Paris, 7 December 2015, 8.00 am

AB Science announces results from Phase 3 randomized placebo-controlled trial of masitinib in adults with severe systemic mastocytosis unresponsive to optimal symptomatic treatment

Results from phase 3 study are both clinically and statistically significant

AB Science SA (NYSE Euronext - FR0010557264 - AB), a pharmaceutical company specializing in the research, development and commercialization of protein kinase inhibitors (PKIs), announced today results from phase 3 study of masitinib, a first in class drug in the treatment of adult patient with severe systemic mastocytosis unresponsive to optimal symptomatic treatment. Masitinib is the first treatment to be evaluated in this indication. Top-line results from this phase 3 were previously announced on 30 November 2015.

The results showed that masitinib 6 mg/kg/day was superior to optimal symptomatic treatment on the primary efficacy analysis as well as secondary efficacy analyses. No new safety signals for masitinib were observed in this phase 3 study.

"We are very pleased to present the results of this study showing efficacy of masitinib in severe systemic mastocytosis, as it is the first phase 3 study ever performed in the treatment of severe systemic mastocytosis," said Professor Olivier Lortholary (APHP Hôpital Necker-Enfants maladies IHU Imagine, Paris, France) Principal Investigator of the study.

The phase 3 randomized study compared masitinib plus optimal symptomatic treatment versus placebo plus optimal symptomatic treatment in adult patients with severe systemic mastocytosis, with or without D816V mutation of c-Kit. Study results showed that masitinib administered at 6 mg/kg/day was superior to the comparator, as measured by the cumulative 75% response rate until week 24 on the handicaps of pruritus or flushes or depression or fatigue (4H75% response). The 4H75% response was 18.7% for the masitinib treatment-arm versus 7.4% for the placebo treatment-arm (p=0.0100, Odd ratio=3.63) in the mITT population (primary analysis). Sensitivity analysis according to the per protocol (PP) population, i.e. the sets of patients who participated in the study as intended, gave a 4H75% response rate of 20.1 % versus 7.4%, respectively (p=0.0146, Odd ratio=3.88).

Success in the primary analysis was supported by positive outcomes in all secondary analyses.

- The cumulative 75% response rate until week 24 on the handicaps of pruritus or flushes or depression (3H75% response) was 24.7% versus 9.8% for the masitinib and placebo treatment-arms, respectively, (p=0.0071, Odd ratio=3.06) in the mITT population. In the per protocol population this response rate was 26.5 % versus 9.8%, respectively (p=0.0038, Odd ratio=3.33).
- The cumulative 75% response rate until week 24 on the handicaps of pruritus or flushes (2H75% response) was 27.2% versus 10.7% for the masitinib and placebo treatment-arms, respectively (p=0.0380, Odd ratio=2.63) in the mITT population. In the per protocol population this response rate was 29.5% versus 10.7%, respectively (p=0.0220, Odd ratio=2.89).
- The cumulative 75% response rate until week 24 on the handicap of pruritus was 22.0% versus 7.3% for the masitinib and placebo treatment-arms, respectively (p=0.0322, Odd ratio=3.13) in the mITT population. In the per protocol population this response rate was24.7 % versus 7.3%, respectively (p=0.0146, Odd ratio=3.69).

When looking at other individual handicaps of flush, Hamilton, and FIS (Fatigue Impact Scale), a consistent superiority was observed for all handicaps, showing that masitinib can reduce each of these symptoms.

- The cumulative 75% response rate until week 24 on the handicap of flush was 39.9% versus 19.0% for the masitinib and placebo treatment-arms, respectively, (Odd ratio=3.03) in the mITT population.
- The cumulative 75% response rate until week 24 on the handicap of depression was 18.6% versus 7.6% for the masitinib and placebo treatment-arms, respectively, (Odd ratio=2.71) in the mITT population.
- The cumulative 75% response rate until week 24 on the handicap of fatigue was 7.7% versus 3.2% for the masitinib and placebo treatment-arms, respectively, (Odd ratio=4.84) in the mITT population. Although the percentage difference with placebo was lower on fatigue than other handicaps, the difference was still statistically significant ($p<0.05$). It is possible that this relatively small difference between masitinib and placebo on fatigue may be due to the choice of the measure using the Fatigue Impact Scale (FIS), as it was published[1] after the start of the study that FIS not sensitive enough to detect change over time (meaning should be used with caution to assess a drug supposed to improve fatigue symptoms). This may also account for the superior response rate observed for the 3H75% criterion when compared with the 4H75% criterion.

1: Whitehead L. The measurement of fatigue in chronic illness: a systematic review of unidimensional and multidimensional fatigue measures. J Pain Symptom Manage. 2009 Jan;37(1):107-28. doi: 10.1016/j.jpainsymman.2007.08.019.

The positive results on patient reported outcomes on the symptoms associated with the disease were also supported with a reduction in the tryptase, which is an objective biological marker of mast cell burden and activity. Indeed, the mean change in tryptase level relative to baseline was minus 18.0% with masitinib versus +2.2% ($p=0.0001$) in the mITT population and minus 20.0% with masitinib versus +2.2% ($p<0.0001$) in the per protocol population.

The effect of masitinib was further substantiated by an observed sustainability in clinical benefit, as evidence by the long-term follow-up data. After the 6-month protocol period, patients were authorized to enter into the study's extension phase. Considering the week 0 to week 96 period (2 years):
- The 4H75% response was 17.2% versus 7.1% for the masitinib and placebo treatment-arms, respectively ($p=0.0102$, Odd ratio=3.37) in the mITT population and 18.7 % with masitinib versus 7.1% ($p=0.0062$, Odd ratio=3.66) in the per protocol population.
- The 3H75% response was 22.1% versus 8.6% for the masitinib and placebo treatment-arms, respectively ($p=0.0030$, Odd ratio=3.10) in the mITT population and 24.1% with masitinib versus 8.6% ($p=0.0013$, Odd ratio=3.42) in the per protocol population.

There was no new safety finding with masitinib through this study.

A patent was filed before disclosure of the detailed results in order to claim a potential 20 year exclusivity period for masitinib in the label of patients with severe systemic mastocytosis.

Professor Olivier Hermine, President of the AB Science Scientific Committee and coordinator of the Reference Center for mastocytosis (CeReMast) said: "The efficacy observed with masitinib on the 3H75% criteria is very relevant from a clinical standpoint because pruritus and flush are well-recognized to be associated with mast cell activation in mastocytosis and depression is a symptom that has a major impact on quality of life of patients suffering from mastocytosis. The fact that masitinib generated efficacy on depression is a major innovation and a major benefit for the treatment of this disease. The effect of masitinib on tryptase level also provides convincing biological evidence of the activity of masitinib. The long-term data show that masitinib can offer a life-time option to normalize the severe symptoms of mastocytosis".

Detailed phase 3 results

Protocol Period (W0-W24 period)			Masitinib	Placebo	p-value	Odd ratio
Primary endpoint	**4H75%**: Cumulative 75% response rate on the handicaps of pruritus or flushes or depression or fatigue	**mITT**	**18.7%**	**7.4%**	**0.0100***	**3.63**
		PP	20.1%	7.4%	0.0146	3.88
Secondary endpoints	3H75%: Cumulative 75% response rate on the handicaps of pruritus or flushes or depression	mITT	24.7%	9.8%	0.0071	3.06
		PP	26.5%	9.8%	0.0038	3.33
	2H75%: Cumulative 75% response rate on the handicaps of pruritus or flushes	mITT	27.2%	10.7%	0.0380	2.63
		PP	29.5%	10.7%	0.0220	2.89
	Pruritus 75%: Cumulative 75% response rate on the handicaps of pruritus	mITT	22.0%	7.3%	0.0322	3.13
		PP	24.7%	7.3%	0.0146	3.69
	Mean change in tryptase level relative to baseline at week 24, in patients with baseline level ≥20 µg/L.	mITT	-18.0%	2.2%	0.0001	-
		PP	-20.0%	2.2%	<.0001	-
Other supportive analyses	Flush 75%: Cumulative 75% response rate on the handicaps of flush	mITT	39.9%	19.0%	NA	3.03
		PP	41.2%	19.0%	NA	3.06
	Hamilton 75%: Cumulative 75% response rate on the handicaps of depression	mITT	18.6%	7.6%	NA	2.71
		PP	19.4%	7.6%	NA	2.87
	FIS 75%: Cumulative 75% response rate on the handicaps of fatigue	mITT	7.7%	3.2%	NA	4.84
		PP	8.4%	3.2%	NA	5.51

* P-value is based on re-randomization
Calculation is based on Missing Data Equal Failure (MDF) method, meaning that if a data is missing at a visit because the patient is not present at the visit, the response is recorded as a failure.
mITT: modified Intention to Treat
PP : Per Protocol
Not applicable: Not a statistical hypothesis of the study

Long-term follow-up (W0-W96 period)		Masitinib	Placebo	p-value	Odd ratio
4H75%: Cumulative 75% response rate on the handicaps of pruritus or flushes or depression or fatigue	mITT	17.2%	7.1%	0.0102	3.37
	PP	18.7%	7.1%	0.0062	3.66
3H75%: Cumulative 75% response rate on the handicaps of pruritus or flushes or depression	mITT	22.1%	8.6%	0.0030	3.10
	PP	24.1%	8.6%	0.0013	3.42

About the phase 3 study in severe systemic mastocytosis

The phase 3 study was designed to evaluate masitinib efficacy and safety in severe systemic mastocytosis patients, with or without D816V mutation of c-Kit. The primary objective of the phase 3 study was to detect a statistically significant difference between masitinib (plus optimal concomitant symptomatic treatments) and placebo (plus optimal concomitant symptomatic treatments) in cumulative response on four severe symptoms, referred to also as handicaps.

Patients enrolled in the phase 3 study had between one and four of the following severe mastocytosis-related symptoms at baseline:

- Pruritus score ≥ 9
- Number of flushes per week ≥ 8
- Depression measured by the Hamilton rating scale (HAMD-17) score ≥ 19
- Asthenia measured by the Fatigue Impact Scale total score ≥75

The study enrolled 135 patients with severe systemic mastocytosis in 15 countries, namely Austria, Czech Republic, France, Germany, Greece, India, Italy, Latvia, United Kingdom, USA, Poland, Russia, Slovakia, Spain, and Switzerland.

Primary objective:

Primary analysis (referred to as "4H75% response") was based on the comparison between masitinib and placebo in the number of actual responses between week 8 and week 24 divided by the total number of possible responses over the same treatment period. At each patient evaluation between weeks 8 and 24, each of the above four severe symptoms was evaluated. An improvement ≥ 75% with respect to baseline in one symptom represented one positive treatment response.

Methodology is based on Missing Data Equal Failure (MDF) method, meaning that if a data is missing at a visit because the patient is not present at the visit, the response is recorded as a failure.

Statistical calculation of the p-value is based on the GEE (generalized estimating equation) model that takes into consideration the correlation between both the responses across symptoms and the responses through time.

Secondary objectives:

Secondary analyses were based on the following endpoints:

- Cumulative 75%-response rate for pruritus (1H75% response)
- Cumulative 75% response rate on the handicaps of pruritus or flushes (2H75% response)
- Cumulative 75% response rate on the handicaps of pruritus or flushes or depression (3H75% response)
- Mean change in tryptase level relative to baseline at week 24, in patients with baseline level ≥20 µg/L.

Targeted population with masitinib in mastocytosis

Mastocytosis is an orphan disease characterized by an abnormal proliferation or activation of mast cells either in the skin or in bone marrow or other organs. Mastocytosis comes in two main forms: indolent and aggressive. Indolent forms of mastocytosis can be either cutaneous or systemic. The prevalence of indolent systemic mastocytosis, including smoldering systemic mastocytosis, is estimated to be 1/26,000 in Europe[2]. The symptoms and handicaps are severe in about one third of the patients; hence, an estimated target population for masitinib of approximately 1/78,000 of the general population.

Since the prevalence of indolent forms of systemic mastocytosis is reputed to be comparable across countries, the target population for masitinib could reach 10,000 adult patients in the USA and in Europe.

2: Prevalence of rare diseases: Bibliographic data, Orphanet Report Series, Rare Diseases collection, July 2015, Number 1: Listed in alphabetical order of disease or group of diseases.
http://www.orpha.net/orphacom/cahiers/docs/GB/Prevalence_of_rare_diseases_by_alphabetical_list.pdf

Orphan Drug Status

Masitinib has been granted orphan drug status in mastocytosis by both FDA and EMA.
There is currently no drug approved for the treatment of indolent mastocytosis.
Masitinib is the first drug to be evaluated in phase 3 in the indolent form of mastocytosis, systemic or not, severe or not.

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 first-line and second-line GIST, metastatic melanoma expressing JM mutation of c-Kit, multiple myeloma, metastatic colorectal cancer, metastatic prostate cancer, pancreatic cancer, T-cell lymphoma, mastocytosis, severe asthma uncontrolled by oral corticosteroid, 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 website: http://www.ab-science.com

This document contains prospective information. No guarantee can be given as for the realization 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.

* * *

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