SynAct Pharma's AP1189 meets primary endpoint and demonstrates favorable safety profile in Rheumatoid Arthritis patients with active joint disease in the Phase 2a BEGIN study

SynAct Pharma AB ("SynAct") today announced top-line results from the Phase 2a study of AP1189 in early rheumatoid arthritis (RA) patients experiencing severe disease activity.

- **In this 4-week study, patients treated once-daily with 100 mg AP1189 achieved a significantly greater reduction in mean Clinical Disease Activity Score (CDAI) as compared to placebo.**
- **Change in disease activity from severe to moderate was numerically higher in groups treated with AP1189 as compared to placebo, with the lack of statistical difference likely explained by higher baseline CDAI and inflammation (CRP) in the 100 mg group.**
- **Consistent dose-dependent effects were also seen across secondary read outs including Disease Activity Score DAS-28, ACR 20 score, and FACIT-fatigue score.**
- **AP1189 was well-tolerated and presented with a favorable safety profile. No serious adverse events were reported in the study.**
- **Based on the positive results, SynAct will seek scientific advice and open an IND with the FDA to prepare for Phase 2b.**

The BEGIN study is a randomized, double blinded, placebo-controlled study evaluating two doses of AP1189 (50 and 100 mg given orally once daily) for four weeks as add-on therapy to methotrexate in patients with newly diagnosed severe active rheumatoid arthritis.

A total of 105 subjects were enrolled in the study. 30 patients were treated with placebo, 29 patients received 50 mg AP1189, and 33 patients 100 mg AP1189. Patient demographics were comparable between groups. A higher baseline disease activity was observed in the AP1189 100 mg group. Two patients discontinued in each of the 3 groups, none judged as related to study medication. In total, 7 patients were taken out of the efficacy evaluation due to protocol violation.

The primary endpoint was reduction in CDAI defined as mean reduction in disease activity and the fraction of patients going from high to moderate/low disease activity. Patients treated with AP1189 achieved a mean reduction of 12.0 and 15.5 points in the 50 mg and 100 mg groups respectively, compared to 9.3 with placebo ($p<0.04$ in the 100 mg group). The number of patients going from severe to moderate disease were 62%, 52%, and 40% for AP1189 50 mg, 100 mg, and placebo, respectively.

Consistent dose-dependent effects were seen across secondary endpoints. ACR20: 31%, 48%, 23% for 50 mg, 100 mg, and placebo. DAS-28 (moderate/low disease activity): 37.8%, 51.5%, and 23.3% for 50 mg, 100 mg, and placebo. FACIT-fatigue scores: 5.9, 8.0, and 4.8 for 50 mg, 100 mg, and placebo.

AP1189 was well-tolerated and presented with a favorable safety profile. No serious adverse events occurred. Adverse events occurred as follows (mild/moderate/severe) in the per

protocol population: 26/12/0 in 31 patients treated with 50mg AP1189, 22/5/0 in 35 patients treated with 100 mg AP1189, and 18/2/1 in 32 patients treated with placebo.

No differences were observed between AP1189 and placebo with regards to liver, kidney, white blood cell count (WBC) or other biochemistry parameters. Clinically significant increases in aminotransferases were seen in 2 patients in the placebo group, 2 patients in the 50 mg group, but none seen in the 100 mg group. With no changes in WBC or rate of infections, no signs of immunosuppression were seen.

“We are very excited with the data of the BEGIN study as it strongly supports further development of AP1189 as a candidate for the treatment of RA and other autoimmune and inflammatory diseases. This is the second time we demonstrate proof of concept with AP1189 in serious inflammatory conditions. Ongoing safety challenges with key classes of RA therapeutics underscore the need for new treatment modalities”, said Thomas Jonassen, CSO and founder of SynAct Pharma.

The company will seek scientific advice and open an IND with FDA to prepare for Phase 2b with AP1189 in RA patients. Phase 2b will utilize the new once-daily tablet formulation and with a longer treatment duration.

“This is a pivotal moment for SynAct. It is what we have been working towards for years. While we are preparing for the phase 2b study, business development activities will continue and we look forward to discussing the BEGIN data with interested parties. We believe that AP1189 has tremendous potential in RA, a $28 billion market, where we believe that AP1189 may have a differentiated efficacy and safety profile over existing treatments”, said Jeppe Øvlesen, CEO of SynAct.

Conference Call Details

SynAct Pharma will host an audiocast and telephone conference on November 30 at 15:00 CET, with the following participants:
Jeppe Øvlesen, CEO
Thomas Jonassen, CSO
Torbjörn Bjerke, Chairman of the Board

Weblink: https://tv.streamfabriken.com/presskonferens-2021
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About SynAct Pharma AB

SynAct Pharma AB conducts research and development in inflammatory diseases. The company has a platform technology based on a new class of drug candidates aimed at acute deterioration in chronic inflammatory diseases with the primary purpose of stimulating natural healing mechanisms. For more information: www.synactpharma.com.

About AP1189

The mechanism of action of SynAct Pharma´s lead compound AP1189 is to promote resolution of inflammation through selective activation of melanocortin receptors 1 and 3. These receptors are located on all immune cell types including macrophages and neutrophils. Activation of these receptors results in two direct anti-inflammatory effects: it turns these cells to produce less pro-inflammatory molecules and also to switching them to perform inflammation "clean-up", known as efferocytosis (J Immun 2015, 194:3381-3388). This effect has shown to be effective in disease models of inflammatory and autoimmune diseases and the clinical potential of the approach is currently tested in clinical programs in patients with rheumatoid arthritis (RA), nephrotic syndrome (NS) and COVID-19. The safety and efficacy of AP1189 is being tested and has not been reviewed by any regulatory authority worldwide.

About BEGIN

The BEGIN study is a multi-center, two-part, randomized, double-blind, placebo-controlled study evaluating two doses of AP1189 (50 and 100 mg given orally once daily) for four weeks against placebo, both given in combination with methotrexate in previously treatment-naïve patients with severe active RA. The primary efficacy endpoint in the study is reduction in disease activity from severe (defined as CDAI >22) to moderate or low disease activity within the four-week treatment period. The current press release comprises results of the final part of the BEGIN study. Results from Part 1 of the BEGIN study were reported November 9, 2020.

https://clinicaltrials.gov/ct2/show/NCT04004429?term=AP1189&draw=2&rank=1