PRESS RELEASE

NEW PEER-REVIEWED DATA PROVIDE STRONG EVIDENCE SUPPORTING MASITINIB'S POTENTIAL FOR THE TREATMENT OF ALZHEIMER'S DISEASE THROUGH A DUAL MECHANISM OF COGNITIVE ENHANCEMENT AND NEUROPROTECTION

THIS PUBLICATION CORROBORATES NEW ANALYSIS FROM THE CLINICAL PHASE 2B/3 STUDY SHOWING COGNITIVE IMPROVEMENT UNDER MASITINIB TREATMENT

PHASE 3 CLINICAL STUDY WITH MASITINIB AS A DISEASE-MODIFYING THERAPY FOR ALZHEIMER'S DISEASE HAS BEEN AUTHORIZED BY THE FDA AND KEY EU COUNTRIES

Paris, June 23, 2025, 8am CET

AB Science SA (Euronext - FR0010557264 - AB) today announced that a new peer-reviewed study from an independent research team based in China (Guangdong Pharmaceutical University and Sun Yat-sen University) presents new evidence showing that masitinib offers a promising new approach to treating Alzheimer's disease, specifically the most common form, sporadic Alzheimer's disease (sAD), which accounts for over 95% of all cases.

Masitinib is a highly innovative drug for Alzheimer's disease because unlike the majority of drug development research in this indication, masitinib targets the brain's innate immune system, including mast cells and microglia. The positioning of masitinib as a treatment of Alzheimer's disease is also different from other drugs.

- **New evidence from peer-reviewed study**

This new publication is accessible online from the *Neuroscience Letters* journal website at: https://doi.org/10.1016/j.neulet.2025.138300 [1]

In the study, researchers used a well-established mouse model that mimics the cognitive and behavioral symptoms of human sAD. When treated with masitinib, the mice showed marked improvements in memory, learning, sense of smell, and anxiety-like behaviors, all of which are early indicators of Alzheimer's progression.

The research also revealed that masitinib:

- Reduced toxic brain proteins such as hyperphosphorylated Tau.
- Alleviated synaptic dysfunction and morphological damage, i.e., it protected synapses, which are essential for brain cell communication.
- Suppressed microglial activation, which in turn inhibited the NF-κB/NLRP3/caspase-1 signaling axis, a key inflammatory signaling cascade linked to Alzheimer's disease, thereby suppressing inflammation in the brain of sAD mice.

The authors emphasized that this is the first study to demonstrate that masitinib attenuates sporadic Alzheimer's disease pathology through dual mechanisms of cognitive enhancement and neuroprotection.

Professor Olivier Hermine, MD, President of the Scientific Committee of AB Science and member of the Académie des Sciences in France said, "*These new, independent findings provide strong evidence supporting*

masitinib as a promising disease-modifying therapy for sporadic Alzheimer's disease and perfectly compliment previously published clinical and preclinical data for masitinib in this indication."

- **New data from phase 2B/3 study in patients with mild Alzheimer's disease**

It has previously been shown that masitinib enhances cognitive function and synaptic integrity in a familial Alzheimer's disease mouse model [2]. Moreover, randomized, placebo-controlled, phase 2 and phase 2B/3 studies demonstrated that masitinib (4.5 mg/kg/day) can effectively delay or mitigate the progression of dementia [3,4]. Clinical and preclinical study findings have also been summarized in a review article [5], with the authors concluding that 'all research studies revealed positive effects concerning the cognitive functions in Alzheimer's disease and generally with good safety and tolerability'.

New analysis from the completed phase 2B/3 study (AB09004), shows that masitinib treatment may not only slow down worsening of cognition in patients with mild Alzheimer's disease, but actually improves it over the treatment period of 24 weeks. Indeed, study AB09004 included patient with both mild and moderate AD (MMSE [12 - 25]). In the overall study population, which included patient with both mild and moderate AD (MMSE [12 - 25]), masitinib 4.5 mg/kg/day plus standard of care (memantine and anticholinesterase) demonstrated a significant reduction in cognitive impairment (ADAS-Cog LS Mean Diff = -2.15; p=0.0003) compared with standard of care alone. However, the clinical benefit on ADAS-Cog was greater in patients with mild impairment (LS Mean Diff = -2.89 ; p=0.0008) than in patients with moderate impairment (LS Mean Diff = -1.74; p=0.0284). Notably, there was a meaningful improvement in cognitive function between baseline and week 24 in the mild AD subgroup under masitinib treatment (LS Mean = -2.47), while it remained stable in the control arm (LS Mean = -0.42), as presented in the table below.

ADAS-COG Change from Baseline to Week 24	**N**	**LS Mean**	**LS Mean Diff.** (97.51% CI)	**p-value**
Mild and moderate AD patients				
Masitinib 4.5 mg/kg/day + SoC	182	-1.45	-2.15 (-3.48, -0.81)	0.0003
Placebo + SoC	176	0.69		

ADAS-COG Change from Baseline to Week 24	**N**	**LS Mean**	**LS Mean Diff.** (97.51% CI)	**p-value**
Mild patients [MMSE (21-25)]				
Masitinib 4.5 mg/kg/day + SoC	63	-2.47	-2.89 (-4.80, -0.99)	0.0008
Placebo + SoC	61	0.42		
Moderate patients [MMSE (12-20)]				
Masitinib 4.5 mg/kg/day + SoC	119	-1.04	-1.74 (-3.52, 0.04)	0.0284
Placebo + SoC	115	0.70		

SoC = Standard of care = memantine and anticholinesterase
Note : Negative change in LS Mean of ADAS-COG means an improvement of cognition. Positive change in LS Mean of ADAS-COG means a worsening of cognition.

- **Authorized phase 3 to support New Drug Application in case of success**

AB Science previously received an Investigational New Drug (IND) approval letter from the FDA and similar authorizations from several European countries to initiate Phase III study (AB21004) in patients with Alzheimer's disease.

Study AB21004 is a randomized, double-blind phase 3 study to evaluate the safety and efficacy of masitinib in patients with mild Alzheimer's disease, as an add-on therapy to standard of care, cholinesterase inhibitors and/or memantine. The study will enroll 600 patients.

The objective of study AB21004 is to confirm results from the first phase 2B/3 study, AB09004, which showed that masitinib administered at 4.5 mg/kg/day significantly slowed cognitive deterioration relative to placebo and also reduced loss of functional ability in activities of daily living in the targeted AD population. Study AB21004 will evaluate the effect of masitinib on absolute change from baseline in cognition (ADAS-Cog-11) as primary endpoint and integrated AD rating scale (iADRS) and daily living (ADCS-ADL) as secondary endpoints.

- **Expected patent protection until 2041**

Based on the results from AB09004 study, AB Science filed a patent application relating to methods of treating Alzheimer's disease (i.e. a medical use patent) with its lead compound masitinib (WO2022129410A1). If granted, this patent will provide intellectual property protection for masitinib in this indication until 2041. A similar strategy was successfully applied in Amyotrophic Lateral Sclerosis, with medical use patent for masitinib in ALS being granted worldwide (press release dated June 1st 2023).

References :

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3. Dubois B, López-Arrieta J, Lipschitz S, et al. Masitinib for mild-to-moderate Alzheimer's disease: results from a randomized, placebo-controlled, phase 3, clinical trial [published correction appears in Alzheimers Res Ther. 2023 Apr 22;15(1):85. doi: 10.1186/s13195-023-01230-9.]. Alzheimers Res Ther. 2023;15(1):39.
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5. Ettcheto M, Cano A, Sanchez-López E, et al. Masitinib for the treatment of Alzheimer's disease. Neurodegener Dis Manag. 2021;11(4):263-276. doi:10.2217/nmt-2021-0019

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.

Forward-looking Statements - AB Science

This press release contains forward-looking statements. These statements are not historical facts. These statements include projections and estimates as well as the assumptions on which they are based, statements based on projects, objectives, intentions and expectations regarding financial results, events, operations, future services, product development and their potential or future performance.

These forward-looking statements can often be identified by the words "expect", "anticipate", "believe", "intend", "estimate" or "plan" as well as other similar terms. While AB Science believes these forward-looking statements are reasonable, investors are cautioned that these forward-looking statements are subject to numerous risks and uncertainties that are difficult to predict and generally beyond the control of AB Science and which may imply that results and actual events significantly differ from those expressed, induced or anticipated in the forward-looking

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