PHASE 2B/3 STUDY EVALUATING MASITINIB IN ALZHEIMER'S DISEASE MET ITS PRIMARY ENDPOINT

MASITINIB DEMONSTRATED SIGNIFICANT EFFECT ON BOTH COGNITION, MEASURED WITH ADAS-COG, AND DAILY ACTIVITY, MEASURED WITH ADCS-ADL

AB SCIENCE WILL HOST A LIVE WEBCAST ON DECEMBER 17, 2020 - 11am-12am EST; 5pm-6pm CET WITH KEY OPINION LEADERS TO FURTHER DISCUSS THE RESULTS

Paris, December 16, 2020, 8am CET

AB Science SA (Euronext - FR0010557264 - AB) today announced that the Phase 2B/3 study (AB09004 - NCT01872598) evaluating oral masitinib in patients with mild and moderate Alzheimer's disease met its predefined primary endpoint.

Study AB09004 was an international, randomized, placebo-controlled, phase 2B/3 study evaluating different doses of masitinib as a treatment of patients with confirmed mild to moderate Alzheimer's disease. This study compared the efficacy and safety of masitinib relative to placebo after 24 weeks of treatment when administered as an add-on therapy to cholinesterase inhibitor (donepezil, rivastigmine or galantamine) and/or memantine. Two doses of masitinib were tested, masitinib 4.5 mg/kg/day and a titrated dose of masitinib from 4.5 to 6.0 mg/kg/day, with each dose having an independent control arm.

The study demonstrated that masitinib 4.5 mg/kg/day (n=182) generated a significant treatment effect compared with the control arm (n=176) on the primary endpoint of change from baseline in the Alzheimer's Disease Assessment Scale-Cognitive Subscale (ADAS-Cog), an instrument that measures the effect on cognition and memory (p=0.0003). The study also demonstrated that masitinib 4.5 mg/kg/day generated a significant change from baseline in Alzheimer's Disease Cooperative Study Activities of Daily Living (ADCS-ADL) score, an instrument that assesses self-care and activities of daily living (p= 0.0381).

There were significantly fewer patients reaching severe dementia stage (MMSE<10) with masitinib 4.5 mg/kg/day compared with placebo after 24 weeks of treatment (p-value= 0.0446).

The safety of masitinib 4.5 mg/kg/day was acceptable and consistent with the known tolerability profile for masitinib:

- 79.5% of patients had at least one adverse event in the masitinib arm versus 74.6% in the control arm
- 5.9% of patients had at least one serious adverse event (non-fatal) in the masitinib arm versus 2.9% in the control arm
- 18.9% of patients had at least one severe adverse event in the masitinib arm versus 16.8% in the control arm

The top-line results will be further discussed during a live webcast with Key Opinion Leaders to be held on Thursday December 17, 2020 from - 11am-12am EST.

A new patent was filed based on results from study AB09004. Said patent, if granted, would permit AB Science to retain exclusive rights on the use of masitinib in Alzheimer's disease until 2041.

Bruno Dubois (MD, PhD), Professor of Neurology at the Neurological Institute of the Salpétrière University Hospital at Paris in France and coordinating investigator of study AB09004 said, "*There is a vacuum of treatment options for patients with Alzheimer's disease and today very few attempts to address the population with confirmed mild or moderate dementia associated with Alzheimer's disease. These data are very encouraging and may provide new hope for patients with Alzheimer's disease. The fact that masitinib could significantly reduce the proportion of patients reaching the stage of severe dementia (MMSE<10) is particularly interesting because this stage of the disease represents a significant burden for the society*".

Philip Scheltens (MD, PhD), Professor of Cognitive Neurology and Director of the Alzheimer Center at the VU University Medical Center in Amsterdam said, "*Results from study AB09004 are refreshing as they provide a radically new approach for the treatment of Alzheimer's disease, and are extremely promising, in particular considering the robustness of the effect observed on cognitive function. I am eager to support AB Science's endeavor to address such a devastating disease.*"

Jeffrey L. Cummings, M.D., Director of the Chamber-Grundy Center for Transformative Neuroscience at UNLV in Las Vegas said "*The preliminary results from this study support efficacy on important outcomes assessing both cognition and function. The observed patient tolerability is encouraging. Masitinib's mechanism is novel in its targeting of the innate immune system via mast cells and microglia. A growing body of evidence suggests that microglia play a central role in Alzheimer's disease and other neurodegenerative disorders."*

Prof. Olivier Hermine (President of the Scientific Committee of AB Science and member of the Académie des Sciences in France) said, "*This positive result in Alzheimer's disease further validates the mechanism of action of masitinib in neurodegenerative diseases [1,2]. Indeed, this is the third evidence delivered by the masitinib in neurology. The first two pieces of evidence were the positive Phase 2B/3 studies with masitinib in amyotrophic lateral sclerosis (ALS) and in progressive forms of multiple sclerosis [3,4]. These three studies clearly demonstrate that targeting the innate immune system including macrophage/microglia and mast cells, through inhibition of tyrosine kinases as masitinib does, is a valid strategy to treat neurodegenerative disorders. This is a true innovation that justifies the long-term efforts from AB Science to develop masitinib in ALS, progressive forms of MS, and Alzheimer's disease."*

Alain Moussy, co-founder and CEO of AB Science said, "*Neurodegenerative diseases, taken together, represent a huge unmet medical need. We are determined after this third positive study, this time in Alzheimer's disease, to continue developing masitinib in consultation with health authorities up to registration, in amyotrophic lateral sclerosis, progressive forms of MS and Alzheimer's disease."*

AB Science plans to present detailed study results at an upcoming medical meeting.

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Webcast

Webcast date: Thursday, December 17, 2020. US: 11am-12am EST; Europe 5pm-6pm CET. Webcast Dial-In and connection details will be provided separately.

The following key opinion leaders will participate in the webcast:

Bruno Dubois
Bruno Dubois is currently Professor of Neurology at the Neurological Institute of the Salpétrière University Hospital at Paris, University Pierre et Marie Curie Paris VI. He is Director of the Behavioural Neurology Department and of the Dementia Research Center at the Hospital. He is also Director of the Research Unit Inserm U-610 of the ICM (Institut du Cerveau et de la Moelle Epinière) of the Hospital. He is coordinator of

the National Reference Center on Rare Dementias and of the National Reference Center for young-onset Alzheimer patients. He is President of the Scientific Committee of France-Alzheimer and of IFRAD (International Fund Raising for Alzheimer's disease), consultant for the Human Frontier Program and Expert of the French Agency of Drugs. He is a member of the European Alzheimer Disease Consortium (EADC). He has published on anatomical and biochemical studies on the central cholinergic systems in rodents and humans; on cognitive neuropharmacology; and on neuropsychology in patients with dementia, with special reference to memory and executive functions. He recently organized an Expert Consensus on the new criteria for Alzheimer's disease and a Task Force on the new criteria for Parkinson's disease dementia. He is principal or co-investigator of a number of research programs focusing on AD, prodromal AD and dementia in Parkinson's disease.

Philip Scheltens

Philip Scheltens, MD, PhD is Professor of Cognitive Neurology and Director of the Alzheimer Center at the VU University Medical Center in Amsterdam, as well as Honorary Professor of Neurology at University College London.

From 2011-2015, he was the scientific director of the Dutch Pearlstring Institute (PSI). In 2013, he was appointed vice-chair of the board of the Dutch "Deltaplan Dementie". Since 2015, he has been a member of the board of the Royal Academy of Sciences and Art. His main clinical and research interests are dementia in the broadest sense, from basic research to care and translational research. He is active in the field of biomarkers and clinical trials and has been the (inter) national PI for many studies, including Phase I–III multicentre clinical trials.

He is founder of, and has directed since 2000, the VUmc Alzheimer Center in The Netherlands, and during this period, he has produced over 50 PhD theses. He also founded the Alzheimer Research Center, a center dedicated to and specialised in Alzheimer clinical trials, where he is now a scientific adviser and member of the Board of Trustees.

Dr. Scheltens is an active member of several societies, including the Dutch Society for Neurology, the AAN, the Alzheimer Imaging Consortium, the ISTAART Consortium, and the ECNP. He has been instrumental in organising several national and international conferences, including the Imaging Symposium attached to AAIC. He is member of the management board of the dementia panel of the EAN.

He is co-editor-in-chief of Alzheimer's Research & Therapy and acts as an ad hoc reviewer of scientific articles for all of the major journals. He has authored >730 peer reviewed papers and >50 book chapters. His current Hirsch factor is 117 (Google Scholar).

Jeffrey L. Cummings

Jeffrey L. Cummings, M.D., is Director of the Chamber-Grundy Center for Transformative Neuroscience at UNLV in Las Vegas. Dr. Cummings is principal investigator/ director of the National Institutes of Health/National Institute of General Medical Sciences-funded Center for Neurodegeneration and Translational Neuroscience.

Dr. Cummings is a world-renowned Alzheimer's researcher and leader of clinical trials. He has been recognized for his research and leadership contributions in the field of Alzheimer's disease through the Henderson Award of the American Geriatrics Society (2006), the Ronald and Nancy Reagan Research Award of the National Alzheimer's Association (2008) and the Lifetime Achievement Award of the Society for Behavioral and Cognitive Neurology (2017). In 2010, he was honored by the American Association of Geriatric Psychiatry with their Distinguished Scientist Award. He was featured in Gentlemen's Quarterly (June 2009) as a "Rockstar of Science." Dr. Cummings' interests embrace clinical trials, developing new therapies for brain diseases and the interface of neuroscience and society.

Dr. Cummings was formerly professor of neurology and psychiatry at the University of California, Los Angeles (UCLA), director of the Mary S. Easton Center for Alzheimer's Disease Research at UCLA and director of the Deane F. Johnson Center for Neurotherapeutics at UCLA. He is past president of the Behavioral Neurology Society and of the American Neuropsychiatric Association. Dr. Cummings has authored or edited 39 books and published over 700 peer-reviewed papers.

Dr. Cummings completed his neurology residency and a fellowship in behavioral neurology at Boston University, Boston. His U.S. training was followed by a research fellowship in neuropathology and neuropsychiatry at the National Hospital for Nervous Diseases, Queen Square, London

Phase 2B/3 study design

Study AB09004 was an international, randomized, placebo-controlled, phase 2B/3 study evaluating masitinib as a treatment of patients with confirmed mild to moderate Alzheimer's disease.

The study enrolled patients having the following main inclusion criteria:

- Patient with dementia of Alzheimer's type, according to the Diagnostic and Statistical Manual of Mental Disorders criteria (DSM-IV)
- Patient with probable Alzheimer' disease according to the NINCDS-ADRDA criteria (National Institute of Neurological and Communicative Disorders and Stroke and the Alzheimer's Disease and Related Disorders Association)
- Patient with MMSE ≥ 12 and ≤ 25 at baseline
- Patient treated for a minimum of 6 months with a stable dose of cholinesterase inhibitors (donepezil, rivastigmine or galantamine) at baseline, and/or a stable dose of memantine for a minimum of 6 months at baseline, with no changes foreseen in therapy throughout the study.

This study compared the efficacy and safety of masitinib after 24 weeks of treatment when administered as an add-on therapy to cholinesterase inhibitor (donepezil, rivastigmine or galantamine) and/or memantine, to placebo as add-on to cholinesterase inhibitor and/or memantine.

Two doses of masitinib were tested, masitinib 4.5 mg/kg/day and a dose titration from masitinib 4.5 to 6.0 mg/kg/day, each dose having its own control arm.

The study was successful if its primary objective to test a significant improvement was reached at a 2.5% level of statistical significance on either ADAS-Cog or ADCS-ADL. That is to say that the Alpha spending was split between ADAS-COG (2.5%) and ADCS-ADL (2.5%), and that the study was successful if the treatment effect was established in at least one of the two primary endpoints at 2.5% level of statistical significance. Type I error was controlled at interim by the Haybittle-Peto alpha spending method. If at interim p-value was superior to 0.001, then the final analysis and efficacy criteria at final analysis was to be tested at 2.499% level for each of the primary endpoints. For the primary analysis, as per guideline, missing values were imputed not based on Last Observation Carried Forward (LOCF) method but by using imputation model based on the patient's previous non-missing score and data from other similar patients (same cluster) that continued treatment. The Jump to Reference approach, which is the most conservation approach, was used as a sensitivity analysis. This methodology imputes the Placebo estimates for all patients who prematurely discontinue due to lack of efficacy and toxicity (related TEAE) in the treatment arm.

The study enrolled 718 patients.

Previous establishment proof of concept

As a reminder, proof of concept for the evaluation of masitinib in Alzheimer's disease was established through a 35-patient, double-blind, placebo-controlled phase 2 study. In this study, the rate of clinically relevant cognitive decline, according to the primary endpoint, ADAS-Cog response (increase > 4 points), was significantly lower with masitinib treatment compared with placebo after 12 and 24 weeks (6% versus 50% for both; p=0.040 and p=0.046, respectively). Moreover, while the placebo treatment-arm demonstrated worsening mean ADAS-Cog, ADCS-ADL and MMSE scores, the masitinib treatment-arm reported improvements with statistical significance between treatment-arms at weeks 12 and/or 24 (respectively, p=0.016 and 0.030; p=0.035 and 0.128; and p=0.047 and 0.031). Adverse events occurred more frequently with masitinib treatment (65% versus 38% of patients); however, the majority of events were mild or moderate and transient. The phase 2 results were published in Alzheimers Res Ther. 2011 Apr 19;3(2):16. doi: 10.1186/alzrt75.

Scientific rationale

The potential therapeutic benefit of masitinib in Alzheimer's disease is linked to two possible mechanisms of action: the role of mast cells in neuroinflammation and regulation of the blood-brain-barrier (BBB)

permeability; and the inhibition of the protein kinase Fyn, which is involved in amyloid-beta signaling and tau phosphorylation.

Neuroinflammation is thought to be a major contributor in the pathogenesis of Alzheimer's disease[1,2,3]. Mast cells release large amounts of proinflammatory mediators and therefore play an important role in sustaining the inflammatory network of the central nervous system. Furthermore; mast cells are found on both sides of the BBB and also have the ability to rapidly cross the BBB, thereby increasing their numbers in response to physiological stimuli. Given that the neural pool of mast cells is influenced by their ability to rapidly cross the BBB, inhibition of mast cells peripheral to the BBB could impact upon neurodegenerative disease outcome. Therefore, masitinib could be an effective drug in Alzheimer's disease because it blocks mast cells through the inhibition of the tyrosine kinases c-Kit and Lyn.

In addition to blocking mast cell activity, masitinib may exert an effect through its inhibition of the tyrosine kinase Fyn[4,5,6]. Alzheimer's disease is associated with the pathological aggregation of amyloid-beta (A-beta) plaques and tau-positive neurofibrillary tangles. Several lines of evidence implicate Fyn in the pathogenesis of Alzheimer's disease through its dual role in A-beta signaling and tau phosphorylation. Masitinib, by inhibiting Fyn, could possibly disrupt the A-beta signaling cascade and modulate the phosphorylation of tau protein, thus and preventing neurofibrillary tangles.

Targeted population

The meta-analysis of epidemiologic studies indicates that between 5 and 10 million people suffer from Alzheimer’s disease in the USA and Europe. Alzheimer’s disease is the most common type of dementia among western countries, corresponding to about 60% of cases. Alzheimer’s disease is already the sixth leading cause of all deaths in USA and the fifth leading cause among Americans over 65 years of age.[7,8,9] Worldwide, it is thought that there are more than 15 million people affected by Alzheimer’s disease.[8]

Currently, there are only five products approved for the treatment of Alzheimer’s disease, four of which belong to the pharmacological class of anticholinesterases, the fifth being an NMDA inhibitor. Therefore, this remains an area of significant unmet medical need. Masitinib may be unique by being both a symptomatic and a disease modifier treatment.

References

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About masitinib
Masitinib is a new orally administered tyrosine kinase inhibitor that targets mast cells and macrophages, important cells for immunity, through inhibiting a limited number of kinases. Based on its unique mechanism of action, masitinib can be developed in a large number of conditions in oncology, in inflammatory diseases, and in certain diseases of the central nervous system. In oncology due to its immunotherapy effect, masitinib can have an effect on survival, alone or in combination with chemotherapy. Through its activity on mast cells and microglia and consequently the inhibition of the activation of the inflammatory process, masitinib can have an effect on the symptoms associated with some inflammatory and central nervous system diseases and the degeneration of these diseases.

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, and inflammatory 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 information and statements. These risks and uncertainties include the uncertainties related to product development of the Company which may not be successful or to the marketing authorizations granted by competent authorities or, more generally, any factors that may affect marketing capacity of the products developed by AB Science, as well as those developed or identified in the public documents filed by AB Science with the Autorité des Marchés Financiers (AMF), including those listed in the Chapter 4 "Risk Factors" of AB Science reference document filed with the AMF on November 22, 2016, under the number R. 16-078. AB Science disclaims any obligation or undertaking to update the forward-looking information and statements, subject to the applicable regulations, in particular articles 223-1 et seq. of the AMF General Regulations.

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