Paris, 25 November 2019, 8.15am



# Summary of webcast with Key Opinion Leaders on Indolent Systemic Mastocytosis

**AB Science SA** (NYSE Euronext - FR0010557264 - AB) is providing a summary of the live webcast on November 20 with key opinion leaders on indolent systemic mastocytosis (ISM) and the role that masitinib may play in treating this disorder.

The presentation of the webcast is available on the company's website. A replay of the webcast is available at the following address: <u>https://viavid.webcasts.com/starthere.jsp?ei=1269879&tp\_key=e0397d61a9</u>

The webcast provides:

- An overview of mastocytosis.
- Current treatment options and new treatments in development for the disease.
- An overview of the masitinib profile and prior Phase 3 results in indolent systemic mastocytosis (published in *The Lancet* in 2017).

## Experts opinion on mastocytosis

Mastocytosis can be categorized into cutaneous mastocytosis and systemic mastocytosis. Systemic mastocytosis (SM) can be further categorized into indolent SM, smouldering SM and aggressive SM (ASM, SM-AHN, MCL). Patients with indolent SM or smouldering SM have a (nearly) normal life expectancy, while patients with aggressive SM have a median overall survival of approximately four years. About 90% of patients express a specific mutation of c-kit (D816V), which is activating mast cells.

The planned indication for masitinib is indolent systemic mastocytosis (ISM) and smouldering systemic mastocytosis (SSM), which are the most prevalent forms of mastocytosis, accounting for approximately 60% of patients.

Patient with ISM or SSMS experience multiple symptoms, which can be severe and considered for some patients as not tolerable. The quality of life of patients with mastocytosis is overall severally affected. Patients suffer from itching, flushing, nausea, diarrhea, brain fog, anxiety, depression, and acute episodes of anaphylaxis among other debilitating symptoms Cognitive impairment and depression are prominent features of the disease.

While aggressive SM therapy is based on registered cytoreductive treatments (cladribine, midostaurin), treatment of ISM and SSM remains a challenge as conventional symptomatic therapies fail to improve severe symptoms.

There is a high unmet need in ISM/SSM for new therapeutic options with demonstrated activity on severe symptoms and adequate safety profile for a life-long treatment.

Masitinib is the leading program in ISM and a viable approach to this goal. It is currently the only drug in phase 3 for a claim on indolent systemic mastocytosis. The key differentiating factors of masitinib are:

 Safety profile: Most frequent AEs occurring at treatment start (rash, diarrhea, nausea) can be managed by judicious dose-escalation in the first two months of treatment. Based on available data, there is no apparent long-term cumulative toxicity with masitinib and no vascular toxicity. Midostaurin and Avapritinib, two tyrosine kinase inhibitors active in aggressive forms of SM, have demonstrated numerous side effects, sometimes life-threatening, challenging their use in classical therapy-resistant ISM/SSM patients. Numerous patients remain on masitinib for years without exhibiting significant adverse effects

- Efficacy on neurology symptoms: Patients complain first about neurological symptoms, and masitinib has proven efficacy on these neurology symptoms, namely depression and asthenia.
- Masitinib has already been proved as highly efficacious on severely handicapped ISM/SSM patients in two well-conducted proof of concept studies and one Phase 3.
- Favorable long-term safety profile is key as patient need life-long treatment, and masitinib fulfill this requirement based on currently available data, unlike other drugs.

In the opinion of certain experts, there is enough evidence to support the use of masitinib in the treatment of ISM/SSM with severe symptoms, and the GCP findings raised during the inspection of the first study AB0006 do not affect the overall positive benefit risk assessment in favor of masitinib.

The European Competence Network (ECNM), the largest network of experts working in the field of mastocytosis, considers that masitinib, thanks to its selectivity on mast cell activation and safety profile, is very adequate to control severe handicaps in symptomatic ISM/SSM patients.

## Masitinib clinical program in mastocytosis

Masitinib is a selective kinase inhibitor that targets mast cells and macrophages/microglia. Masitinib inhibits mast cells, regardless of c-Kit mutation status, through inhibition of c-Kit, Lyn and Fyn kinases. The safety profile of masitinib is sufficiently understood with over 6,000 patients enrolled in clinical studies.

The clinical program in mastocytosis is comprised of two proof of concept studies, one Phase 3 study (*published in the Lancet*), and one Phase 3 confirmatory study.

- Clinical proof of concept has been established both in patients with and without D816V c-Kit mutation. In these two proof of concept studies, masitinib showed a significant reduction of symptoms associated with flush (range from -60% to -74%), pruritus (range from -36% to -45%), fatigue (range from -30% to -38%), and depression (range from -43% to -49%). The majority of patients in phase 2 chose to remain on masitinib over the long term, and some have been treated for more than 7 years. Masitinib also had an effect on mast cells in the skin, as shown by the reduction in urticaria pigmentosa. In addition, imaging showed that masitinib may be able to reverse cerebral hypoperfusion in mastocytosis patient, correlating with improved cognitive function.
- In the first phase 3 study (AB06006) evaluating masitinib versus placebo in 135 patients with ISM and severe symptoms at baseline, the pre-specified primary and secondary analyses on symptoms were positive and supported efficacy based on odds ratio. Study results showed that masitinib administered at 6.0 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=0.0076, Odd ratio=3.63) in the mITT population (primary analysis). Masitinib also demonstrated significant activity on objective markers of mast cell activation and burden (i.e. level of tryptase, body surface area with urticaria pigmentosa, and presence of Darier's sign). The most frequent severe adverse events were related to gastrointestinal disorders and skin cutaneous disorders. No life-threatening toxicities occurred.

A phase 3 confirmatory study (AB15003) is planned in order to request a marketing authorization. Three optimizations of the phase 3 confirmatory study have been implemented based on the first phase 3 and are increasing the probability of success of the study.

 Dose titration: In the first phase 3 study, the starting dose of treatment was 6 mg/kg/day. This led to 20% treatment discontinuation, with discontinuation being counted as treatment failure in the analysis, hence penalizing masitinib. With dose titration from 3.0 to 4.5 and then 6.0 mg over two months period, marginal discontinuation rate is expected, which will favor efficacy assessment of masitinib.

- Recording of rescue therapy: In the first phase 3 study, patients could take rescue treatment in case of
  worsening of symptoms, which favored the placebo arm. In the new study, rescue treatment will be
  counted as treatment failure in the analysis.
- Run-in period: In the first phase 3 study, there was no run-in to ensure that patients were taking
  optimal symptomatic treatment at screening. In new study, one-month run-in period to control failure
  to symptomatic treatment.

This phase 3 confirmatory study is being initiated and patient enrolment is expected to be initiated in Q1 2020. The design benefited from scientific advices and recommendation from health authorities, and from the previous registration procedure of AB06006 study. The study is expected to enroll its first patients in Q1 2020 and plans to enroll 140 patients from around 30 specialized centers.

Masitinib IP rights are secured up to 2031 in the US and potentially 2036 in Europe in ISM.

## **KOL Biography**

The following key opinion leaders participated in the webcast:

**Cem AKIN, MD, PhD**: Dr. Akin is currently a Professor of Allergy and Immunology in the Department of Internal Medicine at the University of Michigan. He is co-chair of the steering committee of the American Initiative in Mast Cell Diseases (AIM) and a member of the Medical Advisory Board of The Mastocytosis Society (TMS).

**Michel AROCK, PharmD, PhD:** Dr. Arock is professor of physiology and hematology at the Ecole Normale Supérieure of Paris-Saclay and is currently heading the Functional Unit for Biological Emergencies within the Hospital Pitié-Salpêtrière Charles-Foix in Paris. He has conducted researches on the physiology of mast cells and on the pathophysiology and treatment of mastocytosis for many years. He has also co-authored more than 180 publications referenced in Medline and is currently the Chair (2015-2020) of the European Competence Network on Mastocytosis (ECNM).

**Mariana CASTELLS, MD, PhD**: Mariana Castells is a Professor at Harvard Medical School. She is a clinician/teacher/researcher at the Brigham and Women's Hospital Rheumatology, Immunology and Allergy Division serving as Director of Drug Hypersensitivity and Rapid Desensitization Center and the Director of the Mastocytosis Center. In 2005, Dr. Castells was the founding Chair of the Task Force on Mast Cell Disorders of the American Academy of Allergy, Asthma and Immunology. Dr. Castells is a member of the American Initiative in Mast Cell Diseases (AIM) Organizing Committee and a member of the Medical Advisory Board of The Mastocytosis Society (TMS).

**Olivier HERMINE, MD, PhD**: Olivier Hermine is Professor of Hematology at Paris V-René Descartes University, Chief of adults Hematology staff at Hospital Necker (Paris), member of the French *Académie des Sciences* and author of 365 international publications. He is founder and coordinator of the reference center of mastocytosis (CEREMAST). He is member of the Medical Advisory Board of The Mastocytosis Society (TMS), a US non-profit organization dedicated to supporting patients affected by Mastocytosis or Mast Cell Activation Diseases. Olivier Hermine is also co-founder of AB Science and Head of its scientific committee.

### 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.

AB Science has developed a proprietary portfolio of molecules and the Company's lead compound, masitinib, has already been registered for veterinary medicine and is developed in human medicine in oncology, neurological diseases, and inflammatory diseases. The company is headquartered in Paris, France, and listed on Euronext Paris (ticker: AB).

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

### 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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