



AB SCIENCE PROVIDES AN UPDATE ON AB8939, A NOVEL MICROTUBULE DESTABILIZER ESCAPING MULTIDRUG RESISTANCE AND STEM CELL TARGETED ALDH INHIBITOR, CURRENTLY IN PHASE 1

Paris, 17 December 2024, 7pm CET

AB Science SA (Euronext - FR0010557264 - AB) today provides an update on its AB8939 program in acute myeloid leukemia (AML).

The webcast presentation is available on the company's website, in the section « Press Releases »: <https://www.ab-science.com/news-and-media/press-releases/>

Highlights of the presentation are the following:

AB8939 target product profile

AB8939 is a next generation synthetic microtubule destabilizer and stem cell targeted ALDH1/2 inhibitor with key differentiating factors for treatment of refractory/relapsing acute myeloid leukemia (AML).

- AB8939 blocks proliferating leukemia cells through microtubules

AB8939 destabilizes microtubule, is not subjected to multidrug resistance as it does not bind to Pgp, responsible of efflux outside the cells and AB8939 is not degraded by the enzyme myeloperoxidase.

- AB8939 targets leukemia cancer stem cells through inhibition of ALDH

AB8939 inhibits ALDH1/2 and favors the bone marrow repopulation of normal progenitors.

- AB8939 is well suited for the treatment of relapsed or refractory AML

AB8939 has activity seen across refractory AML cell lines, has an additive effect with referenced first line treatment for AML, namely cytarabine, azacitidine and venetoclax.

- AB8939 has a potential use in AML with MECOM

AB8939 has shown a signal of efficacy in AML with MECOM gene rearrangement, a subset of patients that show extreme resistance to chemotherapies and exhibit the worst survival prognosis

- AB8939 shows absence of hematological toxicity based on clinical data

Addressable market with AB8939 in relapsed/refractory AML

Treatments in relapsed or refractory AML represent an estimated market size potential above EUR 2 billion per annum.

Region	Incidence Case (1)	% Relapse or Refractory (2,3)	% Insured Patients (4)	Drug Price (€)	Market Size (per in Mio EUR)
USA / CANADA	23,700	50%	90%	100,000 ⁽⁵⁾	1 000 000
EUROPE	27,600		90%	60,000	770 000
APAC	27,800		30%	60,000	250 000
INDIA	11,000		30%	60,000	100,000
LATAM	7,200		30%	60,000	65 000
MENA	3,900		30%	60,000	35 000
TOTAL	90,200				2 200 000

EUROPE = EU27 + Norway + United Kingdom + Switzerland ; APAC = Australia, People's Republic of China , Japan, New Zealand, Singapore, Taiwan ; LATAM = Argentina, Brazil, Chile, Colombia, Costa Rica, Mexico ; MENA = Algeria, Bahrain, Egypt, Israel, Kuwait, Morocco, Oman, Qatar, Saudi Arabia, Tunisia, United Arab Emirates

- (1) Zhou, Y et al. Global, regional, and national burden of acute myeloid leukemia, 1990–2021: a systematic analysis for the global burden of disease study 2021. *Biomark Res* 12, 101 (2024).
- (2) Ravandi F. Relapsed acute myeloid leukemia: Why is there no standard of care *Best Pract Res Clin Haematol.* 2013;26(3):253-9
- (3) Walter RB et al. Resistance prediction in AML: analysis of 4601 patients from MRC/NCRI, HOVON/SAKK, SWOG and MD Anderson Cancer Center. *Leukemia* (2015) 29:312–20. .
- (4) Estimated
- (5) Choi M. et al. Costs per patient achieving remission with venetoclax-based combinations in newly diagnosed patients with acute myeloid leukemia ineligible for intensive induction chemotherapy. *Journal of Managed Care & Specialty Pharmacy* Volume 28, Number 9. <https://doi.org/10.18553/jmcp.2022.22021>

Non clinical pharmacology

Animal experiments have shown the following properties for AB8939 relevant for the treatment of AML:

- AB8939 is active against chemotherapy naive or chemotherapy refractory/relapsing patient's AML cancers cells ex vivo
- AB8939 eradicates blasts in Blood and Bone Marrow in 5-AraC-resistant (Cytarabine) PDX
- AB8939 increases survival and has an additive effect in combination with reference treatment Azacitidine and Venetoclax
- ALDHs expression is a hallmark of cancer stem cells (CSCs) and AB8939 is an inhibitor of ALDH1/2. Therefore, AB8939 is a targeted therapy for leukemia cancer stem cells
- AB8939 eradicates Leukemia Cancer Stem Cells in a human PDX AML model

Phase 1 preliminary safety

The objective of the phase 1 is to determine the maximum tolerated dose (MTD) for three different cycles of AB8939. The first step of the phase 1 has been completed with 28 patients enrolled, evaluating the maximum tolerated dose after 3 consecutive days of AB8939 treatment. The second step of the phase 1 is close to completion and enrolled 10 patients, evaluating the maximum tolerated dose after 10 consecutive days of AB8939 treatment.

The next step is to evaluate the maximum tolerated dose after 14 consecutive days of AB8939 treatment in combination with venetoclax or azacitidine and in combination with venetoclax plus azacitidine, both drugs being widely used on AML and for which AB8939 has shown an additive effect.

Preliminary activity in MECOM

MECOM is associated with a dismal outcome, with almost all patients dying within 12 months after relapse.

AB8939 is a stem cell ALDH targeted therapy with potential use in AML with MECOM.

- ALDH gene expression is a marker of survival prognosis in AML. The higher the expression, the worse the prognosis
- MECOM is associated with the worst prognosis in AML
- MECOM is a rearrangement or a mutation of the chromosome 3 locus Q26 that codes for the transcription factor gene EVI1 (Ecotropic virus integration site-1)
- The expression of ALDH1A1 is regulated by EVI1 and has an outstanding role in the formation and transformation of hematopoietic cells and in particular leukemia stem cells
- The hypothesis is that in MECOM, the rearrangement of chromosome 3 Q26 leads to EVI1 over-expressing ALDH1A and induces high resistance of leukemia stem cells, and AB8939 should have an impact on leukaemia stem cells by inhibiting ALDH1

AB8939 has shown activity on MECOM rearrangement, based on non-clinical data and early clinical data in relapsing/refractory line of treatment, with 50% response rate observed.

Planned phases 2

The next steps in the clinical development will be discussed with FDA and EMA.

The first intended step is to develop AB8939 in patients with MECOM AML, through a single arm study with less than 60 patients supporting an accelerated approval based on response rate.

The second objective is to position AB8939 in broader forms of AML and position AB8939 in relapsed or refractory AML.

The third objective is to capture the full market potential of AB8939 and position AB8939 in first line in combination with standard of care.

Intellectual property

AB8939 intellectual property rights in AML are secured until 2036 through a 'composition of matter' patent and potentially until 2044 in AML with chromosome abnormality, including MECOM, through a 'second medical use' patent.

AB Science is the sole proprietary holder of AB8939 and its family of compounds.

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, inflammatory diseases and viral diseases. 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.

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 published by AB Science. 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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