AB SCIENCE COMMUNICATES RESULTS FROM PHASE 2B/3 STUDY EVALUATING MASITINIB IN ALZHEIMER'S DISEASE

Paris, December 18, 2020, 8.30am CET

AB Science SA (NYSE Euronext – FR0010557264 – AB) today communicates the results from phase 2B/3 study evaluating masitinib in Alzheimer's disease, together with details on the mode of action of masitinib in Alzheimer's disease.

The presentation is available on the company's website and is available here.

Highlights of this presentation are:

The mode of action of masitinib in Alzheimer's disease (AD) is based on four targets, which may have a synergistic effect:

- **Modulation of microglia**: Microglia are involved in neuroinflammartoy processes associated with AD and masitinib modulates microglia activity through inhibition of the CSFR-1 kinase.
- **Protection of synapses**: Synapses are altered in AD and masitinib has been shown to promote recovery of synaptic markers in a mouse model of AD.
- **Inhibition of the tau protein**: The tau protein aggregates in the physiopathology of AD. Masitinib inhibits the FYN kinase, a kinase that mediates tau phosphorylation. Masitinib has also been shown to prevent the accumulation of amyloid fibrils in the hippocampus in a mouse model of AD.
- **Control of mast cell activity**: Mice depleted of mast cells (MCs) do not develop symptoms of AD. Masitinib blocks MC activity through inhibition of the c-Kit, LYN, and FYN kinases. In addition, beta-amyloid plaques activate MCs, and masitinib treatment of transgenic AD mice has been shown to protect against cognition impairment.

The following preclinical data are presented. Experiments in a transgenic mouse model of AD that were carried out by the ICM Brain Institute in Paris, demonstrated that masitinib could:

- Completely restore cognitive impairment in the Morris Water Maze experiment.
- Completely restore the ability to perform navigation strategy in the Morris Water Maze experiment.
- Exerts a neuroprotective effect against synaptic loss through inhibition of MCs.

The masitinib clinical development program in Alzheimer's disease is comprised of one proof of concept study (AB04024) [Piette, 2011] and a phase 2B/3 study (AB09004).

Masitinib is positioned in patients with mild and moderate dementia, with MMSE Score (Mini Mental State Examination) ranging from 12 to 25, which is a different positioning from other compounds.

There are currently four drugs used in the treatment of mild and moderate AD (donepezil, rivastigmine, galantamine and memantine) that were approved about 20 years ago. Masitinib was evaluated in add-on to this standard of care.

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.

Study AB09004 was comprised of two independent sub-studies testing two distinct dosing regimens; masitinib 4.5 mg/kg/day versus its own placebo control (n=358, randomization 1:1), and masitinib 6.0 mg/kg/day titrated dose versus its own placebo control (n=277, randomization 2:1).

The study was to be considered successful if a significant improvement was reached on either ADAS-Cog or ADCS-ADL at a 2.5% level of statistical significance.

Baseline characteristics were balanced. Study AB9004 results were the following:

- The study met its primary analysis, demonstrating a statistically significant reduction in cognitive impairment based on ADAS-Cog (p=0.0003). Treatment-effect with respect to the control arm (i.e., between group difference of least squares mean (LS Mean) and associated standard error (SE) in ADAS-Cog was -2.15 (0.59).
- ADAS-Cog sensitivity analysis based on the jump to reference imputation method remained positive (p=0.0016), demonstrating a robust treatment statistical effect.
- The study demonstrated a statistically significant improvement on daily activity based on ADCS-ADL (p=0.0381). The difference of LS Mean (SE) in ADCS-ADL was 1.82 (0.87).
- ADCS-ADL sensitivity analysis based on the jump to reference imputation method showed a numerical advantage close to statistical significance (p=0.051) in favor of masitinib.
- The study demonstrated a 71% improvement on Clinician's Interview-Based Impression of Change (CIBIC) for masitinib as compared with placebo; a result that was statistically significant (p=0.040).
- The study showed a numerical advantage (not statistically significant) in favor of masitinib on the secondary enpoints of MMSE, CDR, and NPI.
- No further significant treatment-effect was observed either on ADAS-Cog or ADCS-ADL for the high-dose masitinib sub-study (titration up to 6.0 mg/kg/day). This result possibly originated from an improvement under placebo, conceivably influenced by a low number of patients enrolled in the placebo titration arm (n<100). There was no higher efficacy with the masitinib 6.0 mg/kg/day titrated dose versus the misitinib 4.5 mg/kg/day dose. As a result, it could be concluded that the effective dose in Alzheimer's disease for masitinib is 4.5 mg/kg/day.
- As a post-hoc sensitivity analysis, in order to assess the impact of the divergent placebo effect, masitinib 4.5 mg/kg/day was compared with the pooled placebo arms and ADAS-Cog analysis remained significant (p=0.0004).
- There were significantly (log-rank p-value 0.0403) fewer patients reaching severe dementia stage (MMSE<10) and a significant decrease (Hazard ratio 1.19, p= 0.0276) in time to severe dementia with masitinib 4.5 mg/kg/day compared with the pooled placebo arms.
- The safety of masitinib was consistent with its known tolerability profile.

A new patent was filed based on results from study AB09004, which 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 the study said: "*Study AB09004 was a well-designed phase 2b/3 as it compared masitinib on top of standard of care treatment versus the standard of care. These data are very encouraging and may provide new hope for patients with Alzheimer's disease".*

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 bring a novel mechanism of action, which is very interesting considering the need for effective treatment in AD. The positive results from this study provide a robust basis to initiate a phase 3 confirmatory study*".

Jeffrey L. Cummings (M.D), Director of the Chamber-Grundy Center for Transformative Neuroscience at UNLV in Las Vegas said: "*The data from this study are promising and support the use of the dose 4.5 mg /kg/day of masitinib for the future confirmatory study. Based on the mechanism of action of masitinib*

targeting the innate immune system via mast cells and microglia, it should be possible to investigate the correlations between clinical endpoints and biomarkers of neuro-inflammation and neurodegeneration in the next study".

KOL Biographies

The following key opinion leaders participated 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.

Olivier Hermine, MD, PhD

Olivier Hermine, MD, PhD is Professor of Hematology at Paris V-René Descartes University, Chief of adults Hematology staff at Hospital Necker (Paris), member of the French Académie des Sciences and author of over 700 international publications. Olivier Hermine is also co-founder of AB Science and Head of its scientific committee.

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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