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## **Publication of the positive phase 2/3 clinical trial with masitinib in ALS in the journal Amyotrophic Lateral Sclerosis and Frontotemporal Degeneration**

**AB Science SA** (NYSE Euronext - FR0010557264 - AB), announces today that full, peer-reviewed results from its phase 2/3 (AB10015) study of masitinib in amyotrophic lateral sclerosis (ALS) have been published in the journal Amyotrophic Lateral Sclerosis and Frontotemporal Degeneration (ALSFD).

Entitled, *'Masitinib as an add-on therapy to riluzole in patients with amyotrophic lateral sclerosis: a randomized clinical trial'*<sup>1</sup>, this article and its accompanying online supplemental material are freely accessible online from the journal website: <https://doi.org/10.1080/21678421.2019.1632346>.

Professor Mamede de Carvalho, Head of the Neuromuscular Unit and ALS Clinic of University Hospital Lisboa-Norte, Portugal commented: *"These results represent the most positive impact of a study in ALS since the riluzole studies, and I am happy to have contributed to this trial. Publication in a prominent peer-reviewed journal indicates that the scientific community is deeply interested in masitinib as a treatment of ALS. Moreover, study AB10015 represents the first positive phase 3 trial of a tyrosine kinase inhibitor in ALS, with publication of this article being a cornerstone in the development program of masitinib. These results along with previously published preclinical articles, which explain the mechanism of action of masitinib in ALS<sup>2,3,4</sup>, clearly demonstrate that the masitinib program is highly credible. Indeed, this drug had a significant positive impact in a typical population of ALS patients, with a parallel impact on functional and respiratory decay, which supports an unquestionable positive effect on disease progression. Masitinib is a promising therapeutic option in this dreadful disease with continued unmet medical need"*.

*"Like my colleagues, I am proud to have participated to the masitinib clinical study in ALS, the first with a tyrosine kinase inhibitor, the first with a drug that targets both microglia and mast cells. I am convinced that this therapeutic approach is a right one in this disease. Neurologists treating ALS are highly interested by masitinib. This publication represents a significant scientific milestone in the search for a new treatment in ALS"* said Dr. Jesús S. Mora M.D., Director of the ALS Unit at Hospital San Rafael, Madrid, and senior author of this article.

Study AB10015 was a phase 2/3, double-blind, randomized, placebo-controlled trial of masitinib as an add-on to riluzole over 48 weeks. Primary analysis was absolute change of ALSFRS-R from baseline to week 48 in patients receiving masitinib at 4.5 mg/kg/day and with a baseline ALSFRS-R progression rate of less than 1.1 points per month.

Study AB10015 reached its primary endpoint and showed that masitinib at 4.5 mg/kg/day in combination with riluzole was able to significantly ( $p$ -value < 0.05) slow ALSFRS-R decline by 27% as compared with the active riluzole control at week 48.

Several predefined sensitivity analyses (censoring on reason for discontinuation) were performed to test robustness of the primary analysis result, and all were statistically significant. Additional sensitivity analyses based on the EMA recommended multiple imputation technique, which consists to impute a value at week 48 for patients who discontinued before week 48, and based on the highly conservative jump-to-reference technique, which consists to impute the placebo effect at week 48 for masitinib treated patients who discontinued before week 48, were all significant and convergent with the positive primary analysis outcome.

The population of the primary analysis was referred to as 'Normal Progressors' (defined as ALS patients who had a baseline ALSFRS-R progression rate of less than 1.1 points per month), and encompassed around 85%

of all patients suffering from ALS. Study AB10015 had broad inclusion criteria. Patients with disease duration up to 36 months or forced vital capacity (FVC) of at least 60% could be enrolled. There was also no restriction on the functional score (ALSFERS-R) at baseline, meaning that patients who had already lost certain physical functioning or with very severely affected physical function (i.e. respectively, scores of 0 or 1 at inclusion on any of the individual component subscores of ALSFRS-R) could be included.

The key secondary endpoint, PFS (a time-to-event analysis, measuring the earliest event between death and functional decline of at least 9 points in ALSFRS-R)<sup>5</sup>, was also statistically significant ( $p < 0.05$ ), with a clinically meaningful 25% delay in progression (median PFS of 20.0 months for masitinib as compared to 16.0 months for control). This endpoint is of particular importance to account for death. PFS is an endpoint that is recognized by the EMA guideline to support registration in ALS<sup>6</sup>.

Other secondary endpoints were also significant ( $p < 0.05$ ), with a 29% slowing of deterioration in quality-of-life (ALSAQ-40) and a 22% slowing of deterioration in respiratory function (FVC).

Safety was acceptable and consistent with masitinib's known risk profile.

*"Results of the phase 2/3 study on the efficacy and safety of masitinib in ALS have been published. This trial, which enrolled around 400 patients, showed that the dosage of 4.5 mg/kg/day decreased the slope of progression of the ALSFRS-R by 27% after 48 weeks of treatment. These promising results generate hope in the scientific community to have a new treatment in this fatal disease. A confirmatory study will follow with participation of the key reference centers worldwide that should confirm this very encouraging data"* commented Professor Philippe Corcia, Neurology Department, University Hospital Center of Tours, France.

#### ➤ **About amyotrophic lateral sclerosis**

Amyotrophic lateral sclerosis (ALS) is a fatal motor neuron disorder that is characterized by progressive loss of the upper and lower motor neurons at the spinal or bulbar level. The disease belongs to a group of disorders known as motor neuron diseases, which are characterized by the gradual degeneration and death of motor neurons. In ALS, both the upper motor neurons and the lower motor neurons degenerate or die, and stop sending messages to muscles. Unable to function, the muscles gradually weaken, waste away (atrophy), and have very fine twitches (called fasciculations). Eventually, the ability of the brain to start and control voluntary movement is lost.

The prevalence of ALS in western countries is fairly uniform at 6 per 100,000 persons, corresponding to around 30,000 cases in Europe and 20,000 in the USA.

The first drug treatment for ALS, riluzole (Rilutek), was approved in 1995. In Europe, there has been no new treatment approved since riluzole.

#### **References**

[1] Mora JS, Genge A, Chio A, et al. Masitinib as an Add-on Therapy to Riluzole in Patients with Amyotrophic Lateral Sclerosis: A Randomised Clinical Trial. *Amyotrophic Lateral Sclerosis and Frontotemporal Degeneration*. Epub 2019. <https://doi.org/10.1080/21678421.2019.1632346>.

[2] Trias E, et al. Mast cells and neutrophils mediate peripheral motor pathway degeneration in ALS. *JCI Insight*. 2018;3(19):e123249.

[3] Trias E, et al. Evidence for mast cells contributing to neuromuscular pathology in an inherited model of ALS. *JCI Insight*. 2017;2(20):e95934.

[4] 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.

[5] Gordon PH, et al. Outcome measures for early phase clinical trials. Amyotrophic Lateral Sclerosis, 2007, 8:5, 270-273, DOI: 10.1080/17482960701547958

[6] Guideline on clinical investigation of medicinal products for the treatment of amyotrophic lateral sclerosis (ALS). EMA/531686/2015, Corr.1

#### **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](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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