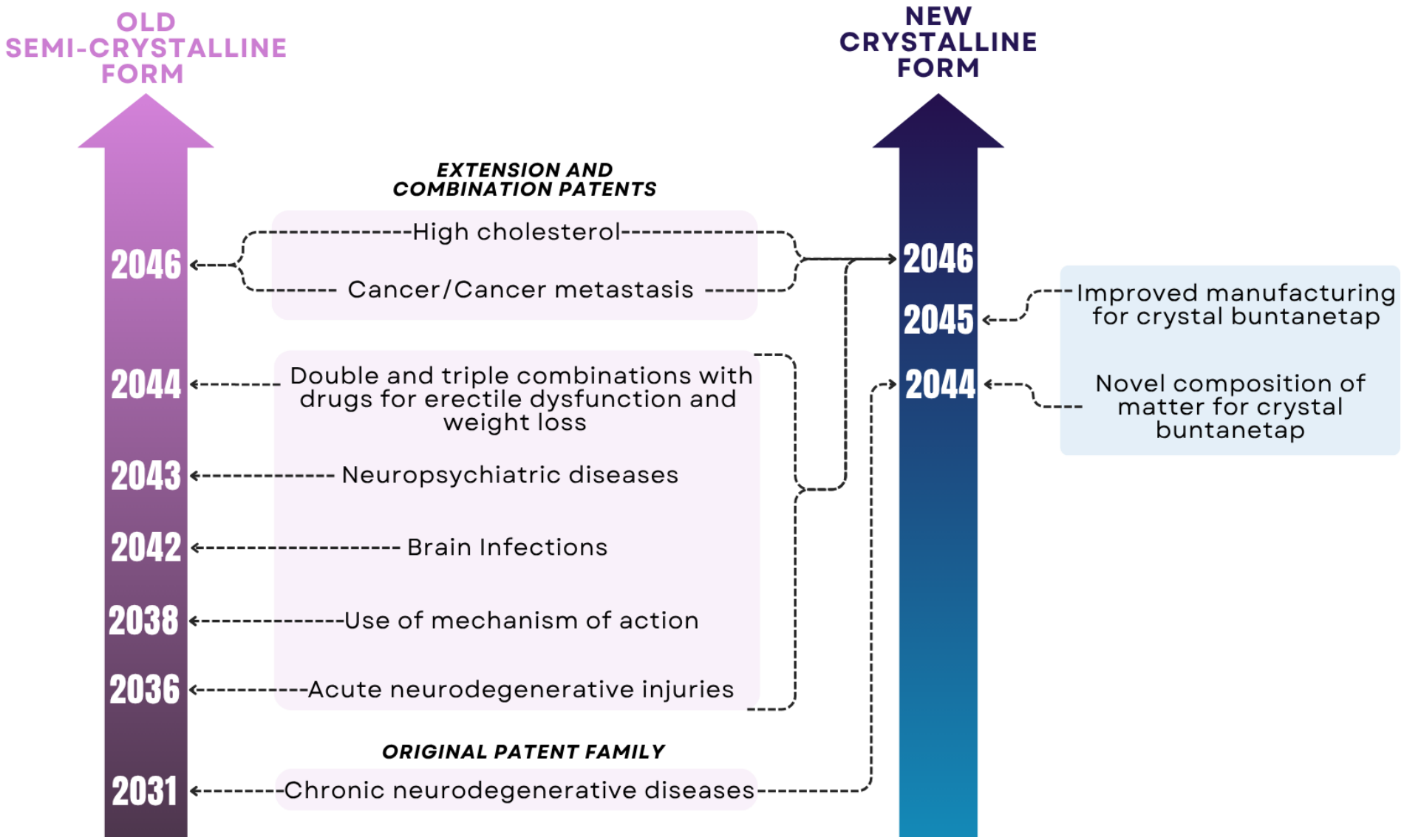
Parkinson's disease

Phase 2 - 1 study (n=58)

Phase 3 - 1 study (n=523)

Over 1000 people treated with buntanetap

Patent portfolio

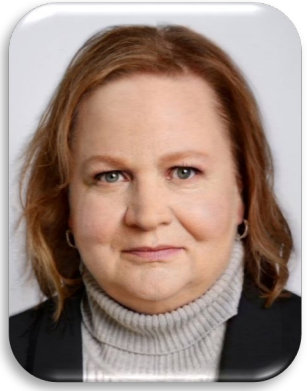


Senior management team

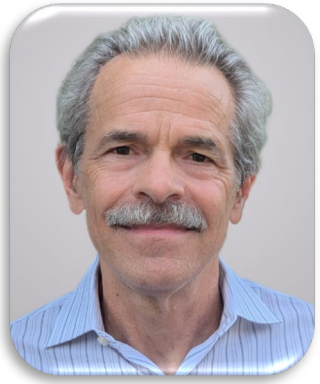
Maria Maccecchini, PhD
Founder, President, CEO

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

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

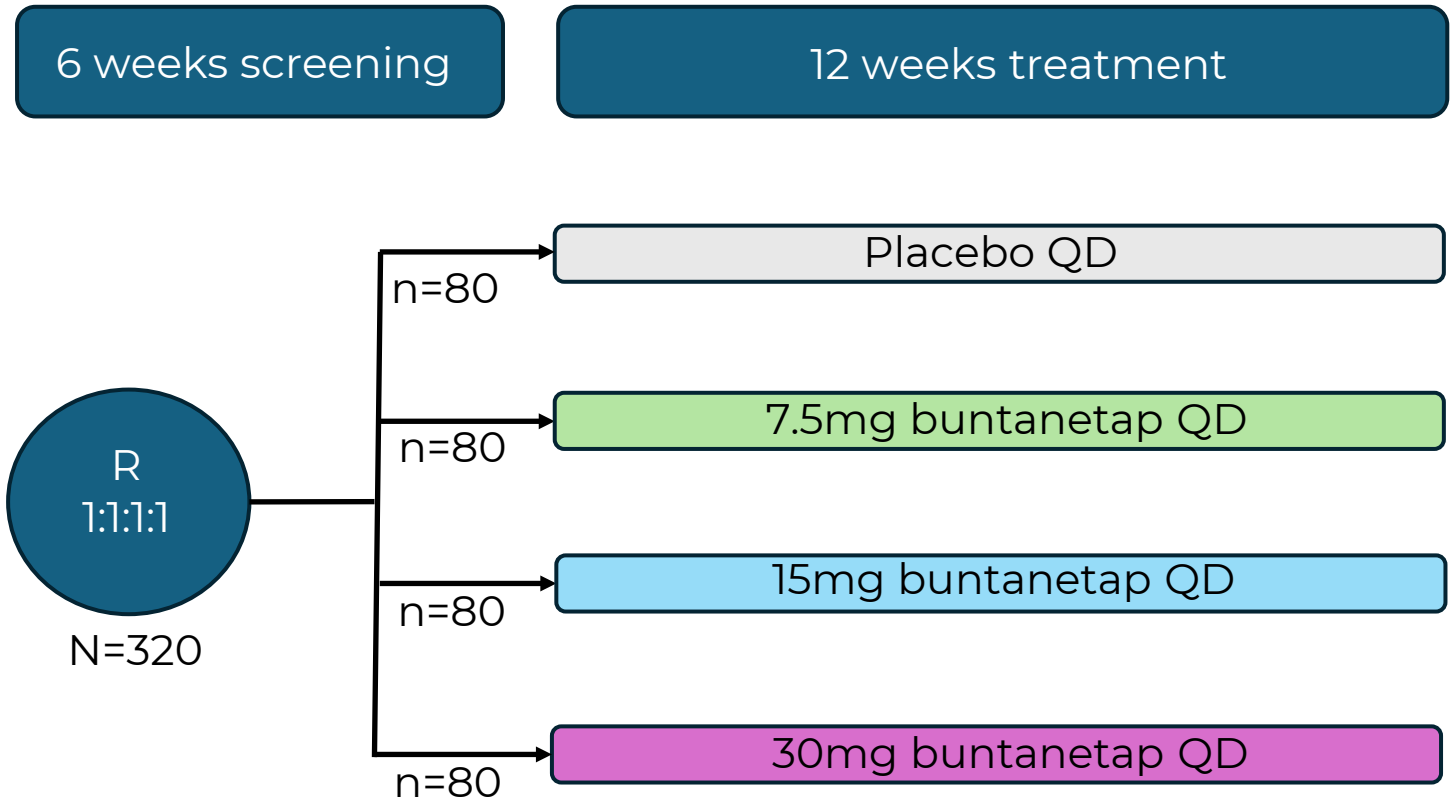
Key clinical outcome:

Primary endpoints:

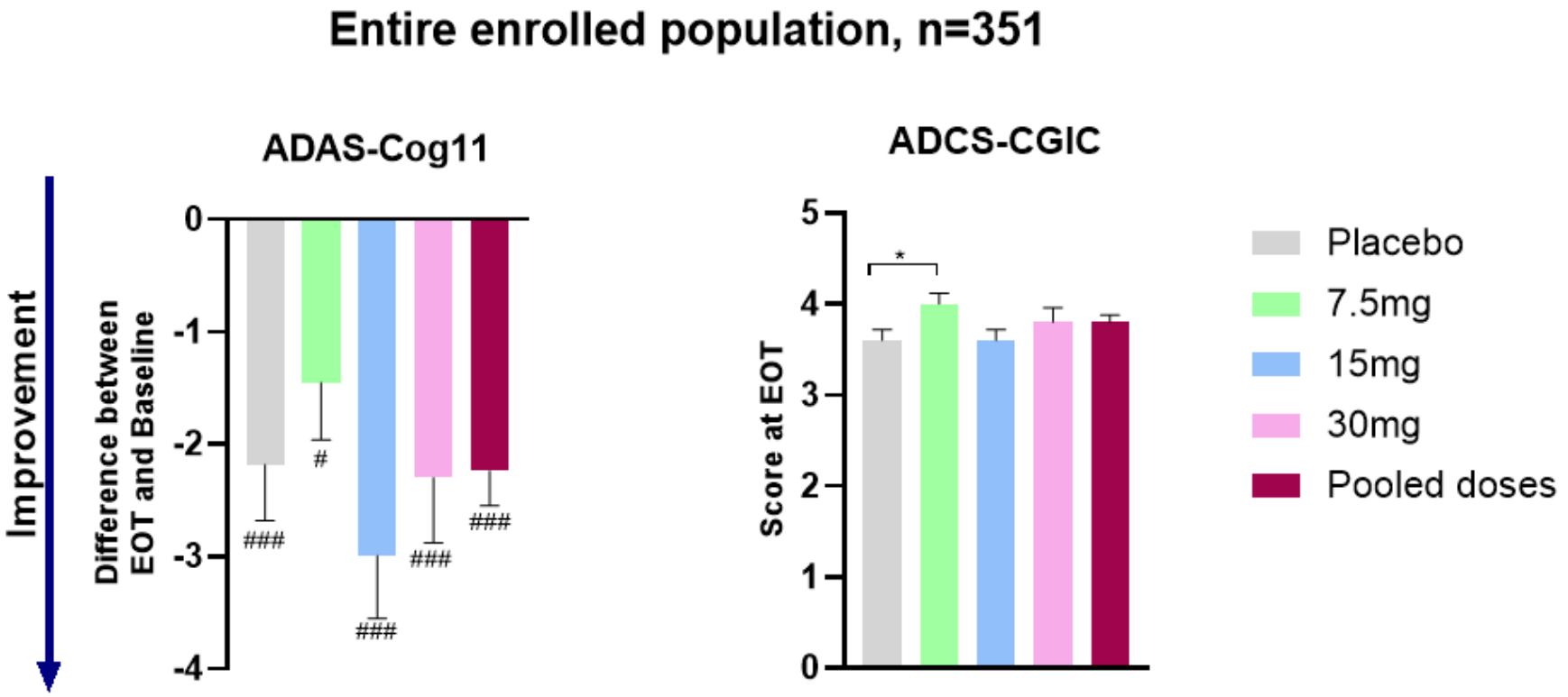
- ADAS-Cog 11
- CGIC

Key secondary endpoint:

- ADCS-ADL



ITT population: ADAS-Cog11 and ADCS-CGIC



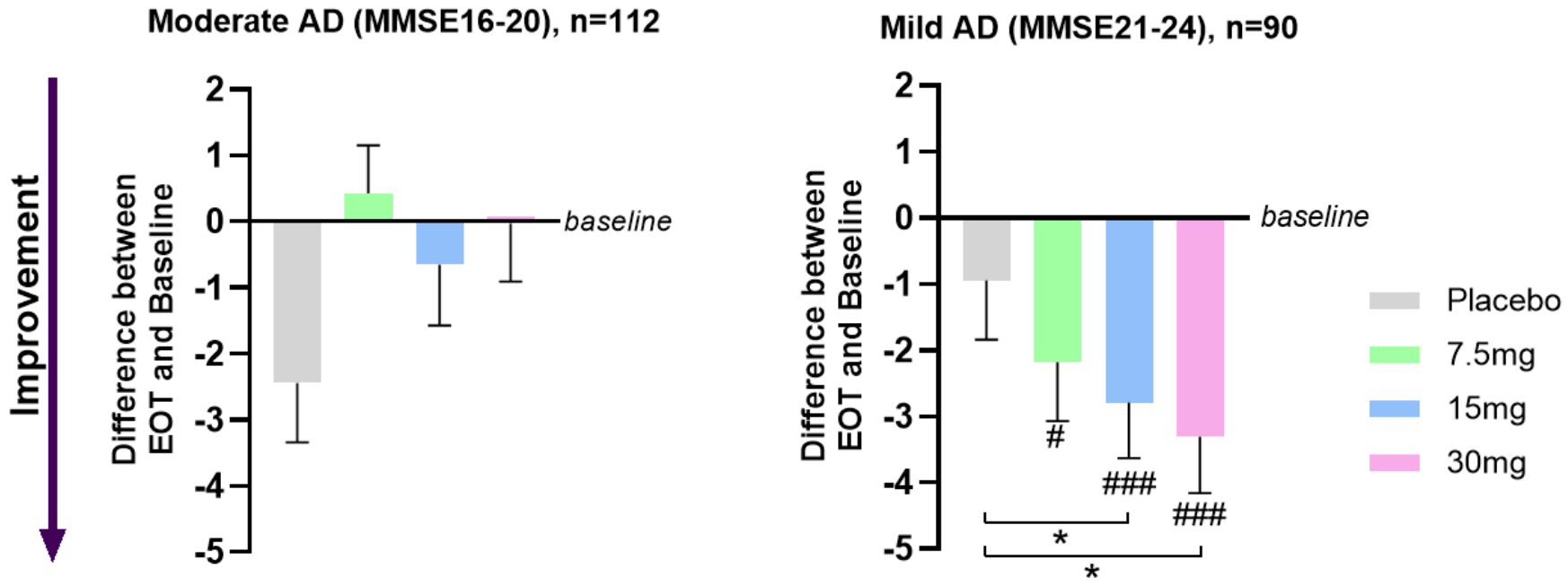
** compared to placebo*

 # compared to baseline

#/* p<0.05
p<0.01
p<0.001

Buntanetap improves cognition in patients with mild, not moderate, AD

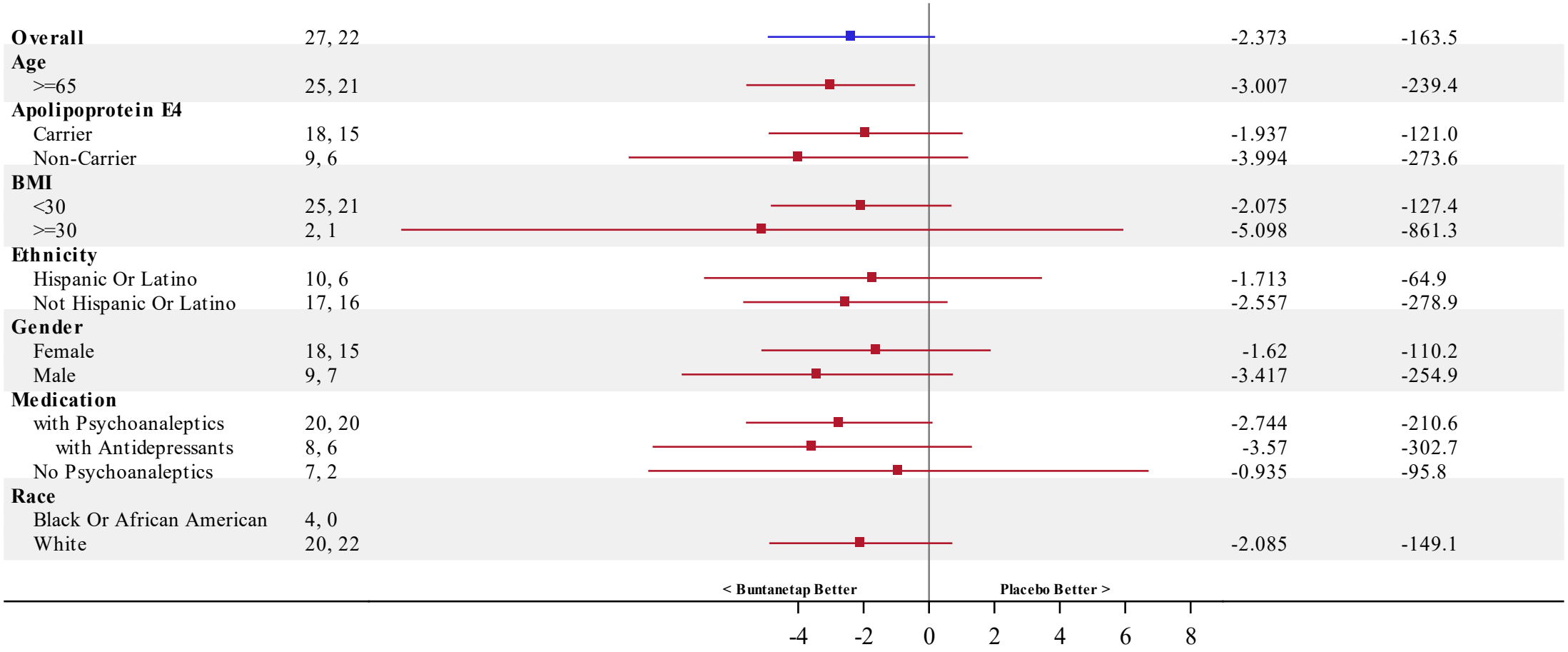
ADAS-Cog11 (pTau217/t-Tau ≥4.2%)



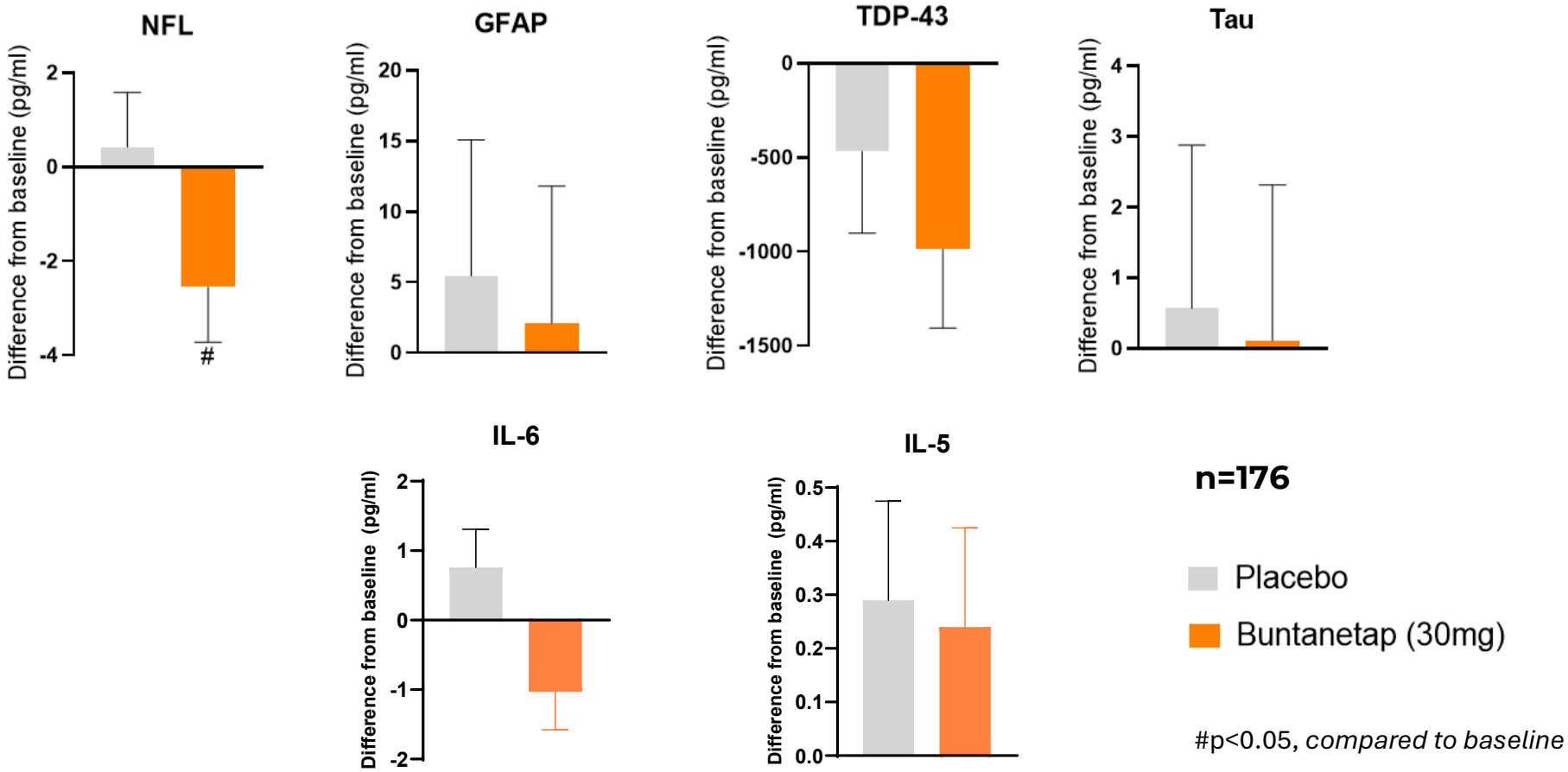
From the ITT population:
- AD patients were selected by pTau217 inclusion/exclusion.
- Mild and moderate AD were determined by MMSE selection.

 # comparing to baseline
** comparing to placebo*
*/# p<0.05
p<0.001

Forest plot shows consistency and robustness of efficacy



Biomarker data support the target and pathway engagement



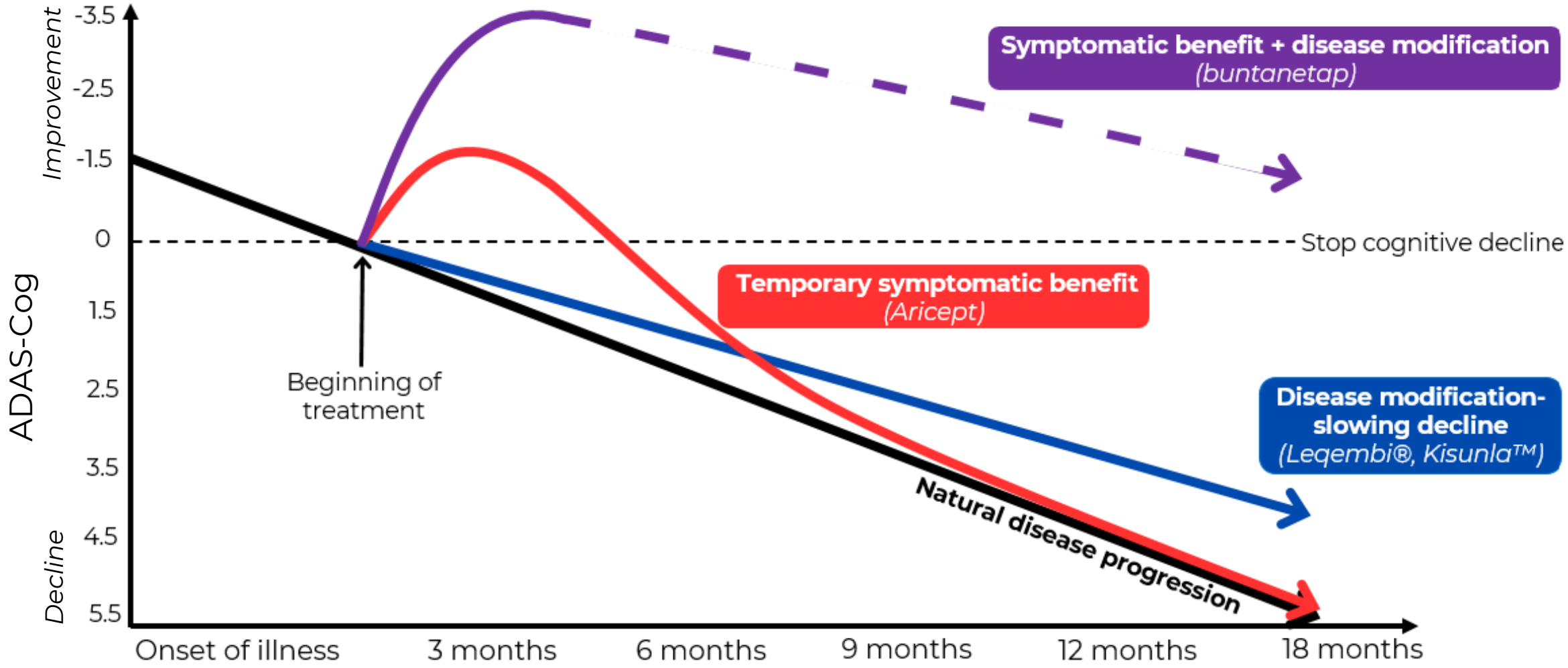
In early AD patients after 3 months of treatment, buntanetap lowers levels of neurotoxic proteins *(target engagement)*, inflammatory factors and nerve health markers *(pathway engagement)*, showing a potential disease-modifying effect.

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

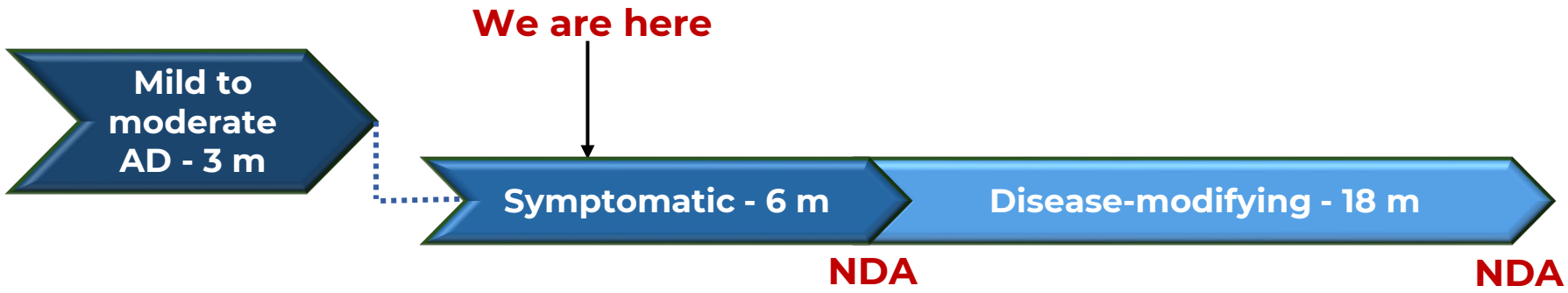
	Placebo	7.5mg Buntanetap	15mg Buntanetap	30mg Buntanetap	All Doses
APOE Carriers (N=159)	38	45	38	38	121
# TEAEs	13 (34.2%)	22 (48.9%)	17 (44.7%)	12 (31.6%)	51 (42%)
# TEAEs Related to Study Drug	1 (2.6%)	8 (17.8%)	6 (15.8%)	3 (7.9%)	17 (14%)
# Serious TEAEs	3 (7.9%)	0	0	1 (2.6%)	1 (2.5%)
# Serious TEAEs 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

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



FDA cleared AD development path



Summary:

1. FDA EOP2 meeting:
   - Granted clearance to proceed with a pivotal Phase 3 study.
   - Aligned on development pathway with new crystal formulation (one 6/18-month trial).
   - Subgroup analyses provided solid rational for design of the next trial.
   - Buntanetap shows promising efficacy in early AD patients.

2. 6/18-month trial started on February 5, 2025:
   - First 6-month readout is expected in fall 2026
   - Second 18-month readout is expected in fall 2027

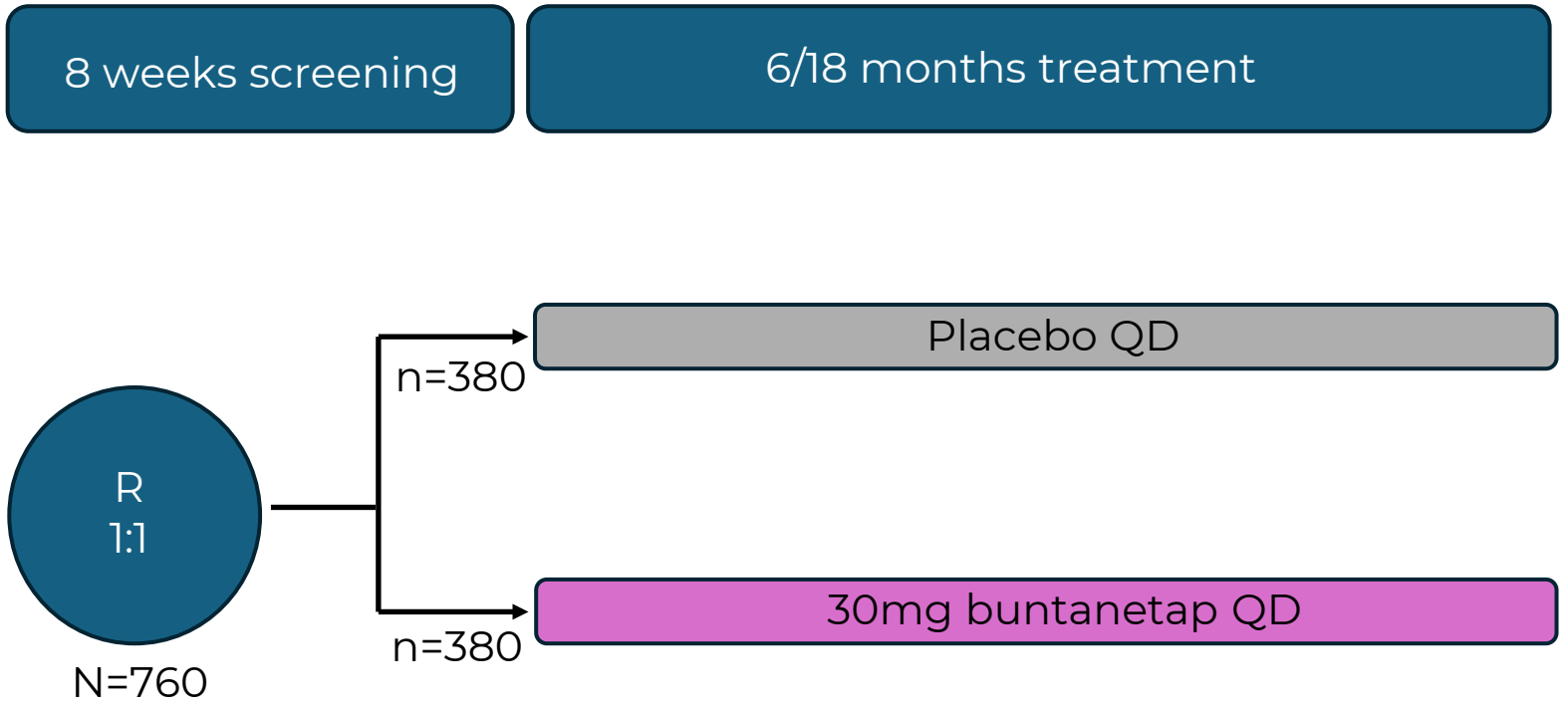
FDA-cleared pivotal Phase 3 study (ANVS-25001):
A randomized, double-blind, placebo-controlled, multicenter study of buntanetap in participants with early Alzheimer's disease

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



Parkinson’s disease

Completed Phase 3 study (ANVS22001):
A randomized, double-blind, placebo-controlled, dose-ranging, multicenter study in early Parkinson's disease

Key inclusion criteria:

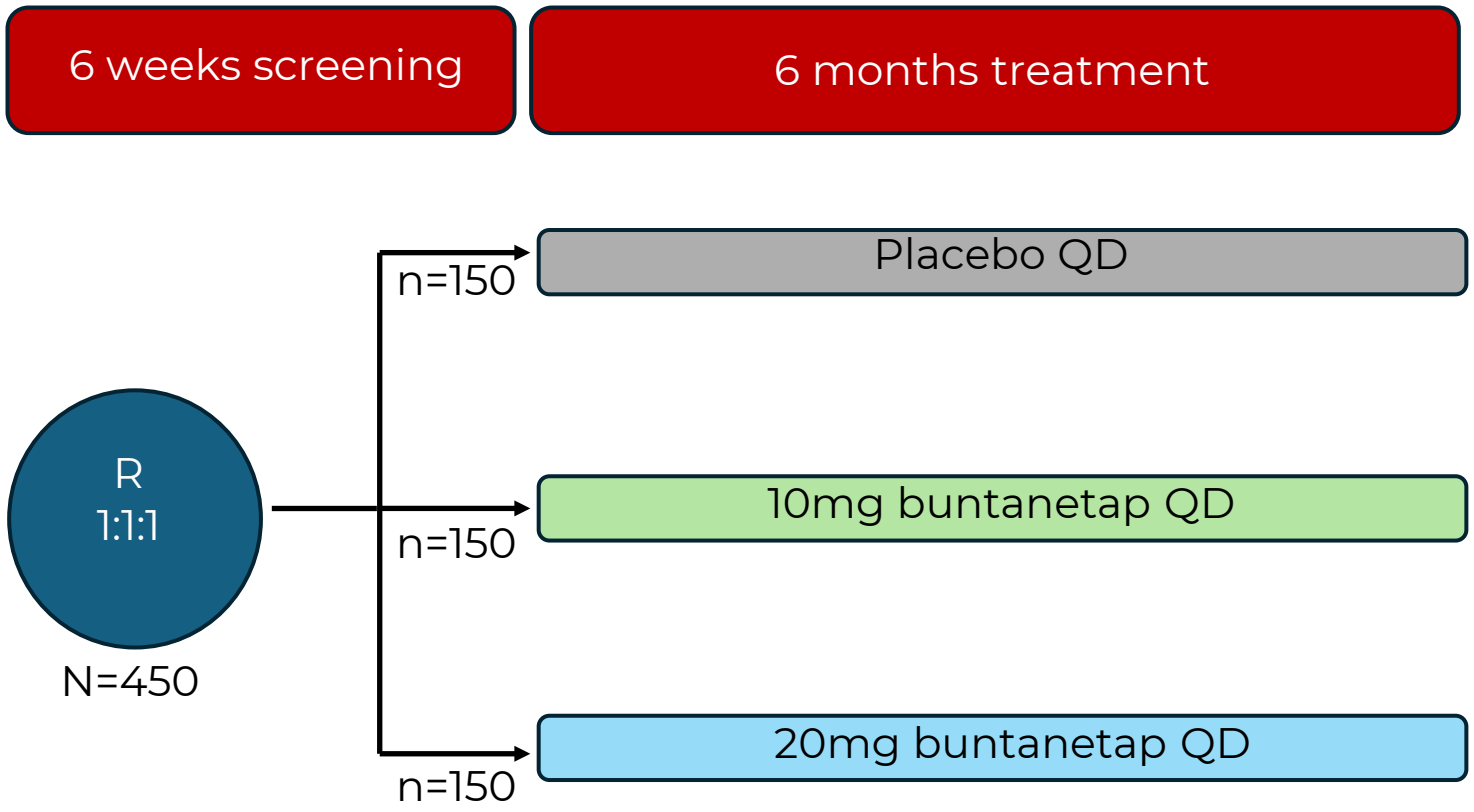
- Diagnosis of idiopathic PD *(Postuma, 2015)*
- H&Y score =1, 2 or 3 during ON-state & OFF-state <2hrs per day.
- 40 – 85 years

Primary endpoints:

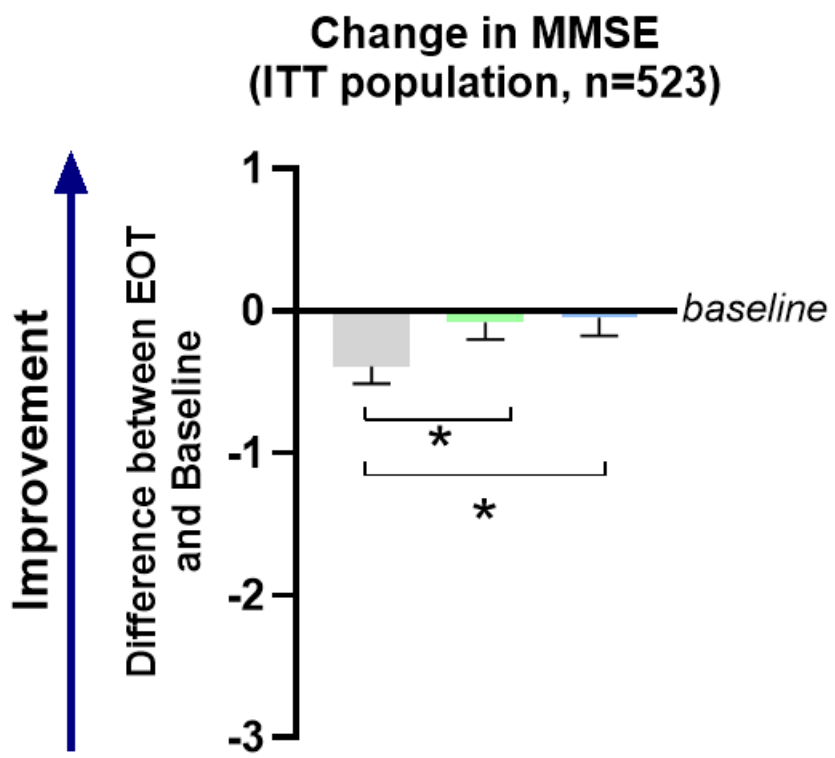
- MDS-UPDRS Part II (OFF state)

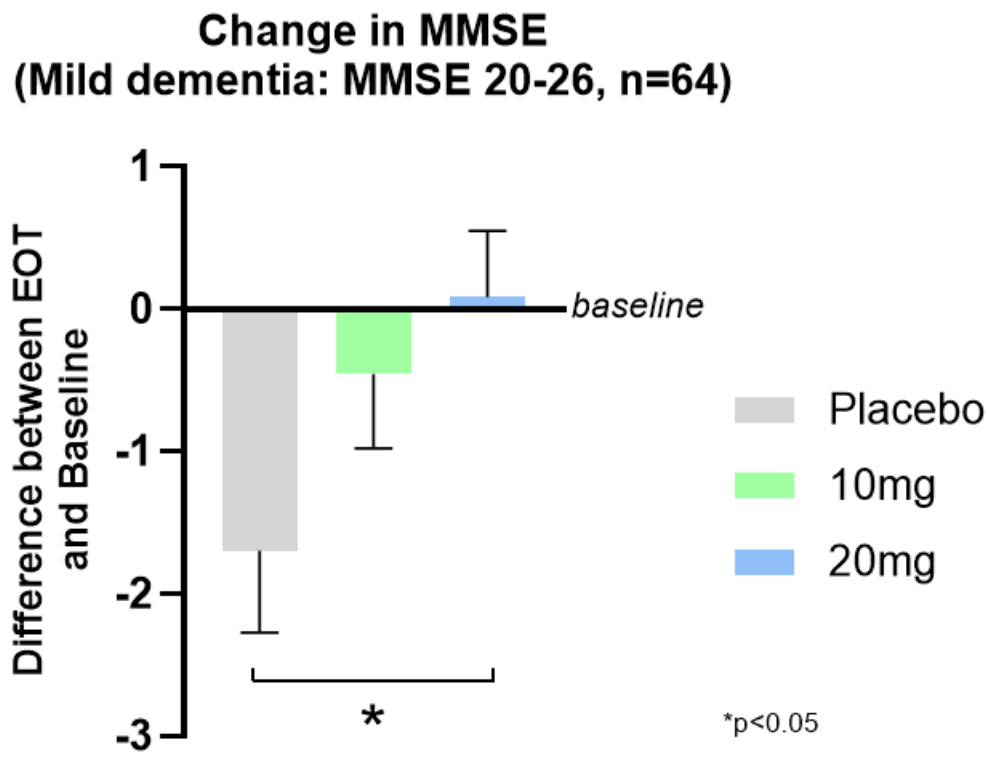
Secondary endpoints:

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

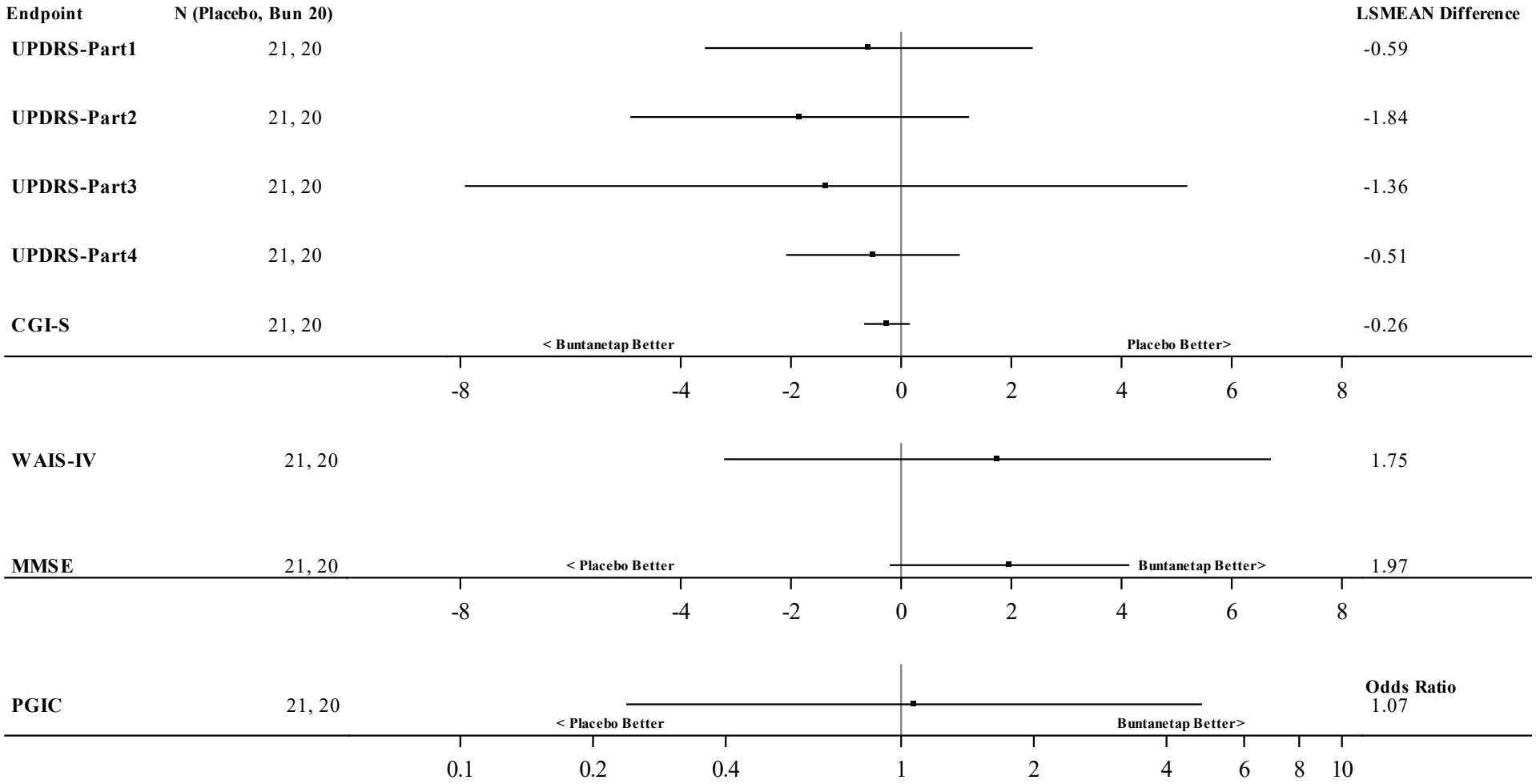


ITT population, cognitive impairment:
MMSE and dementia stage

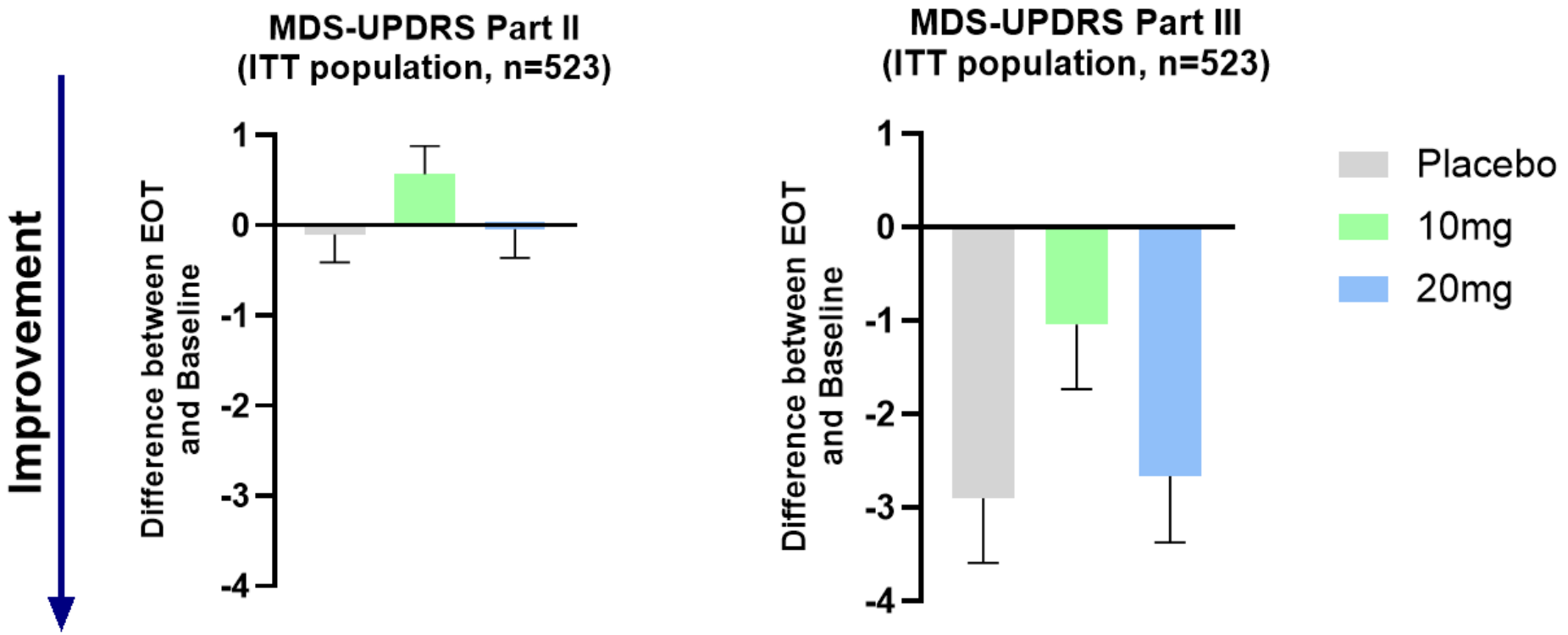




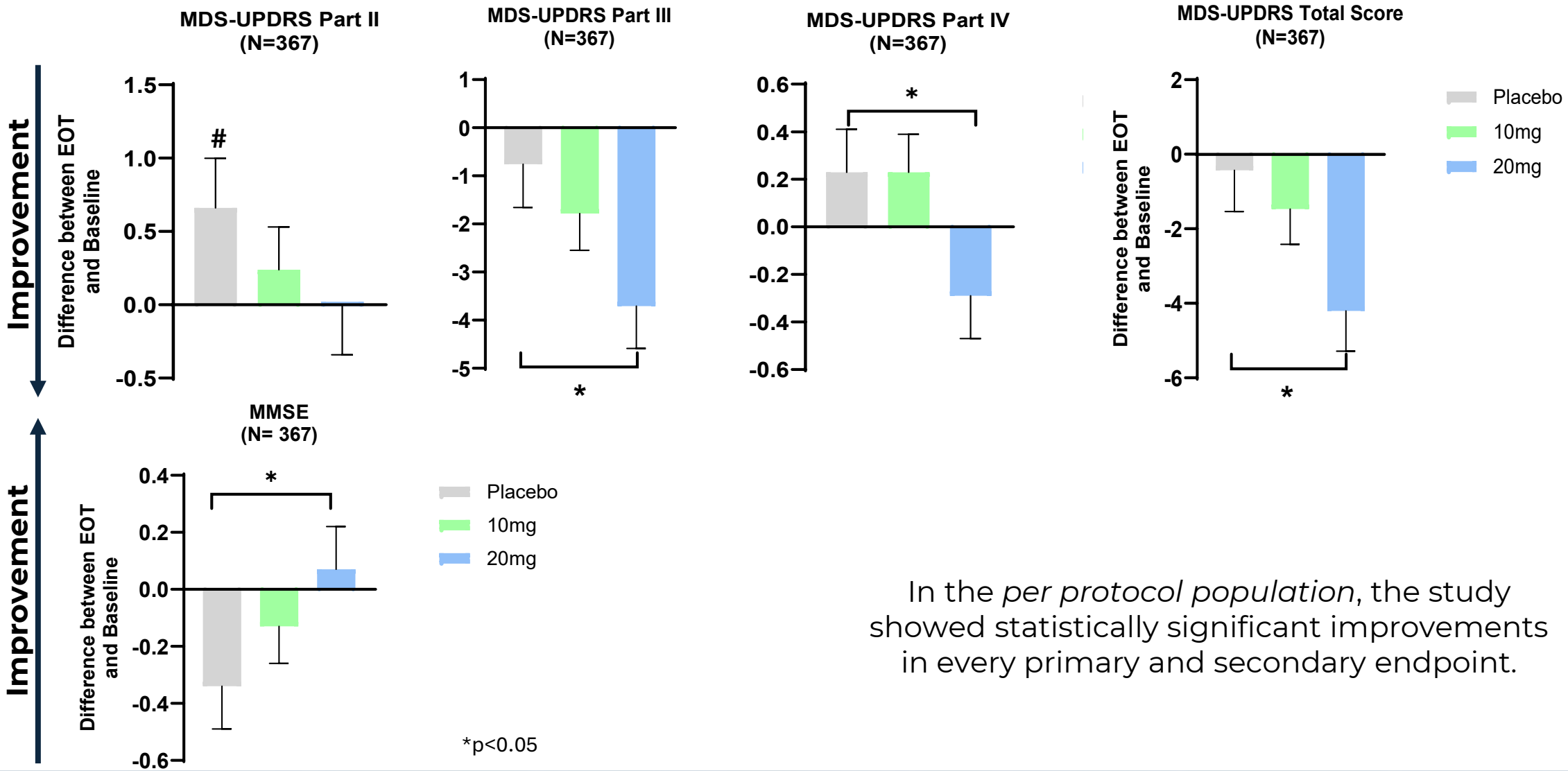
Forest plot shows consistency and robustness of efficacy in PD patients with MMSE 20-26



ITT population: MDS-UPDRS II and III

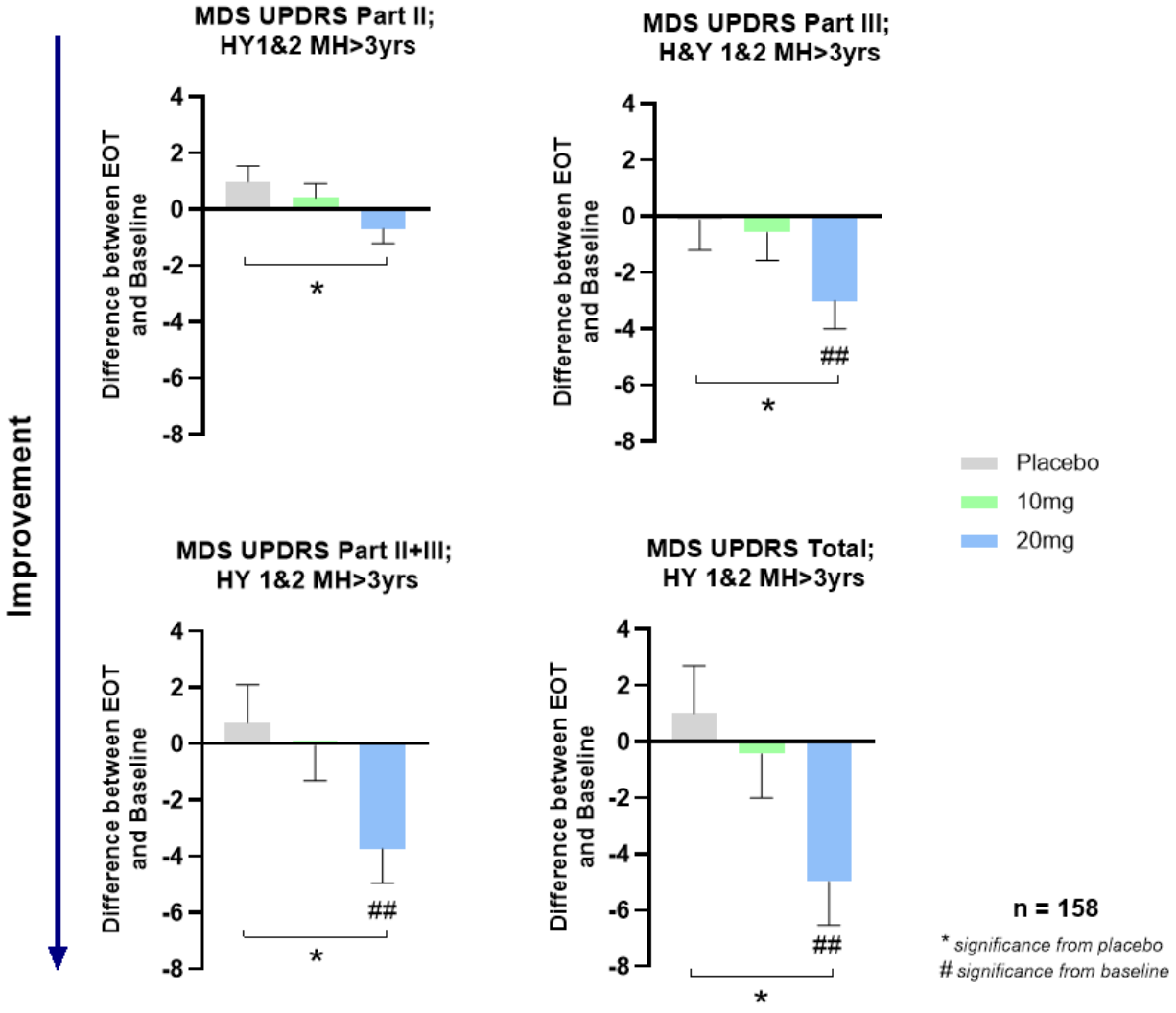


Per protocol population: MDS-UPDRS II, III, IV, total and MMSE



In the *per protocol population*, the study showed statistically significant improvements in every primary and secondary endpoint.

Primary and secondary endpoints in Parkinson's patients with > 3 year and < 10 years diagnosis



Buntanetap statistically and clinically significantly improved scores in all MDS-UPDRS parts in patients with a > 3 and < 10 years PD diagnosis.

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

Key learning and path forward – Parkinson's disease

- Buntanetap prevents worsening of cognition in ITT population.
- Buntanetap demonstrates improved cognitive function in patients with impaired cognition and improved MDS-UPDRS, WAIS, and CGI-S scores.
- In per protocol and in the >3 & <10 years populations, buntanetap shows significant improvement in MDS-UPDRS Part II, III, IV, total and MMSE.
- We are measuring 120 biomarkers in the ITT population to better understand buntanetap's effect in all PD patients.

Next steps:

- Annovis is awaiting FDA feedback for the next steps for the PD program.
- Annovis has also proposed the Open Label Extension (OLE) study protocol for PD.

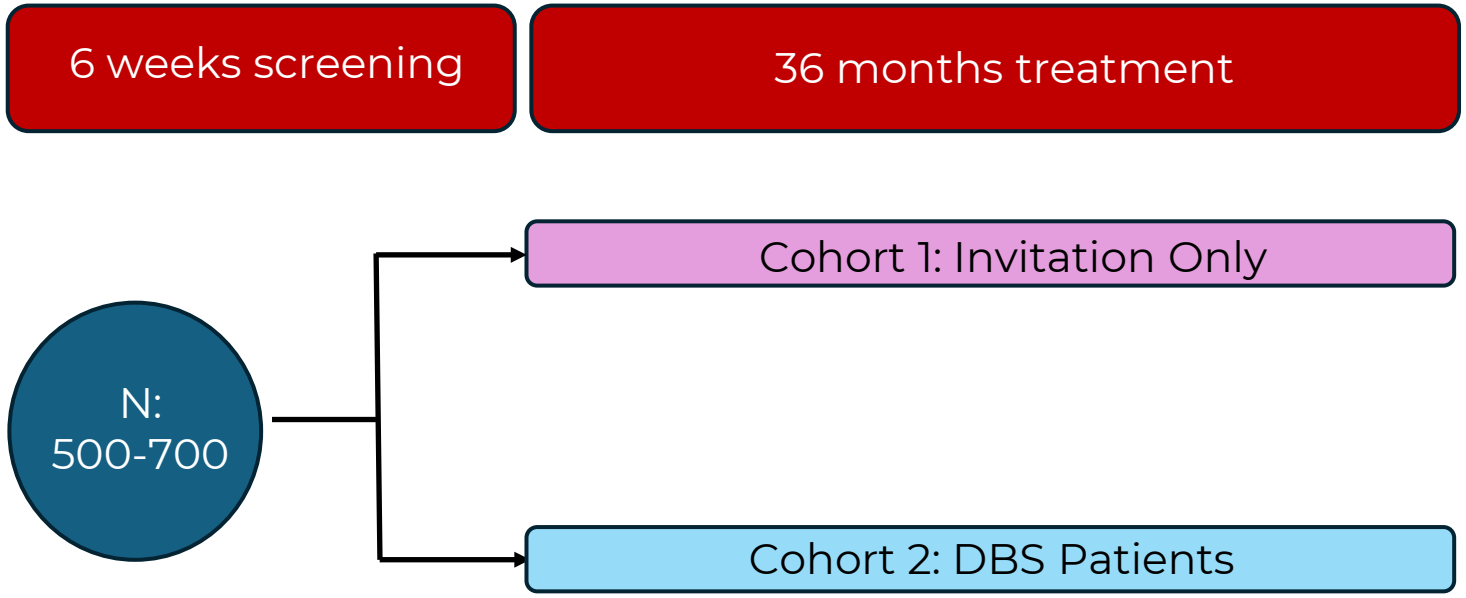
Proposed PD Open Label Extension (OLE) study design

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.

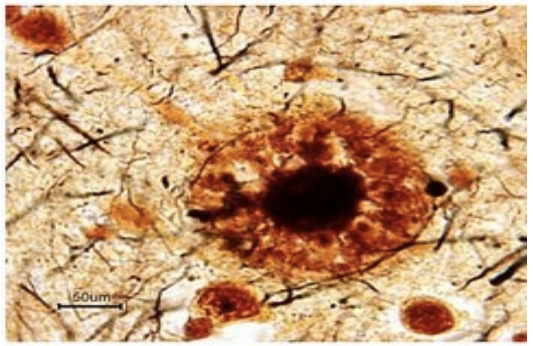


Mechanism of Action

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



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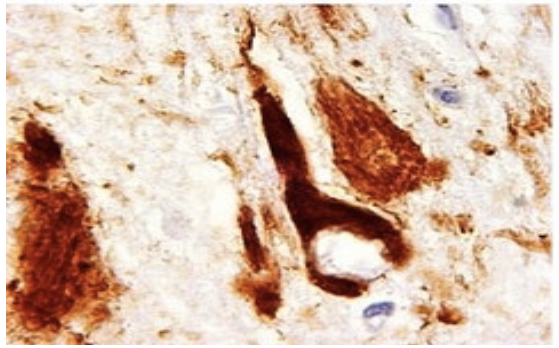

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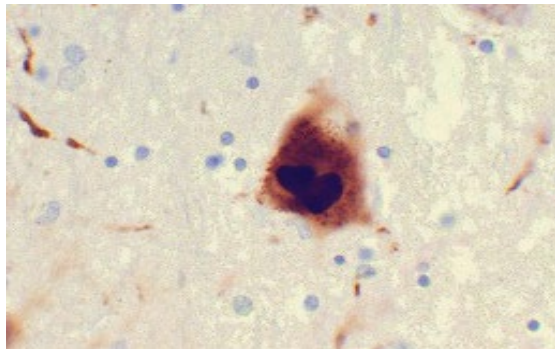

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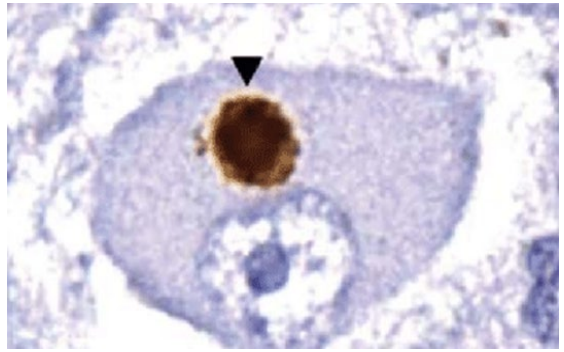

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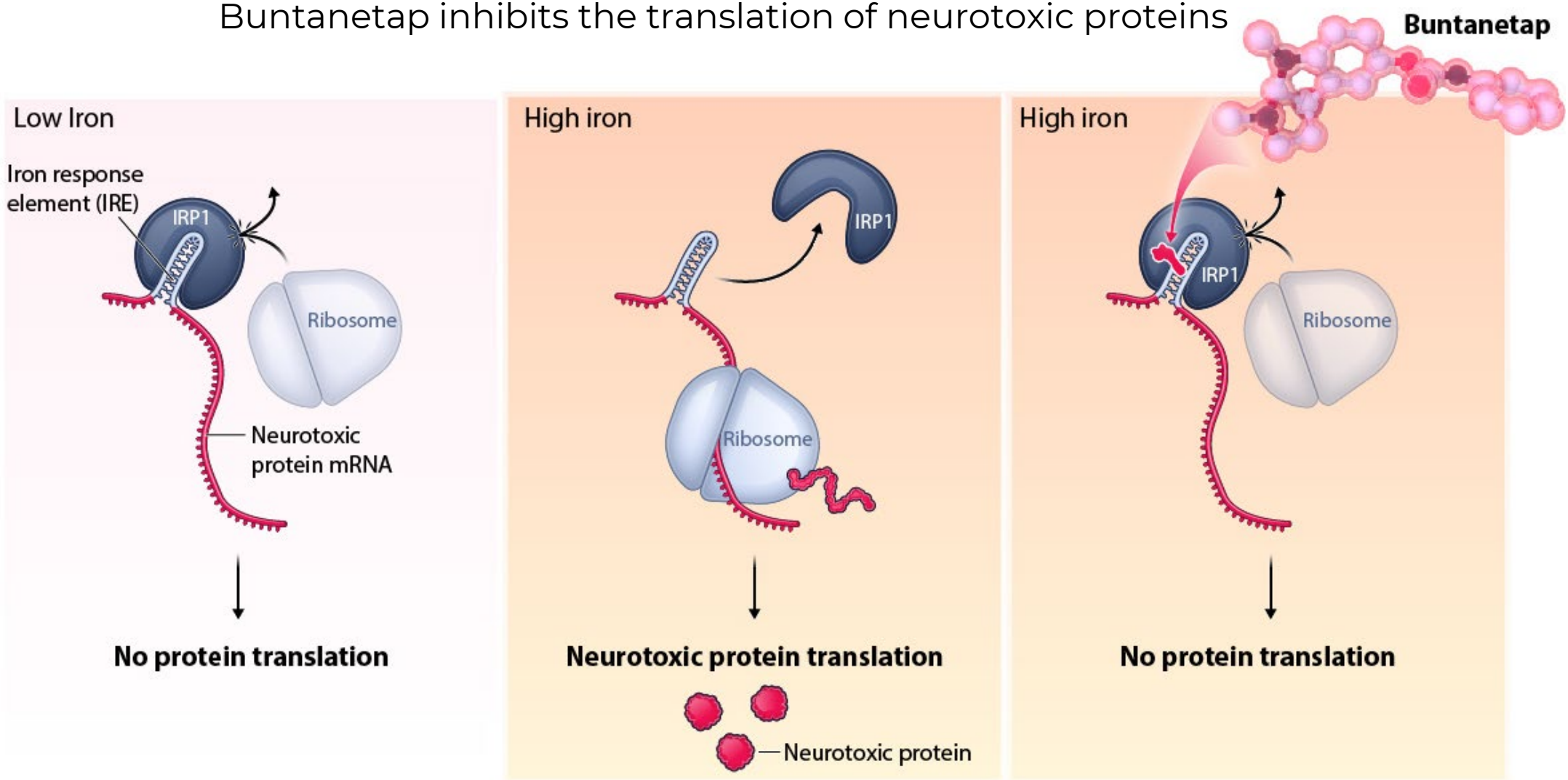
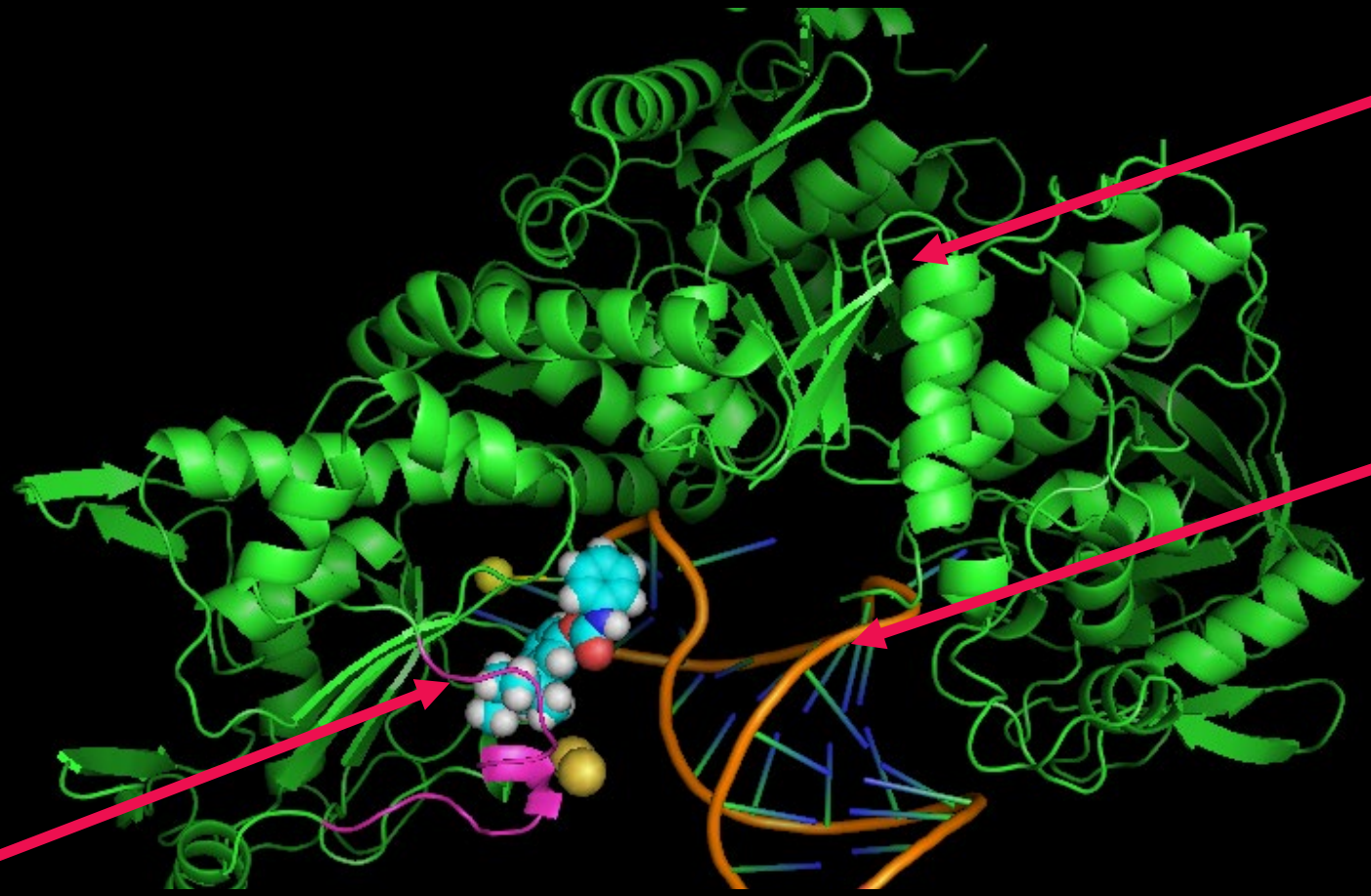
Mechanism of action

Buntanetap inhibits the translation of neurotoxic proteins



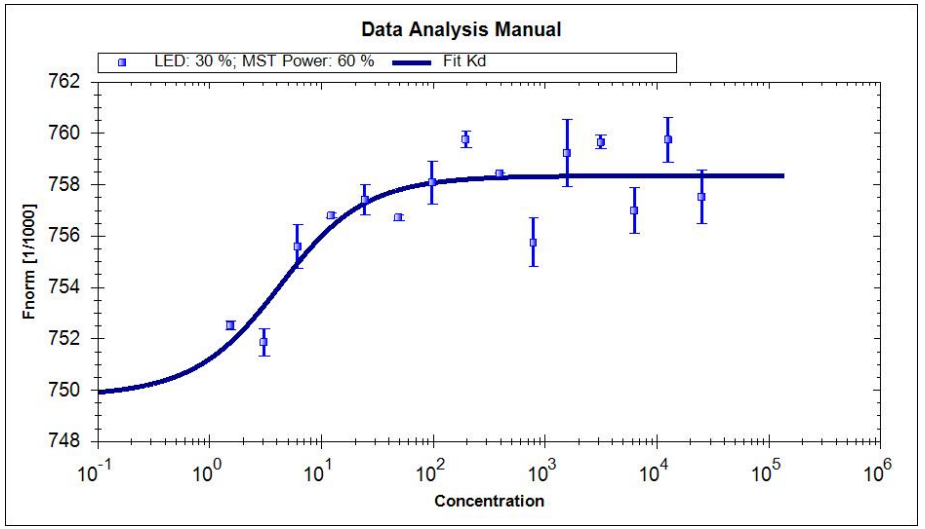
MOA - Chen XQ et al. Pharmaceutics 09-2021.
Iron and Neurodegeneration - Wong F. et al. Frontiers Aging Neuroscience; 03-2022

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



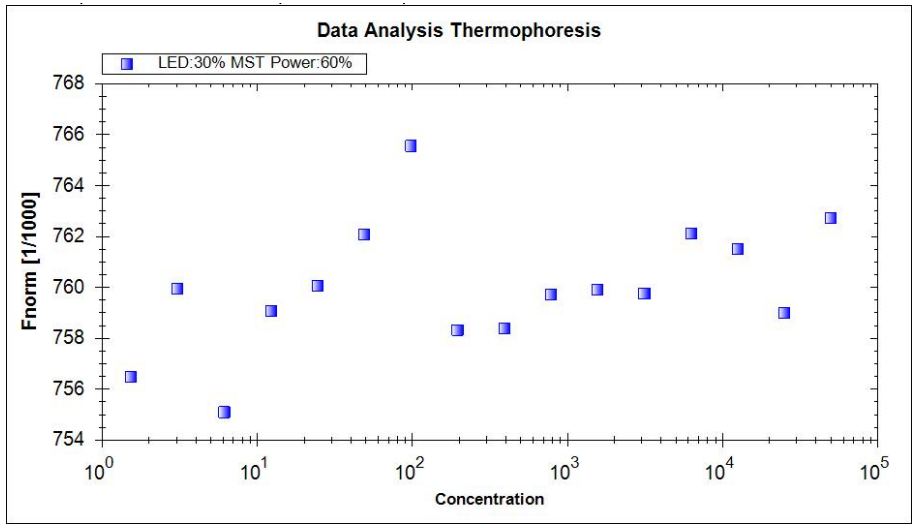
Eric Baldwin, NCI

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	



Ferritin IRE/IRP1/Buntanetap
No Kd

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

Buntanetap lowers neurotoxic proteins in mouse brain

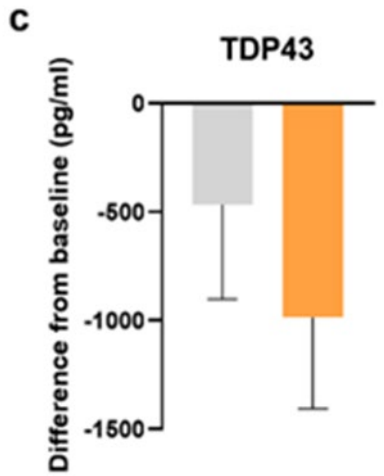
Marker	(%) Drop	p-values
APP	39.8	0.008
CTFβ	46.8	0.0024
CTFα	48.5	0.0031
Aβ42	68	0.0008

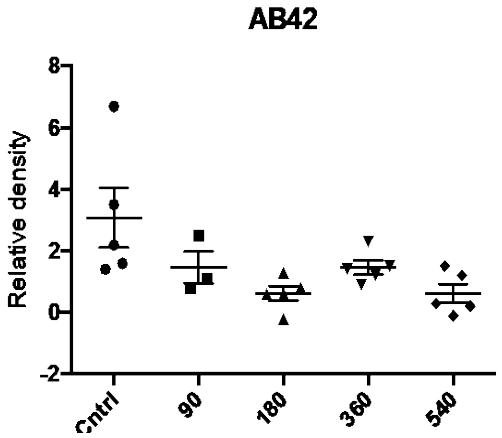
APP/Aβ42

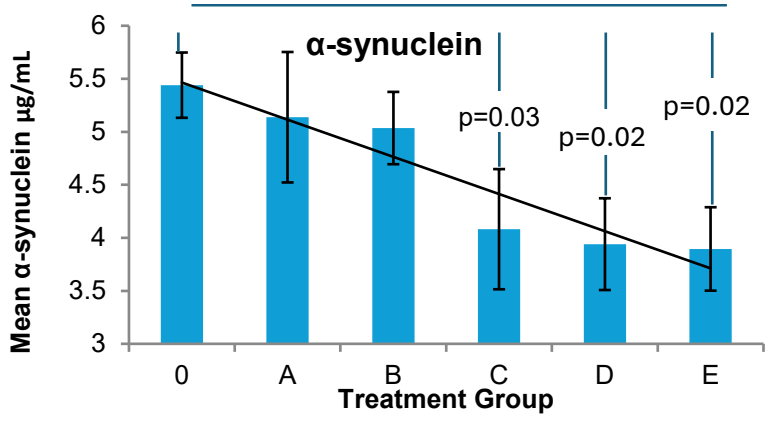
αSYN

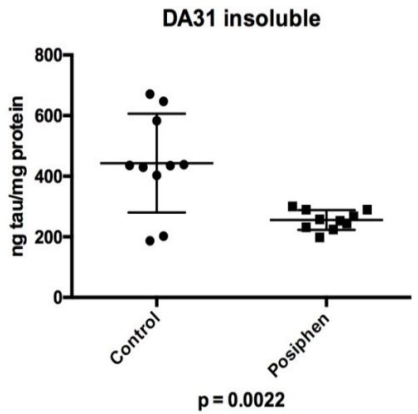
tau

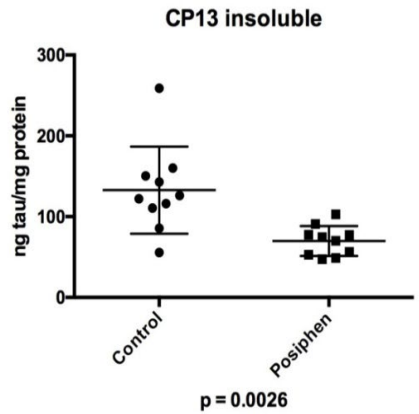
TDP43





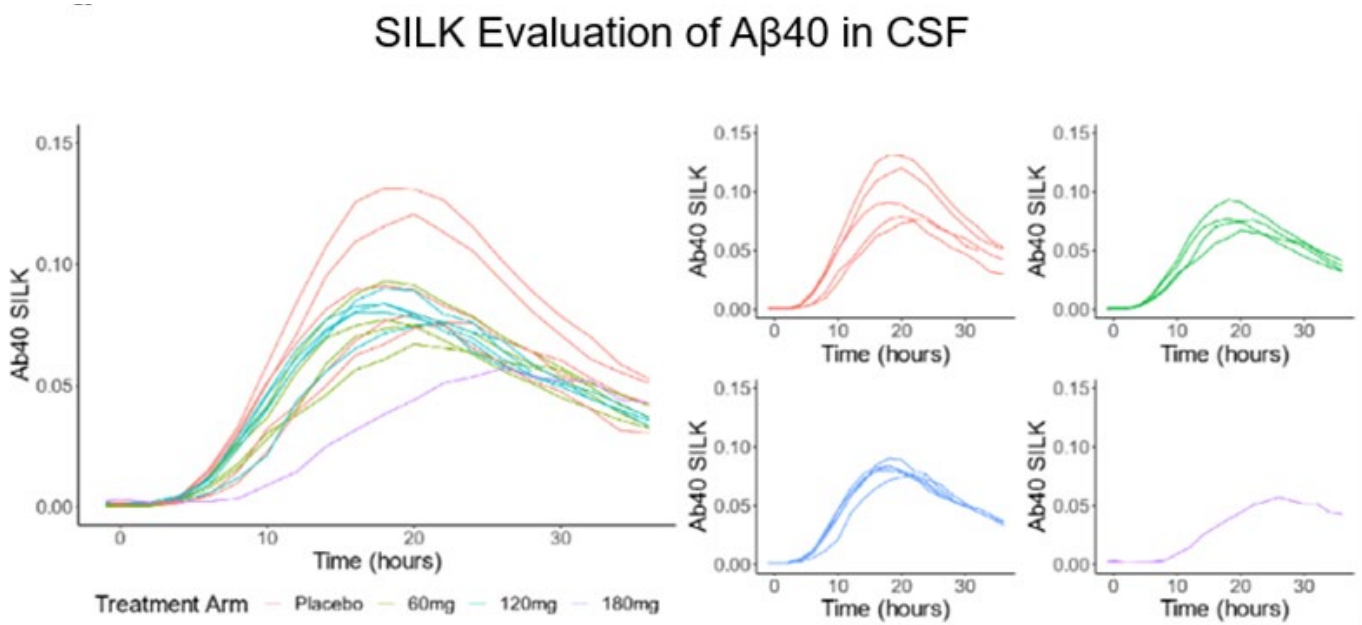






Teich et al: 2018; Kuo et al: 2019; Peter Davies et al.

Target engagement: APP, Aβ42, Aβ40, and Aβ38 synthesis



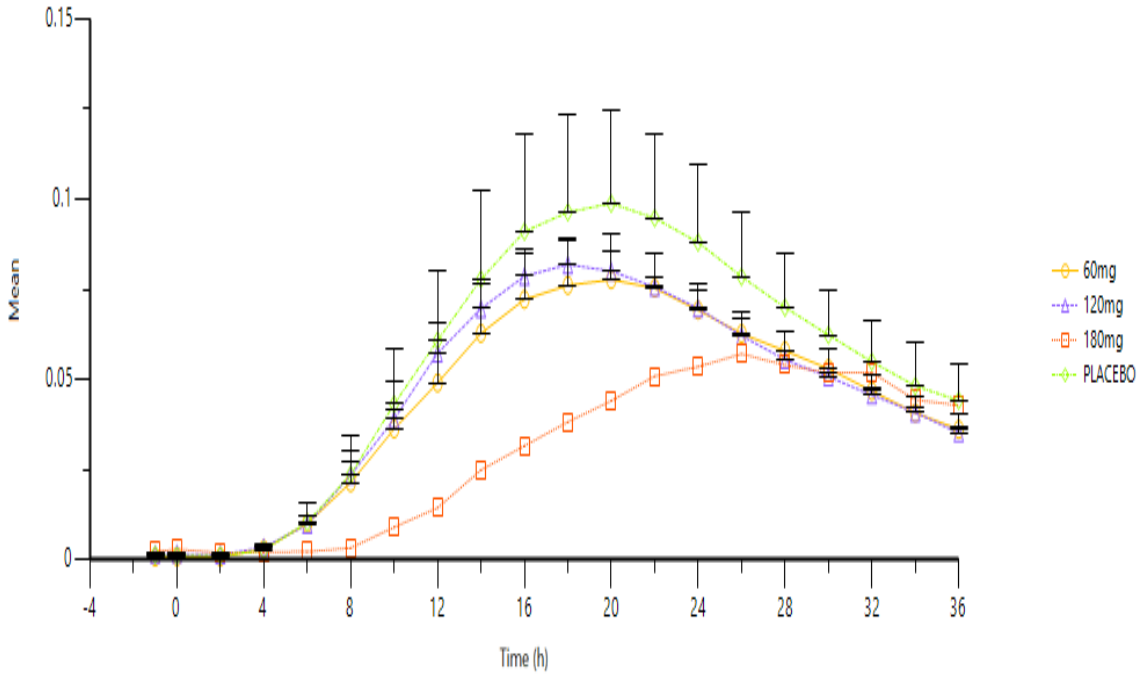
The Discover study was conducted through collaboration with ADCS and was designed to understand buntanetap's effect on synthesis of neurotoxic aggregating proteins – APP, using Stable Isotope Labeling Kinetic (SILK) analysis.

For SILK, lumbar and venous catheters were placed in AD patients and $^{13}C_6$-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, Aβ40, and Aβ42 synthesis was measured by LC-MS differentiation of heavy $^{13}C_6$- leucine labelled APP versus light ^{12}C -leucine normal APP, Aβ40, and Aβ42.

Galasko et al: 2024

Target engagement: buntanetap inhibits translation of Aβ



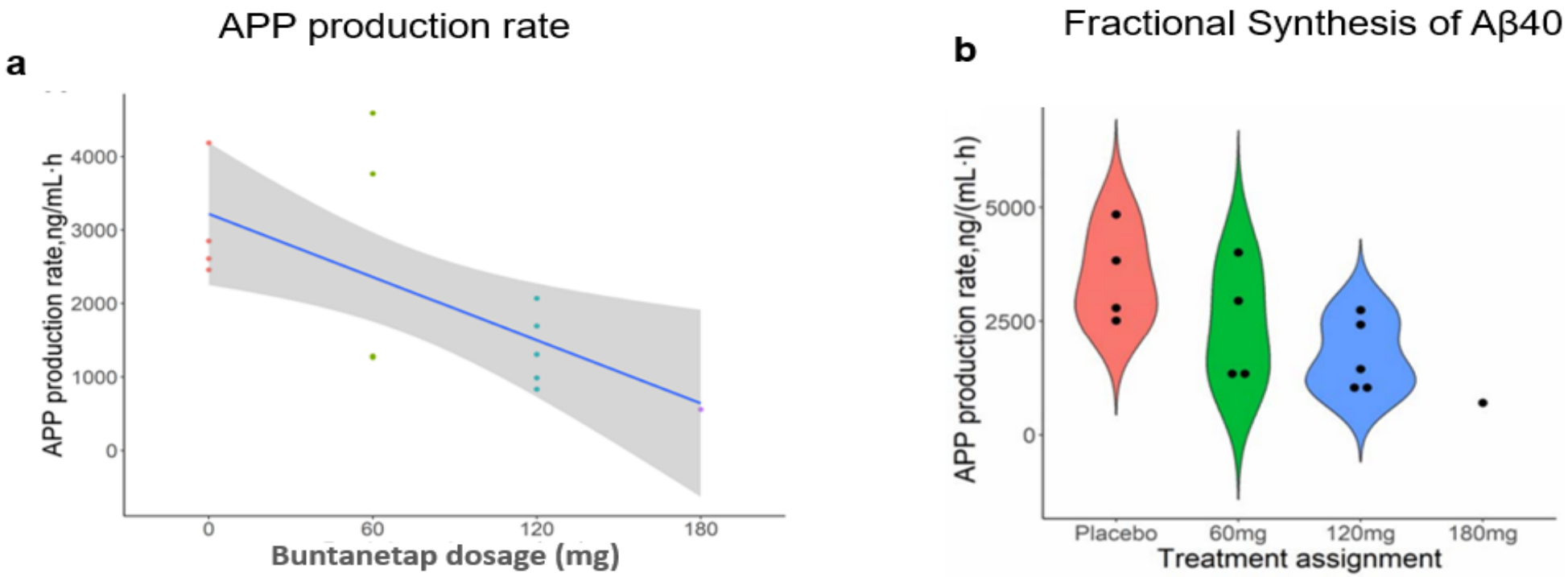
Treatment mg		Start h	Slope	Cmax	Tmax h	AUC
0		0.2	0.0065	0.1	14	1.971
60		0.5	0.0059	0.08	18.8	1.631
120		1.1	0.0053	0.07	19.5	1.529
180		6.2	0.0028	0.05	26	1.033

Buntanetap showed a dose-dependent lowering of Aß40 production as seen by a delayed start, lower synthesis rate, lower Cmax, and smaller Area Under the Curve (AUC) of produced Aß40.

Buntanetap statistically significantly reduced AUC (Aβ38 p=0.039, Ab40 p=0.045), Cmax of Aβ38 and Aβ40 (Aβ38 p=0.04, Aβ 40 p=0.036), proving that buntanetap is a translational inhibitor of APP synthesis.

Annovis/TCM, unpublished

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.

Galasko et al: 2024

Buntanetap improves axonal transport

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

- Nature Review, September 2019

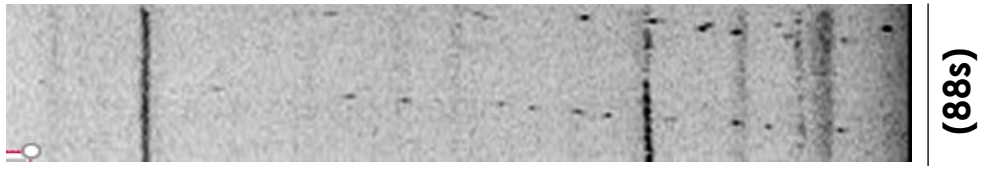
Axonal transport is responsible for:

- 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)

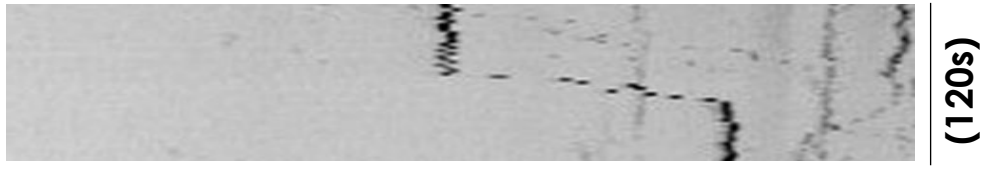
Normal Transport

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

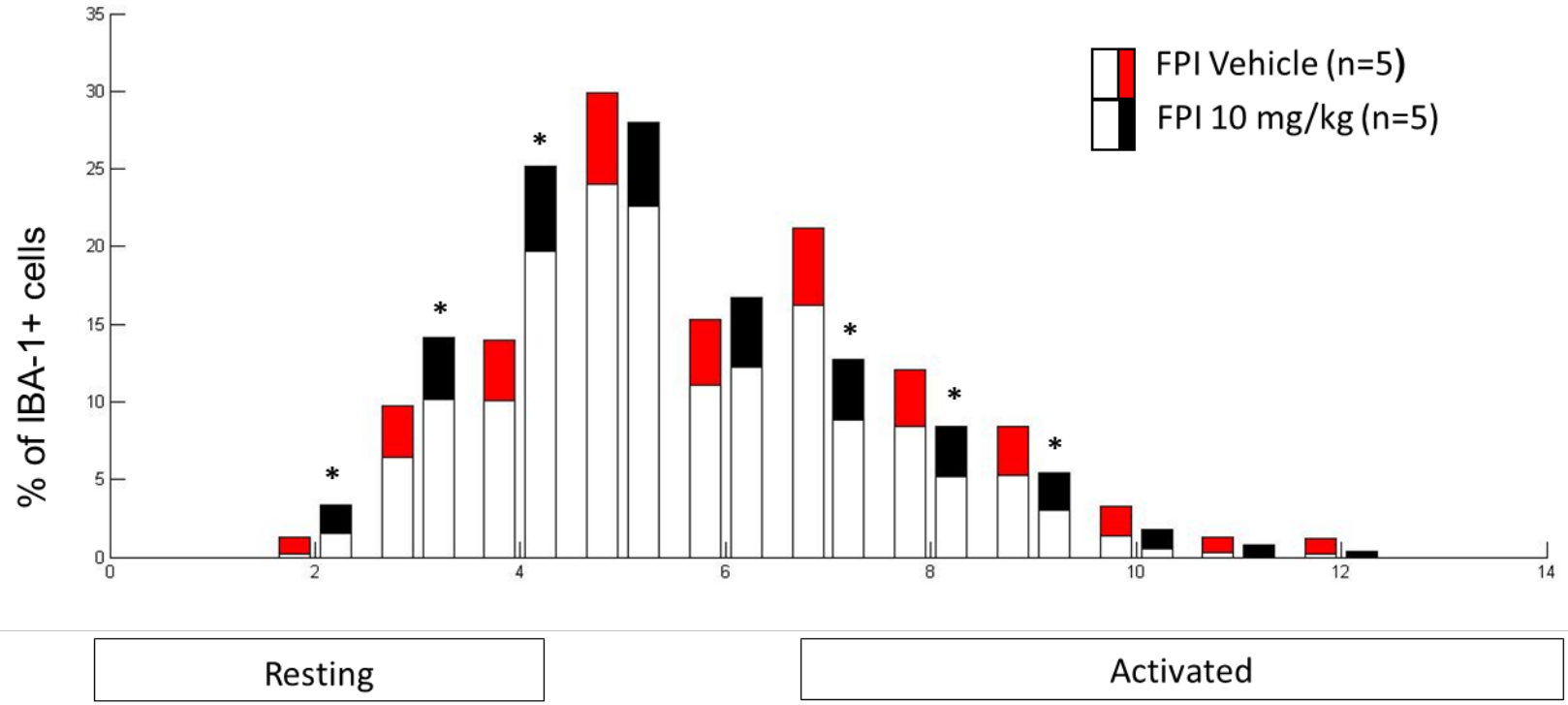
The ***Flow and Speed*** of axonal transport is improved.

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

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

Buntanetap decreases inflammation (microglia activation)

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

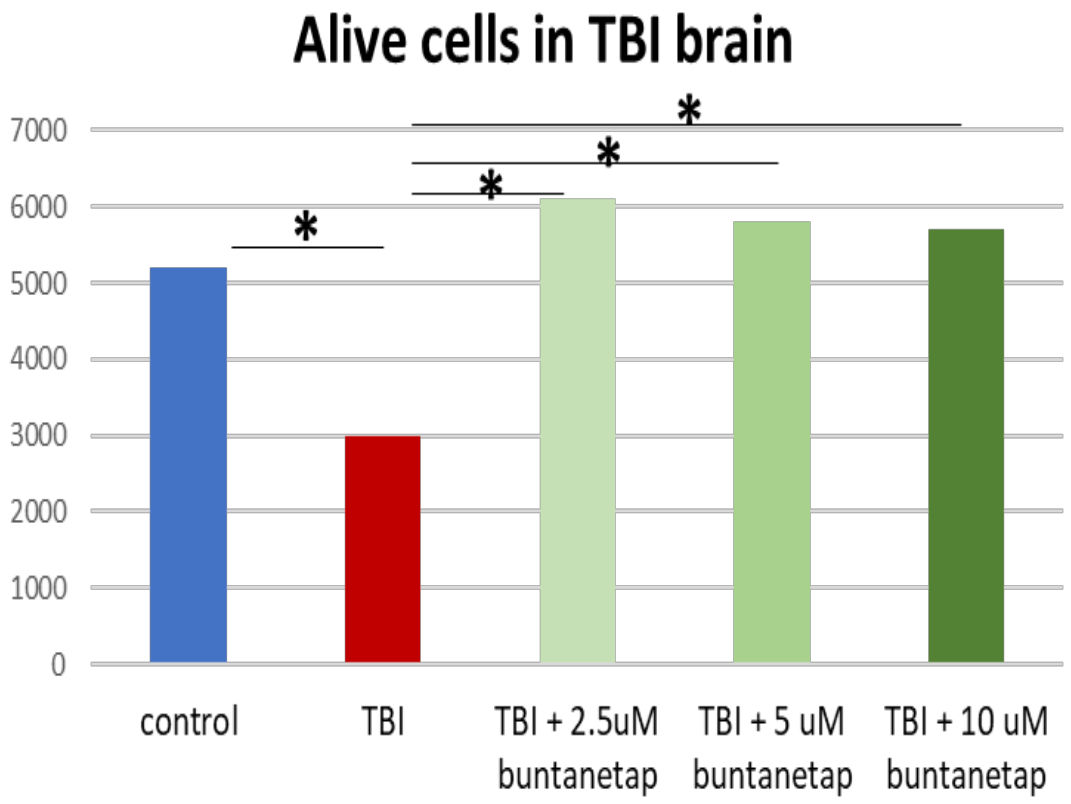


Microglial Cell Diameter (µm)

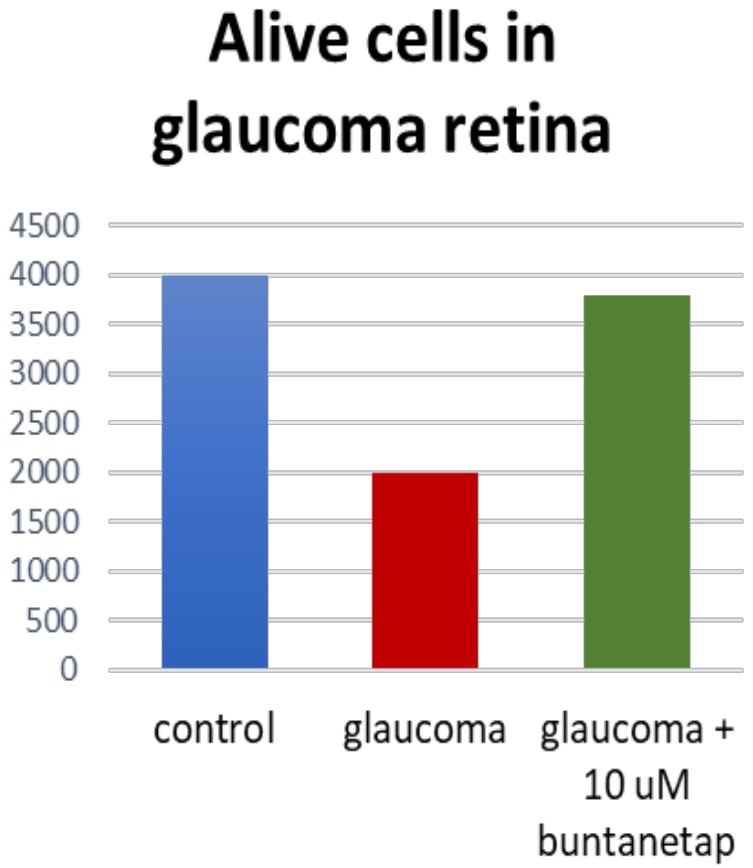
ANVS401 increases the number of resting microglia and reduces the number of activated microglia – it reduces inflammation

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

Buntanetap protects nerve cells from dying



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



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

Hatami A. et al.; Sundstrom J. et al. Hershey Medical Center

Summary of studies in animal models

Evaluated function	Test	Animal model
Memory & Learning	• Mazes	• APP/PS1 Alzheimer's mice • Trisomic Down Syndrome mice • Stroke mice • Traumatic Brain Injury rats
Movement	• Colonic motility • Grip strength	• aSYN Parkinson's mice • Tau Frontotemporal Dementia mice
Vision	• Sight	• Glaucoma rats
Infections	• Cell death	• *P. Gingivalis* mice • COVID mice


ANNOVIS