Thermosome Presents Encouraging Initial Clinical Data from Phase I Trial of Lead Compound THE001

- *THE001 safe and well tolerated in first two dose level, demonstrating encouraging signs of clinical activity*
- *Data presented at The Connective Tissue Oncology Society (CTOS) Annual Meeting 2024*

Munich, Germany – November 19, 2024 – Thermosome, a drug development company focused on targeted tumor therapies, today announced encouraging initial clinical data from the ongoing Phase I study of its lead compound THE001 in patients with heavily pre-treated, locally advanced unresectable or metastatic soft tissue sarcoma (STS). The data were presented as a poster (#P410) titled "*Phase I study of THE001 ($DPPG_2$-TSL-DOX) combined with regional hyperthermia in patients with locally advanced or metastatic soft tissue sarcoma*" at *The Connective Tissue Oncology Society (CTOS) Annual Meeting 2024*, in San Diego, USA.

The Phase I, open-label, interventional dose-escalation study enrolling patients with locally advanced unresectable or metastatic STS is being conducted at two German clinical sites. THE001 is planned to be administered at three dose levels at 20 mg/m² (DL1), 40 mg/m² (DL2), and 50 mg/m² (DL3), respectively, in initially up to 6 cycles every 3 weeks (main study phase). Earlier this year, the independent Data Safety Monitoring Board confirmed the safety of DL1, and the study progressed to DL2. Based on durable clinical benefit in two out of four patients, the study duration has been extended to a total maximum of up to 12 cycles in spring 2024 (treatment continuation phase) in patients with stable disease per RECIST criteria. Primary endpoints of the study are the safety and tolerability of THE001 and the determination of the maximum tolerated dose. A secondary objective is the evaluation of anti-tumor activity.

Following the data cut-off for the CTOS poster, further encouraging clinical data were reported in these heavily (including Doxorubicin) pre-treated patients with locally advanced unresectable or metastatic soft tissue sarcoma (STS). The safety profile observed so far was favorable in both DL1 and DL2, and the study treatment is generally well-tolerated with the majority of adverse events being low-grade as well as expected for doxorubicin with no evidence of adverse events related to the innovative liposomal formulation. With regards to anti-tumor activity, an overall 5 out of 6 efficacy-evaluable patients in DL1 and DL2 achieved local disease control and 4 out of 6 achieved stable disease (SD) per RECIST. In DL2, all 3 out of 3 patients were evaluated as stable disease (SD) per RECIST after the initial tumor restaging (3 cycles). While two patients have not yet reached the tumor staging after 6 cycles (end of the main study period), one patient remained in stable disease per RECIST for 9 cycles (representing a progression-free survival of 7 months) and showed evidence of a pathological response in MRI/PET-CT imaging at the end of the main study period, representing a partial response (PR) per Choi. To put this in context, systemic doxorubicin monotherapy at the standard dose (75 mg/m²) in the first-line setting, which is a 2-4x higher dose compared to THE001 in DL1 and DL2, respectively, is reported with a median progression-free survival of 2.7 months in the MEDISARC Phase 2 study.

"Presenting the first clinical data for THE001 in combination with regional hyperthermia is an important milestone for Thermosome," said Dr. Frank Hermann, CMO of Thermosome. "The data not only confirm the galenic principle of thermosensitive liposomes releasing almost complete doxorubicin upon heat-triggered regional hyperthermia in humans, but also the safe application to date with no formulation-related adverse events. In addition, the first signs of clinical activity in these heavily pre-treated palliative patients are very encouraging and support our efforts to accelerate the clinical development program in soft tissue sarcoma."

"We are very pleased with these encouraging data, in particular with the signs of efficacy shown in our first clinical trial," added Pascal Schweizer, CEO of Thermosome. "The findings clearly demonstrate that THE001 is an innovative approach for tumor-targeted drug enhancement in STS."

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About Thermosome

Thermosome is a clinical-stage drug development company focused on targeted tumor therapy combined with immune stimulation for improved cancer therapy. At its core is a novel, proprietary tumor targeting approach that allows for significantly increased local drug concentrations and improved tumor penetration to achieve improved clinical treatment efficacy.

The first clinical indication for its lead drug candidate THE001 is soft tissue sarcoma, where the Company aims to improve the current standard of care (free doxorubicin). Thermosome's approach enables targeted tumor treatment independent of specific molecular targets and covers patient populations across all tumor subtypes. More information: www.thermosome.com

About THE001

Thermosome's clinical-stage lead drug candidate THE001 is a thermosensitive liposomal formulation of the chemotherapeutic drug doxorubicin ($DPPG_2$-TSL-DOX). It has a different mode of action than conventional liposomes. Thermosome's technology enables intravascular drug release initiated by a mild heat trigger using clinically established hyperthermia devices. This results in up to 15-fold higher local drug concentrations in the tumor and aims to improve clinical treatment efficacy by creating a local boost at the desired site of action. These high local concentrations, which also reach less well perfused areas, are intended to overcome drug resistance. This effect cannot be achieved by administration of conventional doxorubicin due to systemic toxicity. Thermosome intends to further enhance treatment efficacy through an additive immune response induced by regional hyperthermia. THE001 has potential for further development in other anthracycline-sensitive solid tumors, such as breast, bladder, and ovarian cancer.

About Soft Tissue Sarcomas (STS)

STS is an atypical tumor with a patient population that includes many young patients. Locally advanced STS (LA-STS) are large invasive tumors that are difficult or impossible to resect.

Neoadjuvant therapy is used to shrink these tumors preoperatively to allow tumor surgery with curative intent. Free doxorubicin in combination with ifosfamide or dacarbazine has been the gold standard for neoadjuvant therapy of all chemo sensitive LA-STS for several decades. Guidelines also recommend combining DOX-based therapy with regional hyperthermia. However, with response rates of less than 30%, there is a significant unmet need for improved treatment options.

Soft tissue sarcomas occur in more than 50 different subtypes not having a common driver mutation, making biologic targeting more difficult than physically controlled targeting with the most active agent. THE001 has been granted European Orphan Drug Designation for STS.

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