First patient enrolled in Phase Ib/II study SENSITIZE of 4SC-202 in melanoma

- **SENSITIZE study examines the use of 4SC-202 in combination with the checkpoint inhibitor pembrolizumab (Keytruda®, Merck) in patients with advanced-stage melanoma**
- **Topline results expected in H2 2018**

Planegg-Martinsried, Germany, 6 November 2017 – 4SC AG (4SC, FSE Prime Standard: VSC) today announced the enrollment of the first patient in the SENSITIZE study, an open-label, multi-center, Phase Ib/II study to evaluate the combination treatment of 4SC-202 with the anti-PD-1 antibody pembrolizumab (Keytruda®, Merck; an approved checkpoint inhibitor) in patients suffering from advanced-stage cutaneous melanoma.

The SENSITIZE study: 4SC-202 + checkpoint inhibitor pembrolizumab for the treatment of advanced-stage melanoma

According to plan, the SENSITIZE study (ClinicalTrials.gov identifier: NCT03278665) was opened for recruitment from end of September 2017 and will be conducted at 6 certified skin cancer centers in Germany. It will enroll 40 patients suffering from unresectable advanced-stage cutaneous melanoma who are refractory or non-responding to prior treatment with anti-PD-1 antibodies (a checkpoint inhibitor). In the first part of the study, 3 cohorts of 10 patients each will be treated at different dose levels of 4SC-202 in combination with pembrolizumab. In the second part, 10 additional patients will be treated with the recommended dosing regimen defined in the first part of the study.

The primary goal of the study is to determine the safety and tolerability of 4SC-202 in combination with pembrolizumab and key secondary endpoints aim to assess the anti-tumor activity of the combination treatment. Additionally, the study will investigate changes in key immunological biomarkers to better understand how 4SC-202 renders patients more susceptible to treatment with checkpoint inhibitors. 4SC expects topline results to be available in H2 2018.

Prof. Dirk Schadendorf, M.D., principal investigator of the SENSITIZE study, Director and Chair of the Department of Dermatology as well as Director of the Comprehensive Cancer Center at the University Hospital Essen, Germany, commented: “Skin cancer is one of the most common cancers with globally about 2 to 3 million cases each year. Despite the existence of very effective treatment options for early-stage melanoma such as surgery, unresectable advanced-stage melanoma remains associated with a poor prognosis. Novel treatment options particularly in the immuno-oncology field such as checkpoint inhibitors have been proven to be effective in treating advanced-stage melanoma, however, around 40% of the patients do not respond and lack effective therapeutic alternatives. The preclinical data would suggest that the addition of 4SC-202 to the anti-PD-1 antibody pembrolizumab could render these patients more susceptible to treatment with checkpoint inhibitors and allow them to benefit from therapy.”

Jason Loveridge, Ph.D., CEO of 4SC, added: “Enrolling the first patient in the SENSITIZE study is a significant milestone for 4SC. Based on our preclinical work, we are convinced that the combination of 4SC-202 with checkpoint inhibitors is the best route to most rapidly progress 4SC-202 towards market approval. In parallel to the SENSITIZE study, we expect the EMERGE study to start in the upcoming months, which will be conducted by an internationally renowned academic institution. This study will assess the potential of 4SC-202 in combination with another checkpoint inhibitor, the anti-PD-L1 antibody avelumab (Bavencio®, Merck), for treating gastrointestinal

cancer. Taking the data from these two studies we aim to initiate a pivotal clinical trial with 4SC-202 as soon as possible thereafter in the rare skin cancer Merkel-cell carcinoma (MCC)."

- Press release ends -

Related articles

6 July 2017, 4SC AG secures EUR 41 million from successful capital increase

16 May 2017, 4SC AG announces updated and progressive development program

11 April 2017, New mechanistic insights into 4SC-202's epigenetic mode of action

Further information

About 4SC-202

4SC-202 is an orally administered small molecule with a unique mode of action that was designed to strengthen the body's own anti-tumor immune response. 4SC-202 "opens" the tumor microenvironment and encourages infiltration of immune cells into the tumor.

4SC-202 has been investigated in a Phase I study with 24 mostly heavily pretreated patients with several types of highly advanced hematologic cancers, and has proven to be tolerated. Positive signs of anti-tumor efficacy were observed with one complete remission for 28 months and one partial responder for 8 months.

In addition to its therapeutic potential in cancer monotherapy, 4SC is evaluating 4SC-202's capacity as a partner in combination therapies, specifically in the immuno-oncology area. Toward this end, 4SC initiated a Phase Ib/II study of 4SC-202 in combination with the anti-PD-1 checkpoint inhibitor pembrolizumab (Keytruda®, Merck) in patients with advanced-stage melanoma. A second Phase II study of 4SC-202 in combination with the anti-PD-L1 checkpoint inhibitor avelumab (Bavencio®, Merck), which will be conducted by an academic partner in gastrointestinal cancers, is expected to start soon.

As soon as results from the aforementioned trials will be available, 4SC plans to advance 4SC-202 into a pivotal study in combination with a checkpoint inhibitor in PD-(L)1 refractory patients with advanced Merkel cell carcinoma (MCC).

About checkpoint inhibitors

The human immune system is capable of self-regulation via a wide variety of mechanisms to prevent excessive or misdirected defensive reactions. Tumors exploit these immune system "checkpoints" to switch off the immune response that specifically targets them. This is where checkpoint inhibitors are effective: they inhibit the signaling pathways to "release the brakes" on the immune cells and enable them to attack the cancerous tissue again.

Examples of checkpoint inhibitors that have returned promising data after investigation in clinical trials worldwide include drugs that block the PD-1 (Programmed Death-1) receptor on the surface of immune cells. The PD-1 receptor interacts with its ligands PD-L1 or PD-L2 on the surface of cancer cells to prevent the immune cells from attacking the tumor. With the PD-1 receptor or its ligand PD-L1 blocked, cancer cells can no longer escape the immune response.

About 4SC

4SC AG is a clinical-stage biopharmaceutical company developing small-molecule drugs that can target key indications in cancer with high unmet medical needs. Such drugs are intended to provide patients with innovative treatment options that are more tolerable and efficacious than existing therapies and provide a better quality of life. 4SC's pipeline is protected by a comprehensive portfolio of patents and currently comprises three key drug candidates in various stages of preclinical and clinical development: resminostat, 4SC-202 and 4SC-208.

4SC aims to generate future growth and enhance its enterprise value by entering into partnerships with pharmaceutical and biotech companies and/or the eventual marketing and sales of approved drugs in select territories by 4SC itself. 4SC had 47 employees as of 30 September 2017 and is listed on the Prime Standard of the Frankfurt Stock Exchange (FSE Prime Standard: VSC; ISIN: DE000A14KL72).

Forward-looking information

Information set forth in this press release contains forward-looking statements, which involve risks and uncertainties. The forward-looking statements contained herein represent the judgement of 4SC as of the date of this press release. Such forward-looking statements are neither promises nor guarantees, but are subject to a variety of risks and uncertainties, many of which are beyond 4SC's control, and which could cause actual results to differ materially from those contemplated in these forward-looking statements. 4SC expressly disclaims any obligation or undertaking to release any updates or revisions to any such statements to reflect any change in its expectations or any change in events, conditions or circumstances on which any such statement is based.

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