# Investor Update

Development path to NDA for

- Alzheimer's disease
- Parkinson's disease

December 11, 2024

## 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 press release are based on information available to the Company as of the date of this release. 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.

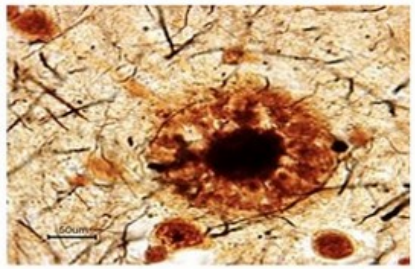
# Multiple neurotoxic proteins are implicated in Alzheimer's disease


*Adapted from R. Peterson, Neurology 2018*

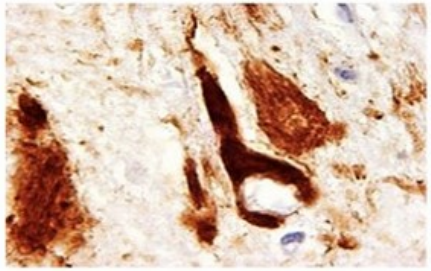
# Annovis' new approach to attack AD and PD

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

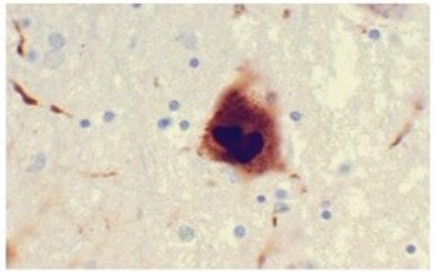
**Amyloid β**
Alzheimer's - Parkinson's



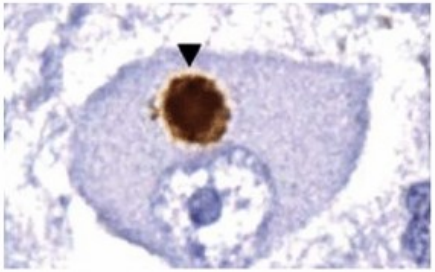
**Tau**
Tauopathies - AD, PD, FTD, CTE



**aSynuclein**
Parkinson's - Alzheimer's



**TDP43**
ALS, AD, PD, FTD, CTE



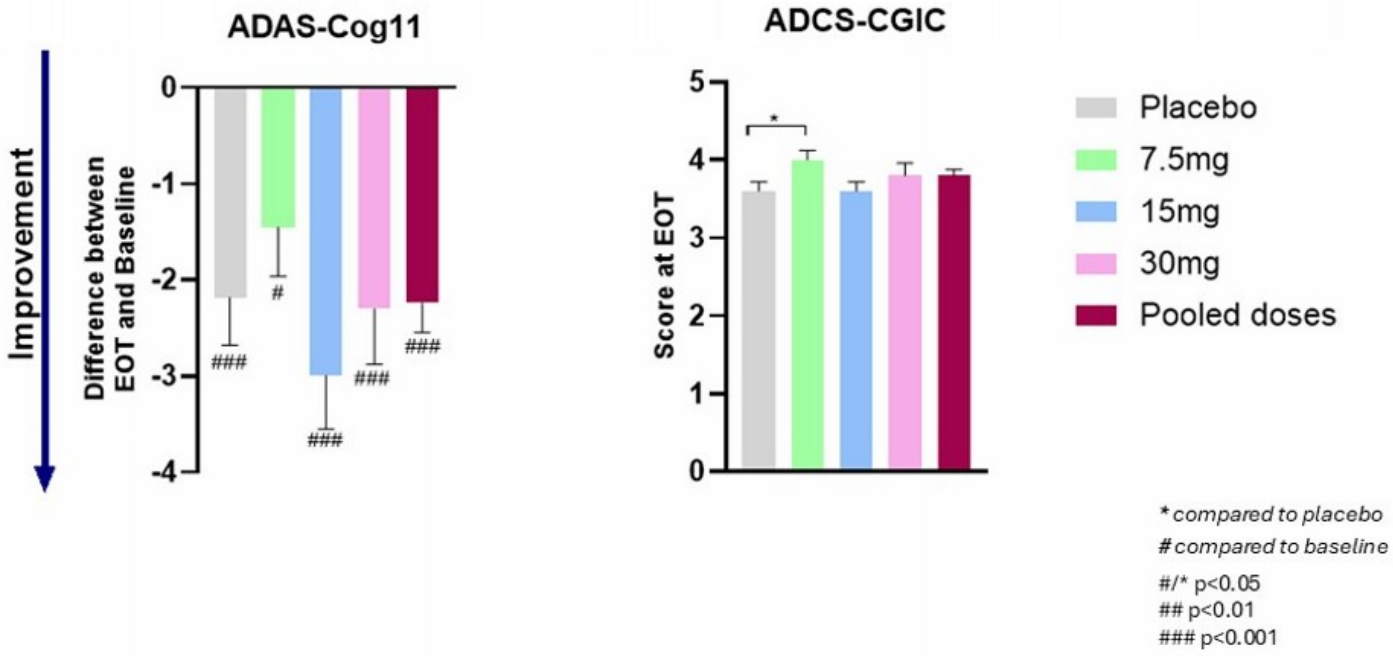
**Attacking one neurotoxic protein results in minimal effect.**

**Buntanetap inhibits the production of multiple neurotoxic proteins simultaneously.**

# Alzheimer’s disease

# ITT population: ADAS-Cog11 and ADCS-CGIC

## Entire enrolled population, n=351



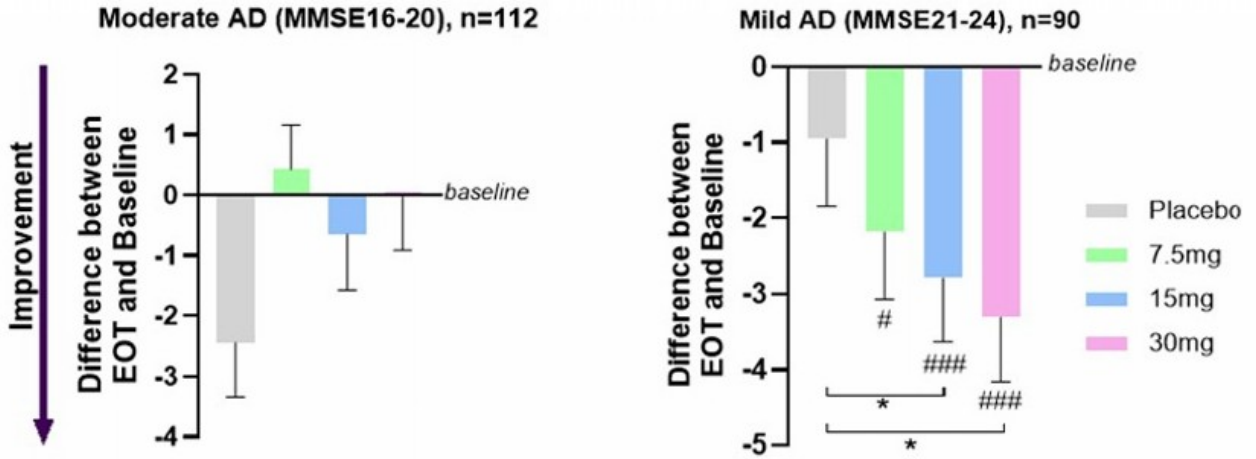

** compared to placebo*

*# 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%)

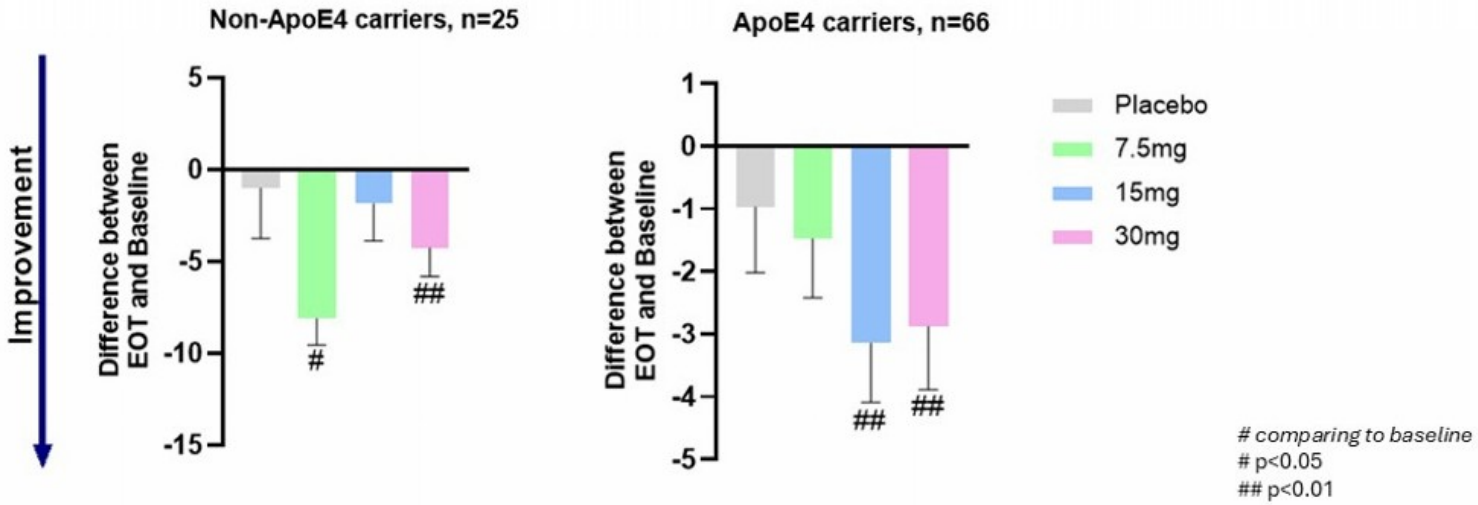



*From the ITT population:*
*- AD patients were selected by pTau217 inclusion/exclusion.*
*- Mild and moderate AD were determined by MMSE selection.*

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

# Buntanetap improves cognition in APOE4 carriers and non-carriers

**ADAS-Cog11 (MMSE 21-24, pTau217/t-Tau ≥4.2%)**

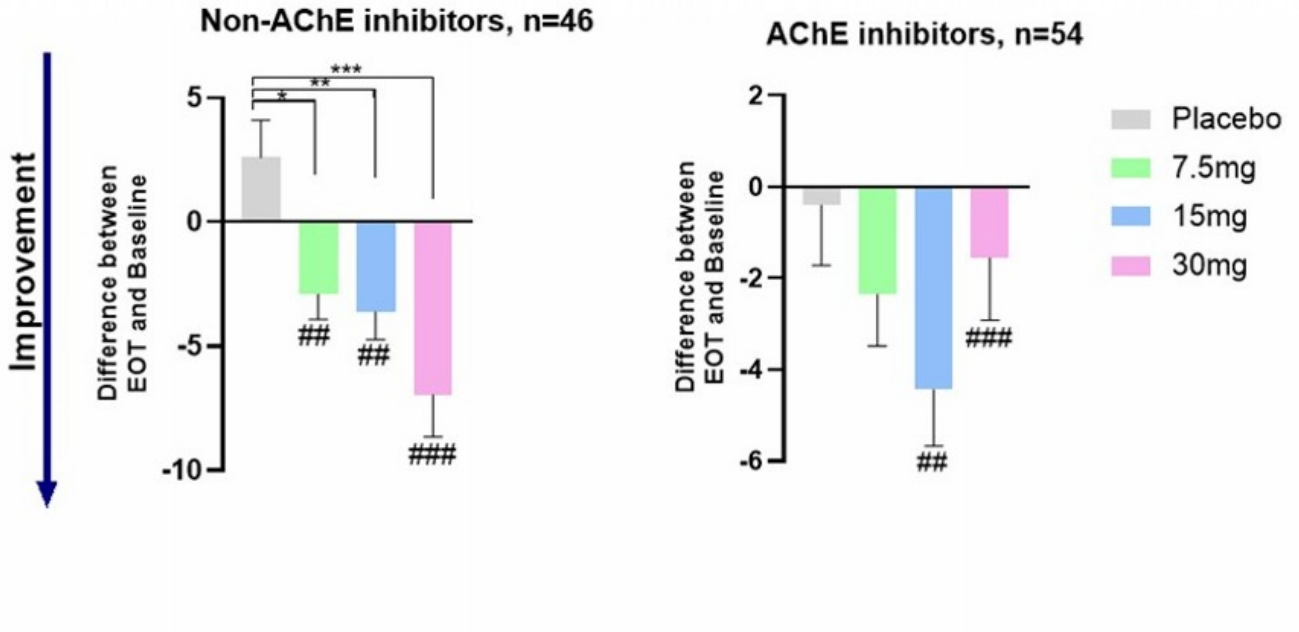



*AD frequency reaches 91% in homo- and 47% in heterozygous ApoE4 carriers.*

*ApoE4 carriers (+/- & +/+): 66.5% in pTau217/t-Tau>4.2% population vs 22.6% in pTau217/t-Tau<4.2% population*

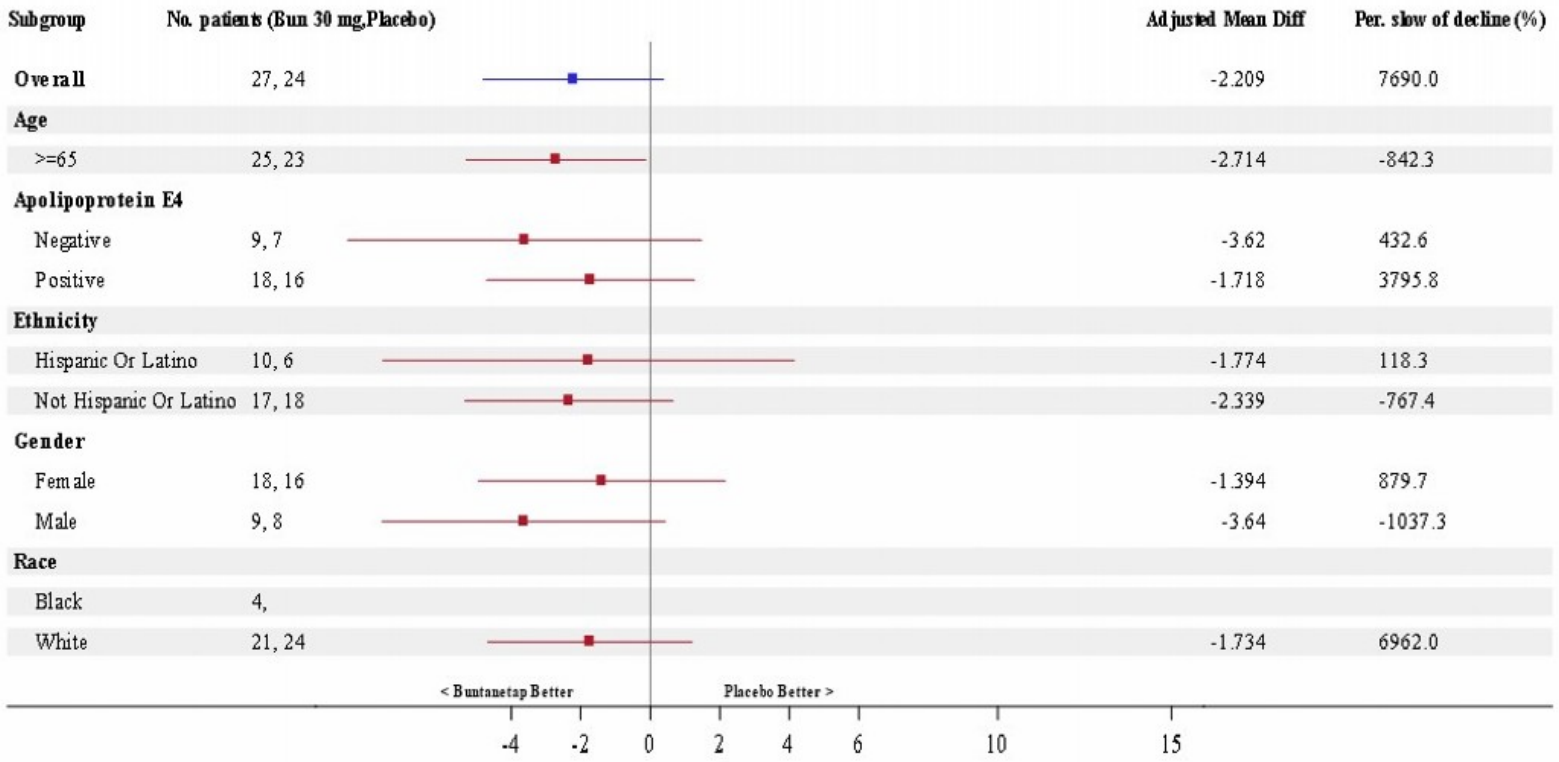
# Buntanetap improves cognition in patients not on AChEIs and on AChEIs

## ADAS-Cog11 (MMSE 21-24, pTau217/t-Tau ≥4.2%)




*# comparing to baseline*
** comparing to placebo*
*/# p<0.05
**/## p<0.01
***/### p<0.001

# Forest plot shows consistency and robustness of efficacy

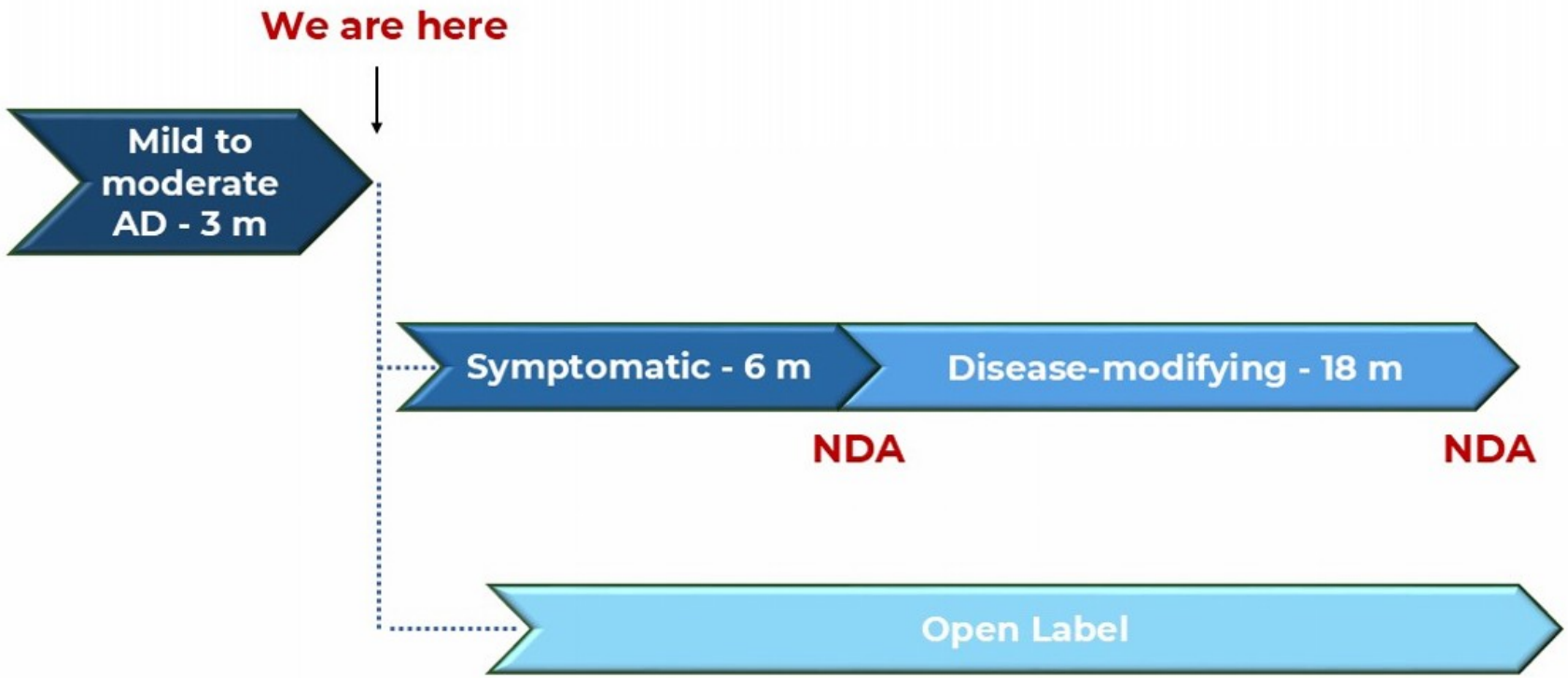


# Buntanetap is safe in APOE4 carriers and non-carriers in ITT AD population

| | 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*

# FDA cleared AD development path



# FDA-cleared Phase 3 study:

## A randomized, double-blind, placebo-controlled, multicenter study of buntanetap in participants with early Alzheimer's disease

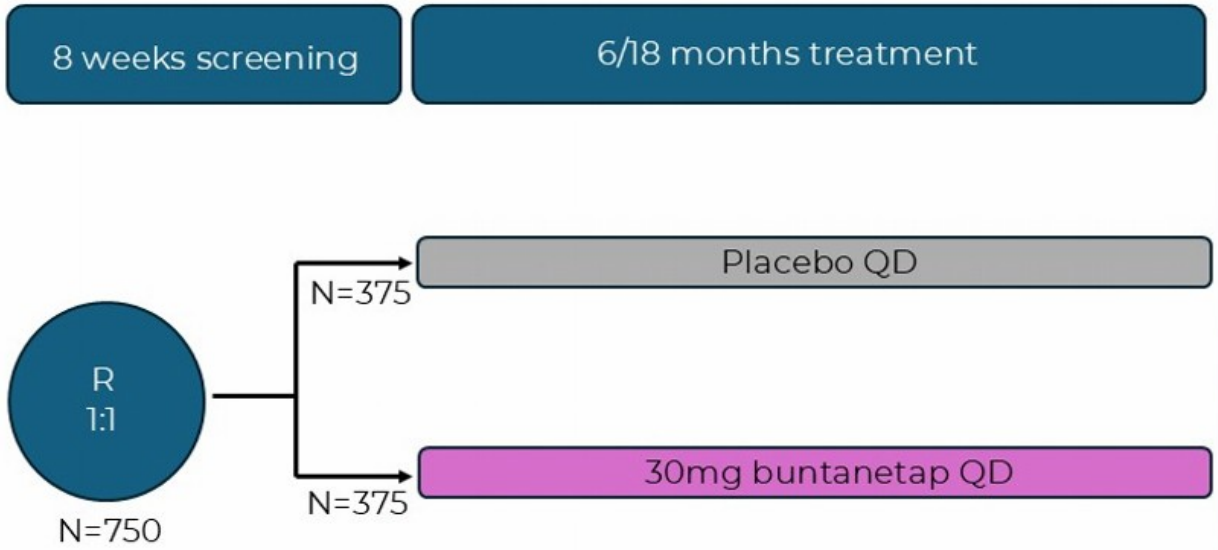
**Key inclusion criteria:**

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

**Key clinical outcome:**

Primary endpoints:

- ADAS-Cog 13
- ADCS-iADL
- vMRI



## Path forward – Alzheimer's disease

1. Buntanetap shows promising efficacy in early AD patients.

2. 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.

3. 6/18-month trial is expected to start in Q1 2025.

# Thanks to all clinical trials participants and their families

**Annovis team:**

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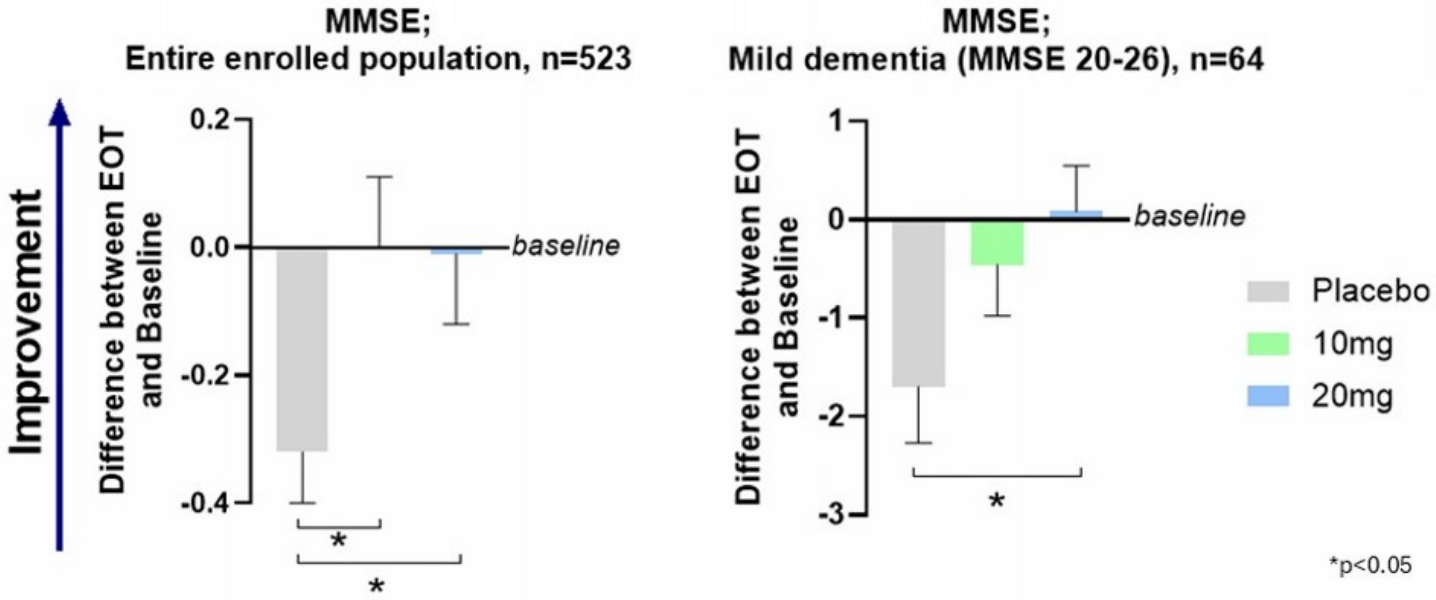
Frontida
Morawek
Pharmaron
Pharmapace
Quanterix
WPI
Wuxi

ANNOVIS

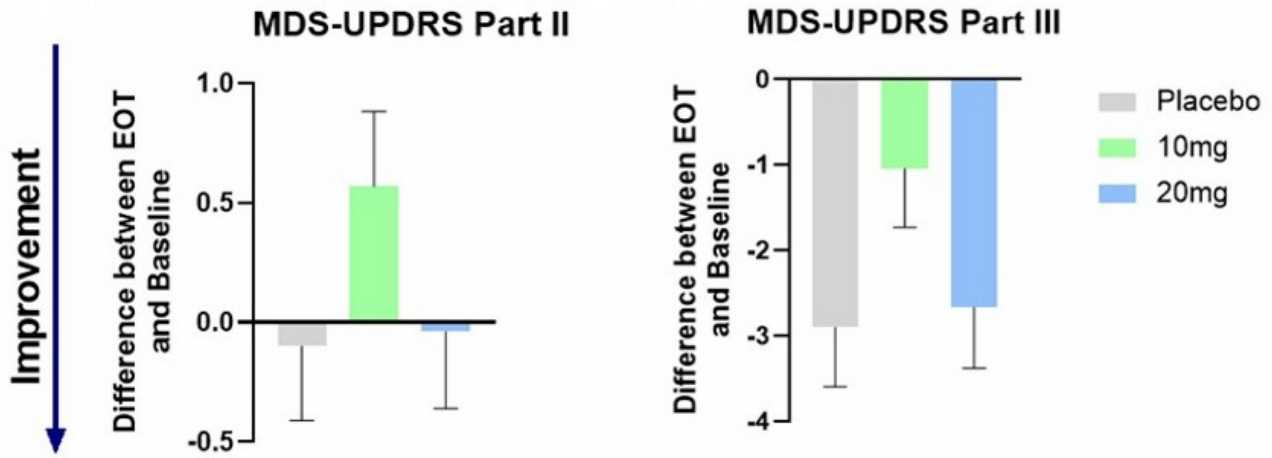
# Parkinson’s disease

# ITT population, cognitive impairment:
## MMSE and dementia stage

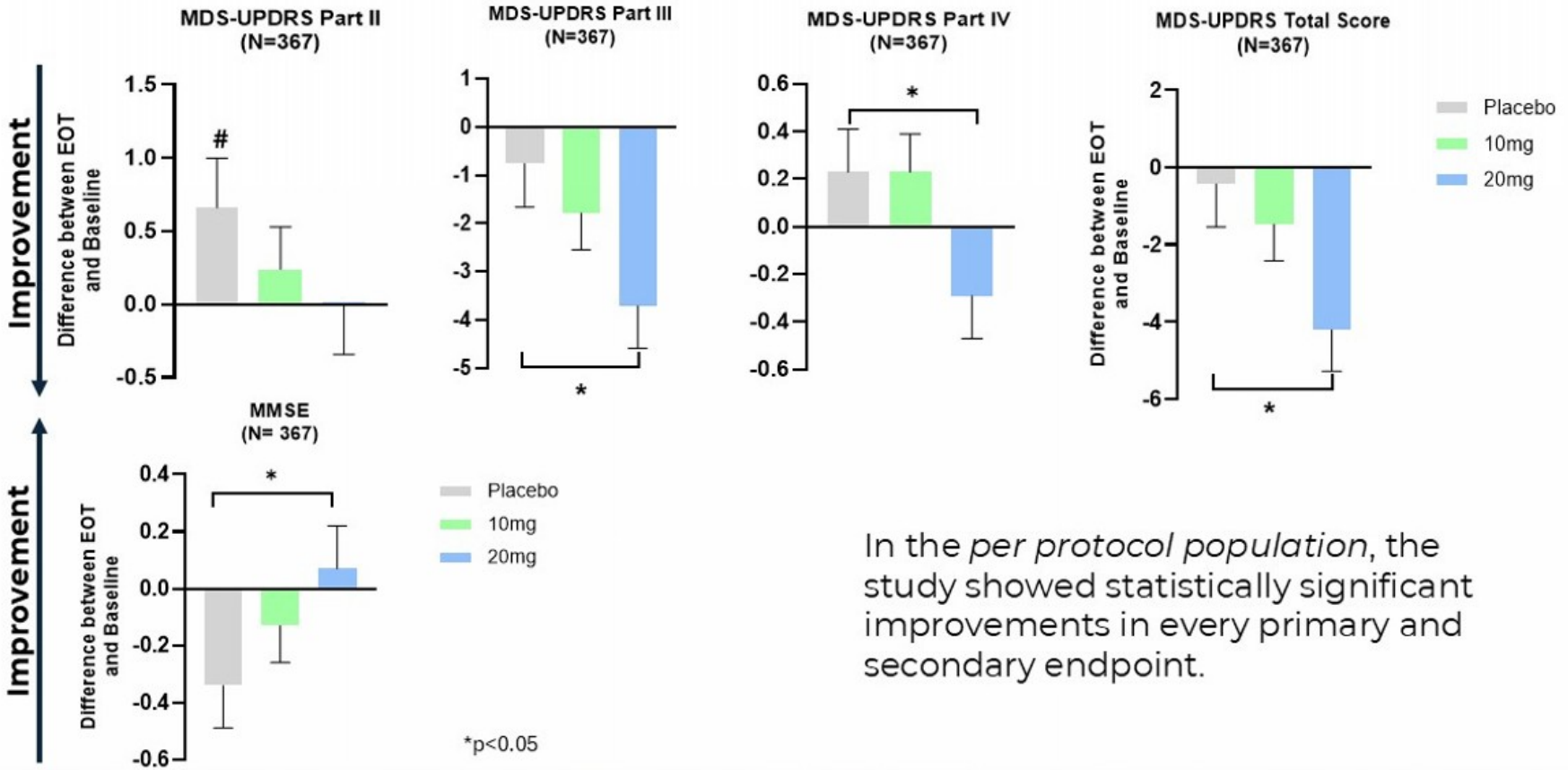


# ITT population: MDS-UPDRS II and III

## Entire enrolled population, n=523



# 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.

# Buntanetap is safe 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

1. Buntanetap prevents worsening of cognition in ITT population - all treated patients.
2. Buntanetap improves cognitive function in patients with impaired cognition.
3. In per protocol population, buntanetap significantly improves MDS-UPDRS Part II, III, IV, total and MMSE.
4. Meeting with the FDA to determine development path forward will be held in Q1 2025.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THANK YOU
QUESTIONS?