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Philogen Publishes New Data on a Fibromun-based treatment combination in Science Translational Medicine in collaboration with the University Hospital Zürich

L19TNF (also known as Fibromun) is an innovative immunotherapy, discovered and developed by Philogen
The new peer-reviewed scientific publication presents recent preclinical and translational results obtained in glioblastoma, the most common and most aggressive primary brain tumor in adults and represents the follow up story of the Science Translational Medicine paper reported in 2020 (see here)
Durable major responses are being observed in a proportion of patients enrolled in the Phase I part of the ongoing clinical trial (NCT04573192)

Siena (Italy), May 24, 2023 - Philogen S.p.A. (BIT:PHIL), a clinical-stage biotech company focused on the development of innovative medicines based on tumor-targeting antibody and small molecule ligands, announces the publication of the latest results of Fibromun (L19TNF, Onfekafusp alfa) in combination with lomustine (an alkylating agent) for the treatment of glioblastoma in *Science Translational Medicine* describing how the combination treatment cured orthotopic glioma-bearing mice and mediated durable objective responses and major tumor shrinkage in patients with recurrent glioblastoma. The paper can be accessed at the following link.

The study demonstrated that the combination Fibromun and lomustine was highly synergistic and relied on an intact immune system. A thorough investigation of the treatment's mechanism of action showed that it could transform tumors from being "invisible" to the immune system ("cold") into being easily recognized and attacked ("hot"). This transformation was proven by several indicators: the activation of the tumor endothelium, enhanced tumor DNA damage signaling pathways, treatment-associated tumor necrosis, increased immunogenicity of cancer cells and elevation of immune cell infiltration within the neoplastic mass.

Prof. Michael Weller and Dr. Tobias Weiss of University Hospital Zürich, commented: ***"****We are excited to release this follow-up work based on the Science Translational Medicine paper published together with Philogen back in 2020. The preclinical anti-tumor activity of the combination of Fibromun with lomustine chemotherapy is very promising and the emerging clinical results of the ongoing Phase I/II trial NCT04573192 provide hope for better therapeutic opportunities for patients affected by this serious disease. We now look forward to exploring this promising approach in the Phase II randomized part which is currently starting****."***

Prof. Dario Neri, co-founder, CEO and CSO of Philogen, commented: *"These latest findings show the promising potential of Fibromun for the treatment of glioblastoma, one of the biggest unmet medical needs. While the Phase II randomized part of the GLIOSTAR clinical trial is about to start, the preliminary evidence collected in the Phase I part demonstrates encouraging, durable objective responses in an indication where responses are very rare. We are committed to advancing our research and development efforts, with the ultimate goal of delivering this innovative treatment to patients in need."*

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About L19TNF (also known as Fibromun)

L19TNF is a fully-human immunomodulatory product consisting of the L19 antibody and tumor necrosis factor (TNF), a strong pro-inflammatory cytokine. The L19 antibody is specific to the EDB domain of fibronectin and mediates selective localization of TNF to the site of disease while sparing healthy organs. The product is currently investigated in multiple clinical trials for the treatment of soft tissue sarcoma and glioblastoma, both in Europe and in the United States.

About glioblastoma

Glioblastoma is the most common and most aggressive primary brain tumor. It affects approximately 5 out of 100'000 people every year (Source: Orphanet). Newly diagnosed patients are typically treated with surgery, radiation and temozolomide (chemotherapy), which result in a median Overall Survival (mOS) in the range of 15 months. Virtually all patients progress and may subsequently receive another systemic or local second-line therapy. The mOS of patients at first progression ranges between 4.7 and 9.8 months in previous clinical trials.

About clinical trial NCT04573192

The Phase I/II clinical trial NCT04573192, which investigates the combination of L19TNF and lomustine for the treatment of patients suffering from glioblastoma at first progression after standard of care radiotherapy and chemotherapy. The Phase I part of the trial with escalating dose levels of L19TNF and lomustine is followed by a randomized Phase II part to investigate the efficacy of the combination treatment compared to standard of care lomustine as monotherapy with overall survival as primary endpoint. The first cohort of the phase I part of the study, comprising 6 patients, is presented in this publication.

About the Philogen Group

Philogen is an Italian-Swiss company active in the biotechnology sector, specialized in the research and development of pharmaceutical products for the treatment of highly lethal diseases. The Group mainly discovers and develops targeted anticancer drugs, exploiting high-affinity ligands for tumor markers (also called tumor antigens). These ligands - human monoclonal antibodies or small organic molecules - are identified using *Antibody Phage Display Libraries* and *DNA-Encoded Chemical Library* technologies.

The Group's main therapeutic strategy for the treatment of these diseases is represented by the so-called *tumor targeting*. This approach is based on the use of ligands capable of selectively delivering very potent therapeutic active ingredients (such as pro-inflammatory cytokines) to the tumor mass, sparing healthy tissues. Over the years, Philogen has mainly developed monoclonal antibody-based ligands that are specific for antigens expressed in tumor-associated blood vessels, but not expressed in blood vessels associated with healthy tissues. These antigens are usually more abundant and more stable than those expressed directly on the surface of tumor cells. This approach, so called *vascular targeting*, is used for most of the projects pursued by the Group.

The Group's objective is to generate, develop and market innovative products for the treatment of diseases for which medical science has not yet identified satisfactory therapies. This is achieved by exploiting (i) proprietary technologies for the isolation of ligands that react with antigens present in certain diseases, (ii) experience in the development of products targeted at the tissues affected by the disease, (iii) experience in drug manufacturing and development, and (iv) an extensive portfolio of patents and intellectual property rights.

Although the Group's drugs are primarily oncology applications, the *targeting* approach is also potentially applicable to other diseases, such as certain chronic inflammatory diseases.

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Forward-Looking Statements

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, also due to the ongoing COVID-19 pandemic; 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; availability and timing of results from preclinical studies and clinical trials; whether the outcomes of preclinical studies will be predictive of clinical trial results; whether initial or interim results from a clinical trial will be predictive of the final results of the trial or the results of future trials; the risk that trials and studies may be delayed and may not have satisfactory outcomes; potential adverse effects arising from the testing or use of Philogen's product candidates; risks related to Philogen's ability to maintain existing collaborations and realize the benefits thereof; expectations for regulatory approvals to conduct trials or to market products; other factors which could cause our actual result to differ from those contained in the forward-looking statements, as also described in greater detail in the Risk Factors section in the prospectus drafted by Philogen and approved by Consob on February 17, 2021. 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