



PRESS RELEASE

AB SCIENCE RECEIVES FIRST AGENCIES AUTHORIZATIONS TO INITIATE CONFIRMATORY PHASE 3 CLINICAL STUDY WITH MASITINIB IN THE TREATMENT OF ALZHEIMER'S DISEASE

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AB Science SA (Euronext - FR0010557264 - AB) today announces that the first authorizations have been received to initiate its phase 3 confirmatory study (AB21004) evaluating masitinib in patients with mild to moderate Alzheimer's Disease (AD) from the French Medicine Agency (ANSM) together with AEMPS (Spain agency) and EOF (Greece agency).

Study AB21004 is a randomized, double-blind phase 3 study to evaluate the safety and efficacy of masitinib in patients with mild to moderate Alzheimer's disease, as an add-on therapy to standard of care, cholinesterase inhibitors and/or memantine. The study will enroll 600 patients with confirmed clinical diagnosis of mild and moderate Alzheimer's disease, corresponding to an Activities of Daily Living (ADCS-ADL) score of less than 73 and a Mini Mental State Examination (MMSE) score of between 14 to 25, inclusive.

The objective of study AB21004 is to confirm treatment effect with masitinib 4.5 mg/kg/day as an adjunct to cholinesterase inhibitor and/or memantine in patients with mild-to-moderate Alzheimer's disease. The primary endpoint of the study will be to evaluate the effect of masitinib on absolute change from baseline in ADCS-ADL score and in ADAS-Cog-11.

The positioning of masitinib is different from other Alzheimer's disease drugs such as lecanemab, aduhelm, donanemab and crenelumab, which target the earliest stages of the AD continuum, including very mild dementia, prodromal or asymptomatic Alzheimer's disease, MMSE>22 and up to 30, whereas patients with MMSE 27-30 have normal cognitive functions.

The mechanism of action of masitinib is also different from other drugs being developed for Alzheimer's disease and possibly complementary in the sense that masitinib targets microglia and mast cells to deliver a disease modifying neuro protective effect, whereas lecanemab, aduhelm, donanemab, and crenelumab are anti-amyloid antibodies that aim to eliminate toxic amyloid-beta (A β) aggregates.

Furthermore, masitinib is an orally administered tyrosine kinase whereas the aforementioned anti-amyloid antibody drugs are administered via injection.

Professor Bruno Dubois, MD, principal investigator of the study and Professor of Neurology at Sorbonne University, France commented, *"We are very excited to initiate this confirmatory phase III study with masitinib in Alzheimer's disease. There is a vacuum of treatment options for patients with mild or moderate Alzheimer's disease. The results from first phase 2B/3 study, AB09004, were very encouraging, especially considering this is a difficult to treat patient population. First, we found the optimal dose out of the three tested. Second, masitinib administered at 4.5 mg/kg/day, significantly slowed cognitive deterioration relative to placebo and also showed reduced loss of functional ability in activities of daily living. Of equal importance, it was shown that the safety of masitinib when administered as an adjunct to cholinesterase inhibitor and/or memantine was in line with its known safety profile and not worsened in this aged population."*

Professor Olivier Hermine, President of the Scientific Committee of AB Science and member of the Académie des Sciences in France, said: *“With these first agency authorizations, AB Science has now launched in the third key indication with masitinib in its confirmatory program; these being amyotrophic lateral sclerosis, progressive forms of multiple sclerosis, and now Alzheimer's disease. Masitinib is a platform program to treat neurodegenerative diseases based on its unique mechanism of action targeting microglia and mast cells, essential cells that are thought to contribute to the neurodegenerative process and if properly controlled contribute to neuro protection ».*

About the results from previous phase 2B/3 AB09004

Study AB09004 was the first successful phase 2B/3 randomized trial in mild-to-moderate Alzheimer's disease of a drug targeting innate immune cells of the neuroimmune system. Masitinib at 4.5 mg/kg/day showed significant benefit over placebo according to the primary analysis, with an acceptable safety profile.

Primary efficacy analysis (based on multiple endpoints, each tested at a significance level of 2.5%) was the least-squares mean change from baseline to week-24 in either the 11-item Alzheimer's Disease Assessment Scale - cognitive subscale (ADAS-cog), or the Alzheimer's Disease Cooperative Study Activities of Daily Living Inventory scale (ADCS-ADL).

Results showed that masitinib can generate a significant treatment effect relative to placebo in the primary endpoint of change from baseline in ADAS-Cog, an instrument that measures the effect on cognition and memory. Specifically, masitinib 4.5 mg/kg/day (n=182) showed significant benefit relative to placebo (n=176), with a respective change in ADAS-cog from baseline of -1.46 (representing an overall improvement in cognition) versus +0.69 (representing increased cognitive deterioration); a corresponding ADAS-cog between-group difference of -2.15 (97.5%CI [-3.48, -0.81]), p=0.0003.

It was also seen that masitinib generated a non-significant trend towards improved overall function relative to placebo as measured by the ADCS-ADL score, an instrument that assesses self-care and activities of daily living. Specifically, masitinib 4.5 mg/kg/day showed a change in ADCS-ADL from baseline of +1.01 (representing an overall functional improvement) versus -0.81 for placebo (representing increased functional deterioration); a corresponding ADCS-ADL between-group difference of +1.82 (97.5%CI [(-0.15, 3.79)]), p=0.038.

The safety of masitinib as an adjunct to cholinesterase inhibitor and/or memantine was acceptable and consistent with its known tolerability profile. It is noteworthy that this result is in the context of a relative elderly population (average age of about 73 years) with comorbidities. The incidence of patients having at least one treatment-emergent adverse event (AE) after 24 weeks of treatment was 87% for masitinib 4.5 mg/kg/day versus 77.5% for the placebo-control group. This corresponds to an incidence rate ratio (masitinib/placebo) of 1.1. The incidence of severe AE for masitinib 4.5 mg/kg/day was 26.5% versus 19.3% in the placebo-control group, corresponding to an incidence rate ratio of 1.4.

About masitinib's mechanism of action in Alzheimer's disease

Masitinib (AB1010) is an oral tyrosine kinase inhibitor that has demonstrated neuroprotective action in neurodegenerative diseases via inhibition of mast cell and microglia/macrophage activity, possibly by switching the neuroimmune system from a neurotoxic state towards a neuroprotective state through remodeling of the neuronal microenvironment. Mast cells, macrophages and microglia are types of innate immune cells that are present in the central nervous system, and for which there is a growing body of evidence implicating them in the pathophysiology of neurodegenerative diseases such as Alzheimer's disease, progressive forms of multiple sclerosis and amyotrophic lateral sclerosis (ALS).

The rationale to use masitinib in Alzheimer's disease patients is supported by preclinical evidence demonstrating that the pharmacological action of masitinib in mast cells can restore normal spatial learning performance in a mouse model of Alzheimer's disease and promotes recovery of synaptic markers [1].

Despite decades of extensive research, the overwhelming majority of human trials (predominantly testing amyloid-based therapeutics) have failed to demonstrate clinical efficacy. This underscores a need for

innovative, non-amyloid based approaches, including therapies that modulate the neuroimmune response in Alzheimer's disease, which has been implicated in the pathophysiology of the disease [2–6].

References :

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- [5] Tchessalova D, Posillico CK, Tronson NC. Neuroimmune Activation Drives Multiple Brain States. *Front Syst Neurosci.* 2018;12:39.
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About AB Science

Founded in 2001, AB Science is a pharmaceutical company specializing in the research, development and commercialization of protein kinase inhibitors (PKIs), a class of targeted proteins whose action are key in signaling pathways within cells. Our programs target only diseases with high unmet medical needs, often lethal with short term survival or rare or refractory to previous line of treatment.

AB Science has developed a proprietary portfolio of molecules and the Company's lead compound, masitinib, has already been registered for veterinary medicine and is developed in human medicine in oncology, neurological diseases, inflammatory diseases and viral diseases. The company is headquartered in Paris, France, and listed on Euronext Paris (ticker: AB).

Further information is available on AB Science's website:

www.ab-science.com.

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For additional information, please contact:

AB Science

Financial Communication & Media Relations

investors@ab-science.com