



NEW INDEPENDENT PUBLICATION CONFIRMS THAT MASITINIB HAS ANTI-VIRAL ACTIVITY AGAINST THE SARS-COV-2 VIRUS *IN VITRO* AND IS A PROMISING CANDIDATE FOR TREATING COVID-19

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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 Institute of Human Virology (Guangzhou, China) has been published in the peer-reviewed journal *mBIO* (a journal of the American Society for Microbiology). The article, entitled 'Engineering a reliable and convenient SARS-CoV-2 replicon system for analysis of viral RNA synthesis and screening of antiviral inhibitors', [1] is freely accessible online from the mBio journal site <https://mbio.asm.org/content/mbio/12/1/e02754-20.full.pdf>

This article reports results of an independent study led by Professor Yewen Luo and colleagues from the Institute of Human Virology (Guangzhou, China), describing development of a replicon system that has been used for high-throughput screening of antiviral drugs. Replicon systems permit convenient and safe simulation of virus replication to analyze the effects of various SARS-CoV-2 genes, the effects of pandemic SARS-CoV-2 gene variants, and the antiviral activities of small compounds.

Starting from a library of 1,680 clinically approved drugs, masitinib was one of just 5 candidate drugs selected for further study due to its potent inhibitory effect upon the replicon system and also its ability to block viral replication of authentic SARS-CoV-2 viruses. In both the replicon system and the authentic SARS-CoV-2 virus, masitinib demonstrated a submicromolar IC_{50} equal to 0.6 μM (this being a quantitative measure of how much of a particular inhibitory substance is needed to inhibit, *in vitro*, viral replication by 50%). This value is equivalent to that of masitinib-dependent SARS-CoV-2 replication inhibition in a model of Human Airway Epithelial cells. Importantly, such active concentration (0.6 μM) is reached in human patients at therapeutic dosing (6 mg/kg/day). The authors concluded that their findings supported a hypothesis that the RNA synthesis of SARS-CoV-2 could be directly dependent on a kind of phosphorylation regulation pathway or indirectly dependent on certain receptor tyrosine kinase pathways. These new results show that masitinib, in addition to be a direct antiviral drug blocking the 3CLPro, as was previously shown by research from the University of Chicago [2], could also probably indirectly block virus replication through inhibition of cellular kinases. Thus, masitinib, as an antiviral and an anti-inflammatory drug, might be used at all stages of the COVID-19 disease, alone or in combination with other drugs, including anti-viral drugs and/or dexamethasone.

*"While vaccines are now available, there is still a need for antiviral and symptomatic treatment for patients infected with the SARS-CoV-2. In addition, the emergence of new, and apparently more transmissible coronavirus variants has prompted concern about whether existing vaccines and monoclonal antibodies will remain effective. This research has shown for a second time that under *in vitro* conditions masitinib exerts a potent anti-viral effect on the SARS-CoV-2 virus. These results considered in conjunction with data published last year from the University of Chicago [2], further underscore the potential of masitinib as an effective treatment of COVID-19. It provides independent verification of masitinib's anti-viral action, and importantly reaffirms that the effective inhibitory concentration is at a level that can be achieved *in vivo*. This latter point strengthens the rationale for the clinical development program of masitinib in COVID-19, and means that extensive clinical testing of masitinib in COVID patients, which is already on-going, is even more essential",* said Professor Olivier Hermine, President of the Scientific Committee of AB Science and member of the Académie des Sciences in France.

As a reminder, the University of Chicago article reported results from an independent study led by Professor Savas Tay from the Pritzker School for Molecular Engineering (University of Chicago, USA) [2,3]. 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 viral replication. Remarkably, the research team elucidated masitinib's mechanism of action against SARS-CoV-2, showing that masitinib inhibits 3CLpro, the main SARS-CoV-2 protease that is crucial for virus infection and reproduction, by directly binding to the protease catalytic site.

AB Science has been granted authorization by French Medicine Agency (ANSM) to initiate a clinical study evaluating masitinib in combination with isoquercetin for the treatment of COVID-19 [4]. 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] Luo Y, Yu F, Zhou M, et al. 2021. Engineering a reliable and convenient SARS-CoV-2 replicon system for analysis of viral RNA synthesis and screening of antiviral inhibitors. *mBio* 12:e02754-20. <https://doi.org/10.1128/mBio.02754-20>.

[2] 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>

[3] AB Science press release. Sept 02,2020. <http://www.ab-science.com/years/2020/>

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

About mBio

mBio is American Society for Microbiology's first broad-scope, online-only, open access journal. *mBio* is a bimonthly peer-reviewed open access scientific journal published by the American Society for Microbiology in association with the American Academy of Microbiology. It covers all aspects of the microbiological sciences, including virology, bacteriology, parasitology, mycology, and allied fields.

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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