SynAct Pharma announces additional data from the EXPAND P2b clinical trial further supporting efficacy and activity seen in patients with elevated CRP

- Additional data supports resomelagon efficacy and activity in the relevant elevated CRP population
- Data indicate that in patients with elevated CRP at baseline (>3mg/L), resomelagon treated patients had:
    - Biggest improvements in the HAQ-Disability Index (HAQ-DI) in areas indicating increased hand strength and dexterity
    - MRI data sub study of wrist and hand joints indicate a reduction in inflammation intensity as compared to placebo supported by matched reductions in tender and swollen joint counts
    - Higher plasma levels of C4M, a biomarker of synovial collagen 4 degradation, indicating a higher reduction in synovial inflammation
- CEO Torbjørn Bjerke will present the data at Redeye's Autoimmune and inflammatory disease event today at 11:35 CEST. The presentation will be posted on SynAct's website after the event. Link to join: https://www.redeye.se/events/915413/redeye-theme-autoimmune-and-inflammatory-disease

SynAct Pharma AB (Nasdaq Stockholm: SYNACT), a clinical stage biotechnology company focused on the resolution of inflammation through the selective activation of the melanocortin system, today reported additional results from the 12-week Phase 2b EXPAND study of 100mg once-daily oral resomelagon (AP1189) in newly diagnosed rheumatoid arthritis (RA) patients experiencing severe disease activity.

SynAct previously announced that while the overall study did not achieve its primary endpoint, resomelagon treatment demonstrated consistent efficacy and activity over placebo in patients with elevated CRP levels (>3mg/L) at baseline as evidenced by a 70.6% ACR20 response rate at 12 weeks Vs 54.3% in the placebo group. Today's release adds more detailed data on the HAQ disability index, data from the sub-study of MRI imaging of wrist and hand joints and biomarker data all supporting resomelagon efficacy and activity in this important and relevant patient population.

SynAct previously announced that in patients with baseline CRP >3mg/L at baseline treated with resomelagon had an average decrease in their HAQ-DI score of 0.64 which is almost 3 times the minimal clinically important difference (MCID). Today's release indicates that the HAQ-DI sections showing the largest mean disability improvements over placebo relate to improvements in hand strength and dexterity. Resomelagon treated patients reported a 50% improvement in activates relating to eating, 43% in dressing and grooming and 38% in grip as compared to 24%, 25% and 18% respectively for placebo.

A sub study using contrast-enhanced MRI to assess joint inflammation in patients with inflamed wrist and hand joints was conducted in 23 patients treated with resomelagon and 18 patients treated with placebo. 74% of the resomelagon patients had CRP>3 mg/L at baseline compared to 33% in the placebo group. The MRI techniques used measure the peak enhancement and rate of enhancement of a contrast agent as indicators of synovial inflammation. Comparing the 12 weeks MRI with the Baseline MRI the resomelagon group showed a larger reduction in both mean peak enhancement (3.8 ml vs 1.2 ml) and mean initial rate of enhancement (0.06 ml/sec vs 0.01 ml/sec) indicating a greater reduction in in inflammation intensity. Matched tender and swollen joint counts of the same patients and joints assessed by MRI supports the finding of lower inflammation in assessed joints. The resomelagon treated patients had a significantly larger reduction in both tender (5.3 vs 2.9; $p<0.05$) and swollen (6.4 vs 3.7; $p<0.05$) MRI-assessed joints than placebo.

SynAct also released data from some experimental plasma biomarkers of synovial collagen turnover as indicator of synovial inflammation. In the patients with CRP>3 at baseline (resomelagon n=34; placebo n=35) comparing circulating levels following 12 weeks treatment to baseline levels C3M a marker of collagen 3 turnover was reduced in both treatment groups in line with previous reports showing that methotrexate treatment is associated with reduction in circulating levels of C3M. C4M a marker of synovial collagen 4 degradation was significantly reduced in the resomelagon group, whereas it was unchanged in the placebo group. Lower levels of C4M mean a lower rate of Collagen 4 degradation which is believed to be a marker for lower synovial inflammation.

“These additional data from the HAQ component scores, the MRI sub study and collagen turnover markers support the positive outcome data for resomelagon over placebo in patients who had systemic inflammation at baseline as indicated by elevated CRP levels. We see a positive signal of hand joint improvement in the HAQ scores that is supported by the MRI findings of lower intensity of inflammation in assessed wrist and hand joints and significant improvements in matched patient joint counts,” said Thomas Jonassen, CSO of SynAct Pharma. “RA is a heterogenic disease but patients with elevated CRP which can be up to 75% or more of patients with longer-standing disease are an important and relevant population and the finding that resomelagon may work at a higher rate in these patients is an important finding.”

“Resomelagon works at least in part to stimulate the body’s own inflammation resolution systems to help restore immune balance. We know that the ability to stimulate inflammatory resolution is associated with induction of the macrophages ability to amplify the clean-up process known as efferocytosis. Then, tissue-reparative, and tissue-protective mechanisms are set in motion. In order to benefit of this ability, a certain degree of inflammation most likely needs to be present,” said Professor Mauro Perretti, PhD William Harvey Research Institute, Barts and the London School of Medicine, Queen Mary University, London, UK.

About SynAct Pharma AB
SynAct Pharma AB (Nasdaq Stockholm: SYNACT) is a clinical stage biotechnology company focused on the resolution of inflammation through the selective activation of the melanocortin

system. The company has a broad portfolio of oral and injectable selective melanocortin agonists aimed at inducing anti-inflammatory and inflammation resolution activity in autoimmune and inflammatory diseases to help patients achieve immune balance and overcome their inflammation. For more information: www.synactpharma.com.

About resomelagon (AP1189)
Resomelagon (AP1189), is a once-daily oral selective melanocortin agonist that selectively activates melanocortin receptors 1 and 3 that are directly involved in inflammation and its resolution. These receptors are located on immune cell types including macrophages and neutrophils. Activation of these receptors can result in both anti-inflammatory effects like lowering the level of pro-inflammatory molecules and in pro-resolution effects like switching macrophages to perform inflammation 'clean-up', known as efferocytosis (J Immun 2015, 194: 3381-3388). This dual 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).

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) In EXPAND, 127 RA patients with high disease activity (CDAI > 22) were randomized 1:1 for treatment with either 100 mg resomelagon (AP1189) tablets or placebo tablets for a once daily dose for 12 weeks, concurrently with the initiation of dosing with methotrexate. 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 included 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 resomelagon (AP1189) on biomarkers and by evaluation of synovial inflammation using magnetic resonance imaging (MRI).

Attachments
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