UCB News

UCB Presents Encouraging Data on Bepranemab in Early Alzheimer's Disease in Phase 2a Study at CTAD 2024

- Results provide first evidence of biological and clinical effect of a mid-domain tau-targeting disease-modifying therapy[1]
- In full study population primary endpoint was not met, however in key secondary endpoints bepranemab slowed cognitive decline and rate of tau accumulation[2]
- In pre-defined patient subgroups, consistent treatment benefit shown across multiple primary and secondary outcome measures, including cognition and function[2]
- UCB is evaluating next steps in the development program

Brussels, Belgium – 31 October 2024 – 6PM CET – UCB today reported Phase 2a data from the TOGETHER (AH0003) study, investigating the safety, efficacy, and tolerability of bepranemab - an investigational anti-tau antibody targeting the mid-region of the tau protein - in people living with prodromal to mild Alzheimer's disease[3]. The results were presented during a late-breaking symposium at the 2024 Clinical Trials on Alzheimer's Disease (CTAD) meeting (Madrid, Spain, October 29 – November 1, 2024).

"We are deeply encouraged by the proof-of-concept data for bepranemab, which highlight its potential to impact early Alzheimer's disease progression. This strengthens our belief in the value of targeting the mid-region of tau as an important strategy in altering the trajectory of the disease," said Alistair Henry, Chief Scientific Officer at UCB. "We extend heartfelt thanks to the patients, families and friends, and dedicated clinical trial teams who have partnered with us on this important research. Their support is invaluable as we continue to explore the next steps in bepranemab's development."

Full study population[2]

In the overall study population, no beneficial effect of low- or high-dose bepranemab compared with placebo was observed on the primary endpoint, Clinical Dementia Rating Scale Sum of Boxes (CDR-SB) total score at Week 80 (CDR-SB is a measure of cognition and function). However, at Week 80, in key secondary endpoints, treatment with bepranemab (45mg/kg and 90mg/kg):

- Slowed the rate of tau accumulation versus placebo in key brain regions by 33%-58%.
- Slowed cognitive decline by 21-25% versus placebo - the change between Baseline and Week 80 in the Alzheimer's Disease Assessment Scale-Cognitive Subscale (ADAS-Cog14) total score.

Consistent treatment effect in sub-group analysis[2]

In two predefined subgroups, low tau burden at Baseline and APOε4* non-carriers, treatment benefits were observed across multiple outcome measures. In a post-hoc subgroup analysis comprising participants with low tau at Baseline or those who are APOε4 non-carriers (approximately 50% of the full study population), high-dose bepranemab (90mg/kg):

- Slowed the rate of tau accumulation versus placebo in key brain regions by 63%-67% at Week 80.

Date of preparation: October 2024

- Slowed clinical disease progression by 29% - as measured by the change in CDR-SB between Baseline and Week 80.
- Slowed disease progression according to secondary/exploratory endpoints, including measures of Activities of Daily Living by 41-54% at Week 80.

In the subgroup comprising participants with high tau at Baseline who were also APOε4 carriers, treatment with high-dose bepranemab showed no benefit across almost all clinical endpoints with effects on CDR-SB, A-iADL-Q and ADCS-ADL scores favoring the placebo arm.

Safety data[2]
Bepranemab had an acceptable safety profile and was generally well tolerated. Brain haemorrhagic and inflammatory changes were similar between placebo and bepranemab treatment arms. Incidence of Treatment Emergent Adverse Events (TEAEs), drug-related TEAEs, and TEAEs leading to dropout were comparable between the treatment arms. Most reported TEAEs were infections and infestations (placebo 50.3% / bepranemab 50.2%), nervous system disorders (placebo 40.1% / bepranemab 35.2%) and musculoskeletal disorders (placebo 26.8% / bepranemab 28.3%).

About TOGETHER study[3]
TOGETHER is a Phase 2a double-blind, placebo-controlled, three-arm study, randomizing patients to placebo, low, or high dose bepranemab. A total of 466 patients participated in the study and were treated in the double-blind phase for 80 weeks. The majority of participants have now entered the 48-week open-label extension (OLE) period with planned bepranemab treatment for 44 weeks, followed by a safety follow-up visit 20 weeks after the last infusion.

About bepranemab
Bepranemab is a monoclonal antibody (mAb) that specifically targets a mid-region epitope of human tau[4,5]. In pathological conditions, the mid-region of tau is thought to be essential for tau aggregation and is a key driver of neurodegeneration in Alzheimer's disease[6].

*APOε4 is the primary genetic risk factor for sporadic Alzheimer's disease.

This release discusses investigational uses of an agent in development and is not intended to convey conclusions about efficacy or safety. There is no guarantee that any investigational uses of such product will successfully complete clinical development or gain health authority approval.

For further information, contact UCB:

Global Communications
Nick Francis
T: +44 7769 307745
nick.francis@ucb.com

Date of preparation: October 2024

UCB News

Corporate Communications
Laurent Schots
T: +32.2.559.92.64
laurent.schots@ucb.com

Investor Relations
Antje Witte
T: +32.2.559.94.14
antje.witte@ucb.com

About UCB
UCB, Brussels, Belgium (www.ucb.com) is a global biopharmaceutical company focused on the discovery and development of innovative medicines and solutions to transform the lives of people living with severe diseases of the immune system or of the central nervous system. With approximately 9,000 people in approximately 40 countries, the company generated revenue of €5.3 billion in 2023. UCB is listed on Euronext Brussels (symbol: UCB). Follow us on Twitter: @UCB_news.

Forward looking statements
This press release may contain forward-looking statements including, without limitation, statements containing the words "believes", "anticipates", "expects", "intends", "plans", "seeks", "estimates", "may", "will", "continue" and similar expressions. These forward-looking statements are based on current plans, estimates and beliefs of management. All statements, other than statements of historical facts, are statements that could be deemed forward-looking statements, including estimates of revenues, operating margins, capital expenditures, cash, other financial information, expected legal, arbitration, political, regulatory or clinical results or practices and other such estimates and results. By their nature, such forward-looking statements are not guarantees of future performance and are subject to known and unknown risks, uncertainties and assumptions which might cause the actual results, financial condition, performance or achievements of UCB, or industry results, to differ materially from those that may be expressed or implied by such forward-looking statements contained in this press release. Important factors that could result in such differences include: the global spread and impact of COVID-19, changes in general economic, business and competitive conditions, the inability to obtain necessary regulatory approvals or to obtain them on acceptable terms or within expected timing, costs associated with research and development, changes in the prospects for products in the pipeline or under development by UCB, effects of future judicial decisions or governmental investigations, safety, quality, data integrity or manufacturing issues; potential or actual data security and data privacy breaches, or disruptions of our information technology systems, product liability claims, challenges to patent protection for products or product candidates, competition from other products including biosimilars, changes in laws or regulations, exchange rate fluctuations, changes or uncertainties in tax laws or the administration of such laws, and hiring and retention of its employees. There is no guarantee that new product candidates will be discovered or identified in the pipeline, will progress to product approval or that new indications for existing products will be developed and approved. Movement from concept to commercial product is uncertain; preclinical results do not guarantee safety and efficacy of product candidates in humans. So far, the complexity of the human body cannot be reproduced in computer models, cell culture systems or animal models. The length of the timing to complete clinical trials and to get regulatory approval for product marketing has varied in the past and UCB expects similar unpredictability going forward. Products or potential products, which are the subject of partnerships, joint ventures or licensing collaborations may be subject to differences disputes between the partners or may prove to be not as safe, effective or commercially successful as UCB may have believed at the start of such partnership. UCB's efforts to acquire other products or companies and to integrate the operations of such acquired companies may not be as successful as UCB may have believed at the moment of acquisition. Also, UCB or others could discover safety, side effects or manufacturing problems with its products and/or devices after they are marketed. The discovery of significant problems with a product similar to one of UCB's products that implicate an entire class of products may have a material adverse effect on sales of the entire class of affected products. Moreover, sales may be impacted by international and domestic trends toward managed care and health care cost containment, including pricing pressure, political and public scrutiny, customer and prescriber patterns or practices, and the reimbursement policies imposed by third-party payers as well as legislation affecting biopharmaceutical pricing and reimbursement activities and outcomes. Finally, a breakdown,

cyberattack or information security breach could compromise the confidentiality, integrity and availability of UCB's data and systems.

Given these uncertainties, you should not place undue reliance on any of such forward-looking statements. There can be no guarantee that the investigational or approved products described in this press release will be submitted or approved for sale or for any additional indications or labelling in any market, or at any particular time, nor can there be any guarantee that such products will be or will continue to be commercially successful in the future.

UCB is providing this information, including forward-looking statements, only as of the date of this press release and it does not reflect any potential impact from the evolving COVID-19 pandemic, unless indicated otherwise. UCB is following the worldwide developments diligently to assess the financial significance of this pandemic to UCB. UCB expressly disclaims any duty to update any information contained in this press release, either to confirm the actual results or to report or reflect any change in its forward-looking statements with regard thereto or any change in events, conditions or circumstances on which any such statement is based, unless such statement is required pursuant to applicable laws and regulations.

Additionally, information contained in this document shall not constitute an offer to sell or the solicitation of an offer to buy any securities, nor shall there be any offer, solicitation or sale of securities in any jurisdiction in which such offer, solicitation or sale would be unlawful prior to the registration or qualification under the securities laws of such jurisdiction.

References:

1. Imbimbo B, et al. Initial failures of anti-tau antibodies in Alzheimer's disease are reminiscent of the amyloid-β story. Neural Regeneration Research. 2023; 18(1): 117-118.
2. Barton M, et al. Results from TOGETHER, a double-blind, placebo-controlled Phase II study evaluating efficacy, safety and tolerability of bepranemab in prodromal–mild AD. Presented at: 17th Clinical Trials on Alzheimer's Disease (CTAD), Madrid (Spain) October 29 - November 1, 2024.
3. https://www.ucb.com/clinical-studies/Clinical-Trials?studyId=AH0003. Accessed October 2024.
4. Albert M, et al. Prevention of tau seeding and propagation by immunotherapy with a central tau epitope antibody. Brain. 2019;142(6):1736–1750.
5. Courade JP, et al. Epitope determines efficacy of therapeutic anti-Tau antibodies in a functional assay with human Alzheimer Tau. Acta Neuropathol. 2018;136(5):729–745.
6. Roberts M, et al. Pre-clinical characterisation of E2814, a high-affinity antibody targeting the microtubule-binding repeat domain of tau for passive immunotherapy in Alzheimer's disease. Acta Neuropathol Commun. 2020;8(1):13.

Date of preparation: October 2024