SYNACT PHARMA

**Press Release**
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# SynAct Pharma enrolls first patient in Phase 2b trial of AP1189 in RA

**SynAct Pharma AB (publ) ("SynAct") today announced enrollment of the first patient to its clinical Phase 2b study EXPAND with the company's candidate drug, AP1189, in patients with newly diagnosed severe rheumatoid arthritis (RA).**

The EXPAND study, aimed at evaluating the safety and efficacy of SynAct Pharma´s lead compound, AP1189, is now initiated according to plan with recruitment of the first patient in Moldova. Enrollment in Bulgaria will be initiated imminently, following approval from local health authorities and ethical committee earlier this month.

"To initiate the EXPAND study, aimed to investigate the full treatment potential of AP1189, 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. A novel treatment concept that we foresee could have major impact on how to treat not only RA, but a large number of autoimmune and inflammatory diseases" said Jeppe Øvlesen, CEO. "The company is working hard to advance its pipeline and right now we are all focused on executing on our plan with primary focus on the development of AP1189."

The aim of the study is to recruit and treat a total of 120 previous treatment naïve patients with severe RA with once daily dosing of 100 mg AP1189 or matched placebo for 12 weeks given in combination with standard therapy, methotrexate (MTX).

In the preceding BEGIN study, AP1189 was found to be safe and well tolerated and induce a statistically significant reduction in disease activity when given once daily for 4 weeks. EXPAND is designed to further evaluate the safety profile and the full treatment potential of the compound when given once daily with the newly developed immediate release tablet during a 12-week treatment period.

To strengthen the position of AP1189 as a novel compound with a unique mode of action in resolution of inflammation, several exploratory endpoints are included in EXPAND, such as MRI-scanning of affected joints, during the study. SynAct expects these data to be pivotal in the interactions with potential partners and for the further development of AP1189.

Key results will be available in the second half of 2023, subject to recruitment to the study being conducted as planned.

*The information was submitted, through the agency of the contact person below, for publication at 07: 00 a.m. CEST on September 27, 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 EXPAND**
The EXPAND (SynAct-CS007) study is a multicenter, randomized, double-blind, placebo-controlled, 12-week study in newly diagnosed, treatment naïve patients with highly active RA (Clinical Disease Activity Score (CDAI) > 22) who are to start treatment with methotrexate (MTX). In EXPAND, 120 RA patients with high disease activity (CDAI > 22) will be randomized 1:1 for treatment with either the newly developed 100 mg AP1189 tablets or placebo tablets for a once daily dose for 12 weeks, concurrently with the prescribed dosing with MTX. The primary efficacy read-out in the EXPAND is proportion of patients achieving 20% improvement in ACR (ACR20) at week 12 relative to placebo. The safety evaluation read-outs include adverse event monitoring, biochemical and hematological evaluation, physical examinations, and vital sign measurements. In addition, several secondary efficacy endpoints are defined, including, ACR50, ACR70, CDAI, and Disease activity score 28 (DAS-28) change over time, Change in Health Assessment Questionnaire – Disability Index (HAQ-DI) and Functional Assessment of Chronic Illness Therapy [FACIT]-Fatigue), as well as use of corticosteroids as rescue medication. Tertiary endpoints are included to further explore the effect of AP1189 on biomarkers and by evaluation of synovial inflammation using magnetic resonance imaging (MRI).

**Attachments**
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