

Paris, 02 September 2020, 8.15pm



New independent research reveals that masitinib has direct anti-viral activity against the SARS-CoV-2 virus *in vitro* and is a promising candidate for treating COVID-19

AB Science SA (NYSE Euronext - FR0010557264 - AB) today announced the publication of preclinical study results with masitinib in COVID-19. Research led by scientists from the University of Chicago has been posted on the bioRxiv preprint service as an article entitled, 'Drug repurposing screen identifies masitinib as a 3CLpro inhibitor that blocks replication of SARS-CoV-2 *in vitro*'. The article [1] is freely accessible online from the bioRxiv site <https://www.biorxiv.org/content/10.1101/2020.08.31.274639v1>

This article reports results of an independent study led by Professor Savas Tay from the Pritzker School for Molecular Engineering (University of Chicago, USA). Starting from a library of 1,900 clinically used drugs, either approved for human use or in late stage clinical development, masitinib stood-out in its ability to completely inhibit activity of the SARS-CoV-2 main protease (3CLpro), thereby blocking viral replication. Remarkably, the research team elucidated masitinib's mechanism of action against SARS-CoV-2, showing that masitinib inhibits 3CLpro, SARS-CoV-2 protease that is crucial for virus infection and reproduction, by directly binding to the protease catalytic site.

*"This research has shown for the first time that masitinib exerts a direct anti-viral effect on the SARS-CoV-2 virus, under *in vitro* conditions. Considering these data in conjunction with masitinib's possible action against life-threatening complications arising from COVID-19 related cytokine storm, suggests that it could be an effective treatment of COVID-19. As such, the clinical development program of masitinib in COVID-19, which includes to date one ongoing phase 2 study, is given a new impetus to determine masitinib's potential to treat COVID-19,"* said Dr Nir Drayman, senior researcher at the Pritzker School for Molecular Engineering (University of Chicago) and one of the article's principal authors.

"Masitinib's dual anti-viral and anti-inflammatory action is a highly attractive approach for combatting severe COVID-19 infections and is one that sets this compound apart from the majority of other drugs currently under development to treat COVID-19," said Professor Savas Tay, principal investigator of the study and author of the article (Pritzker School for Molecular Engineering, University of Chicago).

"These data identify a novel mechanism of action by which masitinib could exert an anti-viral effect against viral diseases by targeting virus protease. In particular, results provide a new compelling biological rationale for the use of masitinib in the treatment of COVID-19. Positive results from masitinib's development in severe uncontrolled asthma also provide a good indication that masitinib could be beneficial in the treatment of respiratory disorders such as COVID-19. Taken together, these data highlight the importance of conducting clinical studies with masitinib in COVID-19," commented Olivier Hermine (President of the Scientific Committee of AB Science and member of the Académie des Sciences in France).

➤ Key points from this research article include:

- The study objective was to identify safe-in-human drugs with potential anti-coronavirus properties from an initial library of 1,900 compounds, either approved for human use or with extensive safety data in humans (Phase 2 or 3 clinical trials).
- Masitinib significantly inhibited SARS-CoV-2 replication in human lung cells.
- Notably, masitinib completely inhibited 3CLpro activity. 3CLpro is the SARS-CoV-2 main protease, necessary for its viral replication cycle.
- X-ray crystallography revealed that masitinib directly binds to the active site of 3CLpro, thereby having a direct antiviral activity by blocking its enzymatic activity.

- Masitinib was also effective in blocking the replication of multiple picornaviruses (human pathogens that cause a range of diseases including meningitis, hepatitis, and poliomyelitis).
- Overall, masitinib was shown to have broad anti-coronavirus and anti-picornavirus activity.
- The study authors concluded that the anti-viral and anti-inflammatory properties of masitinib could be a strong clinical trial candidate for treating COVID-19 a viral disease characterized by lung inflammation.

Masitinib recently received authorization by the French Medicine Agency (ANSM) to initiate a Phase 2 study evaluating masitinib in combination with isoquercetin for the treatment of COVID-19 [2]. This study (AB20001) is a randomized (1:1), open-label Phase 2 clinical trial to evaluate the safety and efficacy of masitinib combined with isoquercetin in hospitalized patients with moderate and severe COVID-19. The study will enroll 200 patients (age ≥ 18 without an upper age limit) at medical centers in France and other countries. The primary objective is to improve the clinical status of patients after 15 days of treatment.

[1] Drayman N, Jones KA, Azizi S-A, et al. Drug repurposing screen identifies masitinib as a 3CLpro inhibitor that blocks replication of SARS-CoV-2 in vitro. bioRxiv 2020.08.31.274639; doi: <https://doi.org/10.1101/2020.08.31.274639>

[2] AB Science press release. May 06,2020. <http://www.ab-science.com/years/2020/>

About bioRxiv

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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: 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 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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