*Paris, 11 August 2014, 5.45pm CET*

**Clarification concerning the French Committee report on health products initial assessment, issued upon the cohort Temporary Authorization Utilization of masitinib with the GIST**

**AB Science SA** (NYSE Euronext – FR0010557264 – AB), a pharmaceutical company specializing in the research, development and commercialization of protein kinase inhibitors (PKIs), would like to bring clarification to the French Committee report on health products initial assessment, issued upon the cohort Temporary Authorization Utilization of masitinib with the GIST.

1. Survival improvement

The report mentions that no difference was observed between masitinib and sunitinib in terms of survival.

*« No difference […] on the secondary survival objectives with a 14 month-median follow-up for masitinib and 15 months for sunitinib, therefore there is no difference».*

This data is not accurate because the survival analysis realized after a 26-month median follow-up showed that the survival median was 29.8 months with masitinib, versus 17.4 months with sunitinib, a survival gain superior to 12 months (HR = 0.40 (95% CI = [0.16; 0.96]; *p*-value = 0.033).

2. Cutaneous toxicity profile different from that of sunitinib

The report mentions that masitinib generates severe syndrome of Lyell type cutaneous reactions, which do not occur with other products.

*"In terms of safety, there were severe syndrome of Lyell type cutaneous reactions, with masitinib in many clinical trials, which did not occur with other products [...]."*

This data is inaccurate because:

- No syndrome of Lyell occurred with masitinib.
- Severe skin disorders have been reported with masitinib, but none in the clinical study supporting the application of a cohort ATU.
- Severe skin disorders have been reported with sunitinib, as indicated by the record of sunitinib: «*Pain or irritation of the mouth has been reported with approximately 14% of patients. Few cases of pyoderma gangrenosum, usually reversible upon discontinuation of treatment, have been reported. Rare cases of severe skin reactions have been reported, including cases of erythema multiforme (EP) and cases suggestive of Stevens-Johnson syndrome (SJS) and toxic epidermal necrolysis (TEN). »*

3. Carcinogenicity study

The report mentions that no carcinogenicity study had been conducted with masitinib.

«*A reviewer would like to clarify that no carcinogenicity study has been conducted on animals. »*

This data is inaccurate because two carcinogenicity studies have been conducted, one on mice and one on rats.

4. Carcinogenicity studies conclusion

The report mentions that masitinib is carcinogenic.

«*Animals can develop spontaneous tumors: it appears that the product is carcinogenic in two rodent strains studied. »*

This data is not precise and cannot be interpreted without additional information:

- Health authorities have a longstanding knowledge of the results of carcinogenicity studies.
  Carcinogenicity studies on two rodent species are only required to allow the registration of a drug administred in long-term care, often for conditions outside of oncology. These two studies by AB Science were completed over five years ago and results were sent to all drug agencies of the countries that have authorized the initiation of clinical studies of large scale outside of oncology, including ANSM.

- The carcinogenicity studies on rodents can generate results that are non-transferable to humans.
  In nearly 50% of carcinogenicity studies of new drugs on rodents, an increased incidence of tumors was observed (see bibliography below *). These tumors are generally considered to be rodent-specific and unrepresentative of a risk to humans. This point is well established and accepted by health authorities, and many medications used daily on humans have generated an increase in tumors in the carcinogenicity studies on rodents.

- The European Medicines Agency considers that the data of carcinogenicity studies do not pose a carcinogenic risk in the target indication.
  Masitinib in and of itself is not genotoxic.
  Both studies were conducted on two rodent species whose metabolic functions behave very differently from that of a man with a production of potentially genotoxic metabolites up to thirty times greater than that of man.
  Carcinogenesis studies have shown a risk only for groups of animals receiving masitinib at the highest dose tested, which is higher than those observed in human concentrations.

- There is no sign of cancer risk based on clinical data.
  No sign of secondary cancer related to masitinib was observed in more than 1600 patients exposed to masitinib to date.

François Bellamy, former director of the Drug Discovery Laboratories Fournier and Head of Preclinical Development at AB Science, who has an experience of over 30 years in the non-clinical development of new drugs says: *« The fact that tumors can occur at a high dose in toxicity studies on animals does not mean that the same will happen to human, especially with lower doses. »*

In conclusion, data on carcinogenesis of masitinib do not prevent registration in oncology and non-oncology indications, especially in the case of indications covered by masitinib, which are serious diseases or diseases with little or no therapeutic alternatives for which masitinib will have demonstrated a clinical benefit.

*** Bibliography**

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Van Ousterhout, J.P.J., van der Laan, J.W., de Waal, E.J., Olenjniczak, K., Hilgenfeld, M., Schmidt, V., Bass, R., (1997). The utility of two rodent species in carcinogenic risk assessment of pharmaceuticals in Europe. Regulatory Toxicology and Pharmacology Vol 25, pp 6–17.

**About masitinib**

Masitinib is a new orally administered tyrosine kinase inhibitor that targets mast cells, important cells for immunity, as well as a limited number of kinases that play key roles in various cancers. Owing to its novel 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. Through its activity of inhibiting certain kinases that are essential in some oncogenic processes, masitinib may have an effect on tumor regression, alone or in combination with chemotherapy. Through its activity on the mast cell and certain kinases essential to the activation of the inflammatory cells and fibrosing tissue remodeling, masitinib can have an effect on the symptoms associated with some inflammatory and central nervous system 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 new class of targeted molecules whose action is to modify signaling pathways within cells. Through these PKIs, the Company targets diseases with high unmet medical needs (cancer, inflammatory diseases, and central nervous system diseases), in both human and veterinary medicines. 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 pursuing thirteen 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, mastocytosis, severe persistent asthma, rheumatoid arthritis, 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's website: www.ab-science.com

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