The information in the press release is intended for investors.

Isofol announces a post hoc per-protocol analysis of the AGENT study, further supporting arfolitixorin's continued clinical development

GOTHENBURG, Sweden, July 5, 2024 - Isofol Medical AB (publ), (Nasdaq Stockholm: ISOFOL), announced today that an external committee of experts has performed a post hoc per-protocol analysis of the clinical phase III study AGENT that shows new results in favor of arfolitixorin. These positive data, together with conclusions from earlier studies and analyses, strengthen the outlook for the continued development of arfolitixorin.

After a new board and management team took office in January, Isofol has concluded several laboratory studies and analyses which have generated further arguments supporting the continued clinical development of arfolitixorin. In addition, an external committee of experts has been assigned to perform an evaluation of available data from the AGENT study and has now delivered its first results. The committee has performed a post hoc per-protocol analysis showing that the outcome may have been affected by a lack of compliance with the study protocol, mainly regarding the time interval between the administration of the 5-FU bolus and arfolitixorin and the duration of the 5-FU injections – factors that were not considered in the original per protocol analysis.

Results from the analysis, in which the expert committee excluded patients who were not treated in compliance with the study protocol, show a numerical difference in objective response rate (ORR) in favor of arfolitixorin (arfolitixorin: 59.3 % ORR; leucovorin: 51.5 % ORR; $p<0.23$). Thus, the study shows a non-significant difference between the arms in favor of arfolitixorin of 7.8 percentage points based on a remaining group of 225 patients.

Similar to the original AGENT analysis, the new analysis further shows that there are regional differences. The only region showing a statistically significant difference in efficacy between the treatment arms is North America, where a strong difference in favor of arfolitixorin is seen (arfolitixorin: 85.7 % ORR; leucovorin: 45.5 % ORR; $p<0.017$; based on 47 patients).

The main conclusions of the previously conducted laboratory studies and analyses have been that there is a clear dose-response relationship, meaning that a higher dose of arfolitixorin led to a higher effect; and that the dose regimen used in the phase III study (AGENT) was probably suboptimal and not comparable with the control arm, based on an extended pharmacokinetic analysis. This may explain why the study showed no significant difference in effect between arfolitixorin and leucovorin.

The overall conclusion is that all available data strengthens Isofol's confidence to be able to show positive data in the planned phase Ib/II study. This is grounded in the per-protocol post hoc analysis, which reveals that even the probably suboptimal dose regimen used in the AGENT study resulted in a numerical difference in favor of arfolitixorin, as well as the previous laboratory studies and analyses that indicate that an optimized dose regimen may have even better effect.

"The results from the per-protocol post hoc analysis show that arfolitixorin has the potential to be more efficacious than leucovorin, if the study protocol is more strictly followed. This is very positive and brings valuable insights to our upcoming clinical trials. Together with the results we received through other studies and analysis, showing that an optimized dose and administration regimen of arfolitixorin could lead to a higher efficacy, these results strengthen the likelihood of success in the continued development of our drug candidate," says Petter Segelman Lindqvist, CEO of Isofol.

Isofol recently signed a collaboration agreement with the leading European university hospital Charité – Universitätsmedizin Berlin and the Clinic for hematology, oncology, and tumor immunology (CCM) led by Professor Dr. med. Sebastian Stintzing, for the continued development of arfolitixorin. The conclusions from the per-protocol post hoc analysis will support the design of the phase Ib/II study that is expected to be initiated before the end of 2024 and the upcoming dialogues with relevant authorities.

For more information, please contact

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This is information that Isofol Medical AB (publ) is obliged to make public pursuant to the EU Market Abuse Regulation. The information was submitted for publication, through the agency of the contact person set out above, at 10:15 CEST on July 5, 2024.

About the post hoc per protocol analysis

The initial ITT population in the AGENT study consisted of 490 patients, split into two arms of 245 patients each. One arm was treated with arfolitixorin (experimental arm) and the other with leucovorin (control arm). In the present post hoc per protocol analysis, patients were excluded based on the following: 1) Missing or incorrect IMP handling 2) The first dose of 5-FU was to be given as a bolus over 2-4 minutes. Patients who received a bolus <2 minutes or >4 minutes in more than 20 % of treatment sessions were excluded. 3) The interval between the first dose of 5-FU and the first arfolitixorin dose would be 30 ± 5 minutes. Patients in whom the time between doses was <25 minutes or >35 minutes in more than 20 % of treatments were excluded. 4) No patients were excluded based on the time interval between the 1st and 2nd arfolitixorin dose or if the duration of the arfolitixorin bolus deviated from 3 minutes as the compliance to these criteria was high. A total of 225 patients (46 %) met these criteria, with 91 patients in the arfolitixorin arm and 134 in the leucovorin arm, and it is this population that was further analyzed by the expert group. Logistic regression, adjusted for randomization strata (region, primary tumor location, previous neo-adjuvant/adjuvant CRC treatment), was used in the analysis of ORR. The committee of experts that has performed the per-protocol post hoc analysis consists of Göran Carlsson, MD, PhD, Sahlgrenska University Hospital; Åke Hjalmarson, MD, Prof in Cardiology at Sahlgrenska University Hospital, and Aldina Pivodic, PhD, APNC Sweden. The analysis was funded by Isofol.

About Isofol Medical AB (publ)

Isofol Medical AB (publ) aims to raise the quality of life and increase the survival rate for patients with severe forms of cancer. The company's drug candidate arfolitixorin is being developed with the purpose of increasing the efficacy of standard first-line treatment for several forms of solid tumours, including colorectal cancer. The next step in the clinical development program is currently being prepared based on a new dosage regimen that is expected to optimize arfolitixorin's efficacy. Isofol Medical AB (publ) is traded on Nasdaq Stockholm.
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