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Masitinib treatment of progressive multiple sclerosis

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AB Science SA (NYSE Euronext - FR0010557264 - AB), a pharmaceutical company specializing in the research, development and commercialization of protein kinase inhibitors (PKIs), announces the publication of results from the human phase 2 study of masitinib carried-out in the treatment of progressive multiple sclerosis. Entitled, '*Masitinib treatment in patients with progressive multiple sclerosis: a randomized pilot study*', this article is freely accessible online from BioMed Central's peer-reviewed journal **BMC Neurology** (http://www.biomedcentral.com/1471-2377/12/36/abstract).

- **Phase 2 study establishes proof-of-concept that oral masitinib has potential therapeutic benefits in patients with progressive forms of multiple sclerosis**

- **Overall, results add new scientific data to the important question of the potential role of anti inflammatory agents in the management of progressive multiple sclerosis**

- **A phase 3 study has been initiated based upon these promising results**

Reported are results from a phase 2 study of 30 patients, conducted by Professor Patrick Vermersch (CHRU Lille - Hôpital Roger Salengro, France) and colleagues from six study centers across France, investigating the hypothesis that masitinib's targeted inhibitory action on mast cells can delay the onset of symptoms associated with progressive forms of multiple sclerosis. There is currently no satisfactory treatment for primary progressive multiple sclerosis or relapse-free secondary progressive multiple sclerosis, which represent approximately 60% of patients diagnosed with multiple sclerosis. Neuroinflammation is thought to be important in progressive multiple sclerosis pathogenesis. Mast cells are a key component of the inflammatory network and participate in the regulation of the blood-brain barrier's permeability. Masitinib is an oral tyrosine kinase inhibitor that effectively down-regulates mast cell functions and therefore, represents a different approach to those therapeutic strategies currently developed. The results showed that for the primary endpoint of Multiple Sclerosis Functional Composite (MSFC) score (which measure symptoms of patients on three aspects: movement of the lower limbs, movement of the upper limbs, and cognitive tests) 32% of patients treated with masitinib were responders against 0% under placebo. Responses were seen in the third month and were more-or-less sustained over the study's 18-month duration. These results suggest that daily administration of masitinib is of therapeutic benefit to progressive forms of multiple sclerosis and could therefore represent an innovative avenue of treatment for this disease.

Professor Vermersch commented: "*Masitinib is a selective inhibitor of specific kinases that play a major role in the activation of mast cells, which are cells involved in the immune response, in the recruitment of lymphocytes to the brain, and also in inflammatory processes associated with multiple sclerosis and many of its resulting symptoms. Masitinib therefore represents an oral treatment different from those drugs already on the market for this indication, with a unique mechanism of action in blocking mast cells. Masitinib showed promising signs of retarding the onset of symptoms associated with progressive multiple sclerosis as compared to placebo, with an acceptable tolerance profile. Although the number of patients in this study was too small to make any definitive conclusions about treatment efficacy, the evidence is sufficiently compelling to warrant further phase 3 investigation.*"

Professor Olivier Hermine, President of the scientific committee of AB Science and co-corresponding author on this paper declared: *"Masitinib differs from those treatments currently available or under development*

in multiple sclerosis. It has a weak immunosuppressive activity, although by inducing a reduction in the number of lymphocytes infiltrating the brain it helps prevent injuries. Masitinib's characteristic selectivity against mast cells also means that it is not associated to date with major toxicities; for example, cardiac toxicity as seen with mitoxantrone, a drug sometimes used in severe progressive multiple sclerosis, or opportunistic infections as seen with Tysabri or Gilenya, which are associated with an increased risk of infection."

Summary of the phase 3 trial in progress

A phase 3 international, multicenter, randomized, double-blind, placebo-controlled study was initiated with the objective of comparing the efficacy and safety of masitinib with placebo in the treatment of patients with progressive forms of multiple sclerosis. This study will enroll approximately 450 patients with primary progressive multiple sclerosis or relapse-free secondary progressive multiple sclerosis across 60 centers around the world, randomized with a ratio of 2:1 between the masitinib and placebo groups. The primary response evaluation will be the proportion of patients to achieve an improvement of at least 100% in their symptoms, as measured by Multiple Sclerosis Functional Composite (MSFC) score, after 96 weeks of treatment. An independent data monitoring committee will analyze the unblinded efficacy and safety data for analysis of the primary criteria at week 48. This analysis will be performed for each stratum (primary progressive and secondary progressive without relapses) and the general population.

About multiple sclerosis

Multiple sclerosis is an inflammatory and neurodegenerative disease of the central nervous system. Commencing at an average age of 30 years (20-40 years) with a female preponderance, it is the leading cause of non-traumatic severe disability in young patients, and affects about 2.5 million people worldwide, including approximately 400,000 in the United States and 80,000 in France. Multiple sclerosis probably results from an interaction of genetic susceptibility and one or more environmental factors including infectious agents such as viruses, the role of which has long been suspected but never proven. This manifests itself as an attack on the myelin sheath that surrounds the nerve fibers and acts to accelerate the flow of nerve impulses. Repeated inflammatory attacks will affect the functioning of these neural pathways by causing movement disorders (decreased muscle strength), sensory disturbances (change in the sensation of hot and cold, touch, tingling, etc.), balance disorders, visual disturbances and urinary problems.
A recent report by visiongain predicts that revenues for disease-modifying treatments for multiple sclerosis will rise to USD$15.8 billion annually in 2015.

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 in veterinary medicine in Europe and in the USA, and is pursuing 10 phase 3 studies in human medicine – one being analyzed in pancreatic cancer and 8 on-going studies including GIST in first-line, GIST in second-line, metastatic melanoma expressing JM mutation of c-Kit, multiple myeloma, mastocytosis, severe persistent asthma, rheumatoid arthritis, and progressive multiple sclerosis. The company is headquartered in Paris, France, and listed on Euronext Paris (ticker: AB).

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.

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