SYNACT PHARMA

Press Release
15 June 2026 06:45:00 CEST

Phase 2b ADVANCE study demonstrates positive effects of resomelagon in Rheumatoid Arthritis – supports phase 3 design, regulatory interactions, and partnering

SynAct Pharma AB (publ) ("SynAct") (Nasdaq Stockholm: SYNACT), a clinical-stage biotechnological company focused on treating inflammation through resolution, reported today that resomelagon in combination with methotrexate showed promising clinical effects on par with previous findings with ACR20 reaching 76,4% in the most effective dose compared to 60,8% in the placebo treated control group (p=0,06, per protocol data set) reaching statistical significance in the subset of patients entering the study with ACR /EULAR class II-III disease, (76,9% vs. 56,5%, p=0,03). The treatment potential was further supported by a significant reduction of CRP (p=0,0037) which was not present in the placebo treated control group. In addition, resomelagon induced a larger reduction in the Simplified Disease Activity Index (SDAI) (p=0,03 vs placebo). Overall, the safety profile of the compound was very good, and the compound was well tolerated. No signs of immune suppression were observed.

- The company is hosting a webcast on Monday June 15th at 10:00 CEST (details below) including a Q&A session.
- A slide presentation outlining results of the ADVANCE study will be made available prior to the webcast on www.synactpharma.com

The ADVANCE (SynAct-CS008) study was a multicenter, randomized, double-blind, placebo-controlled, 12-week study in newly diagnosed, treatment naïve patients with highly active Rheumatoid Arthritis (RA) (Clinical Disease Activity Index (CDAI) > 22; DAS28-CRP >5,1 and hsCRP > 3 mg/L) conducted at sites in Europe and USA. 246 patients were randomized with the aim of confirming the potential of the compound as a novel safe treatment option in RA and identify feasible doses for further (phase 3) clinical development.

"We designed the study with the aim to confirm the potential of resomelagon as a new treatment option for early intervention in RA where there is a large need for novel well tolerated treatment option that can help control disease activity without inducing suppression of the immune system", said Chief Scientific Officer, Thomas Jonassen, and continues "To our knowledge, the ACR20 response for resomelagon is on par with what has been reported for the very potent Janus Kinase (JAK) inhibitors upadacitinib and baricitinib. No other compounds, except glucocorticoids have shown ACR20 response rates above 75% following 12 weeks dosing."

The study identified 40 mg given once daily as the most effective dose showing reduction in all clinical parameters on par with what has been seen in previous studies. The study confirmed the hypothesis of non-linear dose-response for resomelagon. Per protocol, 42 out of 55 (76,4%) (p=0, 06) treated with 40 mg resomelagon reached ACR20 response compared to 31 out of 51 (60,8%) of those treated with Placebo. ACR50 response was reached in 21 of the 55 (38,9%) vs 18 out of 51 (35,3%) in the placebo group. Deeper clinical response like ACR50 continues to improve after

ACR20 saturation, indicating that the ACR50 response will continue to increase with treatment beyond 12 weeks of treatment with resomelagon. In patients entering the study with disease classification ACR/EULAR class II and III further substantiated the potential of resomelagon as ACR20 response reached statistical significance in these patients with 40 out of 52 (76,9%) in the 40 mg resomelagon group versus 26 out 46 (56,5%), (p=0,03) in the placebo treated group.

Resomelagon in all dose-groups induced a statistically significant reductions in CRP. The resomelagon 40 mg group, CRP (mean values) went from 23.0 to 9.5 mg/L (p=0,0037), compared to 17.7 to 12.0 mg/L (not significant) in the placebo treated group. The mean reduction in the clinical relevant Simplified Disease Activity Index (SDAI) was 35.9 in the resomelagon 40 mg group versus 28.5 (p=0.03) in the placebo group. As per FDA guidance, DAS28-CRP and SDAI are interchangeable measures to be used for dose response studies.

Whereas the response to resomelagon was on par with what has been reported previously (BEGIN and subgroup analysis in EXPAND) the least square mean of reduction in DAS28-CRP (primary endpoint) in the per protocol subjects was 1.98 (SE 0.14) vs 1.79 (SE 0.14) in the placebo treated group (p=0.168). The reduction in the placebo treated group was around 50% larger than what was seen in previous studies which made the primary endpoint inadequate to reach significance within the limits of the study design.

Overall, the safety profile of the compound was very good and the compound was well tolerated, no signs of immune suppression were observed, no serious adverse event was reported in the resomelagon treated groups, and reduction in the background treatment with methotrexate due to lack of tolerance was only reported in the placebo treated control group.

Business development and partnering update
“We are excited about the ADVANCE study and we are positive that the results will lay the foundation for a very constructive business development agenda ahead of us”, said Chief Executive Officer, Jeppe Øvlesen.

“The data supports a compelling profile and mechanism of action that could broaden the addressable market in RA, supporting competitive positioning across major patient groups, including those with compromised immune systems and individuals with hyperinflammatory responses to viral infections. Resomelagon is a “first-in-class” and the clinical proof of concept is what makes the results of ADVANCE so exiting”, said Chief Business Officer, Mads Bjerregaard.

The results from the ADVANCE study are expected to further fuel partnering and licensing discussions. SynAct will be engaging with pharmaceutical companies and provide a company presentation on the BIO International partnering conference in San Diego on June 22-25, 2026.

Webcast
SynAct Pharma will present the findings from the study and host a Q&A session during a live webcast on Monday June 15th at 10:00 CEST. Link to the webcast: https://www.youtube.com/live/wWjn0B1CaaI

About Rheumatoid Arthritis:
Rheumatoid Arthritis affects 18 million people and is expected to affect up to 32 million people by 2050 (ref. 1). About 50% of patients present with moderate to severe disease scores at time of diagnosis (ref. 2) and major medical societies recommend progressive treatment to prevent disease from progressing. Resomelagon in addition to 1st line methotrexate therapy may be a safe and effective way to reduce disease symptoms and may prolong or prevent the need for additional therapy typically adding glucocorticoids and biologic DMARDS.

About the Phase 2b ADVANCE study:
The ADVANCE study was a 12-week randomized, double-blind, multicenter, placebo-controlled Phase 2b study with repeated doses of 40mg, 70mg, and 100mg of AP1189 and placebo. The study includes 246 newly diagnosed patients with Rheumatoid Arthritis (RA), with elevated inflammation levels (CRP levels above 3mg/l), severe disease symptoms, and ready to initiate 1st line methotrexate therapy.

References: 1) Lancet Rheumatol 2023;5: e594–610; 2) Z Rheumatol. 2017 Jun;76(5):434-442

For further information, please contact:
Jeppe Øvlesen
CEO, SynAct Pharma AB
Phone: + 45 2844 7567
E-mail: investor.relations@synactpharma.com

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 to help patients achieve immune balance and overcome their inflammation. For further information: https://synactpharma.com/.

This information is information that SynAct Pharma is obliged to make public pursuant to the EU Market Abuse Regulation. The information was submitted for publication, through the agency of the contact persons set out above, at 2026-06-15 06:45 CEST.

Attachments
Phase 2b ADVANCE study demonstrates positive effects of resomelagon in Rheumatoid Arthritis – supports phase 3 design, regulatory interactions, and partnering