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Philogen
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Philogen provides update on pre-planned interim analysis of the Phase III FIBROSARC trial investigating Onfekafusp alfa (L19TNF) in patients with first-line advanced or metastatic Soft Tissue Sarcoma

FIBROSARC (NCT04650984) is a Phase III trial evaluating Onfekafusp alfa (L19TNF, also known as Fibromun) plus doxorubicin versus doxorubicin alone as front-line therapy for patients with advanced or metastatic Soft Tissue Sarcoma

An Independent Data and Safety Monitoring Board reviewed safety and efficacy data of the pre-planned interim analysis and recommended continuing the study as planned by the protocol

L19TNF is also currently studied in pivotal trials for the treatment of newly diagnosed and recurrent Glioblastoma, for which very encouraging data have recently been published

Siena, Italy, 20 February, 2024 - Philogen S.p.A. (BIT:PHIL) is pleased to announce that the Phase III FIBROSARC trial (NCT04650984) will continue as planned by the protocol. The decision was made by an Independent Data and Safety Monitoring Board (DSMB) following the review of efficacy and safety data in the pre-planned interim analysis.

FIBROSARC is a Phase III 1:1 randomized trial (NCT04650984) which studies L19TNF in combination with doxorubicin (Experimental Arm) versus doxorubicin alone (Control Arm) in 118 patients as first-line therapy for advanced or metastatic Soft Tissue Sarcoma (STS). The primary objective of the study is Progression Free Survival (PFS), with an estimated 45% reduction in the risk of progression in the Experimental Arm (Hazard Ratio 0.55). The pre-planned interim analysis was carried out at 50% of the expected events (i.e., one event corresponds to a disease progression or death) necessary for the primary outcome.

The 46 events required to trigger the interim analysis were reached on 9th November 2023, and at the time of this Press Release the study has enrolled 97 out of 118 patients across 24 clinical centers in Germany, Italy, France, Poland, and Spain. The enrolment of 118 patients is expected to be completed in 2024.

Prof. Dario Neri, **co-founder, CEO and CSO of Philogen, commented:** *"We are very pleased with the recommendation of the DSMB to continue the study as planned by the protocol. The Phase III FIBROSARC trial was designed to demonstrate a significant clinical benefit of L19TNF plus doxorubicin compared to doxorubicin alone. If the final analysis is successful, the study is expected to provide an innovative treatment option for patients with advanced or metastatic STS, for whom no new paradigm-shifting therapies have been available in the last decades."*

Alfredo Covelli, MD, **Chief Medical Officer of Philogen, commented:** *"Advanced or metastatic STS are aggressive tumors still treated with chemotherapy-based regimens that were approved in the 1970s. Most innovative therapies, such as immune checkpoint inhibitors, failed to provide a significant benefit to this patient population. We are excited to*

record the outcome of the interim analysis of FIBROSARC and look forward to seeing the final analysis."

L19TNF is also being evaluated in (i) a Phase IIb randomized trial in first-line metastatic Leiomyosarcoma in the United States (NCT03420014), (ii) a Phase II randomized trial in pre-treated advanced or metastatic Soft Tissue Sarcoma in Europe (NCT04733183), (iii) a Phase II randomized trial in Glioblastoma at first progression in Europe (NCT04573192), and (iv) a Phase I/II/IIb trial in newly diagnosed Glioblastoma in Europe (NCT04443010). Philogen is currently launching a new Phase II study in Glioblastoma at first or later progression in the United States, based on the very encouraging preliminary data observed in the European study. These results have already been published in the journal Science Translational Medicine in 2023 (Look at al. Sci. Trans. Med. 2023, 15:eadf2281).

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About Onfekafusp alfa (L19TNF, also known as Fibromun)

L19TNF is a biopharmaceutical product, proprietary to Philogen, studied for the treatment of advanced Soft Tissue Sarcoma and Glioblastoma. It consists of the L19 antibody genetically fused to Tumor Necrosis Factor (TNF). L19 binds selectively to the Extra Domain B of Fibronectin, a protein expressed in tumors (and other diseases) but absent in most healthy adult tissues. TNF is a pro-inflammatory cytokine with anti-tumor activity that is preferentially localized by the L19 antibody to neoplastic masses. L19TNF is administered via a two-hour intravenous infusion. Late-stage clinical trials with registration potential are on-going in Soft Tissue Sarcoma and Glioblastoma. The product has pan-tumoral potential and could be explored for the therapy of other cancer types (e.g., lung, breast, colon, prostate cancers).

About FIBROSARC Phase III study (NCT04650984)

FIBROSARC is a Phase III international, multi-center, randomized, comparator-controlled, parallel-group study in subjects with advanced or metastatic soft tissue sarcoma. In the study, 118 patients will be enrolled and parallel assigned in a 1:1 fashion to one of two different arms, as follows:

Experimental Arm: Patients will receive 13 µg/kg L19TNF on days 1, 3 and 5 every 3 weeks in combination with 60 mg/m2 doxorubicin (once every 3 weeks).

Control Arm: Patients will receive 75 mg/m2 doxorubicin once every 3 weeks.

The sample size is calculated based on a 2-sided significance level of 5% and an 80% power, assuming a 15% rate for permanent early censoring. The statistical analysis is designed to discriminate 8 months median PFS (mPFS) in the Experimental Arm versus 4.4 months mPFS in the Control Arm. The primary analysis of PFS will occur after approximately 92 PFS events.

About advanced or metastatic Soft Tissue Sarcoma

STS is a rare group of mesenchymal cancers originating from connective tissues, which collectively account for 1% of all adult cancers. Surgery is the first line of treatment for early stage and localized disease. However, distant metastases occur in many patients, especially in those with high-grade tumors. For patients with unresectable STS, chemotherapy is the standard of treatment and doxorubicin is the recognized standard of care for first line advanced or metastatic STS.

About Philogen

Philogen (https://www.philogen.com) is an Italian-Swiss biotechnology company specialized in the research and development of innovative pharmaceuticals for the treatment of cancer. The Group's main therapeutic strategy is based on the use of ligands capable to selectively deliver potent payloads (such as pro-inflammatory cytokines, drugs or radionuclides) to the tumor mass, sparing healthy tissues. Over the years, Philogen has discovered and developed monoclonal antibody- and small molecule-based ligands with high affinity to tumor-associated antigens. The Group is headquartered in Siena, Italy, with a subsidiary and research center in Zurich, Switzerland. In addition to its main oncology focus, Philogen is also active in the development of novel pharmaceuticals for the treatment of chronic and debilitating conditions.

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The forward-looking statements contained in this press release may be identified by words such as “aims,” “anticipates,” “believes,” “could,” “estimates,” “expects,” “forecasts,” “goal,” “intends,” “may,” “plans,” “possible,” “potential,” “seeks,” “will” and variations of these words or similar expressions that are intended to identify forward-looking statements, although not all forward-looking statements contain these words. Forward-looking statements in this press release include, but are not limited to, statements regarding anticipated advancement of preclinical development efforts and initiation and progression of clinical trials; anticipated enrollment in and progression of Philogen’s clinical trials; the availability of data from clinical trials and preclinical studies; anticipated regulatory filings; the therapeutic potential of Philogen’s product candidates; Philogen’s ability to achieve planned milestones. Philogen may not actually achieve the plans, intentions or expectations disclosed in these forward-looking statements, and you should not place undue reliance on these forward-looking statements. Actual results or events could differ materially from the plans, intentions and expectations disclosed in these forward-looking statements as a result of various factors, including: risks to site initiation, clinical trial commencement, patient enrollment and follow-up, as well as to Philogen’s and its partners’ abilities to meet other anticipated deadlines and milestones; uncertainties inherent in the initiation and completion of preclinical studies and clinical trials and clinical development of Philogen’s product candidates by Philogen or its partners; the risk that Philogen may not realize the intended benefits of its technology;

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