SYNACT PHARMA

**Press Release**
16 December 2022 07:00:00 CET

# SynAct Pharma initiates dosing in the RESOLVE study in DMARD-IR RA

**SynAct Pharma AB (publ) ("SynAct") today announced that the first patient was dosed in part A of the clinical Phase 2a/b study RESOLVE with the company's candidate drug, AP1189, in rheumatoid arthritis (RA) patients with inadequate response to disease# modifying antirheumatic drugs (DMARD-IR).**

The RESOLVE study, aimed at evaluating the safety and efficacy of SynAct´s lead compound, AP1189, is now initiated according to plan with dosing of the first patient. The study is conducted under an US Investigational New Drug (IND) Application at 17 sites in the US, Bulgaria, and Moldova.

"To initiate dosing in the RESOLVE study is a major milestone for the project. AP1189 addresses an unmet need for a novel treatment option in RA as the compound compared to most current treatment options is aimed to promote immunological resolution. This novel concept could have a major impact on the treatment of RA, where more than 40 % of all patients don't respond adequately to first line treatment" said Thomas Jonassen, CSO. "We are looking forward to seeing the results in the second half of 2023, if recruitment goes as planned."

The AP1189 compound is currently tested in a parallel running Phase 2b study in previous treatment naïve RA patients with high disease activity, the EXPAND study. This study is to be considered as a continuation of the BEGIN study, where AP1189 was found to be safe and well tolerated and induced a statistically significant reduction in disease activity when given once daily for 4 weeks.

*The information was submitted, through the agency of the contact persons set out below, for publication at 07:00 CET on December 16, 2022.*

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**About SynAct Pharma AB**
SynAct Pharma AB (publ) (Nasdaq Stockholm: SYNACT) 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 candidate drug, 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 RESOLVE**
The RESOLVE study (SynAct-CS006) is a two-part, randomized, double-blind, multi-center, placebo-controlled study of the safety, dose-range finding confirmation, and efficacy of 4 (Part A) and 12 weeks (Part B) of treatment with AP1189 in adult RA patients with an inadequate response to MTX alone.

In Part A approximately 120 randomized patients will be treated with either 60 mg AP1189, 80 mg AP1189, 100 mg AP1189 or placebo once daily for 4 weeks as add-on treatment to stable MTX treatment. Part A will conclude with an unblinded assessment for risk/benefit and a recommendation for dose selection for Part B and is due to the sample size not expected to show statistically significant difference between active and placebo on the primary efficacy end point.

In Part B, patients will be randomized into groups of equal size evaluating up to 3 doses of AP1189 versus placebo, all doses will be administered once daily for 12 weeks as add-on treatment to stable MTX treatment. The sample size per dose group/placebo group is 75 patients, by which the total study population of Part B may be up to 300 patients, depending on the number of dose groups of AP1189 selected for evaluation based on Part A.

The objectives of the two-part study are to evaluate the efficacy and safety of multiple doses of AP1189 when combined with MTX in DMARD-IR patients. The safety of AP1189 will be assessed by comparing AP1189 against placebo for adverse events, physical examinations, vital sign measurements, ECG, and clinical laboratory testing (hematology, chemistry, and urinalysis). The primary efficacy endpoint is the effect of AP1189 compared to placebo evaluated by the ACR20 response. The effect will additionally be evaluated by ACR50, ACR70, CDAI, DAS-28, CRP, the need for rescue medication, inflammatory and collagen turnover biomarkers, HAQ-DI and FACIT-Fatigue. In Part B changes in imaging parameters reflecting joint inflammation (DCE-MRI) from Baseline to Week 12 will be evaluated in a subgroup of patients.

**Attachments**
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