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Publication in the Journal of Neuroinflammation of preclinical data showing neuroprotective effect of masitinib in amyotrophic lateral sclerosis, through targeting of microglial cells

AB Science SA (NYSE Euronext – FR0010557264 – AB), a pharmaceutical company specialized in the research, development and marketing of protein kinase inhibitors (PKIs), announces the publication of preclinical study results with masitinib in amyotrophic lateral sclerosis (ALS). Entitled, *‘Post-paralysis tyrosine kinase inhibition with masitinib abrogates neuroinflammation and slows disease progression in inherited amyotrophic lateral sclerosis’* this article and its accompanying Online Supplementary Material are freely accessible online from the peer-reviewed scientific review *Journal of Neuroinflammation*: DOI:10.1186/s12974-016-0620-9; <https://jneuroinflammation.biomedcentral.com/articles>.

‘These findings demonstrate an unprecedented protective effect for masitinib in ALS rat models with respect to other studies found in the scientific literature’ said Professor Luis Barbeito (Head of the Neurodegeneration Laboratory, Institut Pasteur in Montevideo, Uruguay). *‘In particular, masitinib was protective when administered after onset of overt paralysis, a model that closely simulates the clinical condition of ALS patients and therefore better represents their therapeutic needs’*.

This publication is peer-reviewed and therefore validates the plausibility of masitinib’s primary mechanism of action in ALS targeting neurotoxic aberrant microglial cells via CSF1R inhibition to slow down neurodegeneration.

This publication follows the positive interim results of a phase 2/3 study comparing the efficacy and safety of masitinib in combination with riluzole versus placebo in combination with riluzole in the treatment of patients suffering from amyotrophic lateral sclerosis (ALS).

Olivier Hermine, President of the Scientific Committee of AB Science said *“The positioning of masitinib in ALS is based on a novel mechanism of action inhibiting microglial cells without depleting them. It was the first time that a drug was tested in clinical trial aimed at this novel target, and this may explain why the interim analysis was positive whereas previous studies failed in this indication”*.

This publication strengthens the registration dossier of masitinib in ALS that AB Science intends to file in September 2016, because establishing the medical plausibility of a treatment is one of the questions from health authorities when assessing a marketing authorization.

About microglial cells and masitinib non-clinical data in ALS

It is now well-established in the scientific literature that proliferation and accumulation of microglial cells (microgliosis), in particular the emergence of aberrant glial cells, is a major neuropathological feature for ALS animal models. This disease mechanism is regulated by the CSF1/CSF1R signaling pathway.

Masitinib is a potent inhibitor of CSF1R-dependent cell proliferation (IC₅₀ 90 nM). Through targeting the CSF1/CSF1R signaling pathway, masitinib is able to inhibit glial cell proliferation, including aberrant microglial cells that are strongly associated with motor neuron degeneration, and also retard microglia cell migration. Notably, masitinib treatment initiated 7 days after paralysis onset prolonged post-paralysis survival by 40%, with respect to the control group.

Key findings from this series of preclinical studies are summarized below.

- Masitinib significantly prolonged survival in post-paralytic SOD1^{G93A} rats

- Masitinib prevented microglia proliferation by inhibiting CSF1R kinase activity at nanomolar concentrations
- Masitinib prevented microglia migration
- Masitinib prevented microglia transformation into neurotoxic aberrant glial cells
- Masitinib reduced the number of aberrant glial cells in the degenerating spinal cord
- Masitinib inhibited proliferation and accumulation of microglial cells along the degenerating spinal cord
- Masitinib inhibited microglia proinflammatory phenotype

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 in cancers, inflammatory diseases, and central nervous system diseases, both in humans and animal health.

AB Science has developed a proprietary portfolio of molecules and the Company's lead compound, masitinib, has already been registered for veterinary medicine in Europe and in the USA. The company is currently pursuing twelve phase 3 studies in human medicine in first-line and second-line GIST, metastatic melanoma expressing JM mutation of c-Kit, multiple myeloma, metastatic colorectal cancer, metastatic prostate cancer, pancreatic cancer, T-cell lymphoma, severe asthma uncontrolled by oral corticosteroid, Alzheimer's disease, progressive forms of multiple sclerosis, and amyotrophic lateral sclerosis. The company is headquartered in Paris, France, and listed on Euronext Paris (ticker: AB).

Further information is available on AB Science website: <http://www.ab-science.com>

This document contains prospective information. No guarantee can be given as for the realization of these forecasts, which are subject to those risks described in documents deposited by the Company to the Authority of the financial markets, including trends of the economic conjuncture, the financial markets and the markets on which AB Science is present.

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