SynAct Pharma submits CTA for Clinical Phase 2b Study in RA

SynAct Pharma AB ("SynAct") today announced that it has submitted a Clinical Trial Application (CTA) to initiate the clinical Phase 2b study, EXPAND, with the Company's candidate drug, AP1189, in patients with newly diagnosed rheumatoid arthritis (RA).

The EXPAND 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).

EXPAND is a part of SynAct's strategy to further develop AP1189 in RA patients. In the Phase 2a study, BEGIN, 100 mg AP1189 once daily for 4 weeks in combination with MTX treatment was found to be safe and well tolerated and met the primary endpoint of a significantly greater than placebo reduction in clinical disease activity (reduction in CDAI; Placebo: 9.3 points vs 100 mg AP1189: 15.5 points, $P<0.05$). In addition, treatment with AP1189 was associated with a statistically significant higher proportion of patients achieving 20% improvement in American College of Rheumatology (ACR20) score. (ACR20; Placebo: 33% vs 100 mg AP1189: 61%, $P<0.05$).

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. Subject to approval from health authorities, first patient is expected to be enrolled in the study in Q3 2022. The study is expected to benefit from the successful recruitment to the BEGIN study with inclusion of sites in Moldova and Bulgaria.

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).

The purpose of the EXPAND study is to confirm the encouraging effects of AP1189 demonstrated in the BEGIN study showing very good safety and a clinically meaningful effect on both primary and secondary efficacy readouts already after four weeks treatment. A major aim is to identify the full treatment potential of the compound, i.e. how large a proportion of patients who respond to the compound. A just as important purpose of the study is to generate safety data during prolonged treatment.

"With AP1189 we aim to address the treatment in Rheumatoid Arthritis by inducing resolution, i.e. induce treatment effects by balancing the immune system rather than suppress it. If we in addition to identify the full efficacy potential, will be able to confirm the good safety profile of the compound, it could be game changer in the management of RA," said Thomas Jonassen, CSO of SynAct Pharma. "Consequently, we propose that there may be a clinical benefit of initial therapy with a combination of methotrexate and AP1189, as it could demonstrate a better efficacy and a better safety profile than the current treatment option. EXPAND is SynAct Pharma's first Phase 2b study and is an important step in that direction."

"Having developed our novel tablet and performing the three months toxicology studies, now allow us to pass this important milestone and take AP1189 into Phase 2b. We have planned a state-of-the-art study to be completed in second half of 2023. Not only, will it give us very valuable information of the full potential of the compound's efficacy and add equally important data on its safety profile, but also, in our mind, enable late-stage development of AP1189. Thus, with a positive outcome we will have a very attractive asset, that can be benchmarked directly against other treatments in RA," said Jeppe Øvlesen, CEO of SynAct Pharma.

The information was submitted, through the agency of the contact person below, for publication at 07:00 a.m. CEST on June 21, 2022.

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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 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.