



Corporate Presentation

Development path to NDA:

- Alzheimer's disease
- Parkinson's disease

NYSE:ANVS

August 2026

FORWARD-LOOKING STATEMENTS

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Company highlights

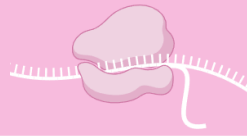
Drug candidate



Buntanetap is a once-daily oral pill that has the potential to stop and even reverse neurodegeneration.

It is the only drug that improves cognition in Alzheimer's as well as cognition and motor function in Parkinson's patients.

Unique mechanism



Buntanetap targets RNA and inhibits the overproduction of multiple neurotoxic proteins associated with neurodegeneration, improving communication between cells, suppressing inflammation, and restoring health of neurons.

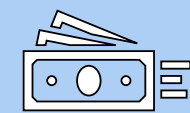
Late-stage development



Buntanetap is now in the very last stages of clinical studies.

After successful completion of this stage, Annovis plans to apply for FDA approval for Buntanetap.

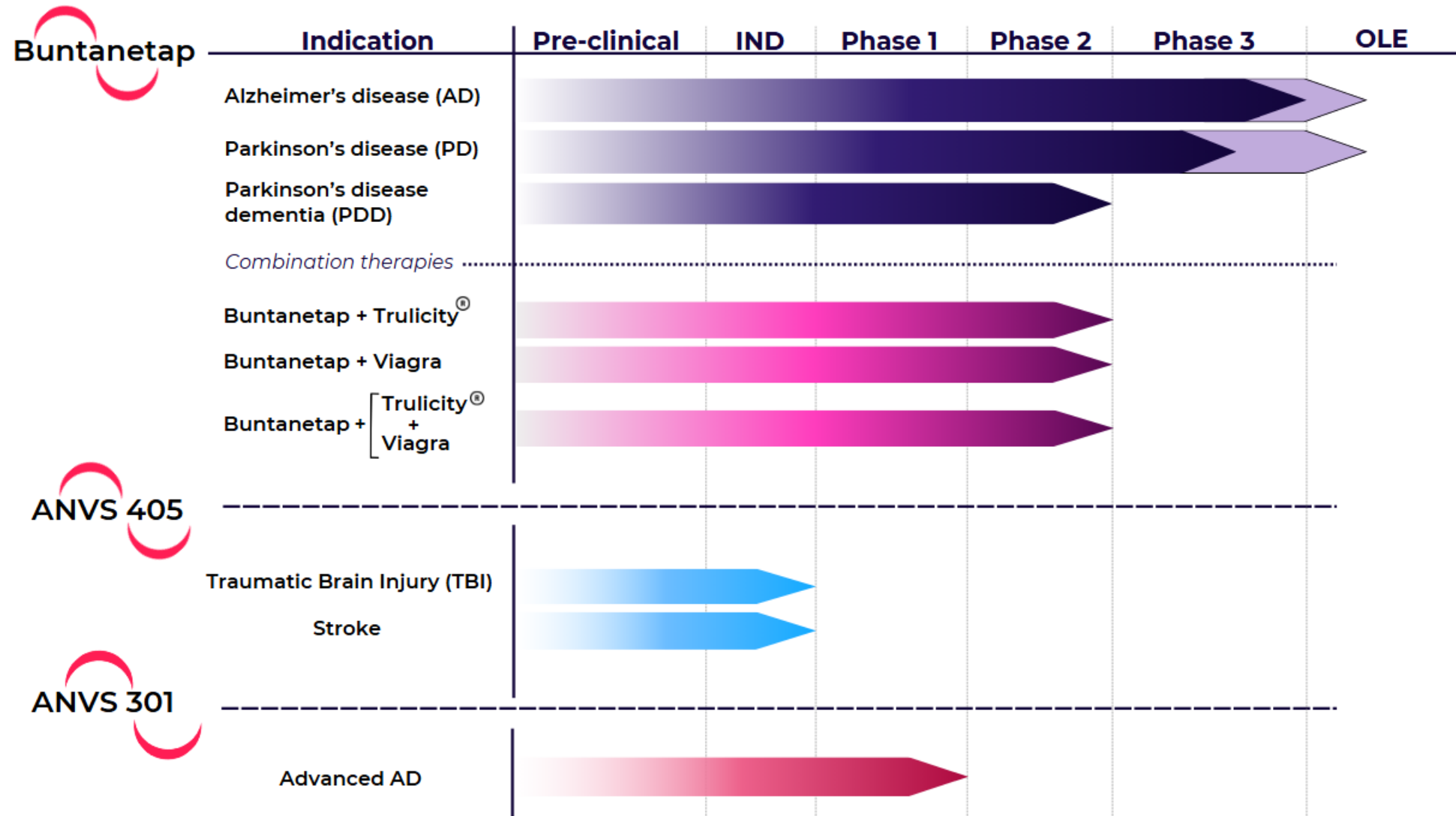
Capital-efficient approach



Current shares outstanding 33m.

Cash balance \$19m., debt \$0 (as of 6.30.2026)

Pipeline



Summary of clinical studies

Healthy volunteers

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

Alzheimer's disease

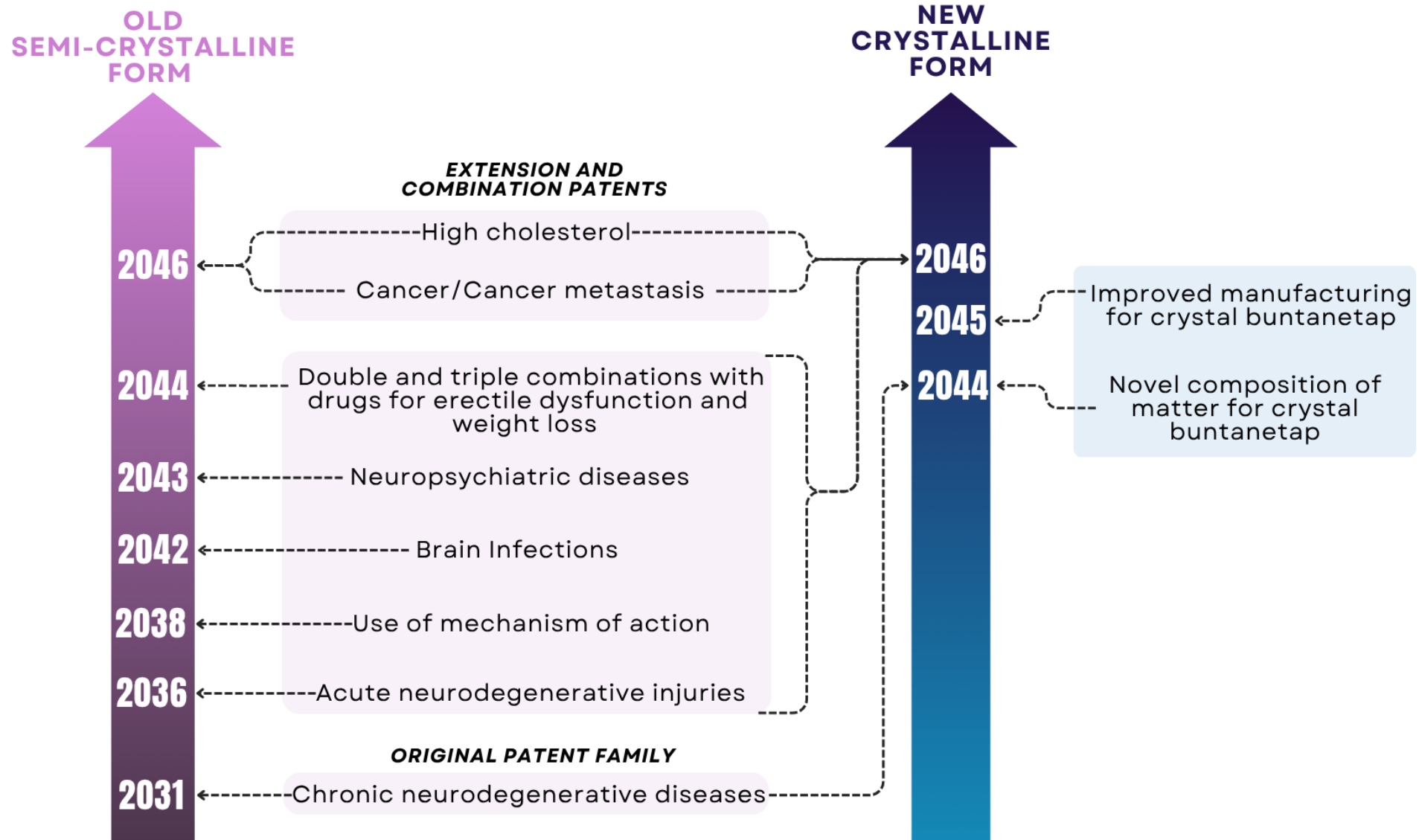
Phase 1/2	2 studies	N=22
Phase 2	1 study	N=17
Phase 2/3	1 study	N=346
Pivotal Phase 3	1 study	N=850 (ongoing)
OLE	1 study	N~400 (planned)

Parkinson's disease

Phase 2	1 study	N=58
Phase 3	1 study	N=523
OLE	1 study	N~500 (ongoing)

Over 1,600 people treated with buntanetap

Patent portfolio



Senior management team



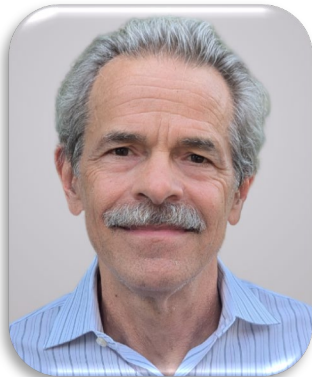
Maria Maccellini, PhD
Founder, President, CEO



Cheng Fang, PhD
CSO



Eve Damiano, MS, RAC
SVP, Regulatory Operations



Mike Christie, PhD
VP, Process Chemistry



Sarah MacCallum
VP, Clinical Operations



Alexander Morin, PhD
Director, Strategic Communications



Hui Liu
Director, Biostatistics

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)
- Positive for plasma pTau217
- Volumetric MRI
- MMSE 20-28

Key clinical outcomes:

Primary endpoints:

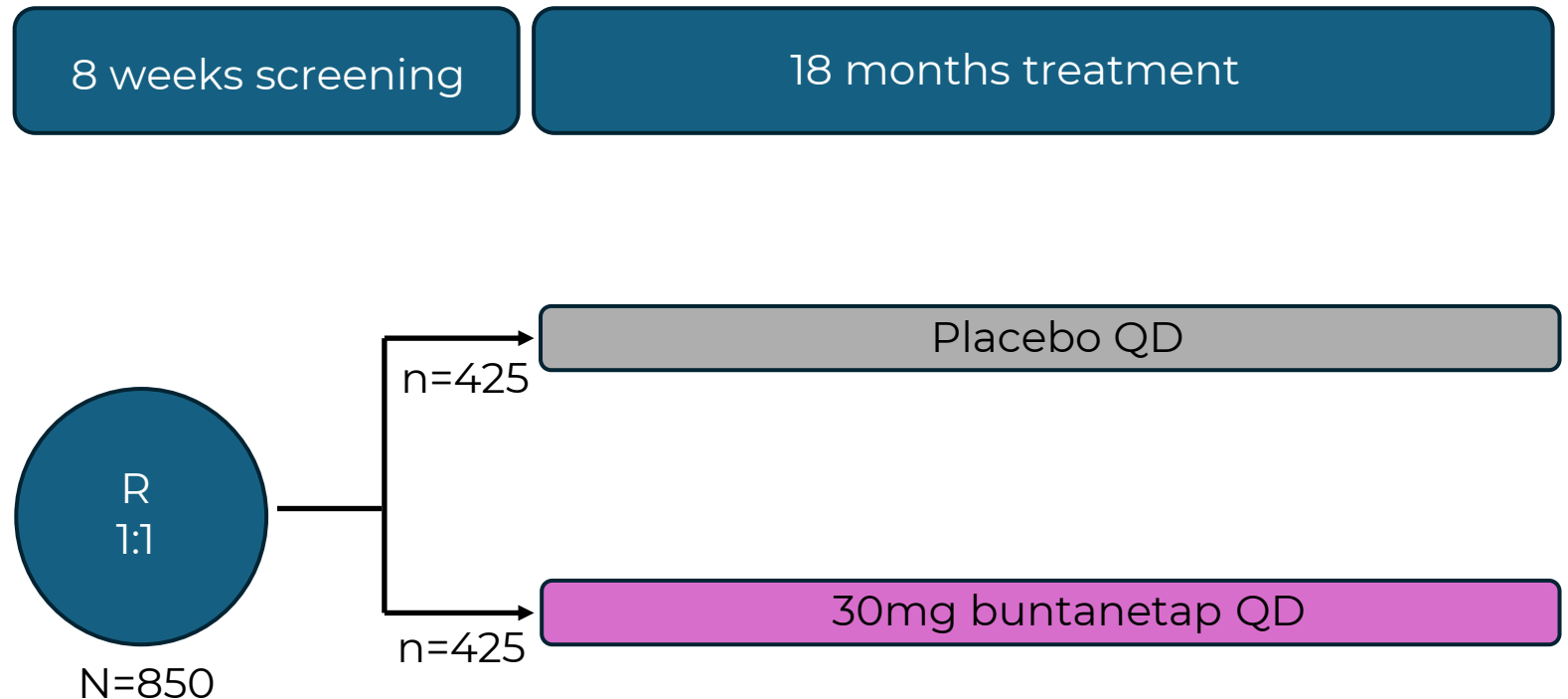
- ADAS-Cog 13; ADCS-iADL

Secondary endpoints:

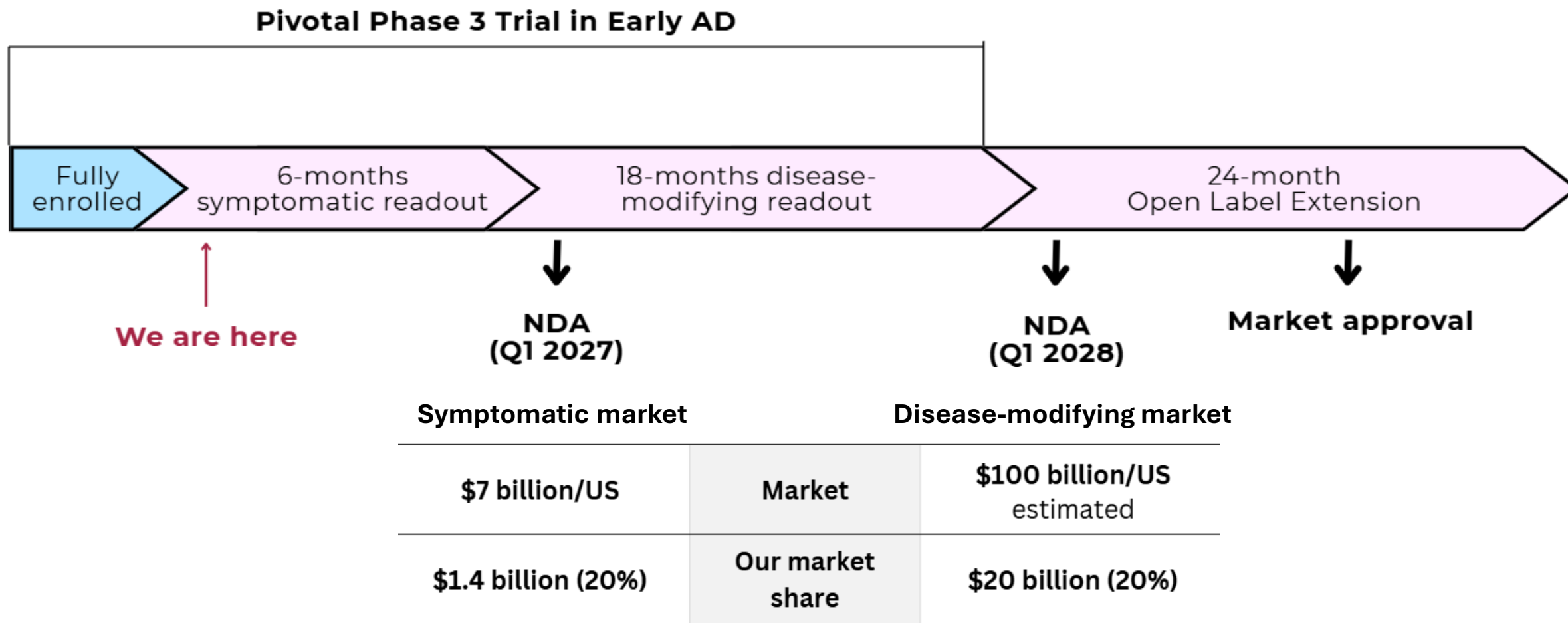
- Volumetric MRI; pTau217

Exploratory endpoints:

- Biomarkers



Milestones toward approval for **Alzheimer's disease (AD)**



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

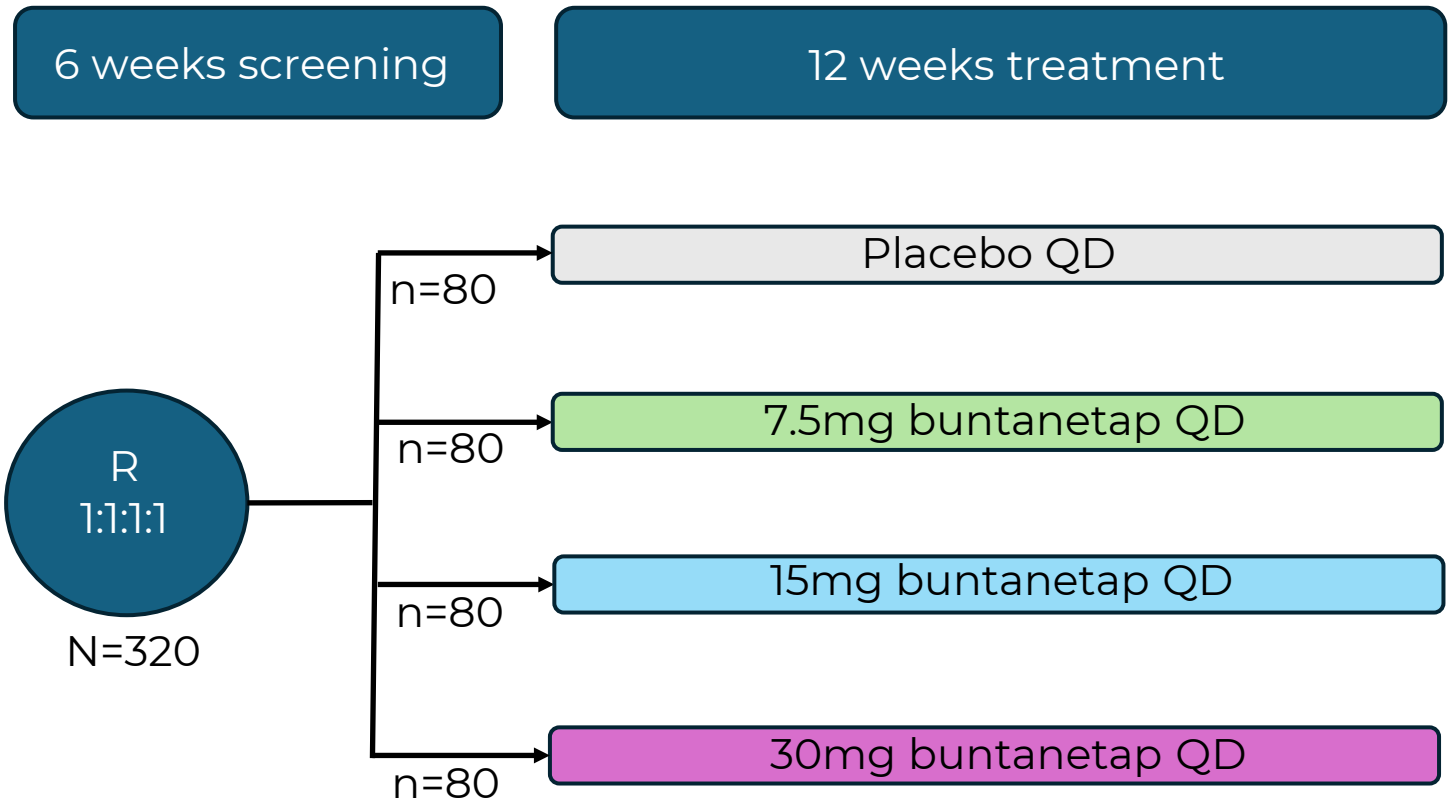
Key clinical outcome:

Primary endpoints:

- ADAS-Cog 11
- CGIC

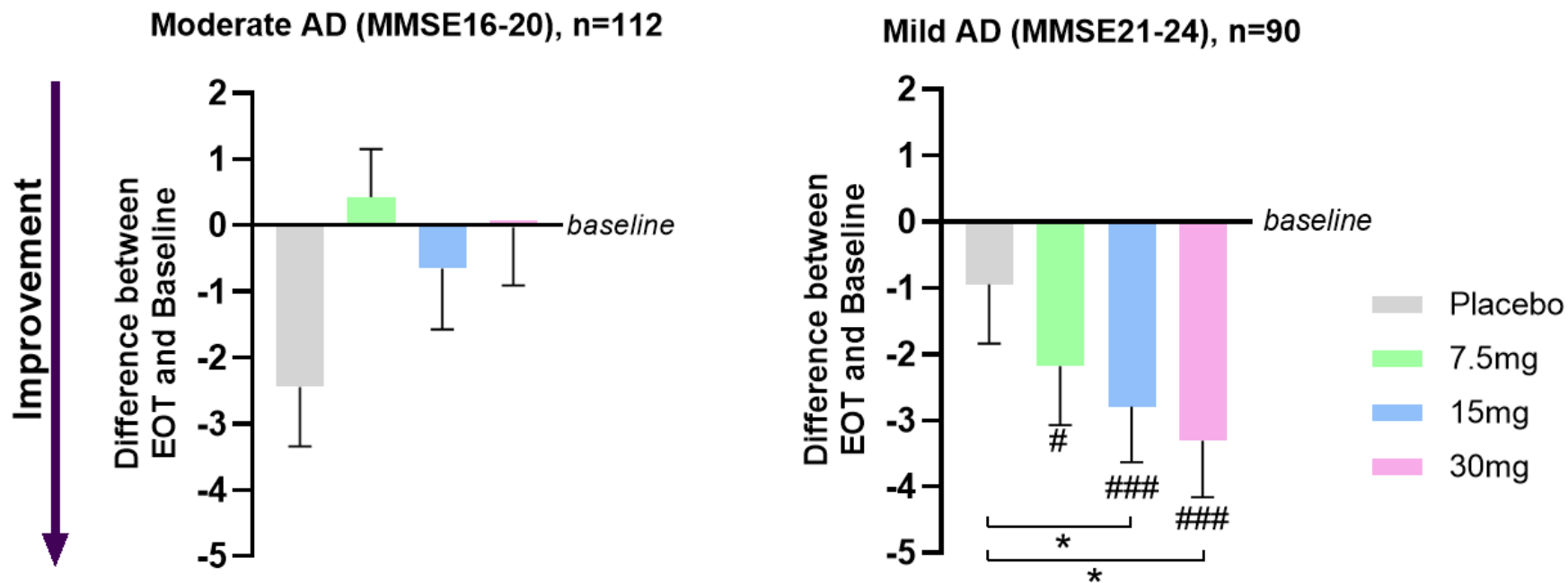
Key secondary endpoint:

- ADCS-ADL



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

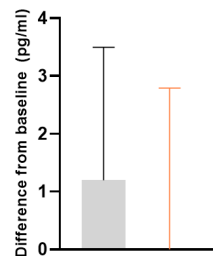
Biomarker data support the **target and pathway engagement**

Mild AD population (MMSE 21-24)

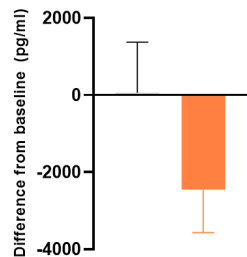
■ Placebo ■ Buntanetap (30mg)

Neurotoxic proteins

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

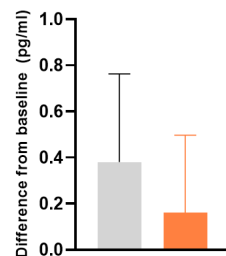


TDP43 (MMSE 21-24, N=43)

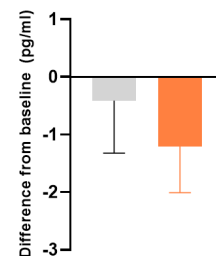


Inflammation

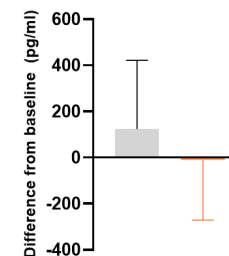
IL5 (MMSE 21-24, N=45)



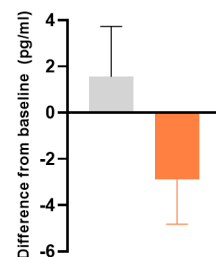
IL6 (MMSE 21-24, N=45)



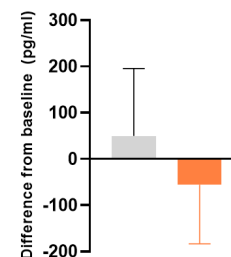
S100A12 (MMSE 21-24, N=49)



IFN-γ (MMSE 21-24, N=49)

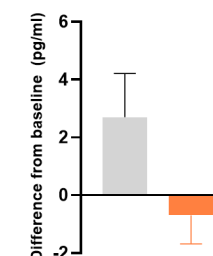


IGF1R (MMSE 21-24, N=49)



Neuronal damage

NFL (MMSE 21-24, N=45)



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

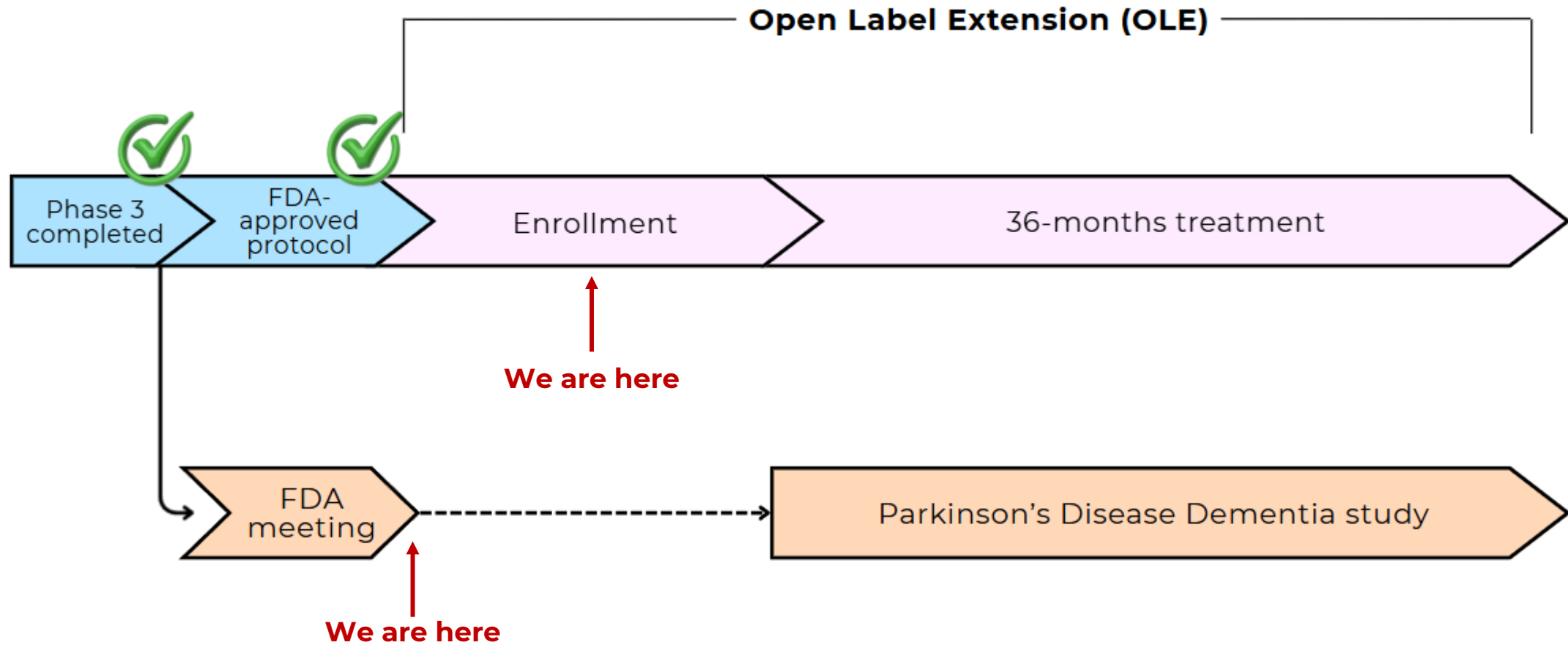
AE = Adverse Event

TEAE = Treatment Related Adverse Event

Parkinson's disease



Upcoming milestones for **Parkinson's** program



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

Key inclusion criteria:

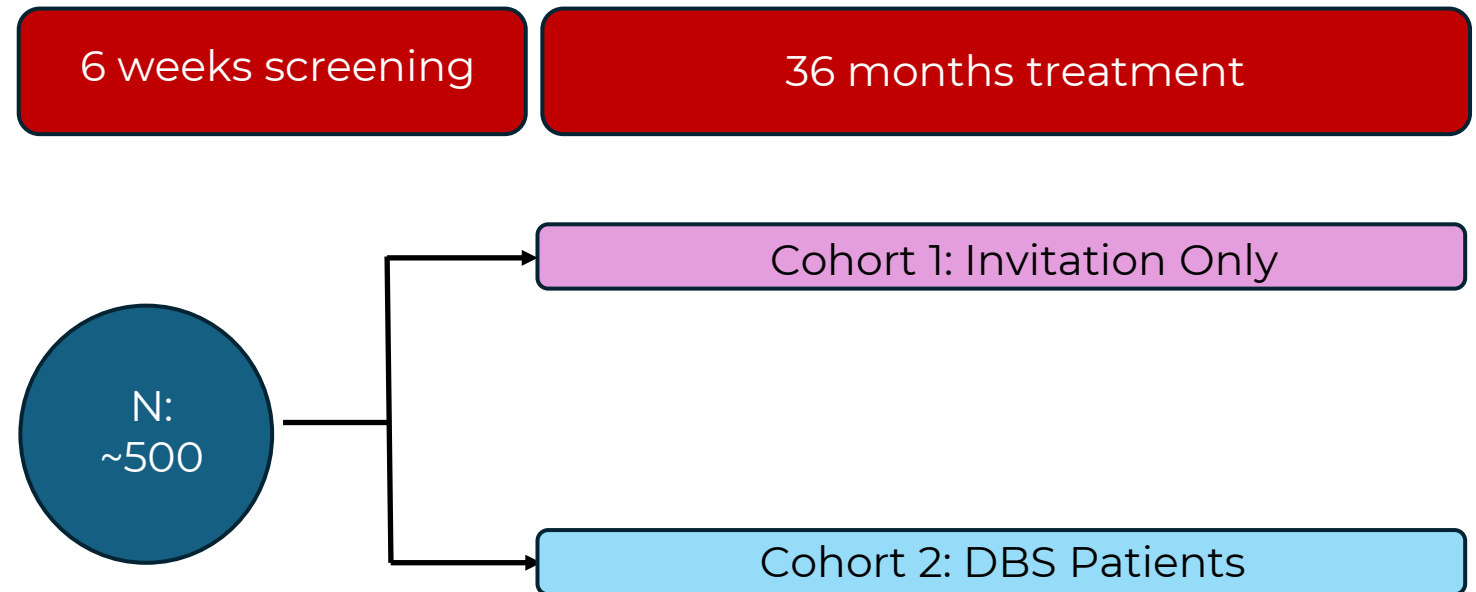
- Adults aged up to 85 years
- Hoehn and Yahr stage 1-3
- MMSE 21-30 at screening

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.



PD OLE study - endpoints and biomarkers

Endpoints

Primary

Safety

Exploratory

- Cognition (MoCA, MMSE)
- Movement (MDS-UPDRS)
- Biomarkers

Innovative biomarkers

Digital biomarker (NeuroRPM app)

- Monitoring primary PD symptoms: bradykinesia, tremor, and dyskinesia.
- Real-time passive data collection
- Medication tracking

Skin biopsy (α SYN biomarker)

- Minimally invasive skin procedure
- Pathological evidence of the disease with >90% diagnostic sensitivity and specificity.

Completed Phase 3 study (ANVS22001):

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

Key inclusion criteria:

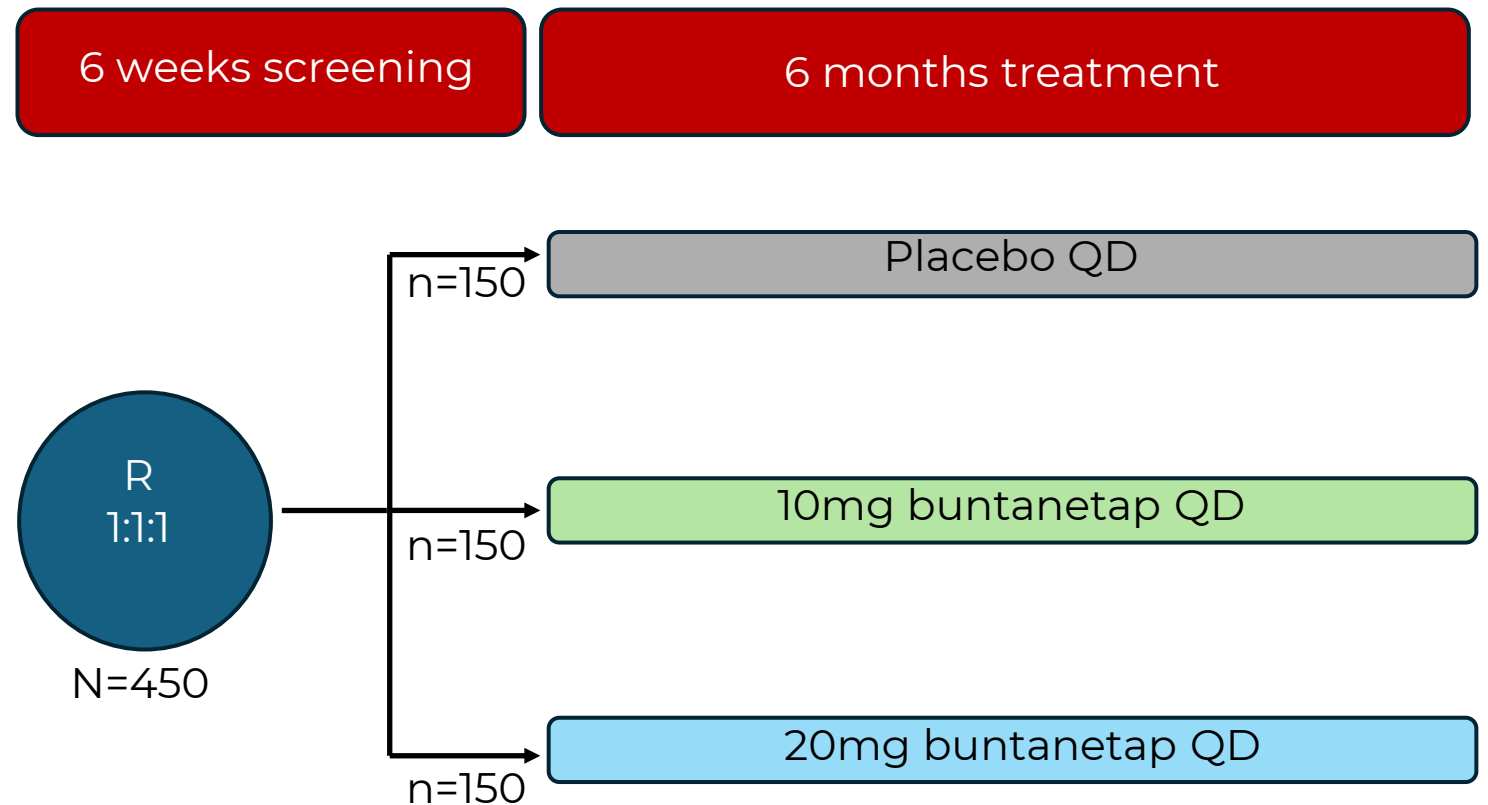
- Diagnosis of idiopathic PD (*Postuma, 2015*)
- H&Y score =1, 2 or 3 during ON-state & OFF-state <2hrs per day.
- 40 – 85 years

Primary endpoints:

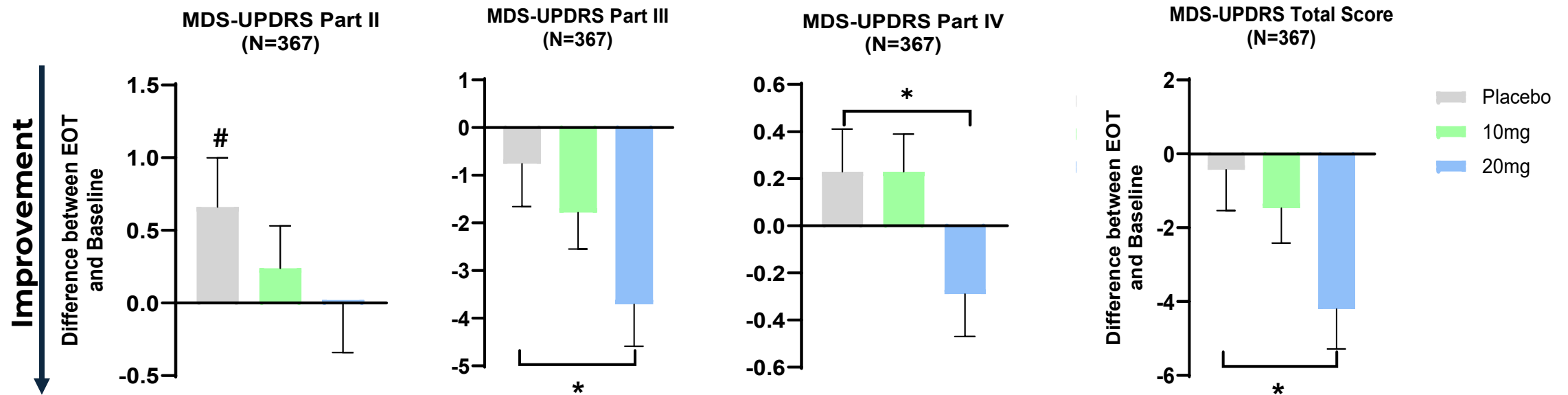
- MDS-UPDRS Part II (OFF state)

Secondary endpoints:

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



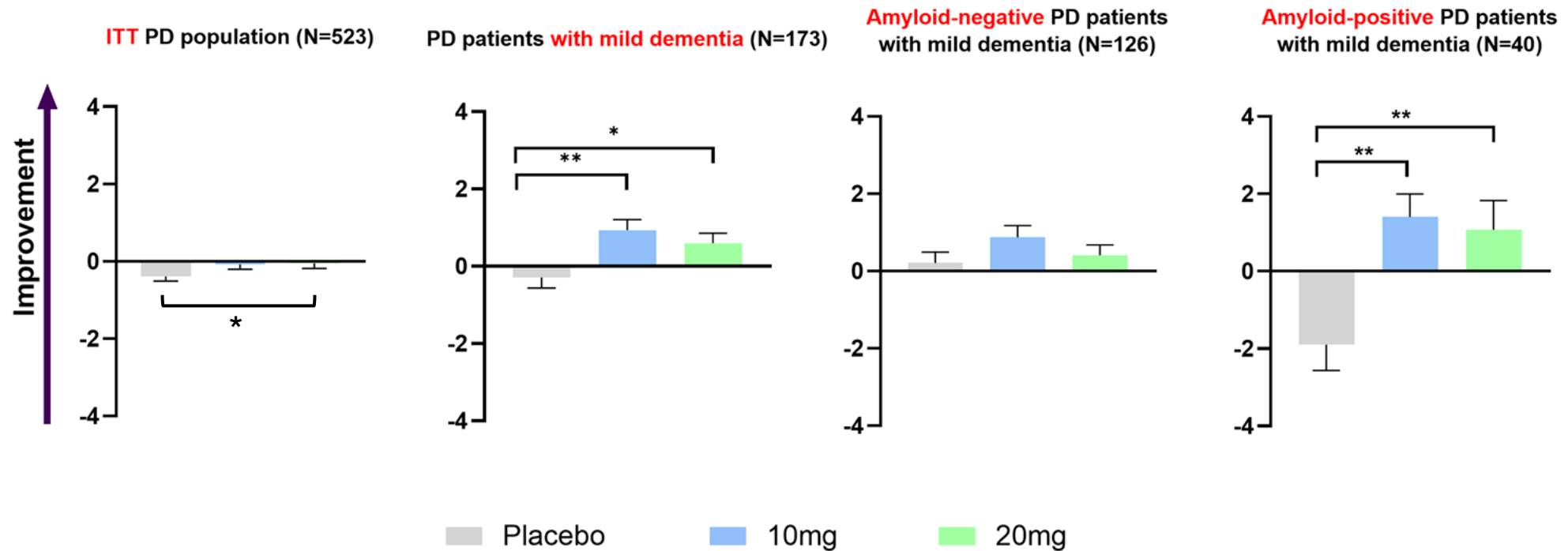
The study met its endpoints in the **per-protocol population**



* 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**

Change in MMSE

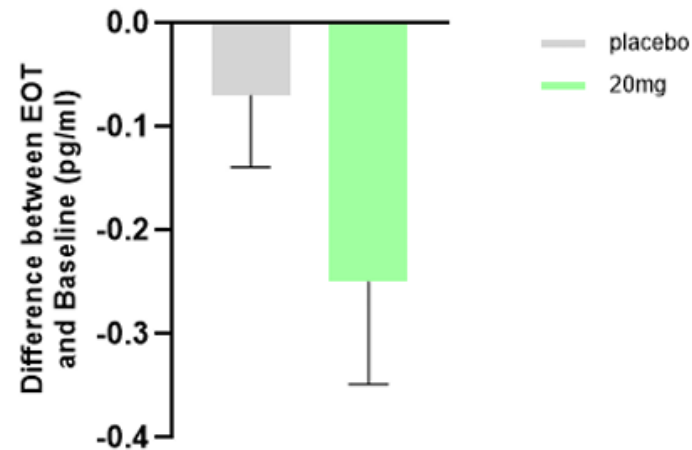


* compared to placebo: * p<0.05; **p<0.01

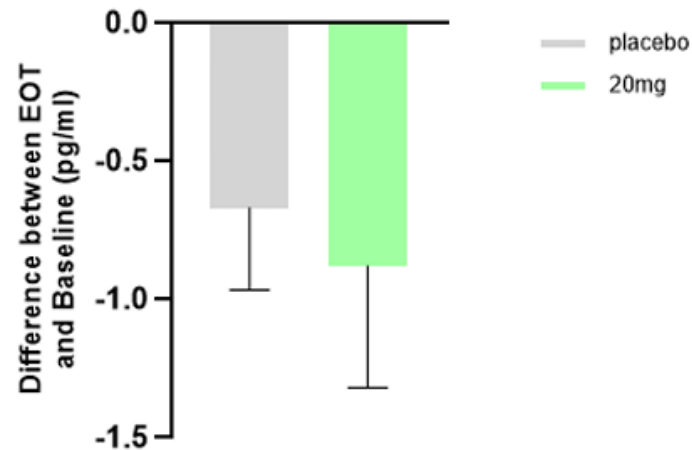
Biomarker data in **cognitively impaired PD patients (MMSE>20)**

Reductions in plasma levels of pTau217, total tau, and brain-derived (BD) tau

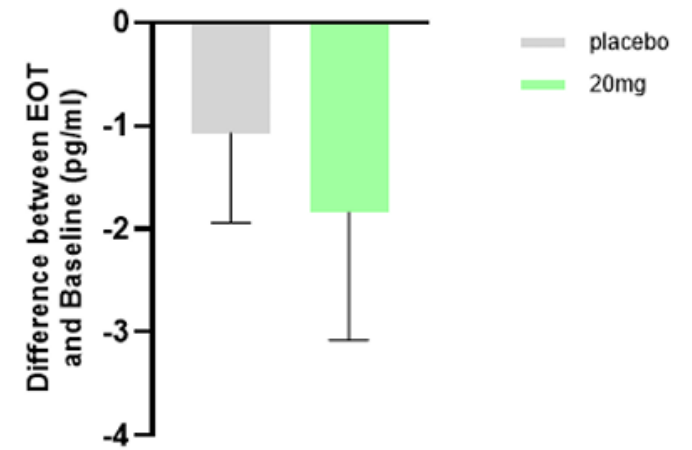
pTau217 in amyloid positive MMSE 20-28 (N=40)



t-Tau in amyloid positive MMSE 20-28 (N=40)



BD Tau in amyloid positive MMSE 20-28 (N=40)



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

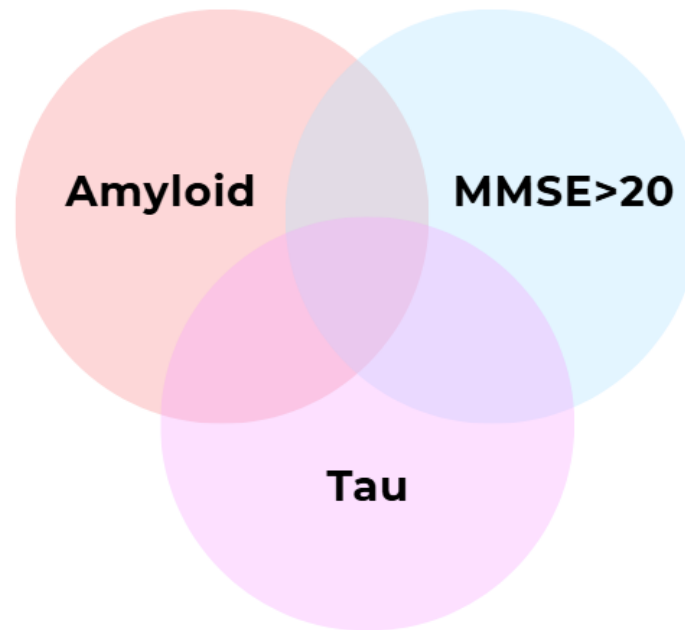
Summary: buntanetap and cognition



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

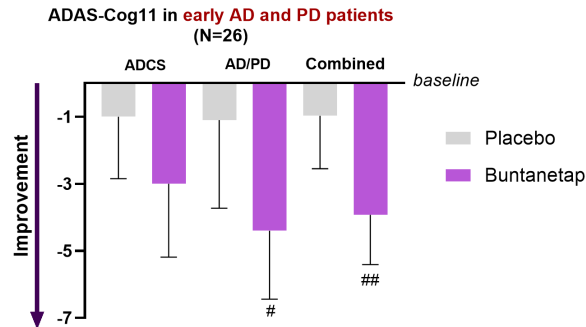
Buntanetap demonstrates the most pronounced cognitive benefit in patients with mild dementia (MMSE >20) and biomarker-confirmed presence of amyloid and tau.

Unified treatment pattern

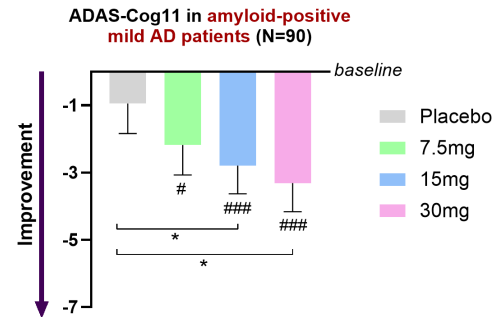


Buntanetap shows a fast improvement of cognition across four studies in Alzheimer's and Parkinson's patients

Phase 1/2 studies



Phase 2/3 AD study

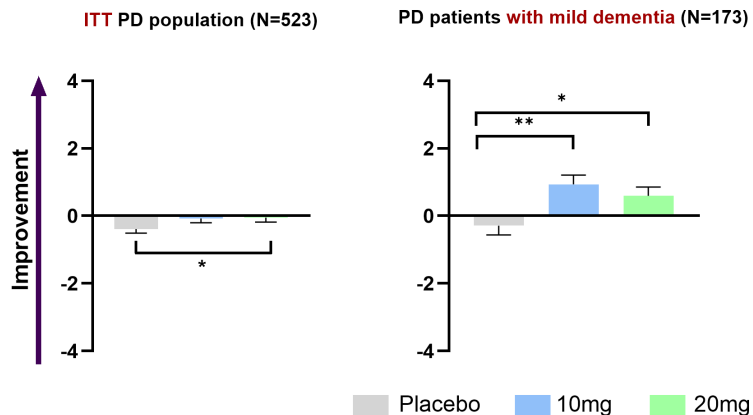


Phase 1/2 studies in early AD and PD

1 month of treatment

Phase 3 PD study

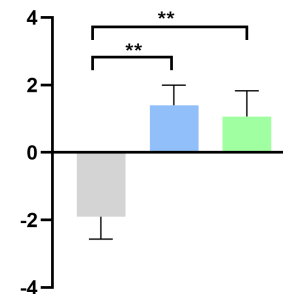
Change in MMSE



Phase 2/3 study in early AD

3 months of treatment

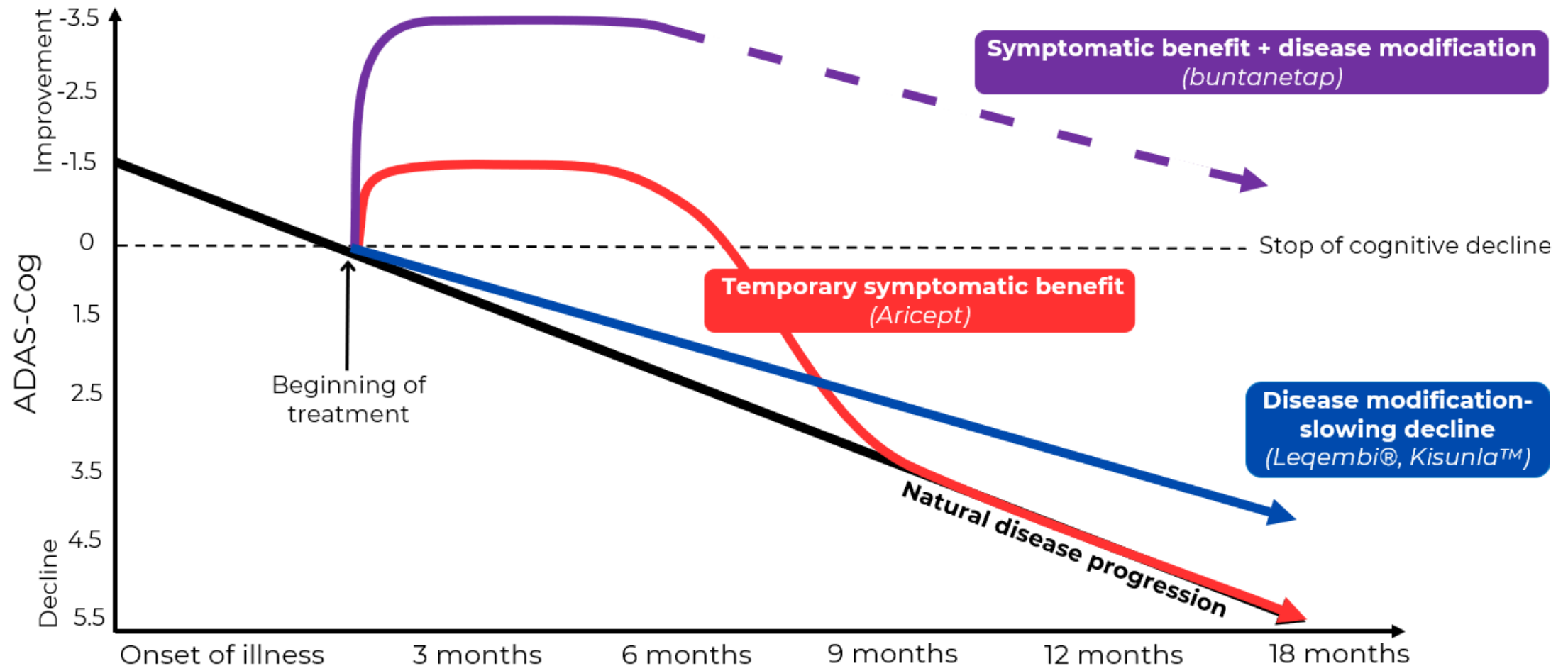
Amyloid-positive PD patients with mild dementia (N=40)



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



Annovis' new approach to attack AD and PD

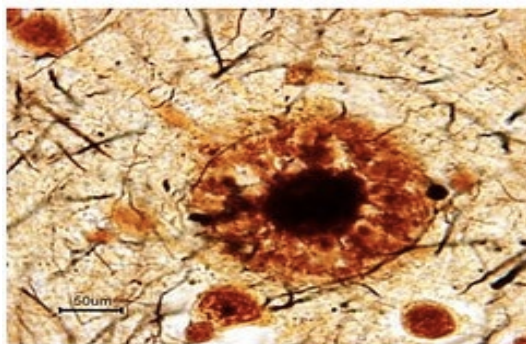
Chronic and acute brain insults lead to high iron levels, resulting in overexpression of neurotoxic proteins, impaired axonal transport, inflammation and neurodegeneration. Attacking one neurotoxic protein results in minimal effect.

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



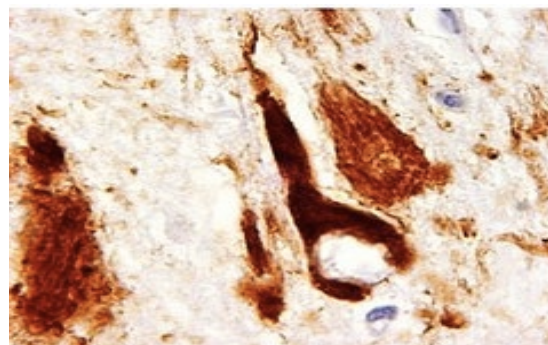
Amyloid β

Alzheimer's - Parkinson's



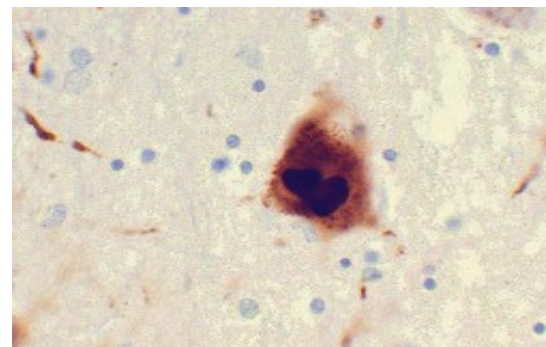
Tau

Tauopathies - AD, PD, FTD, CTE



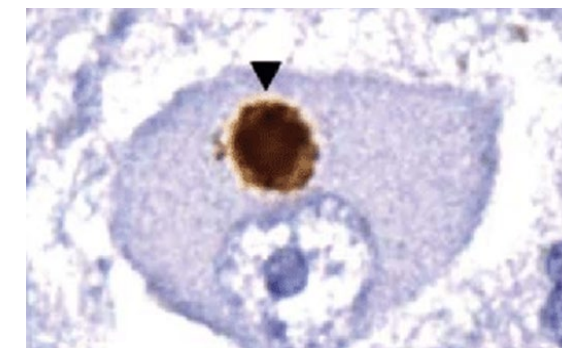
aSynuclein

Parkinson's - Alzheimer's



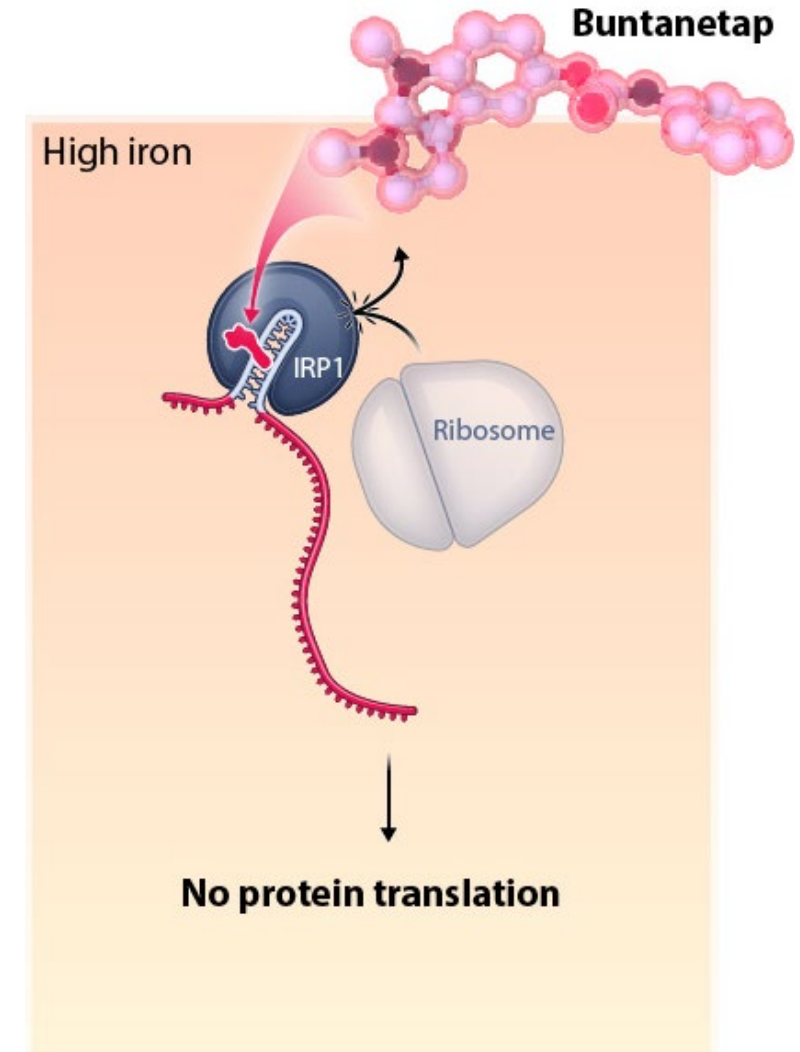
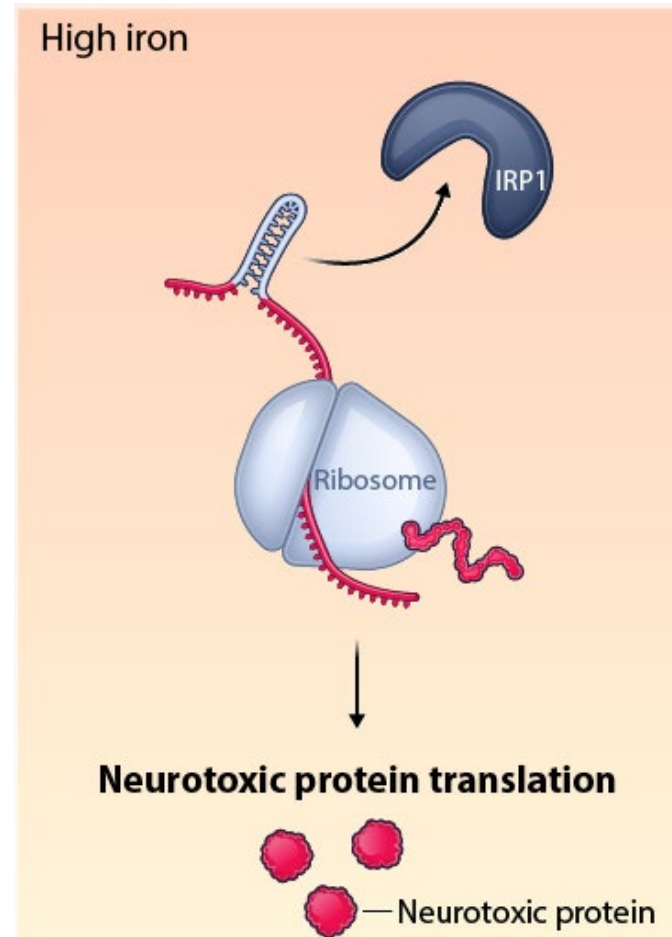
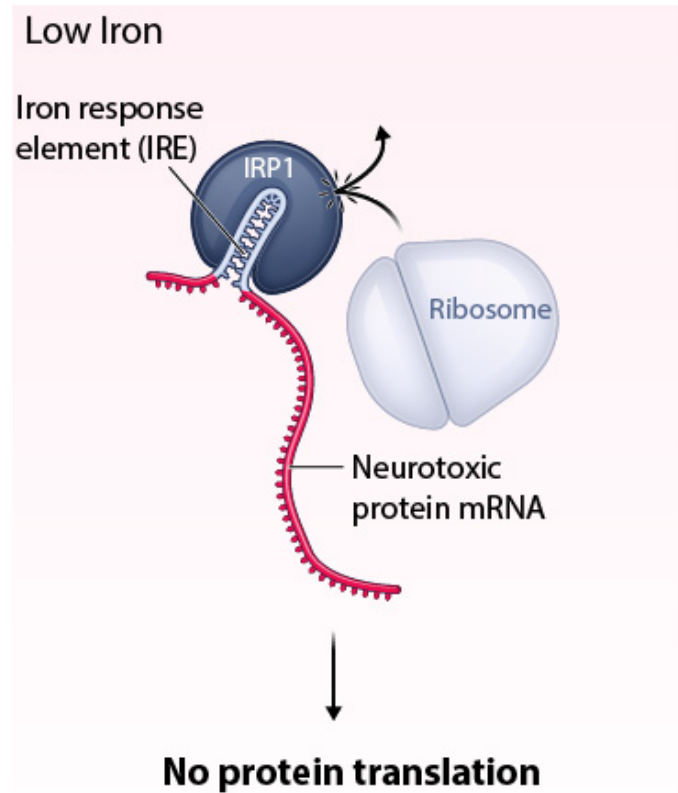
TDP43

ALS, AD, PD, FTD, CTE

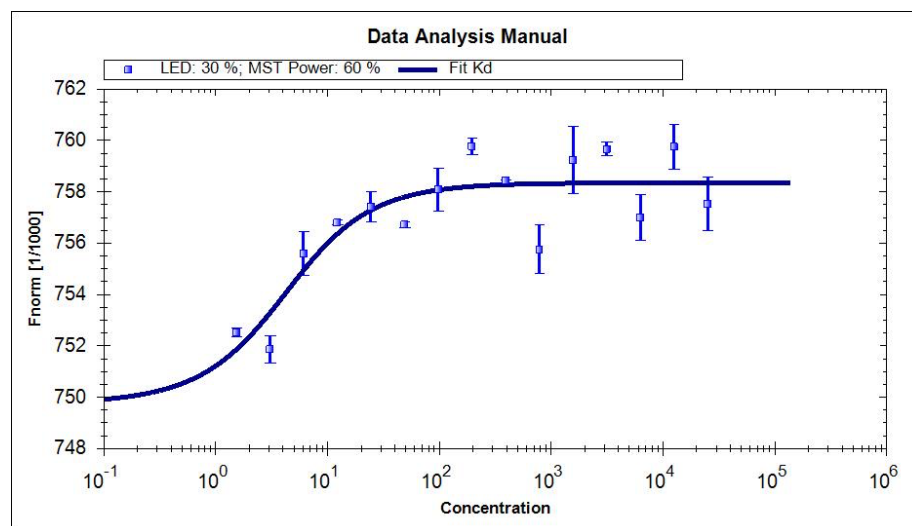


Buntanetap: RNA-targeting small molecule

Mechanism of action



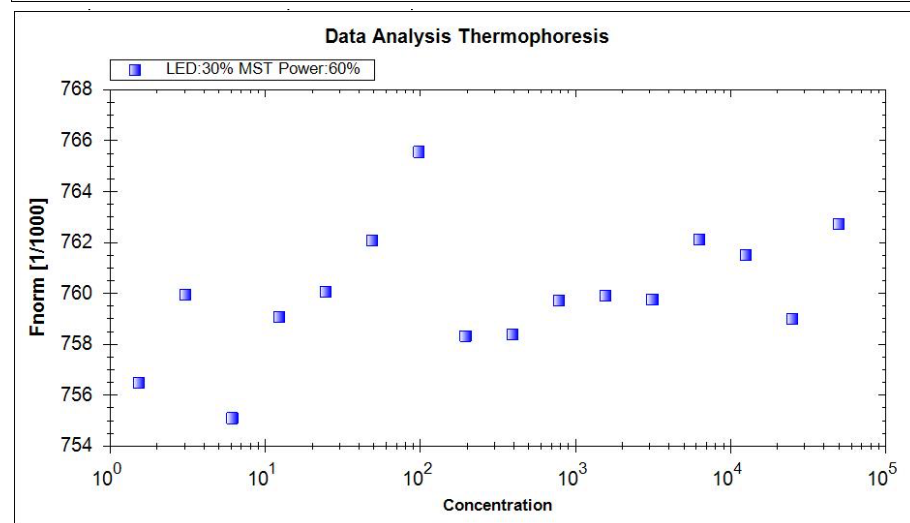
IRE-IRP1 binding is specific for mRNAs coding for neurotoxic proteins



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	
Amplitude	8.59

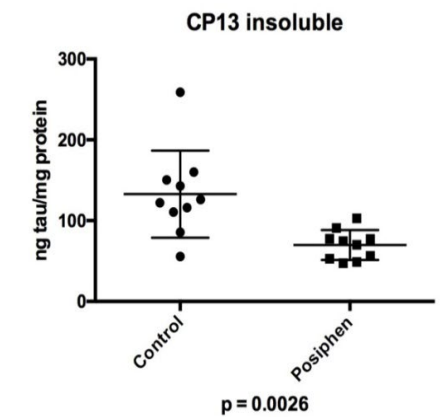
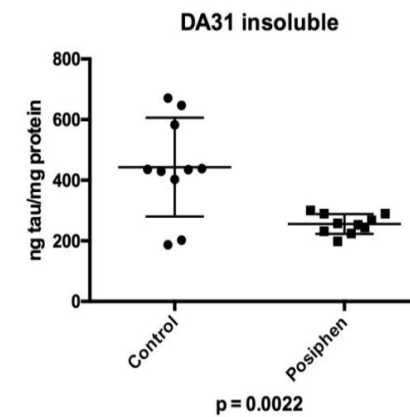
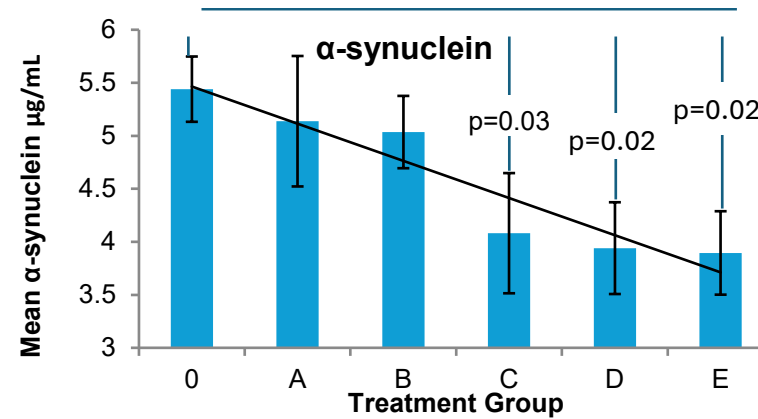
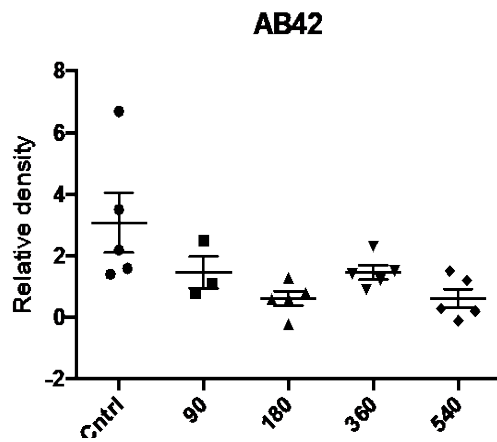
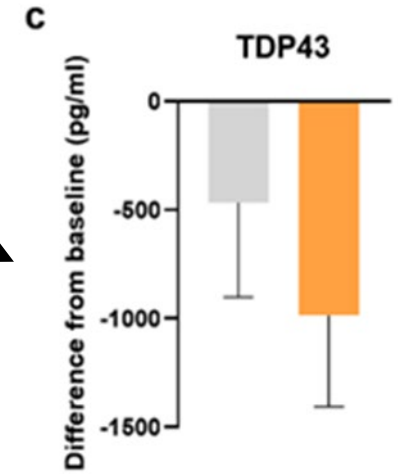
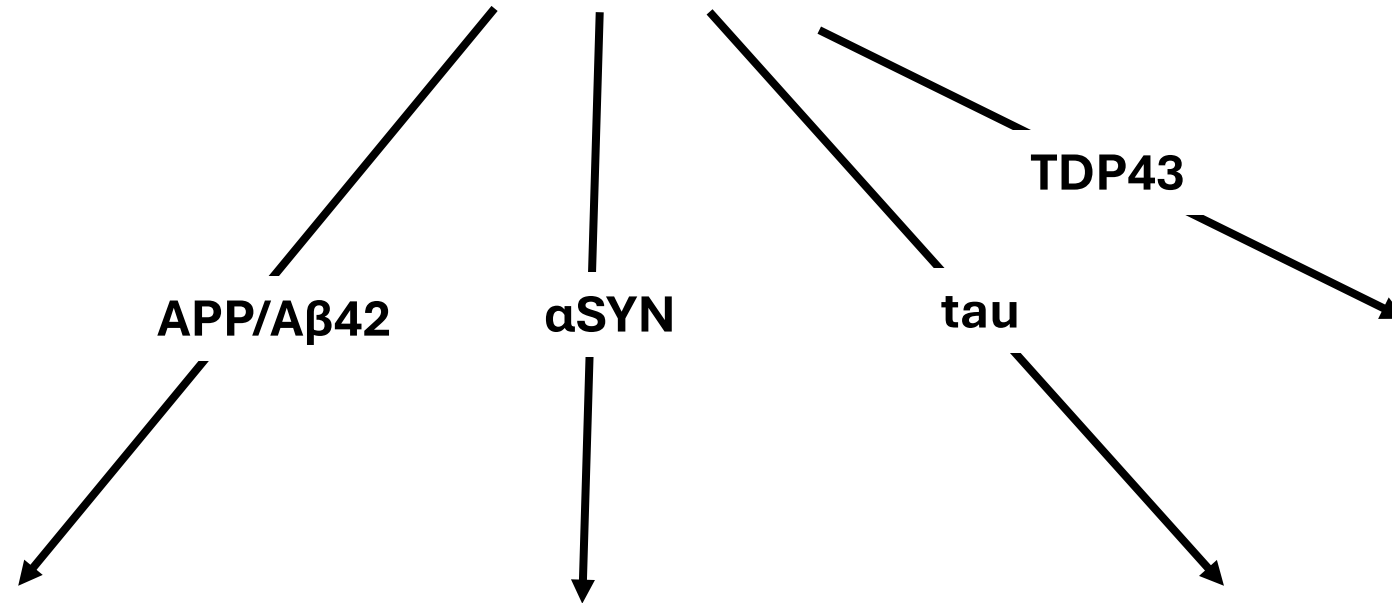
Buntanetap binds specifically to the **APP IRE**, but not to the ferritin IRE



Ferritin IRE/IRP1/Buntanetap
No Kd

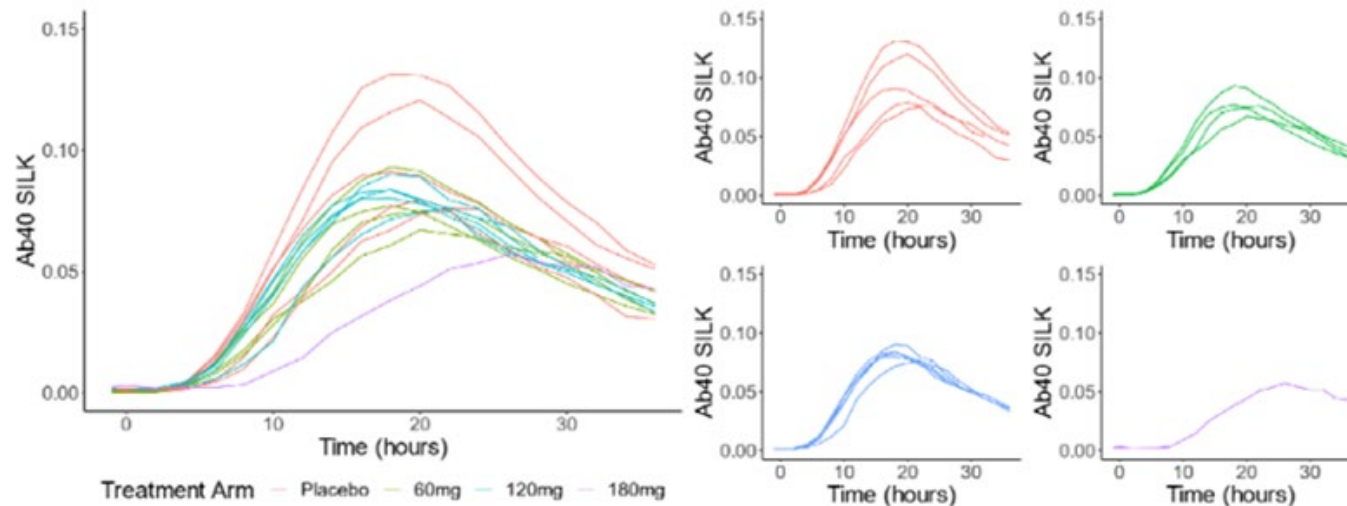
Buntanetap lowers neurotoxic proteins in mouse brain

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

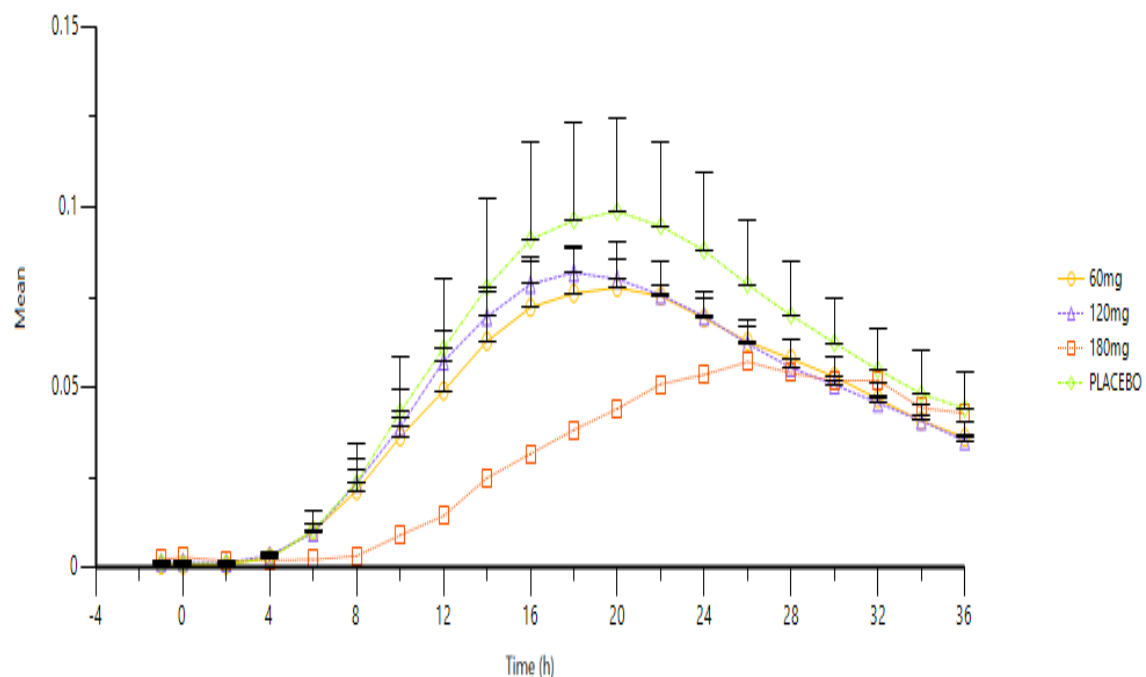


The Discover study was conducted through collaboration with ADCS and was designed to understand buntanetap's effect on synthesis of neurotoxic aggregating proteins – APP, using Stable Isotope Labeling Kinetic (SILK) analysis.

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

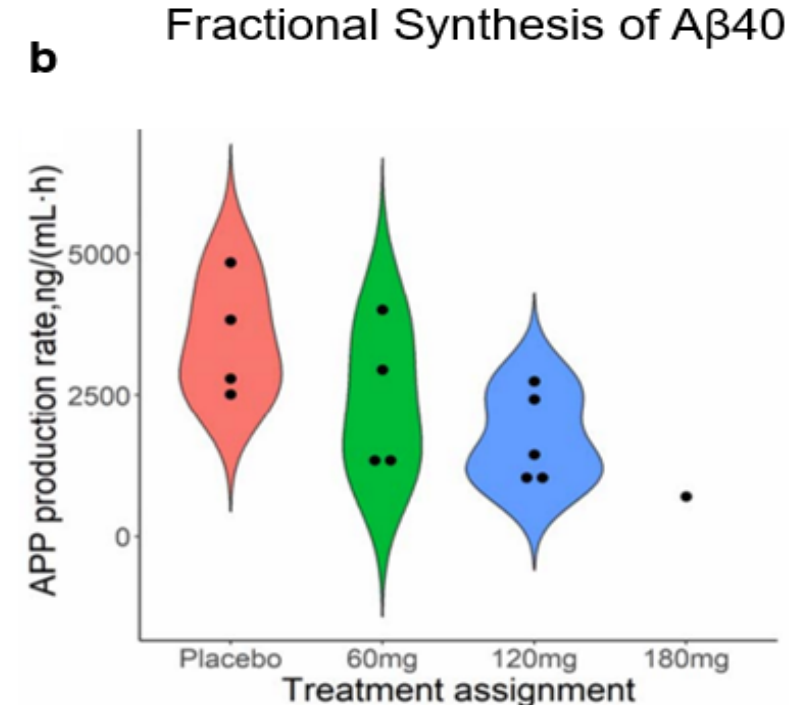
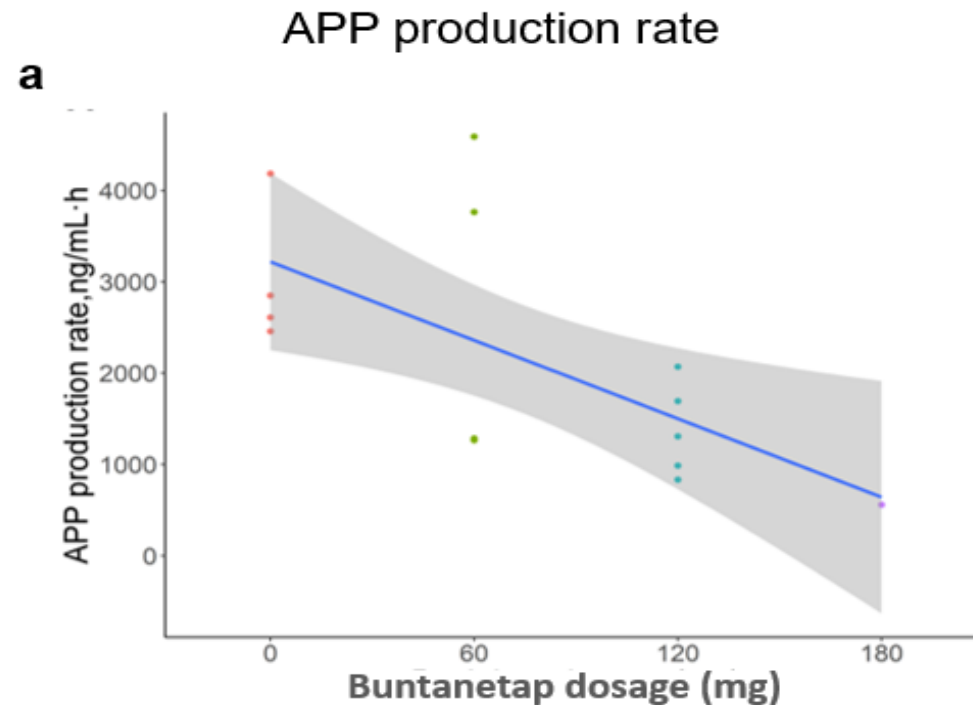


Buntanetap showed a dose-dependent lowering of A β 40 production as seen by a delayed start, lower synthesis rate, lower C_{max}, and smaller Area Under the Curve (AUC) of produced A β 40.

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	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

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

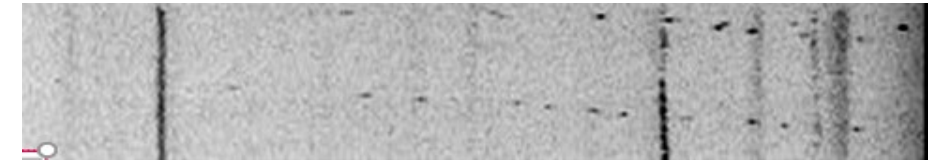
Axonal transport is responsible for:

- 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

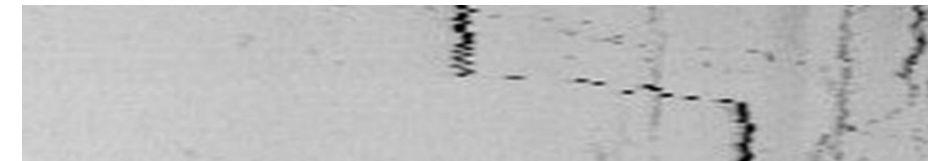
The *Normal Flow and Speed* of vesicles carrying BDNF across the axon.



(88s)

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.



(120s)

TREATED WITH BUNTANETAP

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

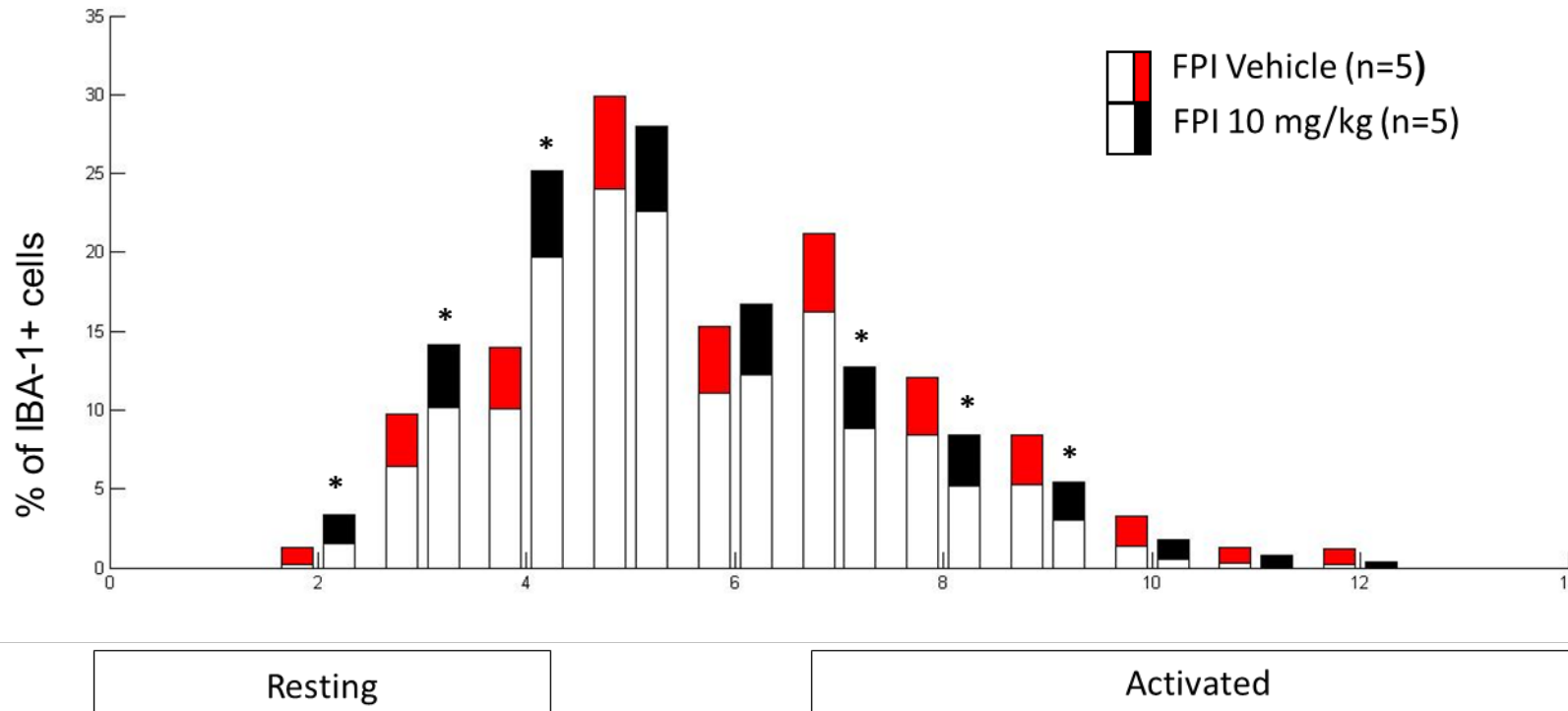


(88s)

APP, Ab42, C99 – Mobley, UCSD; αSYN – 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

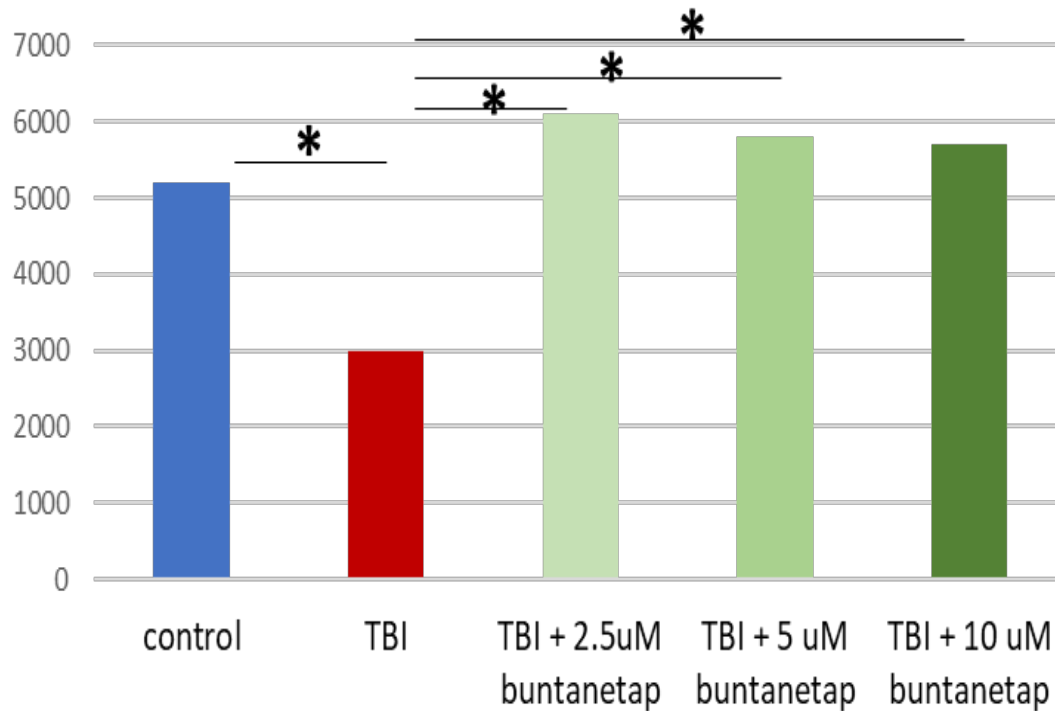


Microglial Cell Diameter (μm)

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

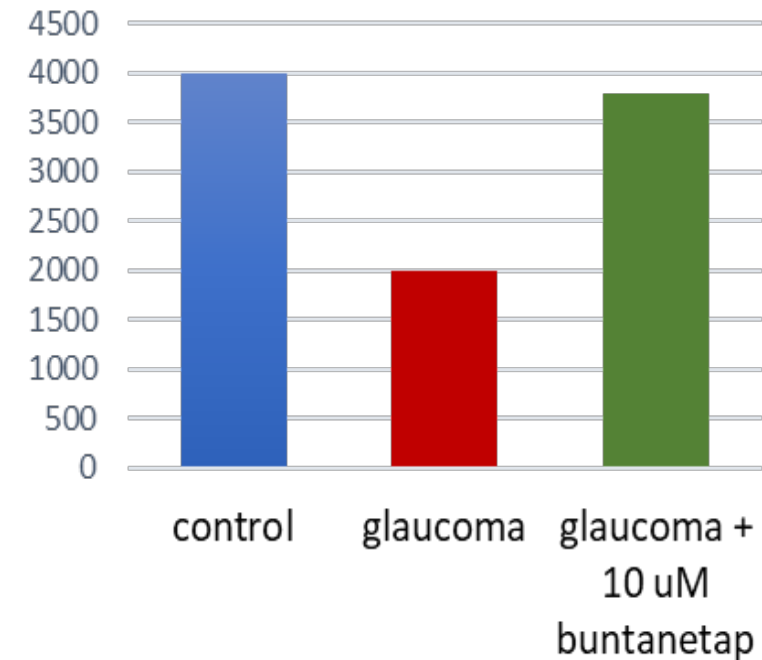
Buntanetap protects nerve cells from dying

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	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	<i>P. Gingivalis</i> mice - COVID mice

