



ABIVAX REPORTS EXCELLENT PHASE 2A CLINICAL SAFETY AND EFFICACY RESULTS WITH 50MG ABX464 IN RHEUMATOID ARTHRITIS

- Primary endpoint met with ABX464 demonstrating good safety and tolerability profile with 50mg once daily oral administration
- A statistically significant difference ($p < 0.03$) was met on key efficacy endpoint ACR20¹ in the PP² population with 60% of ABX464 patients dosed with 50mg reaching that endpoint versus 22% in the placebo group
- Other key efficacy endpoints (ACR50, ACR70, DAS28-CRP³, CDAI⁴) as well as biological markers (CRP, miR-124, IL-6) showed favorable differences with 50mg ABX464 over placebo
- Abivax is preparing to start a clinical phase 2b program in rheumatoid arthritis in early 2022
- Given the demonstrated safety and efficacy of ABX464 in rheumatoid arthritis and ulcerative colitis, Abivax is exploring additional programs in chronic inflammatory indications
 - Abivax to host webcast on Wednesday June 23, 2021 at 2:00 pm CEST (8:00 am EST)

PARIS, France, June 23, 2021 – 8:00 am (CEST) – Abivax SA (Euronext Paris: FR0012333284 – ABVX), a clinical-stage biotechnology company developing novel therapies that modulate the immune system to treat chronic inflammatory diseases, viral infections, and cancer, announces excellent top-line results of the induction phase of its phase 2a clinical study of ABX464 administered in combination with methotrexate (MTX) for the treatment of active moderate to severe rheumatoid arthritis (RA). 60 patients who had either an inadequate response to methotrexate and/or TNF α inhibitors participated in the study.

The primary endpoint of this study, safety and tolerability, was met with 50mg ABX464 once daily demonstrating a good safety and tolerability profile in the overall patient population during the 12-week induction phase.

Although the sample size of this study was not powered to show efficacy, the 50mg group already showed statistically significant differences for the key secondary endpoint ACR20 compared to placebo at week 12 in the Per Protocol population. The ACR20 is the key primary efficacy endpoint required by the FDA for licensure of new drugs in rheumatoid arthritis.

Based on these results, Abivax is preparing to start a clinical phase 2b program in RA in early 2022.⁵

ABX464 is a small molecule for once-daily administration with a first-in-class mechanism of action, centered around the upregulation of the anti-inflammatory microRNA, miR-124. ABX464 was already shown to be efficacious and safe in [phase 2a](#) and [phase 2b](#) clinical studies for the treatment of ulcerative colitis (UC).

¹ The American College of Rheumatology ACR score measures the efficacy of treatments for rheumatoid arthritis patients. The ACR20/50/70 measures a 20/50/70% improvement in the tenderness and swelling in designated joints and a 20/50/70% improvement in at least 3 of the 5 following measures: investigator's and patient's reported global assessment of disease scales, patient's reported pain scale, CRP level, healthy assessment questionnaire.

² PP: Per protocol data

³ DAS28-CRP-Disease Activity Score for 28 joints - C reactive Protein

⁴ The Clinical Disease Activity Index (CDAI) is a composite index based on the tenderness and swelling in designated 28 joints and on investigator's and patient's reported global assessment of disease scales.

⁵ Future clinical development including phase 2b design and initiation is subject to assessment of the overall preclinical, CMC, toxicology, clinical efficacy and safety data of ABX464 by EMA, FDA and other regulatory authorities. These top-line results have not yet been reviewed by regulatory authorities.



Prof. Claire Daien, M.D., Ph.D., rheumatologist at the University Hospital at Montpellier and principal investigator of the study, said: *"I am excited about these positive clinical phase 2a results. 50mg once daily oral treatment with ABX464 shows to be well tolerated and efficacious in patients in the induction study. This is remarkable, as these top-line efficacy results are at par with currently available treatments. Even if the standard of care made some progress during the past years, too many patients still do not respond or lose responsiveness to available drugs, and new molecules with a different mechanism of action, like ABX464, are needed. Therefore, ABX464 should move to phase 2b testing as quickly as possible."*

Prof. Hartmut J. Ehrlich, M.D., CEO of Abivax, added: *"ABX464 has already shown good safety and robust, sustained efficacy in our phase 2a and phase 2b induction and maintenance clinical trials for the treatment of ulcerative colitis. Combined with the phase 2a results in RA, we believe that ABX464 may have an important potential as a novel, highly differentiated anti-inflammatory therapeutic agent across various inflammatory indications. Just as ulcerative colitis and Crohn's disease, rheumatoid arthritis is an irreversible, debilitating, and systemic autoimmune disease that often requires aggressive treatment to control it. This disease represents a major burden for the millions of affected patients, their families and for healthcare systems worldwide and there is an urgent need for new efficacious and well tolerated therapeutic management options."*

50mg once daily oral administration of ABX464 is safe and well tolerated by RA patients with previous inadequate response to MTX and/or to one or more anti-tumor necrosis factor alpha (TNF α) biological therapeutics and shows very promising efficacy results

The clinical phase 2a study was designed to evaluate the safety, tolerability and preliminary efficacy of two oral dose-levels of ABX464 administered once daily (50mg and 100mg), in combination with methotrexate (MTX). 60 patients who had an inadequate response to MTX and/or to one or more anti-tumor necrosis factor alpha (TNF α) biological therapeutics participated in this randomized, double-blind, placebo-controlled trial. Patients received ABX464 (50mg or 100mg) or placebo during the 12-week induction treatment phase. The study was conducted in 21 study centers across four European countries (France, Belgium, Poland and Hungary). The treatment groups were well balanced in terms of disease severity as well as patient demographics.

The primary endpoint of the study was met with 50mg ABX464 once daily being safe and well tolerated during the 12-week induction phase. No deaths or malignancies were reported in the study. One serious adverse event (SAEs) was reported in the placebo group and one in the 100mg dose group, while no SAE was reported in the 50mg dose group. 3 patients in the 50mg group, 12 patients in the 100mg group and 1 patient in the placebo group prematurely discontinued the study. An increased incidence of largely mild to moderate gastrointestinal adverse events in the 100mg treatment group is likely due to an overlapping side effect profile with methotrexate (MTX), leading to a higher drop-out rate of patients, especially as it refers to nausea and emesis. Therefore, the 100mg dose will not be considered for future clinical development of ABX464 in rheumatoid arthritis.

The nature of these adverse events is consistent with what has been observed in more than 800 subjects who have so far been treated in other clinical trials with ABX464 across different indications.



Secondary efficacy endpoints included the proportion of patients achieving ACR20/50/70 responses, change from baseline in DAS28-CRP low disease activity (DAS28-CRP \leq 3.2) and Clinical Disease Activity Index (CDAI).

	Placebo		50 mg		100 mg	
	PP ⁺ (n=18)	ITT (n=20)	PP ⁺ (n=15)	ITT (n=21)	PP ⁺ (n=7)	ITT (n=19)
Early discontinuations	1		3		12	
Mean DAS28-CRP at Baseline	5.3		5.5		5.5	
ACR20	4 (22%)	4 (20%)	9 (60%)*	9 (43%)	3 (43%)	3 (16%)
ACR50	1 (6%)	1 (5%)	5 (34%)	5 (24%)	2 (29%)	2 (11%)
ACR70	1 (6%)	1 (5%)	4 (27%)	4 (19%)	1 (14%)	1 (5%)
DAS28-CRP change from baseline	-0.63	-0.63	-1.78	-1.74	-1.95	-1.95
Low Disease Activity (DAS28-CRP \leq 3.2)	2 (11%)	2 (10%)	4 (25%)	4 (19%)	3 (43%)	3 (16%)
CDAI \leq 10	2 (11%)	2 (10%)	5 (31%)	5 (24%)	3 (43%)	3 (16%)

* P < 0.03 - Statistical tests were only conducted for ACR20 as part of topline results

† PP Per Protocol population set for ACR levels

In addition, a DAS28-CRP remission (DAS-CRP < 2.6) has been reported in 19% of patients dosed with 50mg ABX464 compared to 5% in the placebo group (ITT). Regarding biomarkers, a significant upregulation of miR-124 expression was observed for every patient dosed with ABX464, and a decrease in IL-6 blood levels was observed in both active dose groups compared to placebo.

Patients who completed the induction study could roll over into a two-year open-label maintenance study to evaluate the long-term safety and efficacy of 50mg once daily oral ABX464 in RA. One-year data from this study will become available in Q1 2022.

Epidemiology, unmet medical needs and market size in rheumatoid arthritis

In 2020, there were an estimated 3.8M diagnosed cases of rheumatoid arthritis in G7 countries (US, France, Germany, Italy, Spain, UK and Japan). Despite the existing therapeutic options for RA including biologic disease-modifying antirheumatic drugs 74% of patients report dissatisfaction with their treatment plans mandates more patients-centered therapeutic options which are safe and easy to administer.⁶ The total market size in RA is USD 20.4B annually, based on 2020 pharmaceutical sales estimates for rheumatoid arthritis in these countries, estimated to grow to USD 22.9B by 2025. The currently accessible market for ABX464 in IBD and RA is estimated to grow to USD 48B by 2025, while the overall chronic inflammation market is estimated to exceed USD 110B at that time.⁷

ABX464 phase 3 in UC, phase 2b in Crohn's disease and phase 2b clinical trial in rheumatoid arthritis (RA)

A pivotal phase 3 clinical trial program in UC is expected to be initiated by the end of 2021.

A dose ranging, randomized, placebo-controlled pivotal phase 2b trial in Crohn's disease patients is expected to be initiated before the end of the year.

A phase 2b dose ranging study in RA is expected to start in early 2022.

Based on the encouraging data in UC and RA, Abivax is planning to explore additional chronic inflammatory indications in the near future.

⁶ Radawski C, Genovese MC, Hauber B, et al. Patient perceptions of unmet medical need In rheumatoid arthritis: a cross-sectional survey in the USA. Rheumatol Ther. 2019;6:461-471.

⁷ Source: Informa



About ABX464^{8 9}

ABX464 is a highly differentiated oral drug candidate, with a novel mechanism of action based on the upregulation of a single microRNA (miR-124) with potent anti-inflammatory properties. ABX464 was shown to exert its anti-inflammatory effects through binding to the cap binding complex (CBC), which sits at the 5' end of every RNA molecule in the cell. By binding to the CBC, ABX464 reinforces the biological functions of CBC in cellular RNA biogenesis. Specifically, ABX464 enhances the selective splicing of a single long non-coding RNA to generate the anti-inflammatory microRNA, miR-124, which downregulates pro-inflammatory cytokines and chemokines like TNF- α , IL-6, MCP-1 and IL-17, as well as Th17+ cells thereby "putting a brake" on inflammation and suggesting broad potential as a novel anti-inflammatory therapeutic agent. A seven- to ten-fold increase in miRNA-124 levels was observed in colorectal biopsies of UC patients treated with ABX464. ABX464 does not impact the splicing of cellular genes. Ulcerative colitis [phase 2b top-line results](#) as well as phase 2a induction and maintenance data [after one](#) and [two years](#) of treatment were previously reported.

Investor webcast on phase 2a study results

Abivax will host a **webcast** on **Wednesday, June 23, 2021 at 2:00 pm CEST (8:00 am EST)**, to present the top-line data of its ABX464 phase 2a clinical study in RA. Following the formal presentation, Abivax senior management, will be available to answer questions.

To participate in the webcast, please follow the weblink: <http://media.rampard.com/20210623>

About Abivax (www.abivax.com)

Abivax, a clinical stage biotechnology company, is developing novel therapies that modulate the physiological inflammation and immunological pathways to treat patients with chronic inflammatory diseases, viral infections, and cancer. Abivax is listed on Euronext compartment B (ISIN: FR0012333284 – Mnémo: ABVX). Based in Paris and Montpellier, Abivax has two drug candidates in clinical development, ABX464 to treat severe inflammatory diseases, and ABX196 to treat hepatocellular carcinoma. More information on the company is available at www.abivax.com. Follow us on Twitter @ABIVAX_.

Contacts

Abivax

Communications

Regina Jehle

regina.jehle@abivax.com

+33 6 24 50 69 63

Investors

LifeSci Advisors

Chris Maggos

chris@lifesciadvisors.com

+41 79 367 6254

Press Relations & Investors Europe

MC Services AG

Anne Hennecke

anne.hennecke@mc-services.eu

+49 211 529 252 22

Public Relations France

Actifin

Ghislaine Gasparetto

ggasparetto@actifin.fr

+33 6 21 10 49 24

Public Relations France

DGM Conseil

Thomas Roborel de Climens

thomasdeclimens@dgm-conseil.fr

+33 6 14 50 15 84

Public Relations USA

Rooney Partners LLC

Marion Janic

mjanic@rooneyco.com

+1 212 223 4017

⁸ J. Tazi et al.: [Specific and selective induction of miR-124 in immune cells by the quinoline ABX464: a transformative therapy for inflammatory diseases](#), Drug Discovery Today, Volume 26, Issue 4, April 2021, Pages 1030-1039

⁹ S. Vermeire et al.: [Induction and long-term follow-up with ABX464 for moderate-to-severe ulcerative colitis: Results of phase 2a trial](#), Gastroenterology, March 2021



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