PRESS RELEASE

AB SCIENCE ANNOUNCES A NEW PUBLICATION ON BIORXIV THAT IDENTIFIES AND CHARACTERIZES A NOVEL SMALL SYNTHETIC MOLECULE, AB8939, AS A PROMISING DRUG CANDIDATE FOR TREATING REFRACTORY ACUTE MYELOID LEUKEMIA (AML) AND POTENTIALLY OTHER CANCERS

- **AB8939 is a promising drug candidate for refractory AML, especially for cases with poor prognoses such as complex karyotypes, MECOM rearrangements, and TP53 mutations**
- **AB8939 has dual action against both proliferating tumor cells (via tubulin disruption) and quiescent, resistant stem cells (via ALDH inhibition) making it a unique therapeutic agent**
- **Based on these findings, AB8939 is being evaluated in a Phase I/II clinical trial for relapsed or refractory AML**

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AB Science SA (Euronext - FR0010557264 - AB) today announced the publication of a new article on the preprint platform bioRxiv. This article is entitled 'Identification of AB8939, a novel synthetic microtubule destabilizer and ALDH inhibitor that overcomes multidrug resistance in tumor cells as a drug candidate for the treatment of refractory acute myeloid leukemia' and is freely accessible online from the bioRxiv website [1].

Professor Olivier Hermine, President of AB Science's Scientific Committee, member of the French Academy of Sciences and Head of the Hematology Department at Necker Hospital, commented: *"Our preclinical research has identified AB8939 as a powerful compound with a novel dual mechanism of action, which holds potential for treating high-risk acute myeloid leukemia. The data indicate that AB8939 disrupts microtubule formation, a classic anti-cancer strategy, and inhibits ALDH enzymes, which are implicated in therapy resistance and the survival of leukemic stem cells. We demonstrated that AB8939 overcomes formidable drug resistance pathways, such as P-gp efflux, and is highly effective against patient-derived AML cells that are resistant to standard therapies. Most importantly, our work in advanced preclinical models shows that it can eradicate the leukemic stem cells that fuel this disease, a critical step toward preventing relapse. These robust findings provide a strong scientific rationale for the ongoing clinical trials and represent a tangible step toward developing a new, effective therapy for patients with high-risk and refractory AML."*

The key findings are as follows.

- **AB8939 has a novel dual-targeting mechanism of action**
  - **Microtubule Destabilizer:** It acts as a microtubule-targeting agent (MTA) by binding to the colchicine-binding site on β-tubulin. This interaction disrupts the microtubule network, leading to cell cycle arrest in the G2/M phase and subsequent apoptosis (programmed cell death).
  - **ALDH Inhibitor:** Through reverse proteomics, aldehyde dehydrogenases (ALDH), specifically ALDH1 and ALDH2, were identified as secondary targets of AB8939. AB8939 is a potent inhibitor of these enzymes, which are often overexpressed in tumors and are associated with cancer stem cells, tumor progression, and resistance to therapy.
- **AB8939 has potent and broad antiproliferative activity**

- AB8939 demonstrated strong and broad-spectrum antiproliferative activity against a wide variety of human cancer cell lines, with particularly high potency against hematopoietic cancers, with IC_{50} values in the nanomolar range.

- **AB8939 can overcome several major mechanisms of drug resistance in cancer cells**
  - **P-glycoprotein (P-gp) Efflux:** Unlike many conventional chemotherapeutics (e.g., doxorubicin and vincristine), AB8939 is not a substrate for the P-gp efflux pump. This allows it to remain effective in cancer cells that overexpress P-gp, a common cause of multidrug resistance (MDR).
  - **β3-tubulin Expression:** The molecule retains its efficacy in cell lines with high expression of β3-tubulin, another factor linked to resistance against microtubule-targeting agents.
  - **Chemoresistance in AML:** It shows high cytotoxicity against AML patient blasts, including those resistant to standard-of-care agents such as cytarabine (Ara-C) and vincristine.

- **In vivo evidence supporting the therapeutic potential of AB8939 in AML**
  - In an Ara-C-resistant AML mouse model (MOLM-14), AB8939 treatment significantly inhibited tumor growth and increased survival rates.
  - In a patient-derived xenograft (PDX) model of high-risk AML (TG-LAM-75 with MECOM rearrangement), AB8939 monotherapy was effective, and its combination with azacitidine led to near-complete disease clearance with a manageable safety profile.
  - AB8939 effectively eradicated leukemic stem cells (LSCs) in an AML PDX model (TG-AML-36), suggesting that it could reduce the risk of disease relapse.

Clinical study AB18001

AB8939 is currently being evaluated in a Phase I/II clinical trial (AB18001, NCT05211570) in patients with refractory and relapsed AML. AB Science recently received regulatory approval to initiate the third stage of this study, which combines the molecule AB8939 with venetoclax for the treatment of acute myeloid leukemia [2].

The objective of the Phase 1 study was to determine the maximum tolerated dose (MTD) for different treatment cycles of AB8939.

- Stage 1: Determination of the MTD after three consecutive days of treatment with AB8939 alone.
- Stage 2: Determination of the MTD after 14 consecutive days of treatment with AB8939 alone.
- Step 3: Determination of the MTD after 14 consecutive days of treatment with AB8939 in combination with venetoclax.
- Stage 4: Determination of MTD after 14 consecutive days of treatment with AB8939 in combination with venetoclax and azacitidine.

The first two stages of Phase 1 were completed with 28 and 13 patients enrolled, respectively, and the MTD of AB8939 was determined after 3 consecutive days of treatment (21.3 mg/m^2) and after 14 consecutive days of treatment (21.3 mg/m^2). The third stage now consists of evaluating the MTD after 14 consecutive days of treatment with AB8939 in combination with venetoclax, a standard treatment for AML.

Intellectual property protection until 2036 or even 2044 and orphan drug protection

AB8939 was discovered by AB Science, which retains full ownership of the intellectual property rights, reflecting AB Science's priority to develop innovative drugs aimed at improving patients' lives.

The composition of AB8939, including its use in the treatment of AML, is covered until 2026 by a patent granted in all geographical areas where AB8939 could be marketed, including Europe (patent EP 3253749), the United States (US 10,570,122), Canada (CA 2975644), China (CN 107531685), South Korea (KR 10-2544132), Japan (JP 6713000), Hong Kong (HK 1243700), Israel (IL 253779), Australia (AU 2016214283), Russia (RU 2758259), Brazil (BR 112017016883-9), Mexico (MX 377742), India (IN 480996), and South Africa (ZA 2017/05537).

A second patent application for medical use was filed to protect the use of AB8939 in the treatment of AML with specific chromosomal abnormalities. If this application is accepted, the protection for AB8939 will be extended until 2044 for these subpopulations of AML patients.

In addition to patent protection, AB8939 is eligible for regulatory data protection in numerous countries, preventing generic competition for up to 8 years from product registration.

AB8939 has also received orphan drug designation for AML by both the European Medicines Agency (EMA) and the US Food and Drug Administration (FDA). This orphan drug designation confers 10 and 7 years of marketing exclusivity in Europe and the US, respectively, from the date of the product registration.

References

[1] Humbert M, Letard S, Goubard A, et al. Identification of AB8939, a novel synthetic microtubule destabilizer and ALDH inhibitor that overcomes multidrug resistance in tumor cells as a drug candidate for the treatment of refractory acute myeloid leukemia. bioRxiv 2025.12.10.692519; doi: https://doi.org/10.64898/2025.12.10.692519.

[2] AB Science press release 30/07/2025. https://www.ab-science.com/ab-science-receives-regulatory-approval-from-european-countries-to-initiate-third-stage-of-phase-i-ii-study-combining-its-molecule-ab8939-with-venetoclax-for-the-treatment-of-aml/

About bioRxiv

BioRxiv (pronounced "bio-archive") is a free online archive and distribution service for unpublished preprints in the life sciences. It is operated by Cold Spring Harbor Laboratory, a not-for-profit research and educational institution. By posting preprints on bioRxiv, authors are able to make their findings immediately available to the scientific community and receive feedback on draft manuscripts before they are submitted to journals.

About AB8939

AB8939 is a new synthetic molecule that targets cancer cells by destabilizing the microtubules essential for cell division and cancer stem cells by inhibiting enzymes (ALDH1A1 and ALDH2) essential for maintaining their physiological state and survival. The molecule '1-{4-[2-(5-ethoxymethyl-2-methylphenylamino)-oxazol-5-yl]phenyl}imidazolidin-2-one' is the chemical name of AB8939. The intellectual property of AB8939 is 100% owned by AB Science.

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 is 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.

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 being developed for human medicine in oncology, neurological diseases, inflammatory diseases, and viral diseases. The company is headquartered in Paris, France and is 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

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