Abivax provides an update on the ABX464 clinical data and development strategy in ulcerative colitis

September 14, 2021

Excellent once-daily oral ABX464 efficacy and safety data in the phase 2b clinical trial in ulcerative colitis (UC) patients, previously reported at 8-weeks, are further improved at 16-weeks

Additional analyses (incl. miR-124 levels, histopathology, quality of life, etc.) underpin the potential of ABX464 to become a safe short- and long-term efficient treatment option in UC

Novel and highly differentiated mechanism of action of ABX464 confirmed, showing specific upregulation of a single microRNA, miR-124

Additional long-term data of the ABX464 phase 2a open-label maintenance study in UC confirm the good safety and potent efficacy of ABX464 after 3 years of continuous chronic treatment

For the launch of its phase 3 program in UC, Abivax is getting ready for the mandatory consultations with the regulatory authorities, starting with feedback from the US regulatory agency (FDA) expected by year end

Abivax' late breaking abstract on the phase 2b data in UC was selected for oral presenta-tion during UEG Week Virtual 2021 (Monday, October 4). The data will be presented by the study's principal investigator, Prof. Séverine Vermeire, M.D., Ph.D.

Also, on the same day at UEG Week Virtual 2021, Abivax will host a Live Industry Symposium with presentations by key opinion leaders Prof. Bruce Sands, M.D., M.S. and Prof. William Sandborn, M.D.

PARIS, France, September 14, 2021 – 6:00 pm (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, today provides an update on its clinical development strategy of lead compound ABX464 in UC and releases complementary data supporting the recently announced positive phase 2b top-line results. According to the latest additional analysis, the results after 16 weeks of once-daily oral treatment with ABX464 confirm and further extend the data with respect to the efficacy and the good safety profile already observed after 8-weeks of induction treatment.

Prof. Séverine Vermeire, M.D., Ph.D., Head of the IBD Center at the University Hospitals Leuven, Belgium, and principal investigator of the study, said: *"These new data add to the promising outcomes of our ABX464 phase 2b study in UC, communicated in May this year. The consistency observed between the 8- and 16- week data is very reassuring in terms of the sustainability of the positive efficacy and the tolerability of ABX464, which is further strengthened by the very encouraging 3-year maintenance data of the phase 2a maintenance study. We are very excited to focus now on the implementation of the global phase 3 program in UC for the treatment of patients suffering from this debilitating disease, still in need for novel safe and long-term effective therapeutic management options."*

Prof. Hartmut J. Ehrlich, M.D., CEO of Abivax, added: *"In addition to its convenient once-daily oral administration, its fast onset of action, durable and maintained efficacy and good safety profile, the recent data analysis once again demonstrated the unique and novel mechanism of action of ABX464. This mechanism of action fundamentally differentiates this first in-class small molecule from any other drug or drug-candidate in the inflammatory field. At present, Abivax is preparing the upcoming consultations with the key regulatory agencies to discuss the phase 3 program in UC and the overall clinical development strategy of ABX464. We expect feedback from the FDA by the end of this year."*

Complementary data analysis of the ABX464 phase 2b induction clinical trial in UC

In May 2021, Abivax announced the top-line data of its ABX464 randomized, placebo-controlled phase 2b trial in UC after the 8-week induction treatment, which demonstrated significant clinical efficacy in the overall patient population, as well as in patients previously refractory to biologics and/or JAK inhibitors, on primary and key secondary endpoints and a good safety profile of ABX464.

The baseline disease characteristics were well balanced across all ABX464 dose groups and the placebo group. Enrolled patients suffered from longstanding UC with an overall median duration of 5.45 years. At inclusion, 71.4% of the patients showed a severe disease profile, with a baseline modified Mayo Score[1] of 7 to 9 points. About 50% of the patients in each ABX464 treatment group and placebo were previously refractory to biologic treatments and/or JAK inhibitors. The majority of the patients was treated with concomitant UC medication at a stable dose (52% corticosteroids, 76.6% 5-ASA and 13.9% immunosuppressants).

At week 8, 35%, 40%, 44% of patients treated with 25mg, 50mg, 100mg respectively achieved endoscopic improvement compared to 14% in the placebo group. As per the clinical study protocol, only patients without an endoscopic improvement[2] at week 8, had another endoscopy performed at week 16. This criterion was chosen for ethical reasons to not require an additional endoscopy for patients who already had an endoscopic improvement at week 8. Among the patients, who had another endoscopy at week 16, higher percentages of clinical remission[3] were achieved at week 16 in the ABX464 treatments groups (25mg, 50mg and 100mg) with 15%, 20% and 23% respectively and 13% in the placebo group.

These results confirm the potency of ABX464 to maintain and to further improve clinical remission rates over time. Similar trends were observed for reduction of the modified Mayo Score, presence of clinical response[4], and endoscopic improvement as well as reduction in fecal calprotectin in patients treated with ABX464 both in the entire population as well as in the subset of patients who were previously exposed refractory to biologic treatments and/or JAK inhibitors.

Complementary laboratory analysis at week 8 have now been completed, showing a highly statistically significant upregulation of the specific microRNA, miR-124, in rectal tissue in all patients treated with ABX464, compared to baseline. Increased miR-124 levels were observed in colorectal biopsies after 8 weeks of treatment with ABX464: The median increases were 13-fold for the 25mg group, 25-fold for the 50mg group and 25-fold for the 100mg group, while no upregulation was observed in the placebo group (1.02-fold increase), indicative of the positive pharmacological effect of ABX464.

Furthermore, a statistically significant reduction of the level of inflammation in the rectal tissue, assessed by the Robarts Histopathology Index (RHI), has been observed in UC patients treated with the lowest dose of 25mg ABX464 at week 8, compared to placebo (least square mean difference of 3.9 (7.3, 0.5) and p=0.03).

Importantly, the quality of life of patients treated with ABX464 showed a superior improvement at week 8 compared to the placebo group (40, 41 and 51-point improvement in 100/50/25mg compared to a 31-point improvement in the placebo). The “Health Related Quality of Life (HRQOL)” was measured from baseline using the standardized “Inflammatory Bowel Disease Questionnaire (IBDQ)” total score.

The pharmacokinetic (PK) data collected during this study confirmed the previous observation of dose-linearity and will allow Abivax to validate the population PK modelling approach, necessary for upcoming clinical studies and licensure.

Consistent with the other clinical studies, ABX464 was found to be safe and well tolerated at all dose levels during the 16-week induction period. Within the ABX464 phase 2b induction study, the most frequently reported adverse events were mild and transient (i.e. headache, nausea, gastrointestinal pain) and manageable with or without over-the-counter medication. Similarly, low rates of infections were observed in the active treatment groups (8.4%) compared to placebo (9.4%). No deaths or malignancies were reported in this study. In the ABX464 groups, serious adverse events (SAEs) occurred in 1.6% (25mg), 6.3% (50mg) and 6.2% (100mg) of patients and in 6.2% of patients in the placebo group.

These safety data are in line with what has been observed in more than 650 healthy volunteers and patients who have so far been treated in other clinical trials with ABX464 across different indications.

New clinical data on the phase 2a maintenance study in UC

Separately, today, Abivax reports for the first time the 3-year efficacy data from its ongoing phase 2a maintenance study in UC. 15 out of the 22 patients who were initially enrolled into the phase 2a maintenance study in 2018, completed the third year of treatment with once-daily oral 50mg ABX464.

Among the 13 patients who underwent centrally read endoscopies at the completion of year 3, 11 patients (85%) were still in clinical remission, among which 7 patients (54%) had an endoscopic remission (endoscopic subscore=0) and 11 patients had an endoscopic improvement (endoscopic subscore=0 or 1).

The long-term safety profile of chronic ABX464 administration continues to be very favorable.

Novel and unique mechanism of action of ABX464[5],[6]

Besides its convenient once-daily oral administration, its fast onset of action, durable and maintained efficacy and good safety profile, the recent data analysis once again demonstrated the unique and novel mechanism of action of ABX464. This mechanism of action fundamentally differentiates this first in-class small molecule from any other drug or drug-candidate in the inflammatory field. It is based on the upregulation of a single physiological microRNA (miR-124), a potent down-regulator of excessive inflammation. ABX464 was shown to exert its inflammation dampening 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 key 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 inflammation modulation therapeutic agent. Increased miR-124 levels were observed in colorectal biopsies after 8 weeks of treatment with ABX464: The median increases were 13-fold for the 25mg group, 25-fold for the 50mg group and 25-fold for the 100mg group, while no upregulation was observed in the placebo group (1.02-fold increase), indicative of the positive pharmacological effect of ABX464. More than 80% of patients dosed with ABX464 had an upregulation of miR-124 of at least 2-fold compared to 12% in the placebo group. ABX464 does not impact the splicing of cellular genes.

Abivax’ late-breaking abstract on the phase 2b data in UC was selected by UEG for oral presentation during UEG Week Virtual 2021

This abstract will be presented by Prof. Séverine Vermeire, M.D., Ph.D, the principal investigator of the study, on Monday, October 4, 2021, between 10:30-11:30 am CEST (4:30-5:30 am EDT).

Abivax to host an Industry Symposium at UEG Week Virtual 2021

Abivax will be hosting an Industry Symposium at the UEG Week Virtual 2021 on Monday, October 4, 2021 at 1:00-2:00 pm CEST (7:00-8:00 am EDT) on “ABX464, a novel anti-inflammatory drug-candidate for the treatment of ulcerative colitis”. Presentations on the continued need for novel drugs in IBD and the potential of ABX464 to address them will be given by the internationally renowned key opinion leaders Prof. Bruce Sands, M.D., M.S. and Prof. William Sandborn, M.D. In addition, Didier Scherrer, Ph.D., Vice-President R&D at Abivax, will provide more details on the novel and unique mechanism of action of ABX464.

UEG Week Virtual subscribers can follow the live symposium and view the subsequently provided on-demand replay under the following link: https://virtualweek.ueg.eu/symposium/is-10

Epidemiology and market size in inflammatory bowel diseases

In 2020, there were an estimated 3.5M diagnosed cases of ulcerative colitis in G7 countries (US, France, Germany, Italy, Spain, UK and Japan). The total market opportunity for ABX464 is USD 6.0B annually, based on 2020 pharmaceutical sales estimates for ulcerative colitis in these countries. For inflammatory bowel diseases (ulcerative colitis and Crohn’s disease), sales were USD 17.9B in 2020 and are estimated to grow to USD 25.0B by 2025, i.e. the year ABX464 is expected to reach the market for ulcerative colitis.

Next update

Abivax will provide the half-year 2021 financial results as well as an operational update before the end of next week.

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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 chronic inflammatory diseases, and ABX196 to treat hepatocellular carcinoma. More information on the company is available at www.abivax.com. Follow us on Twitter @ABIVAX_.

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[1] Modified Mayo Score refers to stool frequency, rectal bleeding and endoscopy sub score.

[2] Endoscopic improvement is defined as endoscopic subscore ≤1.

[3] Clinical remission (per Modified Mayo Score) is defined as stool frequency subscore (SFS) ≤1, rectal bleeding subscore (RBS) of 0 and endoscopic subscore ≤1.

[4] Clinical response (per Modified Mayo Score) is defined as a decrease from baseline in the Modified Mayo Score ≥2 points and ≥30% from baseline, plus a decrease in RBS ≥1 or an absolute RBS ≤1.

[5] 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

[6] 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