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AB Science announces authorization to initiate phase 2 in stomach cancer with masitinib

Masitinib clinical development program in solid tumors now accounts for 11 indications

AB Science SA (NYSE Euronext - FR0010557264 - AB), a pharmaceutical company specialising in the research, development and commercialisation of protein kinase inhibitors (PKIs), announced today the authorisation granted by Afssaps to start a phase 2 clinical study in stomach cancer.

AB Science is now evaluating masitinib in eleven indications in solid tumors, eight in phases 2, in second line treatment of gastro-intestinal stromal tumor (GIST), lung cancer, prostate cancer, colorectal cancer, triple negative breast cancer, metastatic breast cancer, metastatic melanoma, and stomach cancer, and three in phase 3 in pancreatic cancer, first line treatment of GIST and in metastatic melanoma expressing JM mutation of c-Kit.

Except for GIST and melanoma bearing the JM mutation of c-kit, where masitinib is tested in monotherapy because the main target is the JM mutation of c-kit, in the remaining 9 indications masitinib is tested in combination with standard of care chemotherapy. Indeed, masitinib has proved to sensitize in vitro and in grafted mice models several standard of care chemotherapies in various solid tumors cell lines.

Alain Moussy, Chairman and CEO of AB Science declared « *Besides the three phase 3 studies already launched in pancreatic cancer, GIST first line and melanoma bearing the JM mutation of c-kit, the objective of these proof of concept phases 2 studies in solid tumors is to define in which cancers masitinib can improve progression free survival and survival. The position of masitinib is mainly in resistance to first line treatment and in metastatic tumors, where the medical need is the maximum. In case of success, this set of indications represents a huge potential, as overcoming resistance to chemotherapy remains a daunting problem. These eight phase 2 studies and three phase 3 studies in oncology are fully financed*».

Details of the clinical development program (on next page).

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 tumour 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 remodelling, 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 specialising in the research, development and commercialisation of protein kinase inhibitors (PKIs), a new class of targeted molecules whose action is to modify signalling 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. Thanks to its extensive research and development capabilities, AB Science has its own portfolio of molecules. Masitinib, a lead compound, has already been registered in veterinary medicine in Europe and is pursuing nine phase

3 studies in human medicine, including four studies on-going in pancreatic cancer, GIST, in metastatic melanoma expressing JM mutation of c-Kit, and mastocytosis.

Further information is available on AB Science's website: www.ab-science.com

This document contains prospective information. No guarantee can be given as for the realisation of these forecasts, which are subject to those risks described in documents deposited by the Company to the Authority of the financial markets, including trends of the economic conjuncture, the financial markets and the markets on which AB Science is present.

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DETAILS OF THE CLINICAL DEVELOPMENT PROGRAM IN SOLID TUMORS

Status of program of clinical studies of masitinib in solid tumors

Clinical Studies	Status at IPO	Current status
Masitinib in monotherapy (JM mutation of c-Kit)		
1 - Gist first line (phase 3)	Recruitment on-going	Recruitment on-going
2- Metastatic melanoma bearing JM mutation of c-Kit (phase 3)	Not initiated	Recruitment on-going
3 - GIST second line (phase 2)	Recruitment on-going	Recruitment on-going
Masitinib in combination with chemotherapy		
4- Pancreatic cancer (phase 3)	Recruitment on-going	Recruitment completed
5 - Lung cancer (phase 2)	Authorised (Afssaps)	Recruitment on-going
6 - Prostate cancer (phase 2)	Authorised (Afssaps)	Recruitment on-going
7 - Colorectal cancer (phase 2)	Authorised (Afssaps)	Recruitment on-going
8 - Breast cancer triple negative (phase 2)	Authorised (Afssaps)	Recruitment on-going
9 - Metastatic breast cancer (phase 2)	Authorised (Afssaps)	Recruitment on-going
10 - Metastatic melanoma (phase 2)	Not initiated	First patient enrolled
11 - Stomach cancer (phase 2)	Not initiated	Authorised (Afssaps)

Scientific rationale for developing masitinib in solid tumors in combination with chemotherapies

Masitinib is a novel inhibitor targeting specifically c-kit, FAK, PDGFR, and FGFR3, thus it could limit cell proliferation, cell migration and/or tumour vascularisation. It has also been shown that it can potentiate chemotherapeutic agents or sensitize resistant cells to chemotherapeutic agents.

Masitinib is an effective antimastocyte, exerting a direct anti-proliferative and pro-apoptotic action on mast cells and reducing secretion of mast cell mediators through its inhibition of KIT signalling. Evidence indicates that recruitment of inflammatory cells, especially infiltration by mast cells, facilitates the growth and spread of some cancers by producing molecules that enhance tumour invasiveness. Therefore, inhibition of mast cell function may prove to be therapeutically beneficial in restraining the growth of numerous cancers, even those without a direct association with mast cell proliferation. In addition to its

antiproliferative properties, masitinib can also regulate the activation of mast cells through its targeting of Lyn and Fyn, key components of the transduction pathway leading to IgE induced degranulation. This can be observed in the inhibition of FcεRI-mediated degranulation of human cord blood mast cells. It is thought that inhibition of Lyn kinase activity may also inhibit IgE independent degranulation and as such has potential benefits in defence against metastasis and drug-resistance.

Masitinib may reduce angiogenesis and enhance the chemotherapy sensitivity and availability at the tumour site via inhibition of PDGFR. Recent studies have suggested that PDGFR-β inhibition reduces tumour interstitial pressure and thus, increases the uptake of concomitantly administered drugs. Inhibition of PDGFR kinase activity may also result in direct tumour cell growth arrest and apoptosis if PDGFR is constitutively activated.

FAK influences cell proliferation, survival, and migration, and has been associated with tumour progression, metastasis and chemoresistance. Masitinib can block the FAK pathway in cells through the inhibition of FAK phosphorylation activity, without blocking its enzymatic activity.

Altogether, this could provide a mechanism of action for masitinib's chemosensitisation properties, i.e. through the reduction of tumour progression and/or improved drug delivery and/or the inhibition of mast cell migration and activation; thereby explaining the observed therapeutic benefits of masitinib.

Characteristics of the phase 3 GIST first line

A prospective, multicenter, randomized, open-label, active-controlled, 2-parallel group, phase 3 study to compare efficacy and safety of masitinib at 7.5 mg/kg/day to imatinib at 400 or 600 mg in treatment of patients with gastro-intestinal stromal tumour in first line medical treatment

Patients will be randomized in two groups:

- Group 1: Patients will receive masitinib at 7,5 mg/kg/day
- Group 2: Patients will receive imatinib at 400 or 600 mg per day

The primary criterion will be the Overall Progression Free Survival (PFS), defined as the delay between the date of randomisation to the date of documented progression or any cause of death during the study. Overall Survival will be the main secondary criterion.

Characteristics of the phase 3 study in metastatic melanoma bearing JM mutation of c-kit

A prospective, multicenter, randomized, open-label, active-controlled, two-parallel groups, phase 3 study to compare the efficacy and safety of masitinib at 7.5 mg/kg/day to dacarbazine in the treatment of patients with non-resectable or metastatic stage 3 or stage 4 melanoma carrying a mutation in the juxta membrane domain of c-kit.

Patients will be randomized in two groups:

- Group 1: Patients will receive masitinib
- Group 2: Patients will receive dacarbazine

The primary criterion will be the Overall Progression Free Survival (PFS), defined as the delay between the date of randomisation to the date of documented progression or any cause of death during the study. Overall Survival will be the main secondary criterion.

Characteristics of the phase 2 GIST second line

A prospective, multicenter, randomized, open-label, 2-parallel group, Phase 2 study to compare efficacy and safety of masitinib at 12 mg/kg/day to sunitinib at 50 mg/day in treatment of patients with gastrointestinal stromal tumor resistant to imatinib

Patients will be randomized in two groups:

- Group 1: Patients will receive masitinib at 12 mg/kg/day
- Group 2: Patients will receive sunitinib at 50 mg/day

The primary criterion will be the Overall Progression Free Survival (PFS), defined as the delay between the date of randomisation to the date of documented progression or any cause of death during the study. Overall Survival will be the main secondary criterion.

Characteristics of the phase3 in pancreatic cancer

A prospective, multicenter, randomized, double-blind, placebo-controlled, 2-parallel group, Phase 3 study to compare efficacy and safety of masitinib at 9 mg/kg/day in combination with gemcitabine, to placebo in combination with gemcitabine, in treatment of patients with advanced/metastatic pancreatic cancer.

Patients will be randomized in two groups:

- Group 1: Patients will receive masitinib at 9 mg/kg/day plus gemcitabine
- Group 2: Patients will receive matching placebo plus gemcitabine

The primary criterion will be the Overall Survival. Progression Free Survival (PFS) will be the second criterion.

Characteristics of the phase 2 study in lung cancer

A prospective, multicentre, randomised, open-label, 2-parallel groups, phase 2 study to evaluate efficacy and safety of masitinib at 9 mg/kg/day in combination with docetaxel or in combination with gemcitabine in the treatment of patients with metastatic non-small cell lung cancer in progression after first line treatment.

Patients will be randomized in two groups:

- Group 1: Patients will receive masitinib at 9 mg/kg/day in combination with docetaxel
- Group 2: Patients will receive masitinib at 9 mg/kg/day in combination with gemcitabine

The primary criterion will be the Overall Progression Free Survival (PFS), defined as the delay between the date of randomisation to the date of documented progression or any cause of death during the study. Overall Survival will be the main secondary criterion.

Characteristics of the phase 2 study in prostate cancer

This is a prospective, multicenter, randomized, open-label, 2-parallel group, Phase 2 study to evaluate the efficacy and the safety of masitinib at 9 mg/kg/day in combination with docetaxel or with gemcitabine in metastatic Hormone Refractory Prostate Cancer (HRPC) in progression after first line of treatment.

Patients will be randomized in two groups:

- Group 1: Patients will receive masitinib at 9 mg/kg/day in combination with docetaxel and prednisone
- Group 2: Patients will receive masitinib at 9 mg/kg/day in combination with gemcitabine

The primary criterion will be the Overall Progression Free Survival (PFS), defined as the delay between the date of randomisation to the date of documented progression or any cause of death during the study. Overall Survival will be the main secondary criterion.

Characteristics of the phase 2 study in colorectal cancer

This is a prospective, multicentre, randomized, open-label, 3-parallel groups, phase 2 study to evaluate efficacy and safety of masitinib at 9 mg/kg/day in combination with oxaliplatin, 5-fluorouracil (5-FU) and folinic acid (FOLFOX) or in combination with irinotecan, 5-fluorouracil (5-FU) and folinic acid (FOLFIRI) or in combination with gemcitabine (GEM) in the treatment of patients with metastatic colorectal cancer in progression after a first line treatment.

Patients will be randomised in three groups:

- Group 1: Patients will receive masitinib in combination with oxaliplatin 5-fluorouracil (5-FU) and folinic acid (modified FOLFOX protocol);
- Group 2: Patients will receive masitinib in combination with irinotecan, 5-fluorouracil (5-FU) and folinic acid (FOLFIRI protocol);
- Group 3: Patients will receive masitinib in combination with gemcitabine.

The primary criterion will be the Overall Progression Free Survival (PFS), defined as the delay between the date of randomisation to the date of documented progression or any cause of death during the study. Overall Survival will be the main secondary criterion.

Characteristics of the phase 2 study in breast triple negative cancer

This is a prospective, multicentre, open-label, randomised, phase 2 study to evaluate efficacy and safety of masitinib at 9 mg/kg/day in association with gemcitabine or carboplatin or gemcitabine plus carboplatin in patients with a triple negative metastatic or locally advanced breast cancer.

Patients will be randomised in three groups:

- Group 1: Patients will receive masitinib at 9 mg/kg/d in association with gemcitabine;
- Group 2: Patients will receive masitinib at 9 mg/kg/d in association with carboplatin;
- Group 3: Patients will receive masitinib at 9 mg/kg/d in association with gemcitabine plus carboplatin.

The primary criterion will be the Overall Progression Free Survival (PFS), defined as the delay between the date of randomisation to the date of documented progression or any cause of death during the study. Overall Survival will be the main secondary criterion.

Characteristics of the phase 2 study in metastatic cancer

This is a prospective, multicentre, open-label, randomised, phase 2 study to evaluate efficacy and safety of masitinib in combination with gemcitabine or carboplatin or capecitabine in patients with a metastatic or locally advanced breast cancer (all hormonal status tumour except triple negative tumour) and who relapsed after a first line chemotherapy.

Patients will be randomised in three groups:

- Group 1: Patients will receive masitinib at 9 mg/kg/d or 6 mg/kg/day in association with gemcitabine
- Group 2: Patients will receive masitinib at 9 mg/kg/d or 6 mg/kg/day in association with carboplatin
- Group 3: Patients will receive masitinib at 9 mg/kg/d or 6 mg/kg/day in association with capecitabine

The primary criterion will be the Overall Progression Free Survival (PFS), defined as the delay between the date of randomisation to the date of documented progression or any cause of death during the study. Overall Survival will be the main secondary criterion.

Characteristics of the phase 2 study in metastatic melanoma

This is a prospective, multicentre, open-label, two-parallel groups, phase 2 study to evaluate efficacy and safety of masitinib at 9 mg/kg/day in monotherapy and combination with dacarbazine in the treatment of patients with non-resectable or metastatic stage 3 or stage 4 melanoma not carrying a mutation in the juxta membrane of c-kit.

Patients will be randomized in two groups:

- Group 1: Patients will receive masitinib in association with dacarbazine
- Group 2: Patients will receive masitinib.

The primary criterion will be the Overall Progression Free Survival (PFS), defined as the delay between the date of randomisation to the date of documented progression or any cause of death during the study. Overall Survival will be the main secondary criterion.

Characteristics of the phase 2 study in stomach cancer

This is prospective, multicentre, open-label, randomised, phase 2 study to evaluate the efficacy and safety of masitinib in combination with 5-fluorouracil (5-FU) or capecitabine, or masitinib in combination with irinotecan, or masitinib in combination with irinotecan, 5-fluorouracil (5-FU) and folinic acid (FOLFIRI protocol), as second line therapy in patients with gastric or gastro-oesophageal junction metastatic adenocarcinoma.

Patients will be randomized in three groups:

- Group 1: Patients will receive masitinib at 6 mg/kg/day or 9 mg/kg/day, in association with 5-Fluorouracil or Masitinib at 6 mg/kg/day or 9 mg/kg/day in association with capecitabine
- Group 2: Patients will receive masitinib at 6 mg/kg/day or 9 mg/kg/day, in association with irinotecan
- Group 3: Patients will receive masitinib at 6 mg/kg/day or 9 mg/kg/day in association with FOLFIRI protocol

The primary criterion will be the Overall Progression Free Survival (PFS), defined as the delay between the date of randomisation to the date of documented progression or any cause of death during the study. Overall Survival will be the main secondary criterion.