SYNACT PHARMA

Press Release
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SynAct Pharma receives IND clearance from the FDA for Phase 2a/b trial of AP1189 in RA

SynAct Pharma AB (publ) ("SynAct"), a clinical stage biotech company with a unique portfolio of melanocortin receptor agonists, today announced it has received clearance from the US Food and Drug Administration (FDA) of its Investigational New Drug (IND) application for a Phase 2a/b study in Rheumatoid Arthritis (RA) with the company's lead compound AP1189.

The IND was submitted to the FDA Division of Rheumatology and Transplant Medicine (DRTM) on September 30, 2022, sponsored by SynAct. On October 31, FDA confirmed by email that as of October 30, 2022, the IND-initiating study, RESOLVE, was safe to proceed.

Dr. Thomas Jonassen, CSO at SynAct stated: "This IND clearance is an important milestone for SynAct and for AP1189. It marks the initiation of regulatory and clinical processes in the US and a true globalization of the development program for AP1189. We are looking forward to collaborating with investigators and well renowned key opinion leaders in the further development of AP1189 in the US and in the conduct of the RESOLVE study. We believe AP1189 can make a great impact with its new and unique mode of action for oral treatment of inflammatory and auto-immune diseases."

"Inclusion of the US in the development program is very important for our discussions with potential business partners. Also, it opens up the US market, the world's biggest and most important pharma market, where RA in itself has an estimated market value of approximately USD 20 billion annually," **he added**.

SynAct expects that AP1189, a selective melanocortin receptor agonist, could be very well suited as a once-daily oral treatment therapy for inflammatory and auto-immune diseases, such as RA. AP1189 has been effective, safe and well-tolerated in previous clinical studies. Also, it has a favorable patent situation, with coverage beyond 2040.

RESOLVE, which is SynAct's fifth approved clinical Phase 2 study in three different diseases of which two are completed, will be conducted at five clinical sites in the US as well as 12 sites in Bulgaria and Moldova, where Clinical Trial Applications are pending review by the local authorities and ethics committees. The successful outcome of the IND application review implies that SynAct can initiate the clinical development of AP1189 in USA immediately.

The information was submitted, through the agency of the contact person below, for publication at 07: 00 a.m. CEST on November 1, 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.

In Part B patients will be randomized into groups of equal size evaluating 2-3 doses of AP1189 versus placebo, all doses will be administered once daily for 12 weeks as add-on treatment to stable MTX treatment. The proposed sample size per dose group/placebo group is 75 patients, by which the total study population of Part B may be either 225 or 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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