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Preclinical data published in *Nature Communications* shows that masitinib is capable of counteracting resistance to oncology treatments, including gemcitabine

Phase 3 clinical studies on-going for masitinib-gemcitabine combination in pancreatic cancer, refractory peripheral T-cell lymphoma and refractory ovarian cancer

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 showing that masitinib is capable of counteracting resistance to oncology treatments, including gemcitabine.

Entitled, 'Dual protein kinase and nucleoside kinase modulators for rationally designed polypharmacology' this article and its accompanying Online Supplementary Material are freely accessible online from the peer-reviewed scientific journal Nature Communications https://www.nature.com/articles/s41467-017-01582-5.[1]

Research conducted to identify the signaling pathways involved in the ability of masitinib to re-sensitization cancer cells to chemotherapies has identified human deoxycytidine kinase (dCK) as a potential new target for masitinib. This kinase is very important for the phosphorylation and activation of certain molecules used in cancer chemotherapy, called nucleoside analogues, such as gemcitabine (but also cytarabine, cladribine, fludarabine and decitabine).

This research demonstrates that masitinib enhances the dCK-dependent activation of gemcitabine, as well as several other pro-drugs of therapeutic interest from the same class. Indeed, masitinib was found to be the most active of the kinase inhibitors tested.

dCK is involved in both drug resistance and sensitivity. Masitinib can therefore potentiate the activity of nucleoside analogue agents. This is of potential clinical benefit through either reducing toxicity of dCK-associated therapeutic agents or by counteracting drug resistance.

"These findings represent a novel mechanism of action for masitinib that is of relevance to its oncology development program" said Dr Patrice Dubreuil, Director of Research at the INSERM Center for Cancer Research of Marseille and senior author of the article. *"This property of masitinib is of potential clinical benefit through either reducing toxicity of dCK-associated therapeutic agents by maintaining therapeutic efficiency at lower doses, or by amplifying the effectiveness of such agents in order to counteract drug resistance. Furthermore, because nucleoside-like drugs are among the most important therapeutic agents currently used to treat tumors and viral diseases, this discovery could also be of benefit for a variety of other diseases."*

The combination of masitinib plus gemcitabine is currently under phase 3 clinical development in three indications:

- Pancreatic cancer in a patient subpopulation initially selected for treatment based upon the predictor factor of disease related pain intensity (masitinib plus gemcitabine)
- Relapsed or refractory peripheral T-cell lymphoma (masitinib / dexamethasone plus gemcitabine)
- Relapsed or refractory advanced/metastatic epithelial ovarian cancer (masitinib plus gemcitabine)

"*The findings reported in this article provide additional justification for the development of masitinib in combination with nucleoside-like anticancer drugs such as gemcitabine*" said Professor Olivier Hermine, President of the Scientific Committee of AB Science. *"For example, a confirmatory phase 3 randomized clinical*

trial is currently ongoing in pancreatic cancer with an objective to replicate the first study's promising results in a prospective manner."

As a reminder, this confirmatory phase 3 study was based on data generated from the AB07012 phase 3 study of masitinib in treatment of advanced pancreatic ductal adenocarcinoma. Results have previously been published in the peer-reviewed journal Annals of Oncology under the title of, '*A randomized, placebo-controlled phase III trial of masitinib plus gemcitabine in the treatment of advanced pancreatic cancer*'[2]. This article is freely available at http://annonc.oxfordjournals.org/lookup/doi/10.1093/annonc/mdv133.

Key findings from that study are described below:

- It was revealed that the marker of baseline pain intensity, assessed via a visual analog scale (VAS) at baseline, has prognostic value, with patients from this subgroup experiencing aggressive disease progression while receiving Gemzar® (gemcitabine, from Eli Lilly and Company).
- This subgroup represents a critical unmet medical need as evidenced from a shorter median OS of approximately 5.5 months.
- In the pain subgroup, administration of masitinib in combination with Gemzar® produced a statistically significant overall survival advantage of +2.6 months (Hazard Ratio=0.62[0.43;0.89]) when compared with placebo administered in combination with Gemzar®.
- Safety of the combination remained acceptable with no overall detrimental effect on quality of life.
- There is evidence from the scientific literature in support of biological plausibility for the observe masitinib treatment-effect in patients with baseline pain (VAS ≥ 20). The presence of pain in pancreatic ductal adenocarcinoma is thought to flag an increased mast cell activity within the tumor microenvironment which promotes disease progression.
- Masitinib's highly selective inhibition of mast cell activation is expected to be of therapeutic benefit by impacting on mast cell related remodeling of the tumor microenvironment.

[1] Hammam K, et al. Dual protein kinase and nucleoside kinase modulators for rationally designed polypharmacology. Nature Communications 8, Article number: 1420 (2017).

[2] Deplanque G, et al. A randomized, placebo-controlled phase III trial of masitinib plus gemcitabine in the treatment of advanced pancreatic cancer. Ann Oncol. 2015 Jun;26(6):1194-200.

About pancreatic ductal adenocarcinoma

Incidence of pancreatic cancer has markedly increased over the last few decades. Pancreatic cancer is now the twelfth most common cancer in the world, with 338,000 new cases diagnosed in 2012[1]. The estimated 5-year prevalence of people in the world living with pancreatic cancer is 4.1 per 100,000. This cancer is almost always fatal, and is the seventh most common cause of death from cancer. Patients diagnosed with pancreatic cancer often have a poorer prognosis compared with other cancers in part because early detection is difficult. At the time of diagnosis, most patients with pancreatic ductal adenocarcinoma present with locally advanced or metastatic disease and only 10-20% of cases are candidates for curative surgery. For over a decade single-agent gemcitabine has been the standard first-line treatment for unresectable, locally advanced or metastatic pancreatic ductal adenocarcinoma. Median overall survival is between 6 to 7 months and 1-year survival rates range between 17 to 25% [2, 3].

[1] http://globocan.iarc.fr/Pages/fact_sheets_population.aspx

[2] Heinemann V, et al. BMC Cancer. 2008;8:82.

[3] Von Hoff DD, et al. N Engl J Med. Oct 31 2013;369(18):1691-1703.

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.

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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