



*Paris, May 12 2017, 3am*

**AB Science announces that ANSM requested the temporary suspension of clinical studies conducted in France following deviations from Good Clinical Practice (GCP) standards**

**AB Science corrected these deficiencies and an audit plan confirming the GCP compliance will be performed in the coming months**

**ANSM accepted the principle of restarting the clinical studies on the basis on the findings of this independent audit**

**AB Science SA** (NYSE Euronext - FR0010557264 - AB), a pharmaceutical company specializing in the research, development and commercialization of protein kinase inhibitors (PKIs), received yesterday the notification from the Agence Nationale de la Sécurité des Médicaments (ANSM) requesting the temporary suspension of the ongoing masitinib studies until their compliance is confirmed by an external audit.

AB Science is actively collaborating with ANSM in order to restart the recruitment of patients in clinical studies in France.

This decision follows the findings of the inspection that was carried out as part of the procedure for the marketing authorization of masitinib in mastocytosis, which showed deviations from the Good Clinical Practice (GCP) in the conduct of the mastocytosis pivotal study (AB06006) and deviations related to the pharmacovigilance system.

GCP compliance and pharmacovigilance system

The EMA inspection focused on study AB06006 conducted between 2009 and the beginning of 2015 and does not therefore reflect the quality system put into place since mid-2015. Indeed, since mid-2015, the company has implemented a new quality system to ensure compliance with the GCP requirements.

As an evidence that other studies have no unreported adverse events, the last 11 site inspections carried out by national health authorities outside France since mid-2015 have not identified any serious or severe adverse events that would have been left unreported. In particular, a site inspection performed by the Canadian Health Authority on the amyotrophic lateral sclerosis phase 3 study concluded that the study is conducted under GCP compliance.

Additionally, all the deficiencies identified in the pharmacovigilance system have been corrected following the inspection and the pharmacovigilance system currently in place is now GCP compliant.

An independent audit will be performed in the coming months in order to provide ANSM with confirmation that the system meets the GCP standards. ANSM confirmed that the clinical studies could restart in France following the positive results of this audit plan.

### Reliability of efficacy and safety data

As part of the implementation of the new quality system, data from all studies, clinical sites and patients have been remonitored since mid-2015. This remonitoring of all studies concerned key efficacy data and adverse events. This full remonitoring was performed between mid-2015 and November 2016 for all studies except mastocytosis and following EMA inspection between January 2017 and March 2017 for mastocytosis study. The masitinib's safety profile was not modified following this full remonitoring. The 2017 Investigational Brochure will include the remonitored data and will be sent to health authorities in the coming months.

Additionally, independent quality audits of key efficacy data and adverse events in mastocytosis and ALS studies will be conducted in order to ensure the data reliability and secure registration in both indications.

Clinical batches records, including treatment number correspondence lists, have been received by AB Science's Pharmaceutical Operations department in preparation for an inspection, without AB Science being informed of the presence of these lists, and discovered during EMA inspection. These lists only concern a very small number of the patients included in the mastocytosis study and have no impact on other studies, including the ALS study. Regarding the mastocytosis study, the inspection showed that no modification of the protocol had occurred after the receipt of these lists and showed no use of these lists before unblinding.

### Masitinib safety profile

The masitinib safety profile is known on the basis of more than 5,000 patients, has not increased, and is acceptable in the targeted indications.

The masitinib safety profile has been assessed as acceptable in all ongoing indications by the Independent Data Monitoring Committees (IDMC) of the studies, which have access to unblinded data, as well as by health agencies of more than 25 countries where masitinib is currently developed and finally by the ethics committees which have authorized the studies.

Concerning the risk of severe skin toxicity, since the implementation of the new risk management plan in 2012, the suspected Stevens Johnson syndrome cases have been reviewed by two independent experts and no case of Stevens Johnson syndrome have occurred on the 3500 recruited patients, proving the control of this risk. 2 cases of possible or probable Stevens Johnson syndrome were reported before 2012 in cancer patients receiving masitinib at high doses (7,5 mg and 9 mg) in combination with chemotherapy.

Similarly, the risk of severe neutropenia was minimized by the risk management plan in 2012, around 1% and remained stable.

Clinical risk analysis does not indicate an identified risk of death or renal toxicity or cardiac toxicity. A vigilance plan has been implemented for this latter risk given the class effect, but masitinib appears to be unique because of its very selective kinase inhibition profile and no toxicity signal has been identified in clinical studies. A follow-up on 250 patients of the left ventricular ejection fraction showed no risk increase. Similarly, a QT/QTc study did not show an increase in this risk.

Additionally, the carcinogenic risk observed in non-clinical studies in animals was evaluated in detail by the EMA during the procedure for the marketing authorization of masitinib in mastocytosis and this assessment shows that the risk of tumors is specific to evaluated animal species and not transposable to humans, and that the genotoxic risk is below the acceptable limits set in EMA guidelines for a lifetime treatment in a non-life-threatening indication. It is therefore now established that this residual risk is not an obstacle to the registration of masitinib in indications outside oncology.

### Impact on clinical studies

The clinical studies have not been stopped. The decision applies in France only. In France, studies are not prohibited, only suspended. The study suspension in France has a low impact on the recruitment of ongoing studies, France accounting for less than 5% of patient recruitment in these ongoing studies. Additionally, patients who could be discontinued account for less than 1% of the number of patients to be recruited in phase 3 studies, which does not threaten the data interpretation. For these patients, the discontinuation is not certain as ANSM informed AB Science that the decision to discontinue the treatment for ongoing patients may be subject to an appeal and a review of individual benefit for each patient.

#### Impact on amyotrophic lateral sclerosis study (ALS)

The findings identified during this inspection do not affect the ALS study for the following reasons:

- This study was conducted between mid-2013 and beginning of 2017 and therefore benefited from the quality system implemented since mid-2015
- This study was not conducted in France
- The audits demonstrating the GCP compliance will be available before the EMA inspections conducted as part of the procedure for the marketing authorization.

#### Webcall :

A webcall will be hosted on May 12, 2017 at 4.30pm (CET) for French speakers and at 6.30pm (CET) for English speakers. To participate please send an email at [linda.carlet@ab-science.com](mailto:linda.carlet@ab-science.com).

#### **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 thirteen phase 3 studies 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, 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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