

Abivax publishes in Nature Scientific Reports ABX464's unique mechanism of action leading to both anti-inflammatory and antiviral effects

Abivax lead candidate ABX464 selectively upregulates anti-inflammatory microRNA miR-124

Selective miR-124 upregulation in inflamed tissue explains ABX464's broad potential to treat inflammation

ABX464 binds cap binding complex (CBC) making it more efficient, favoring miR-124 upregulation

ABX464 enhances viral – but not cellular – splicing to prevent HIV replication

PARIS, January, 28, 2019, 7:00 a.m. CET - Abivax (Paris:ABVX) (Euronext Paris: FR0012333284 – ABVX), a clinical-stage biopharmaceutical company harnessing the immune system to develop novel treatments for patients with inflammatory/autoimmune and viral diseases as well as cancer, today published new data characterizing the novel mechanism of action of its lead drug candidate, ABX464 in *Nature Scientific Reports*, a prestigious, highly rigorous peer-reviewed scientific journal.

The research, entitled “*Both anti-inflammatory and antiviral properties of novel drug candidate ABX464 are mediated by modulation of RNA splicing,*” concludes that ABX464’s ability to selectively upregulate anti-inflammatory miR-124 and selectively splice viral RNA, but not endogenous cellular RNA, may have applicability for treatment of both inflammatory diseases and HIV infection.

“*The elucidation of the unique mechanism of action of ABX464, particularly with respect to its anti-inflammatory properties, is a major breakthrough for Abivax*” said **Prof. Hartmut Ehrlich, MD, Chief Executive Officer of Abivax**. “*This mechanism of action, i.e. the stimulation of local synthesis of miR-124 in inflamed tissue, together with the impressive clinical efficacy and safety data from our completed placebo-controlled phase 2a proof-of-concept study in patients with ulcerative colitis, holds strong promise for ABX464 as a potentially novel treatment in the \$ 70+ billion anti-inflammatory market. As a consequence, Abivax is aggressively pursuing the next wave of clinical trials in inflammatory indications, representing areas of high unmet need, like ulcerative colitis, Crohn’s disease and rheumatoid arthritis.*”

The research, conducted in the cooperative ABIVAX-CNRS laboratory directed by Prof. Jamal Tazi, demonstrated that ABX464 enhances the splicing of HIV RNA in infected peripheral blood mononuclear cell (PBMCs) from healthy individuals, and enhances the expression and splicing of a single long noncoding RNA to generate the anti-inflammatory miR-124 in patients.

Prof. Jamal Tazi, PhD, VP Research of Abivax and Director of the collaborative laboratory between Abivax and the CNRS, commented: “*It has been a long-held belief of Abivax that the highly positive clinical efficacy data observed in studies of ABX464 in ulcerative colitis are a result of its potent, and promising anti-inflammatory mechanism of action. To have finally determined how this mechanism of action reduces inflammation and have these findings published in a prestigious scientific journal such as Nature Scientific Reports is very encouraging for the Company as we continue to pursue developing*



ABX464 for treatment of ulcerative colitis and other prevalent and under-addressed inflammatory diseases.”

The data further demonstrate that ABX464 binds to an mRNA-binding protein complex known as the cap binding complex (CBC) and enhances its functioning, resulting in the enhanced splicing of two types of RNA: 1.) a segment of HIV RNA which the HIV virus needs in an unspliced form for replication, thus inhibiting replication; and 2.) a long non-coding human RNA (lncRNA 0599-205), which, upon splicing results in specific increased expression of miR-124, a microRNA with potent anti-inflammatory properties. MicroRNAs are known to dampen gene expression, and miR-124 is known to specifically downregulate the expression of a number of pro-inflammatory cytokines, thereby mitigating inflammation. Furthermore, by binding to CBC, ABX464 reinforces the biological functions of CBC in cellular RNA biogenesis including splicing, which is especially important in tissues suffering from perturbations, like inflammation. Therefore, the molecule acts inside injured immune cells to preserve the integrity of newly synthesized RNA.

Importantly, ABX464 did not modulate the rate of splicing of cellular genes, a key requirement for a safe and well tolerated drug.

ABX464 is a first-in-class small molecule for oral administration that has been tested in Phase 2a clinical trials for ulcerative colitis (UC) and HIV infection. In the proof-of-concept clinical trial in UC patients, ABX464 statistically significantly improved UC signs and symptoms on both clinical and endoscopic endpoints, achieving a clear and clinically meaningful magnitude of effect in a small exploratory study. Based on these exciting data, Abivax is currently preparing the imminent regulatory submission of a phase 2b clinical trial in 232 ulcerative colitis patients, as well as phase 2a proof-of-concept studies for two additional inflammatory indications, Crohn’s disease and rheumatoid arthritis.

Research details:

TITLE: “Both anti-inflammatory and antiviral properties of novel drug candidate ABX464 are mediated by modulation of RNA splicing”

Authors: Audrey Vautrin, Laurent Manchon, Aude Garcel, Noëlie Campos, Laure Lapasset, Abdelhamid Mahdi Laaref, Roman Bruno, Marie Gislard, Emeric Dubois, Didier Scherrer, Hartmut Ehrlich and Jamal Tazi

Weblink: www.nature.com/articles/s41598-018-37813-y

About Ulcerative Colitis

Ulcerative colitis is a debilitating inflammatory bowel disease in adults and children, with limited therapeutic management options for many patients. It is estimated that close to 1 million patients with ulcerative colitis live in the United States, 650,000 in the EU and >2.7 million globally. Pharmaceutical sales for this disease in the major global markets are estimated to be around \$5.5 billion in 2017. For inflammatory bowel disease (IBD), which includes both ulcerative colitis and Crohn’s disease, the sales in the major global markets are estimated to be around \$15 billion for the same period. The financial potential of treatments in the anti-inflammatory space are exemplified by anti-TNF monoclonal antibodies (Humira, Remicade, Simponi) with estimated global annual sales of > \$30 billion, including at least \$2.5 billion for ulcerative colitis.

About ABIVAX (www.abivax.com)

ABIVAX is mobilizing the body’s natural immune machinery to treat patients with inflammatory/autoimmune diseases, viral diseases and cancer. A clinical-stage company, ABIVAX leverages its anti-inflammatory/antiviral and immune enhancing platforms to optimize candidates to treat inflammatory diseases, HIV and liver cancer. ABIVAX is listed on Euronext compartment B (ISIN: FR0012333284 – Mnémo: ABVX). More information on the company is available at www.abivax.com/en. Follow us on Twitter @ABIVAX_



Contacts

Abivax

Finance

Didier Blondel

didier.blondel@abivax.com

+33 1 53 83 08 41

Investors

LifeSci Advisors

Chris Maggos

chris@lifesciadvisors.com

+41 79 367 6254

Press Relations and Investors EU

MC Services AG

Anne Hennecke

anne.hennecke@mc-services.eu

+49 211 529 252 22

French Media

ALIZE RP

Aurore Gangloff/Catherine Mégélas

abivax@alizerp.com

+33 6 49 57 82 68 / +33 6 31 05 66 05

US Media

LifeSci Public Relations

Matt Middleman, M.D.

matt@lifescipublicrelations.com

+1 646 627 8384