PRESS RELEASE

AB SCIENCE HAS RECEIVED APPROVAL FROM SEVERAL EUROPEAN COUNTRIES TO INITIATE THE CONFIRMATORY PHASE 3 STUDY OF MASITINIB IN AMYOTROPHIC LATERAL SCLEROSIS

THIS APPROVAL FOLLOWS PROTOCOL VALIDATION BY THE EMA AND FDA AUTHORIZATION

Paris, July 24, 2025, 8am CET

AB Science SA (Euronext - FR0010557264 - AB) today announced that the confirmatory Phase 3 study with masitinib in amyotrophic lateral sclerosis (ALS), study AB23005, has been authorized by the first set of European countries (Spain, Greece, Slovenia) in Step 2 of *the Clinical Trials Information System* (CTIS) procedure. This authorization follows EMA's validation of the harmonized protocol, approved at the end of Step 1 of the CTIS procedure, and followed the authorization from the FDA. Consequently, AB Science can now initiate this registration study in Europe and the United States.

Professor Albert Ludolph, MD, PhD (University of Ulm, Germany), principal investigator of the study, said: "*Masitinib ALS study AB23005 has great potential because it's design is based on strong clinical and preclinical data. That is to say, results from the first 48-week Phase 2B/3 study, AB10015, which generated a strong hypothesis with significant survival of several months in the patient population being targeted in this confirmatory study, and also numerous preclinical studies that provide compelling insight into masitinib's mechanism of action in ALS and its effect on biomarkers such as neurofilaments (NfL) by targeting mast cells and microglia.*"

- **Alignment with the FDA and EMA on the Phase 3 design and, in particular, the study population focused on patients who respond best to masitinib.**

Study AB23005 is a prospective, multicenter, randomized, double-blind, placebo-controlled, two-arm study in patients with amyotrophic lateral sclerosis (ALS), to confirm the efficacy and safety of masitinib (at a dose of 4.5 mg/kg/day in combination with riluzole) as compared against riluzole in combination with placebo after 48 weeks of treatment.

The study will include 408 patients (randomized 1:1) with ALS, with normal disease progression (i.e., functional decline of less than 1.1 points per month) and no total loss of function (i.e., a score of at least 1 on each of the 12 items of the ALSFRS-R score). US patients receiving edaravone will also be eligible to participate in the study, with the use of this drug being a stratification factor.

This design has been validated in discussions with European health authorities, particularly with regard to the criteria for the optimal population selected for the confirmatory study:

- Patients without rapid progression: Experts of the EMA's Scientific Advisory Group on Neurology (SAG-N) considered the categorization of the study population with normal progressors, defined as an average rate of change in the ALSFRS-R of less than 1.1 points per month, as clinically relevant and consistent with the expected progression of the disease, and therefore acceptable when predefined, which is the case for this study.
- Patients without complete loss of function: The SAG-N experts considered that the ALSFRS-R scale is widely used in clinical practice and that administration criteria are available for healthcare

professionals. Therefore, the subgroup of patients with very severe ALS (who have a score of zero on at least one of the 12 individual items of the ALSFRS-R) can be easily identified in clinical practice.

In this subgroup, defined as patients before complete loss of function and with normal disease progression, which corresponds to the optimal population of best responders to masitinib that is targeted in study AB23005, the AB10015 study generated extremely robust results, with a median survival increase of +12 months.

This optimal population represents approximately 75% of the total patient population.

Masitinib 4.5 mg/kg/day vs placebo		AB10015 Primary Analysis	**Subgroup Analysis of Patients Meeting the Criteria for Study AB23005**
Main EMA criterion ΔALSFRS-R *	Difference in means	2.6	3.1
	p-value	0.0462	0.0308
FDA primary endpoint CAFS	Relative benefit	+ 14.8	20.
	p-value	0.0776	0.0290
Quality of Life (ALSAQ-40*)	Difference in means	-6.04	-6.22
	p-value	0.030	0.044
Respiratory function (FVC *)	Difference in means	5.8	7.5
	p value	0.0931	0.038
Median PFS	Gain	+ 4 months	+ 9 months
	Median [95% CI]	20 vs 16	25 vs 16
	p-value (log rank)	0.015	0.0057
Median survival (SG)	Gain	+ 6 months	+ 12 months
	Median [95% CI]	46 vs 40	53 vs 41
	p-value (log rank)	0.076	0.019

* Analysis CIR: Copy Increment in Reference; FVC: Forced Vital Capacity; PFS: Progression-Free Survival; OS: Overall Survival

- **Optimization of statistical sample size to maximize chances of success**

The optimal population included approximately 90 patients per treatment group in the AB10015 study. The effect of masitinib was statistically significant (p=0.0290) on the CAFS endpoint, which is the endpoint recognized by the FDA.

The AB23005 study will enroll approximately 200 patients per treatment group, more than double the number in the AB10015 study, in order to achieve high statistical power for this test and maximize the chances of statistical success.

- **Demonstrated mechanism of action targeting mast cells and microglia**

Masitinib, thanks to its well-demonstrated mechanism of action, particularly its immunomodulatory properties targeting mast cells and microglia, preserves neuromuscular function.

- The immunomodulatory properties of masitinib in ALS have been well demonstrated in a preclinical setting using a relevant model that replicates the complexity of a multicomponent immune response with concomitant evidence of neurodegeneration [1-4].
- The mechanism of action of masitinib in ALS has been confirmed by independent research. Harrison and colleagues showed that treatment of SOD1G93A mice with masitinib significantly reduced macrophage infiltration, prevented the loss of terminal Schwann cells and , and improved reinnervation of partially denervated plantar muscles [5].

- Recent pharmacological data have shown that mast cells infiltrate the degenerating spinal cord in both mouse models of ALS and in patients with ALS [6]. The results indicate a protective effect of masitinib.
- Masitinib has demonstrated its ability to reduce blood levels of neurofilament light (NfL) in a model of neurodegenerative disease (EAE model) [7].
- Masitinib has demonstrated its ability to restore motor performance in zebrafish expressing the TDP-43 mutant.

Overall, these preclinical results establish the biological plausibility of masitinib for use in ALS and support the hypothesis that masitinib may offer clinical benefit if administered early in the disease course (i.e., before the point of permanent loss of function).

- **Intellectual property protection until 2037 or even 2042 and Orphan Drug Designation**

Based on the results of the AB10015 study, AB Science has filed a patent application for methods of treating ALS (i.e., a secondary medical use patent) with its lead molecule, masitinib, and this patent has been granted in all jurisdictions where it has been filed.

This patent provides strong protection for masitinib in the treatment of ALS until 2037 and in all geographical areas where masitinib could be marketed, including Europe (patent EP 3240538), the United States (US 10092564), Canada (CA 3018635), China (ZL201780019760. 9), South Korea (KR 10-2293847), Japan (JP 7250312B2), Singapore (SG 11201808106Y), Hong Kong (HK 1261581), Israel (IL 261856), Australia (AU M53001274), Eurasia (EA 201800499), Mexico (MX 390495), New Zealand (NZ 745778) and South Africa (ZA 2018/05810).

An extension of this protection for 5 years is possible in certain countries.

In addition, masitinib has been designated as an orphan drug for ALS by both the European Medicines Agency (EMA) and the US Food and Drug Administration (FDA). This orphan drug designation confers 10 and 7 years of marketing exclusivity in Europe and the United States, respectively, from the date of product registration. Such status may also be sought in Japan. If granted, the period of commercial exclusivity is extended to 10 years (compared with 4 to 6 years for conventional drugs).

References:

[1] Trias E, Kovacs M, King PH, et al. Glia. 2020;68(6):1165-1181.
[2] Trias E, King PH, Si Y, et al. JCI Insight. 2018;3(19):e123249.
[3] Trias E, Ibarburu S, Barreto-Núñez R, et al. JCI Insight. 2017;2(20):e95934.
[4] Trias E, Ibarburu S, Barreto-Núñez R, et al. J Neuroinflammation. 2016;13(1):177.
[5] Harrison JM, Rafuse VF. Neurobiol Dis. 2020;145:105052.
[6] Kovacs M, Alamón C, Maciel C, et al. Acta Neuropathol Commun. 2021;9(1):136.
[7] Hermine O, Gros L, Tran T-A, et al. (2025) PLoS ONE 20(4):e0322199.

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, inflammatory diseases and viral 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 published by AB Science. 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.

For additional information, please contact:

AB Science
Financial Communication & Media Relations
investors@ab-science.com