Main Office: Loc. Bellaria, 35 - 53018 Sovicille (SI), Italy
e-mail: info@philogen.it – website: www.philogen.com

Philogen
innovating targeting

Philogen provides Corporate Update

- **Nidlegy™ and Fibromun pivotal clinical trials on track**
- **Fibromun shows potent activity in last-line glioblastoma in combination with Lomustine**
- **OncoFAP platform shows promising results in both radio-conjugates and drug-conjugates**
- **Philogen's management team to hold a Webinar today (December 1st, 2022) at 10:00 ET / 15:00 GMT / 16:00 CET (please find the link to attend here)**

Siena (Italy), December. 1, 2022 - 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, is pleased to provide an update on its R&D programs.

Dario Neri, co-founder, CEO and CSO of Philogen, commented: *"We are very pleased with the recent progress of our pipeline. We currently have seven pivotal clinical trials underway with Nildegy™ and Fibromun for which we expect important readouts in the coming years. Our most advanced study is the one of Nidlegy™ in stage IIIB,C melanoma and we expect to reach 95 events to complete the trial in 2023.*

Based on the complete remissions being observed with Nidlegy™ in high-risk Basal Cell Carcinoma (BCC), the Company is committed to expand the number of clinical centers to speed up timelines. It is important to highlight that the market potential in high-risk BCC is potentially larger than the melanoma market. We have the ambition to turn Nidlegy™ into a broad applicable dermato-oncology drug.

Fibromun's registration studies remain on track, both in Soft Tissue Sarcoma and in Glioblastoma.

Our Discovery Center has been very productive, having published more than 15 scientific peer reviewed publications and has initiated two novel collaborations with Bracco imaging and Janssen which are currently ongoing.

Our Group is increasing its investments in the discovery of small molecule tumor-targeting agents, which may facilitate the selective delivery of therapeutic radionuclides (Small Molecule Radiolabeled Conjugates, or "SMRCs") and of non-radioactive drugs (Small Molecule Drug Conjugates, or "SMDCs"). The excellent targeting properties of our OncoFAP small molecule ligand bode well for delivering both therapeutic radionuclides and cytotoxic drugs to tumors. Stimulated by curative activity observed in "difficult-to-treat" preclinical models of cancer, preparation activities for therapeutic trials with the OncoFAP platform are ongoing."

MAIN EVENTS AND RECENT HIGHLIGHTS

- **Nidlegy™** - consists of two active ingredients, L19IL2 and L19TNF which are given intratumorally. The L19 antibody is specific to the Extra Domain B of Fibronectin, a protein expressed in tumors (and other diseases) but absent in most healthy tissues. Interleukin 2 (IL2) and Tumor Necrosis Factor (TNF) are inflammatory cytokines with anti-tumor activities
  - Phase III European study in neoadjuvant (i.e., prior surgery) Stage IIIB,C melanoma (Pivotal)
    - 214 patients have been enrolled, in line with the protocol of the study
    - The trial will read-out when 95 events are reached. One event occurs when a patient's tumor relapses or when the patient passes away. As of December 1st, 80 out of 95 events have been recorded
    - The study is ongoing in Germany, Italy, Poland, and France at 22 clinical centers
    - The study has successfully passed two interim analyses in March 2019 (at 25% of total events) and December 2020 (at 50% of total events). An independent Data and Safety Monitoring Board supported the continuation of the trial based on Safety and Futility analyses
  - Phase III USA study in neoadjuvant Stage IIIB,C melanoma (Neodream)
    - The study is ongoing in the United States, Switzerland, and Spain at 23 clinical centers. More than 30 centers are expected to be open by 1H 2023.
    - A larger number of centers are being activated, compared to the European trial described above to speed up recruitment rate
  - Phase II study in high-risk Basal Cell Carcinoma and cutaneous Squamous Cell Carcinoma (cSCC) (Duncan)
    - Nine out of 40 patients have been enrolled. Eight patients were suffering from high-risk BCC and one had cSCC

        - The study is ongoing in Switzerland, Germany, and Poland. Seven clinical centers are currently open and at least an additional site is expected to be activated by 1H 2023. Evidence of potent therapeutic activity has emerged from the study and results have been presented at congresses in the field.
    - Phase II study in a basket of Non-Melanoma Skin Cancers (NMSC) (Intrinsic)
        - The trial has just started and foresees the treatment of 70 patients
        - NMSC included in the trial are Kaposi's sarcoma, cutaneous T-cell lymphoma, malignant adnexal tumors of the skin, Keratocanthoma, Merkel Cell Carcinoma, cutaneous Squamous Cell Carcinoma, and Basal Cell Carcinoma
        - The study is ongoing in Italy and France. Three centers are currently open and at least two additional sites are expected to be activated by 1H 2023
- **Fibromun** - a fully-human immunomodulatory product consisting of the L19 antibody and TNF (a strong pro-inflammatory cytokine). Fibromun is administered by systemic intravenous infusion
    - Phase III European study in newly diagnosed advanced or metastatic Soft Tissue Sarcoma (Fibrosarc)
        - Fibromun is given in combination with Doxorubicin
        - 47 out of 118 patients have been enrolled
        - The study is ongoing in Germany, Italy, Spain, Poland, and soon also in France. 17 centers are currently open and more than 25 are expected to be activated by 1H 2023
        - The opening of the centers and the recruitment of patients are on track. The projections support the completion of patient enrolment by the end of 2023
    - Phase IIb USA study in newly diagnosed metastatic Leiomyosarcoma (Fibrosarc US)
        - Fibromun is given in combination with Doxorubicin
        - Leiomyosarcoma is the most common Soft Tissue Sarcoma subtype
        - 9 clinical centers are currently open
    - Phase II EU study in advanced or metastatic Soft Tissue Sarcoma patients that failed at least 2 prior systemic therapies (Flash)
        - Fibromun is given in combination with Dacarbazine
        - 20 out of 92 patients have been enrolled
        - Seven centers are currently open and more than 15 are expected to be activated by 1H 2023
    - Phase I/II study in progressive High-Grade Stage III-IV Glioma (Gliomoon)
        - Fibromun is given as monotherapy
        - 20 out of 20 patients have been enrolled. The last patient was recruited in December 2020
        - The study has been conducted at three clinical centers in Switzerland
        - Data clean-up is ongoing and full results will be presented in a peer-reviewed scientific publication
    - Phase I/II study in progressive Glioblastoma (Gliostar)
        - Fibromun is given in combination with Lomustine
        - 14 patients have been enrolled in the Phase I part. Cohort 1 and 2 have been completed, while Cohort 3 is ongoing. Cohort 3 is the last one before proceeding to the Phase II randomized part
        - **Substantially improved survival benefit and major durable responses observed both in Cohort 1 and Cohort 2. Objective responses are very uncommon with lomustine alone**
        - More mature data of Cohorts 2 and 3 will be available in 1H 2023
        - The randomized Phase II part of the study foresees 158 patients and is expected to start in 1H 2023
        - The Phase I trial is currently ongoing at the University Hospital Zürich. Philogen has alreadycontacted several centers in Switzerland, Italy, France, Germany, and in the USA, with the aim to open 18-20 sites for the Phase II randomized part of the study
    - Phase I/II/IIb study in newly-diagnosed Glioblastoma (Gliosun)
        - Fibromun is given in combination with radiotherapy and temozolomide
        - 9 patients have been enrolled in the Phase I part. Cohort 1 and 2 have been completed, while Cohort 3 is ongoing. 5 Cohorts in total are planned for Phase I, before proceeding to the Phase II single-arm part
        - The Phase II part with 32 patients is expected to start in 2023
        - The randomized Phase IIb part, with registration potential, foresees 166-206 and is expected to start when consolidated data of Phase II become available
- **OncoFAP** is a small molecule ligand with ultra-high affinity for Fibroblast Activation Protein (FAP). The product is suitable for diagnostic and therapeutic applications of a variety of metastatic solid tumors, as FAP is overexpressed in more than 90% of epithelial cancers (e.g., malignant breast, colorectal, ovarian, lung, skin, prostate, and pancreatic cancers, as well as in some soft tissue and bone sarcomas)
    - OncoFAP - radio-conjugate for imaging applications
        - Several patients suffering from different cancers have already been imaged in Germany with ^{68}Ga-OncoFAP
        - The Italian Medicines Agency AIFA approved the Clinical Trial Application to formally initiate a Phase I clinical trial in Italy. The first patient of the study is expected in the upcoming weeks

- OncoFAP-23 - radio-conjugate for therapy applications
  - OncoFAP-23 is an innovative derivative which shows excellent tumor targeting properties in pre-clinical studies. The product selectively localizes rapidly into neoplastic lesions, with a stable uptake in the tumor for at least 96h. The long-tumor residence time of the novel OncoFAP derivative bodes well for therapeutic applications
  - ^{177}Lu-OncoFAP-23 exerts potent anti-cancer activity in pre-clinical studies, which are superior to other FAP-targeting agents
  - The GMP production and central labelling of OncoFAP-23 are ongoing at the dedicated Contract Research Organization
  - ^{177}Lu-OncoFAP-23 is expected to enter in clinical trials by the end of 2023
- OncoFAP-GlyPro-MMAE - small molecule drug conjugate
  - The Chemistry Group at Philochem (discovery center of the Philogen Group) has identified and tested novel OncoFAP-based drug conjugates showing excellent tumor targeting and therapeutic properties in pre-clinical models.
  - OncoFAP-GlyPro-MMAE shows superior performance compared to other derivatives featuring commonly used linkers in Antibody-Drug Conjugates (e.g., Valine-Citrulline linker)
  - Small Molecule Drug Conjugates are an attractive alternative to ADCs, based on their superior targeting performance and much lower Cost of Goods

- **Ongoing partnerships** include those on Dodekin (undisclosed), Dekavil (Pfizer), small molecule for diagnostic applications (Bracco), and discovery of novel small molecule therapeutics (Janssen)
- **GMP Facility in Rosia**
  - The construction and the equipment of the novel GMP facility in Rosia with state-of-the-art equipment have been completed within the foreseen timelines.
  - Three Aseptic Process Simulations (APS) have recently been successfully accomplished. APS simulates the aseptic process of the so-called "fill and finish" step of a GMP production campaign and represents a crucial step before initiating the manufacturing of commercial batches
  - Authorization from the Italian Medicines Agency, AIFA of the new GMP production facility in Rosia for the production and marketing of drugs is expected in 2023
  - It should be noted that this new facility will complement the existing GMP plant in Montarioso (Siena), which will be dedicated to the production of investigational drugs

The Group remains engaged in the strengthening of its in-house R&D, as well as contractual activities related to discovery and/or manufacturing. It also runs Business Development activities with potential industrial partners in order to seek new scientific collaborations on an opportunistic basis.

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PHILOGEN GROUP DESCRIPTION

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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FOR MORE INFORMATION:

Philogen - Investor Relations

IR@philogen.com - Emanuele Puca | *Investor Relations*

Consilium Strategic Communications contacts

Mary-Jane Elliott, Davide Salvi

Philogen@consilium-comms.com

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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, 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. Any forward-looking statements contained in this press release speak only as of the date hereof, and Philogen expressly disclaims any obligation to update any forward-looking statements contained herein, whether as a result of any new information, future events, changed circumstances or otherwise, except as otherwise required by law. The information and contents of this press release do not: (i) constitute an order or an offer to purchase or to sell financial products or financial services; (ii) relate to special investment goals or to the financial situation or particular requirements of specific users. All information presented, reports published, and opinions expressed are intended purely for information purposes, and do not constitute an offer for the conclusion of a contract or other legal transaction. In particular, the content of the press release is not to be understood as an invitation or recommendation to buy or sell securities of Philogen, or as an advertisement for securities of Philogen. Neither does it constitute an offer to participate in any other transaction, including (but not restricted to) trading in derivatives. The mere use of the website does not give rise to any contractual relationship of any kind between the user and Philogen. Philogen expressly draws your attention to the fact that its share price is subject to fluctuation, and that the future development of the share price cannot be derived either from the previous price history or from the information and content shown on this website. Results achieved in the past provide no guarantee in regard to the future development of the share price. Philogen provides no guarantee of any kind that the capital invested will increase in value or maintain its value. In light of these given risks, we strongly advise you to seek professional advice before making any investment decision. The material contained on the website does not relieve the user from having to make his own decisions. This press release may contain links to external websites of third parties (external links) the content of which is outside the sphere of influence of Philogen. Visiting and using such websites

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