Paris, 11 April 2016, 8.00am

Masitinib in Amyotrophic Lateral Sclerosis (ALS)

Summary of Webcast

AB Science SA (NYSE Euronext – FR0010557264 – AB), a pharmaceutical company specialized in research, development and marketing of protein kinase inhibitors (PKIs), provides a summary of the key points of the web conference held on 08 April 2016 with key opinion leaders on masitinib in the treatment of amyotrophic lateral sclerosis.

Amyotrophic lateral sclerosis (ALS), also known as Lou Gehrig's disease and Charcot disease, is a life-threatening neurological disease that causes muscle weakness, disability and eventually death. Only around 10% of patients live past 10 years with 80% of patients die within 5 years. ALS represents a high unmet medical need with an estimated combined target population in the USA and EU of 50,000 patients.

The only drug registered in this indication is Riluzole, which was registered in 1996. There has been no advance in availability of effective therapeutic agents over the last 20 years. All studies in this indication failed.

Design of study AB10015

The study was initiated as a phase 2, transformed at early stage into a phase 3. The study remained blinded. A resampling was done while endpoints and hypothesis on treatment effects remained similar. The study followed a classical design and used the endpoints recommended by the guideline.

Study AB10015 is a blinded, placebo controlled, 3-treatment arms (randomisation 1:1:1), testing 2 doses of masitinib (3 and 4.5 mg/kg/day) in add-on to riluzole, versus placebo plus riluzole. Treatment duration is 48 weeks. Efficacy assessment was based on endpoints validated by regulatory authorities.

- Primary endpoint: ALSFRS-R (Amyotrophic Lateral Sclerosis Functional Rating Scale)
- Secondary endpoints : FVC (Forced Vital Capacity) , CAFS (Combined Assessment of Function and Survival)
- Supportive endpoints : ALS-AQ40 (Quality of life), survival

The planned enrolment was 381 patients, with a pre-planned futility analysis with 30% of patients enrolled treated for 48 weeks, and a pre-planned interim analysis with 50% of patients enrolled treated for 48 week.

The interim analysis was based on 192 patients in 3 arms, equivalent to 64 patients per arm. The objective of the interim analysis was to conclude on efficacy prior to completion of the study and to discuss with regulatory authorities about early filing based on interim result, or to adjust the sample size if the study was under-powered. The protocol did not specify to stop the study in case interim analysis was successful.

The primary hypothesis was to detect a difference in the mean change of ALSFRS-R between placebo group and masitinib group after 48 weeks with a 0.0311 significance level, using a Pocock alpha spending method. Efficacy analyses were conducted in a stepwise manner. Fixed sequence method was used to control the global family-wise error rate at the 0.0311 level for the primary analysis for each dose. Secondary analyses (FVC, CAFS, ALS-AQ40, OS) were performed only if primary analysis was significant, therefore at a 0.05 significance level. The dataset was analysed in the ITT population, using LOCF method (last observation carried forward).

Status of study AB10015

Patients were enrolled in sites in Europe, Argentina and Canada, (not USA).

The patient recruitment was completed in December 2015 with 392 patients. Recruitment at interim and final analysis was made 2/3 in Europe and 1/3 outside Europe.

Next steps

AB Science will initiate discussion with EMA and FDA regarding the possibility to file for marketing authorization.

Outcome of interim analysis

The study is not stopped at this time for the following reason.

- Obtain more mature survival data
- Obtain long term safety data
- Protect the scenario of conditional approval with condition being that analysis with 392 patients at week 48 is confirmatory

The recruitment is completed therefore there is no impact on recruitment. Follow-up data will be available in Q1 2017.

To protect the follow-up phase of the study, no data can be disclosed at this time such as providing exact p-value, treatment effect or dose effect which is considered by the authorities as a potential bias.

All precautions were taken to ensure that the follow-up part of the study is unbiased. A procedure was documented describing who performed the analysis and who accessed the interim analysis results. Furthermore, it is not feasible for investigators or patients to predict if treatment received is masitinib+riluzole or placebo+riluzole based on adverse events of masitinib or riluzole. Indeed, most frequent adverse events with masitinib are gastro-intestinal disorders (diarrhea, nausea, vomiting) and skin and subcutaneous disorders (rash, pruritus, erythema) and rarely neutropenia. Riluzole generates the same disorders (diarrhea, nausea, vomiting, and rash, pruritus, erythema) and rarely neutropenia.

The phase 2/3 was a success at the interim analysis based on pre-specified primary endpoint on ALSFRS-R. ALSFRS-R is a validated([1]) rating score for monitoring the progression of disability in patients with ALS, which takes into account both quality of life and survival. Primary analysis in ITT population is successful with p-value <1%. P-value <1% can be considered as a substantial evidence of efficacy based on guideline for registration under single pivotal study. The hypothesis of the study was to detect a difference of around 3 points in ALSFRS-R at week 48 between the two treatment arms with a 0.0311 significance level. The placebo in the ALS studies typically deteriorates by 1 point per month, so 12 points in 12 months. The objective was therefore to detect a 25% difference in deterioration, a difference considered clinically relevant. Given the p-value was below 1%, this means that the treatment effect was clinically significant.

The primary analysis was supported by all sensitivity analyses. The first method of sensitivity analysis was based on reasons for discontinuation and was positive. Different methods of missing data imputation based on the reasons of discontinuation were used, in line with “Guideline. EMA/CPMP/EWP/1776/99 Rev. 1”. The second method of sensitivity analysis was based on multiple imputation and was successful. Multiple imputation is a statistical technique based on regression model permitting to analyze data sets that are incomplete because of missing entries, such as discontinuation. Values at week 48 for patients who discontinued are calculated from the values of patients who reach week 48. The simulation is repeated 500 times.

The phase 2/3 was a success at the interim analysis based on the forced vital capacity (FVC) [(1)]. FVC is the vital capacity (VC) measured when the patient is exhaling with maximal speed and effort. Significant benefit

---

1 http://www.ema.europa.eu/docs/en_GB/document_library/Scientific_guideline/2015/12/WC500199241.p

confirmed with sensitivity analyses with different data censoring method based on reason of discontinuation.

The phase 2/3 was a success at the interim analysis based on CAFS[(2)]. CAFS ranks each patient against all other patients based on survival time and change in ALSFRS-R score. CAFS is a recognized as a valid endpoint by FDA.

The phase 2/3 was a success at the interim analysis based on ALS-AQ40. ALS-AQ40 is a questionnaire to assess the quality of life.

There was no bias at the interim analysis

- There was no bias in baseline characteristics
- There was no unexpected placebo effect
- There was no bias due to center effect or country effect.

The safety profile of masitinib in combination with riluzole appeared acceptable.

- The Independent Data and Safety Monitoring Board (DSMB) reviewed safety data frequently during the study and always recommended the continuation of the study on this basis.
- The frequency of adverse events was comparable between the two treatment arms (for the first dose tested)
- The frequency of serious adverse events was comparable between the two treatment arms (for the first dose tested)
- The frequency of adverse events leading to treatment discontinuation was comparable between the two treatment arms (for the first dose tested)
- One isolated case autoimmune hepatic toxicity was reported. Masitinib can generate ALT increase and riluzole appears to have potential hepatotoxic effects with cytolytic and cholestatic effects and may cause liver dysfunction.
- ALS is a life threatening disease

Furthermore, the safety profile of masitinib is well characterized, The safety database includes over 4,000 patients enrolled in various clinical studies, including more than 2,500 exposed to masitinib.

Study rationale

- Glia is a key therapeutic target in ALS. Indeed, there is a proliferation of microglia and aberrant microglia in ALS patient, and dysfunctional glial cells contribute to progressive motoneuron death in ALS.
- Masitinib targets microgia via M-CSFR1. The IC50 of masitinib on M-CSFR1 is 90nM and masitinib dose of 3 mg/kg/day or 4.5 mg/kg/day provide a concentration above the IC50.
- In-vivo and in-vitro data show that masitinib decreases glia proliferation, astrocytes migration and potently reduces microgliosis (accumulation of microglia cells) in $SOD1^{G93A}$ rats. In $SOD1^{G93A}$ rats, masitinib reduces motor neuron death and protects motor neuron atrophy.
- Masitinib generated positive preclinical results at therapeutic dose for human. Masitinib delayed the onset of symptoms and improves grip strength in ALS $SOD1^{G93A}$ mice. In two randomized, blinded trials, masitinib increased the survival of $SOD1^{G93A}$ rats whether given immediately at the onset of gait abnormalities or 7 days after gait onset.

The phase 2/3 study with masitinib suggests that microglia is a relevant target in ALS.

Intellectual property

[2] A new endpoint for ALS clinical trials., Berry JD1, Miller R, Moore DH, Cudkowicz ME, van den Berg LH, Kerr DA, Dong Y, Ingersoll EW, Archibald RRY & al 2013

IP rights for masitinib are secured in ALS until 2028 and potentially until 2036 based on a recently filed phase 3 patent.
Masitinib has been granted orphan drug status in ALS by FDA (filing at EMA pending). This status provides exclusivity of 7 years in USA and 10 years in Europe.

Targeted population with masitinib in ALS

ALS incidence is high but prevalence is low due to the rapid fatal outcome of the disease. There are approximately 50,000 people with ALS in the European Union and in the US, with more than 16,000 new cases diagnosed each year in Europe and in the US.

Commercial approach in case of registration

In case of registration, a stand-alone strategy for commercialization in the USA and Europe would be pursued.

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 lines of treatment in cancers, inflammatory diseases, and central nervous system diseases, both in human 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 twelve 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, 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's website: 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