



**Preclinical data showing protective effect of masitinib on the peripheral nervous system in amyotrophic lateral sclerosis (ALS) published in the *Journal of Clinical Investigation Insight***

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, *'Evidence for mast cells contributing to neuromuscular pathology in an inherited model of ALS'* this article and its accompanying Online Supplementary Material are freely accessible online from the peer-reviewed scientific journal *JCI-Insight* <https://insight.jci.org/articles/view/95934>.

This research links increased mast cell activity to the degeneration of neuromuscular junctions and paralysis progression in a relevant model of ALS. Such findings represent a novel pathogenic mechanism in ALS that is shown to be therapeutically targeted by masitinib. Masitinib therefore appears capable of exerting a protective effect on the peripheral nervous system via mast cell inhibition, in addition to its main mechanism of action on aberrant microglia of the central nervous system.

This article provides a detailed description and interpretation of these findings, which have been validated by the rigorous peer-review process necessary for acceptance. Preliminary results from this research have been previously reported at the ENCALs 2017 meeting and will be the topic of an upcoming presentation at the International Symposium on ALS/MND (Boston, USA) in December.

*"These findings represent a significant mechanism of action for masitinib, which may have clinical therapeutic relevance for ALS",* said Professor Luis Barbeito, Head of the Neurodegeneration Laboratory (Institut Pasteur in Montevideo, Uruguay) and senior author of the article. *"Taken together with our previously published preclinical finding<sup>2</sup>, we now have evidence that masitinib generates a protective effect via two independent mechanisms of action involving immune cells interacting with motor neurons. One predominantly impacts on the central nervous system, via targeting of deleterious microglial cells in the brain, while the other impacts on the peripheral nervous system, via prevention of neuromuscular junction denervation."*

➤ **Key findings from the new *Journal of Clinical Investigation Insight* article<sup>1</sup> showing that masitinib exerts a protective effect on the peripheral nervous system in ALS**

- It has been demonstrated that disease progression in an animal model of ALS is accompanied by massive infiltration and accumulation of mast cells around degenerating motor axons and neuromuscular junctions.
- In particular, the increased number and degranulation of mast cells correlated with paralysis progression, suggesting mast cells may be deleterious for the maintenance of functional neuromuscular junctions.
- Because neuromuscular junctions serve as a critical link between skeletal muscles and the nervous system, this finding represents a novel pathogenic mechanism in ALS that can be therapeutically targeted by masitinib.
- Masitinib-induced mast cell reduction significantly reduced the rate of neuromuscular junction denervation and motor deficits.
- Masitinib also prevented morphological changes in Schwann cells and capillary networks that are typically observed in advanced paralysis.

➤ **Reminder of key findings from the previously published Journal of Neuroinflammation article<sup>2</sup> showing that masitinib exerts a protective effect on the central nervous system in ALS**

Survival data showed that:

- Masitinib treatment significantly prolonged survival in post-paralytic SOD1<sup>G93A</sup> rats

Immunohistochemistry data showed that masitinib treatment:

- Prevented microglia proliferation by inhibiting CSF1R kinase activity at nanomolar concentrations
- Prevented microglia migration
- Prevented microglia transformation into neurotoxic aberrant glial cells
- Reduced the number of aberrant glial cells in the degenerating spinal cord
- Improved microgliosis and motor neuron pathology (microgliosis is defined as the presence of microglia in nervous tissue secondary to injury)
- Inhibited microgliosis along the degenerating spinal cord
- Inhibited microglia proinflammatory phenotype

➤ **Reminder of the key findings from the clinical phase 3 study**

Masitinib orally administered at 4.5 mg/kg/day as an add-on to riluzole demonstrated benefit in ALS patients with a baseline ALSFRS-R progression rate of <1.1 points/month.

- Significant (p<0.05) 27% slowing of ALSFRS-R deterioration (primary endpoint)
- Significant 29% slowing of deterioration in quality-of-life (ALSAQ-40)
- Significant 22% slowing of deterioration in respiratory function (FVC)
- Significant 25% delay in disease progression (survival-to-event analysis)
- Safety was acceptable

[1] Trias E, et al. Evidence for mast cells contributing to neuromuscular pathology in an inherited model of ALS. JCI Insight. 2017;2(20):e95934. <https://doi.org/10.1172/jci.insight.95934>.

[2] Trias E, et al. Post-paralysis tyrosine kinase inhibition with masitinib abrogates neuroinflammation and slows disease progression in inherited amyotrophic lateral sclerosis. J Neuroinflammation. 2016;13(1):177.

**About Amyotrophic Lateral Sclerosis**

Amyotrophic lateral sclerosis is a rare degenerative disorder that results in progressive wasting and paralysis of voluntary muscles. There are approximately 50,000 people with ALS in the European Union and in the US, with more than 16,000 new cases diagnosed each year in Europe and in the US. Almost 80% of ALS patients die within 5 years and 90% die within 10 years.

**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 and is developed in twelve phase 3 indications in human medicine in metastatic prostate cancer, metastatic pancreatic cancer, relapsing metastatic colorectal cancer, relapsing metastatic ovarian cancer, GIST, metastatic melanoma expressing JM mutation of c-Kit, relapsing T-cell lymphoma, mastocytosis, severe asthma, amyotrophic lateral sclerosis, Alzheimer's disease and progressive forms of multiple sclerosis. 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](http://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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