SynAct Pharma Announces Positive Interim Phase 2 Data of AP1189 in Rheumatoid Arthritis

- The Data Safety Monitoring Board (DSMB) finds no safety concerns in the 50 mg and 100 mg dose cohorts
- Signs of efficacy against rheumatoid arthritis was observed. Thus, the number of patients changing from the severe to the moderate Clinical Disease Activity Index (CDAI) score was higher than placebo in both treatment groups in a dose dependent manner
- The DSMB recommends that the study continues to Part 2 in which the patients are randomized to 50 mg AP1189, 100 mg AP1189 and placebo plus methotrexate (MTX)
- Full Phase 2 topline data is expected by the end of Q2 2021

Lund, Sweden, November 9, 2020. SynAct Pharma AB ("SynAct"), a clinical stage biopharmaceutical company developing novel therapies of inflammatory diseases, today announced that an independent Data Safety Monitoring Board (DSMB) has reviewed unblinded and validated data from part 1 of the company's Phase 2a study in patients with rheumatoid arthritis (RA) with high disease activity with the aim to recommend which dose(s) of AP1189 to be brought into part 2 of the study. The DSMB is composed of independent clinical experts and has the responsibility to recommend further dosing and continuation of the study. The company remains blinded to the data.

"We are very excited that DSMB observes good safety and promising signals of efficacy in the interim analysis of AP1189 in patients with severe and newly diagnosed rheumatoid arthritis. This may indicate that we might see a clinical effect already following 4 weeks of treatment. We look forward to initiate recruitment in part 2 of the study this week. As we are testing newly diagnosed patients, we have decided to name this study BEGIN," said Thomas Jonassen, MD, CSO at SynAct Pharma AB.

The BEGIN study is designed as a placebo-controlled double-blind multicenter study with a 2:1 randomization ratio of once-daily dosing of AP1189 vs placebo in RA patients referred to rheumatological departments due to uncontrolled disease activity defined as a Clinical Disease Activity Index (CDAI) score higher than 22. AP1189 or placebo is dosed once daily for 4 weeks in parallel with the initiation of a treatment with the disease-modulating, anti-rheumatic drug methotrexate (MTX). The full study consisting of part 1 and 2 will include up to 90 patients. The second part of the study will be initiated this week according to the DSMB recommendation.

The data analysis conducted on the first 26 patients who has completed treatment indicates that AP1189 is safe and well tolerated at the current dose schedule. There are no reports of any serious adverse events. The overall frequency of adverse events is similar in the two treatment groups, and slightly higher than the placebo group. The most common adverse event was nausea.

The median CDAI at the point of inclusion in the study was 34 (low: 23; high: 49). The fraction of patients that had a reduction in CDAI to 22 or lower upon 4 weeks of therapy, i e going from severe to moderate or low disease activity, was as follows:

Placebo + MTX	AP1189 50 mg + MTX	AP1189 100 mg + MTX
44%	67%	75%

Based on these findings the DSMB concludes the following:

"The efficacy data indicated an effect of AP1189 on rheumatoid arthritis which was larger than placebo (may also be dose-dependent), the number of patients going from severe to moderate CDAI score was higher in both treatment groups than in the placebo group. However, the small number of patients precluded any statistical evaluation of significant differences."

Based on the interim analysis, the DSMB recommend continuing into part 2 of the BEGIN study with AP1189 dosed at either 50 mg, or 100 mg as well as a placebo group, and in all three groups MTX in a 1:1:1 randomization according to the protocol.

SynAct to Host Investor Conference Call

The company will host an investor call and webcast today, Monday, November 9, 2020 at 1:30 p.m. CET to discuss the interim data from the BEGIN study

To participate in the conference call, click on the following link: https://financialhearings.com/event/13379

In addition, a replay of the webcast will be available on the company website for 30 days following the event.

This information is such information that SynAct Pharma AB is obliged to publish in accordance with the EU Market Abuse Regulation. The information was submitted, through the agency of the contact person below, for publication on November 9, 2020.

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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. SynAct Pharma is listed on the Spotlight Stock Market (ticker: SYNACT). For more information, please visit https://synactpharma.com.

About AP1189

The mechanism of action of SynAct Pharma´s lead compound AP1189 is to promote resolution of inflammation through melanocortin receptor activation directly on macrophages, thereby reducing the pro-inflammatory activity of macrophages and by stimulating so-called macrophage efferocytosis, a specific ability to clear inflammatory cells (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 a clinical phase 2 study in patient with active rheumatoid Arthritis, in nephrotic syndrome and COVID-19 inflammation ARDS.

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

https://clinicaltrials.gov/ct2/show/NCT04456816?term=AP1189&draw=2&rank=2

About BEGIN Phase 2 Study

The BEGIN study is a multicenter, two-part, randomized, double-blind, placebo-controlled, 4-week study with repeated doses of AP1189. The study population consist of newly diagnosed subjects with severe active RA (Clinical disease activity score, CDAI >22) who are to start up-titration with methotrexate (MTX).

The first part of the study that now has been completed consisted of two cohorts. In the first cohort a total of 14 patients were treated with 50 mg AP1189 or placebo oral dosing once daily for 4 weeks as add on treatment to MTX naïve patients. The dosing of MTX given were in the range of 10-25 mg given orally once weekly

In the second part of the study that will be initiated in the week of November 9, 2020, 50 mg AP1189, 100 mg AP1189 or placebo given orally in a 1:1:1 randomization will be dosed once daily for 4 weeks as add on to MTX as in part 1 of the study. The total number of patients in both parts of the study is 90. The study is conducted at sites in Denmark, Sweden and Norway.

The primary safety objective is to compare AP1189 against placebo by evaluating adverse events (AEs), serious adverse events (SAEs), and laboratory abnormalities.

The primary efficacy objective is to evaluate the effect of AP1189 vs. placebo in subjects with severe active RA (CDAI >22), undergoing up-titration with MTX, by showing a change in CDAI from severe (CDAI >22) to moderate (CDAI ≤22) after 4 weeks treatment compared to baseline.

Secondary efficacy objectives are to compare the effects of AP1189 against placebo by assessing:

- Proportion of subjects achieving a reduction of more than 10 swollen and/or tender joints at week 4 compared to baseline
- Proportion of subjects achieving a change in CDAI score at week 4 compared to baseline (Proportion of subjects with a 5-10 and 15-point decrease)
- Proportion of subjects achieving a change in value to ≤3.2 as measured by DAS28 (disease activity score 28) at week 4 compared to baseline
- Change in subject-reported quality of life (using Health Assessment Questionnaire – Disability Index (HAQ-DI)) at week 4 compared to baseline
- Change in subject-reported fatigue (using Functional Assessment of Chronic Illness Therapy [FACIT]-Fatigue) at week 4 compared to baseline
- Proportion of subjects achieving ACR (American College of Rheumatology) response assessed by ACR 20, ACR 50, and ACR70

Tertiary efficacy objectives include evaluation of treatment effect with AP1189 relative to placebo on circulating levels of chemokines and cytokines.

In addition, samples to determination of melanocortin receptor polymorphism will be collected which gives the possibility to address treatment effect on an individual basis to the expression of the specific melanocortin receptor variants. In parallel experimental studies aimed to characterize the efficacy of AP1189 as a biased agonist in number of melanocortin receptor variants has been initiated. This approach opens for a unique possibility to apply a personalized medicine approach for further development.