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Isofol reports FDAs feedback from the ongoing special protocol assessment (SPA) process

In March 2018, Isofol Medical AB (publ) submitted a Special Protocol Assessment (SPA) to the United States Food and Drug Administration (FDA). The SPA process aims to confirm the specific targets to be met in the ISO-CC-007 study, the pivotal study with arfolitixorin in first line metastatic colorectal cancer (mCRC). In the feedback received from the FDA the company has reached a consensus with the FDA on the most important parameters for an SPA agreement and will now complete the SPA submission with the outstanding issues commented on by the FDA.

The FDA agreed:

- that the primary outcome for the ISO-CC-007 study will be objective response rate (ORR), the proportion of patients with tumor size reduction according to the RECIST criteria 1.1.
- that a significant improvement of 9,7 percent units for ORR in the arfolitixorin arm will be sufficient to support an New Drug Application (NDA), if Isofol also can demonstrate a clinically meaningful improvement in the key secondary endpoint, progression free survival (PFS).
- on the sample size of 440 patients and the outline of the statistical plan and the adaptive study design described, with the possibility to increase sample size based on the outcome of an interim analysis of ORR and PFS performed after approx. 75 % of the patients being treated for at least 16 weeks.

In addition, the FDA requires;

- safety data from a total of 9 patients treated with the selected study dose of arfolitixorin in combination with 5-FU, oxaliplatin and bevacizumab from the ongoing phase I / II study ISO-CC-005 in patients with mCRC before Isofol can resubmit the SPA application to the FDA. Today, 7 patients have initiated treatment with the selected dose regimen intended for the ISO-CC-007 study.
- an addition of statistics for OS (overall survival) to be able to rule out a clinically meaningful decrement in survival for the arfolitixorin arm.

Isofol estimates that an updated SPA application will be submitted to the FDA during July/August this year. Based on this, it is indicated that Isofol's previously communicated time plan for the ISO-CC-007 study, including the first patient in June, is postponed with approx. 4 months. The company's assessment, however, is that this does neither delay a scheduled interim analysis of 330 patients at the turn of the year 2019/2020 nor the time for the last patient included in the study, scheduled for Q4 2020.

In order for Isofol to get an approved SPA, thereby launching the ISO-CC-007 study in the United States, the company also needs to adapt the study protocol for the planned ISO-CC-007 study in accordance with recommendations from the FDA. An update of the protocol is expected to be completed in June.

Anders Rabbe, CEO of Isofol Medical, commented: *"It is encouraging that we in the ongoing SPA process have reached a consensus with the FDA on the overall study design and the most important parameters in the ISO-CC-007 study. The additional feedback from the FDA also guides us in adopting the study protocol to FDAs recommendations to support an NDA for arfolitixorin in the US. We also have to adapt the SPA process to the fact that the FDA would like to see data from 9 patients treated with the intended study regimen in the ongoing ISO-CC-005 study, before we can resubmit the SPA. This will lead to a postponing of the initiation of the ISO-CC-007 study. We plan to conduct the interim analysis year end 2019/2020 as well as completing the patient recruitment during q4 2020 in accordance with the original time plan for the ISO-CC-007 study".*

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This information is information that Isofol Medical AB) 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(s) set out above, on 3 May 2018, at 15:00 CET.

About arfolitixorin
Arfolitixorin is a new drug developed to increase the efficacy of the cytotoxic agent 5-fluorouracil (5-FU) and as a rescue drug after high-dose methotrexate treatment. The active ingredient in arfolitixorin, [6R]-5,10-methylenetetrahydrofolate, is the key active metabolite of the widely used folate-based drugs leucovorin and levoleucovorin. Arfolitixorin is suitable for all patients irrespective of their capacity to activate folates since it does not require metabolic activation to exert its effect.

About Isofol Medical AB (publ)
Isofol Medical AB (publ) is a drug development company within the field of oncology developing arfolitixorin, primarily as a treatment for advanced colorectal cancer and as a rescue drug after high-dose methotrexate treatment in osteosarcoma (bone cancer). Through a worldwide exclusive license agreement, Isofol holds the rights to develop and commercialise arfolitixorin within oncology with access to the unique patented production process and the production capabilities of Merck KGaA, Darmstadt, Germany. Isofol Medical AB is traded on the Nasdaq First North Premier. Certified Adviser is FNCA Sweden AB.

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