CELSION ANNOUNCES PUBLICATION OF THERMODOX® PHASE I CLINICAL STUDY RESULTS IN THE LANCET ONCOLOGY

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– The TARDOX Study, in Collaboration with University of Oxford, Evaluates the Use of Focused Ultrasound in Combination with ThermoDox® to Treat Primary and Metastatic Liver Cancer –

– Imaging Studies in Patients Treated with ThermoDox® and Focused Ultrasound Demonstrated Clinical Response After a Single Dose –

– Demonstrates in Actual Patients that Tumor Concentrations of Doxorubicin Increased up to 10-fold With Targeted Heating Using Focused Ultrasound –

LAWRENCEVILLE, N.J, July 10, 2018 (GLOBE NEWSWIRE) -- Celsion Corporation (NASDAQ: CLSN), an oncology drug development company, today announced that results from a Phase I trial of ThermoDox® were published in the peer-reviewed journal, *The Lancet Oncology* [1]. Conducted by a multi-disciplinary team of biomedical engineers, oncologists, radiologists and anesthetists at the University of Oxford, United Kingdom, the trial evaluated the safety and efficacy of ThermoDox®, Celsion's proprietary heat-activated liposomal encapsulation of doxorubicin, along with focused ultrasound for the treatment of liver cancer. Referred to as the TARDOX Study, the trial demonstrated that the ThermoDox® plus focused ultrasound technique increased doxorubicin delivery to tumors between two- and ten-fold in the majority of patients in this 10-patient trial.

"Reaching therapeutic levels of cancer drugs within a tumor, while avoiding side effects for the rest of the body is a challenge for all cancer drugs, including small molecules, antibodies and viruses," said Professor Constantin Coussios, Director of the Oxford Centre for Drug Delivery Devices ($OxCD^3$) and of the Institute of Biomedical Engineering at the University of Oxford. "Our study is the first to trial this new technique in humans and finds that it is possible to safely trigger and target the delivery of chemotherapy deep within the body from outside the body using focused ultrasound. Once inside the tumor, the drug is released from the carrier, supplying a higher dose of chemotherapy directly to the tumor, which may help to treat tumors more effectively for the same or a lower systemic dose of the drug."

"The findings published in *The Lancet Oncology* prove that ThermoDox® combined with targeted thermal therapy can increase the concentration of doxorubicin up to 10 times in actual tumors in liver cancer patients," said Nicholas Borys, M.D., Celsion's senior vice president and chief medical officer. "The most dramatic finding was that a single dose of thermally activated ThermoDox® produced a clinical response in some of the tumors treated."

A lysolipid thermally sensitive liposome encapsulating the chemotherapy agent, doxorubicin, ThermoDox® is designed to release targeted levels of doxorubicin into and around liver tumors with heat activation. In this Phase I study, and consistent with the ThermoDox® heat-activated design, the amount of drug passively reaching the tumor was low and estimated to be below therapeutic levels before ultrasound exposure. Following focused ultrasound application with ThermoDox®, chemotherapy concentrations within the liver tumor were between two and ten times higher in seven out of 10 patients, with an average increase of 3.7 times across all patients.

"Only low levels of chemotherapy entered the tumor passively. The combined thermal and mechanical effects of ultrasound not only significantly enhanced the amount of doxorubicin that entered the tumor, but also greatly improved its distribution, enabling increased intercalation of the drug with the DNA of cancer cells," explained Dr. Paul Lyon, clinical research fellow at the Nuffield Department of Surgical Sciences at the University of Oxford and lead author of the study.

The Phase I trial evaluated patients with inoperable primary or secondary liver tumors and who had previously received chemotherapy. The procedure was carried out under general anaesthesia, and patients received a single intravenous dose of 50 mg/m^2 of ThermoDox®. The target tumor was selectively heated to over 39.5^{o} C using an approved ultrasound-guided focused ultrasound device at the Churchill Hospital in Oxford. In six patients, the temperature at the target tumor was monitored using a temporarily implanted probe, while in the remaining four patients, ultrasonic heating was carried out non-invasively. Side effects were monitored for 30 days after the procedure, and apart from the existing side effects caused by general anesthetic and chemotherapy, no additional side effects were observed. Five patients experienced grade 4 neutropenia, but their symptoms were resolved without treatment, and one patient experienced mild confusion after the procedure, which was resolved.

"This study adds to the ever growing body of evidence supporting thermally activated ThermoDox® has the potential to deliver potent and concentrated levels of doxorubicin to liver tumors – an effect that we believe may result in enhanced tumor killing," said Michael H. Tardugno, Celsion's chairman, president and chief executive officer. "The efficacy of ThermoDox® continues to be evaluated, and the OPTIMA Study, a 550-patient, multinational, double-blind, placebo-controlled, pivotal Phase III clinical study of ThermoDox® in combination with radiofrequency ablation (RFA), is well underway. The OPTIMA Study will evaluate overall survival in patients with primary liver cancer. We expect to complete enrollment in this pivotal study in the third quarter of 2018 and look forward to the first prespecified interim efficacy analysis in the first half of 2019."

The TARDOX Study, supported by the National Institute for Health Research (NIHR) Oxford Biomedical Research Centre, was carried out as a multi-disciplinary collaboration between Celsion, the Oxford University Institute of Biomedical Engineering, the Oncology Clinical Trials Office (OCTO) and the Oxford University Hospitals NHS Foundation Trust.

[1] For today's news release issued by NIHR Oxford Biomedical Research Centre regarding *The Lancet Oncology* publication, please visit www.ox.ac.uk .

About ThermoDox®

Celsion's most advanced program is a heat-mediated, tumor-targeting drug delivery technology that employs a novel heat-sensitive liposome engineered to address a range of difficult-to-treat cancers. The first application of this platform is ThermoDox®, a lyso-thermosensitive liposomal doxorubicin (LTLD), whose novel mechanism of action delivers high concentrations of doxorubicin to a region targeted with the application of localized heat at 40°C, just above body temperature. In one of its most advanced applications, ThermoDox®, when combined with radiofrequency thermal ablation (RFA), has the potential to address a range of cancers. For example, RFA in combination with ThermoDox® has been shown to expand the "treatment zone" with a margin of highly concentrated chemotherapy when treating individual primary liver cancer lesions. The goal of this application is to significantly improve efficacy.

Celsion's LTLD technology leverages two mechanisms of tumor biology to deliver higher concentrations of drug directly to the tumor site. The first: Rapidly growing tumors have leaky vasculature, which is permeable to liposomes and enables their accumulation within tumors. Leaky vasculature influences a number of factors within the tumor, including the access of therapeutic agents to tumor cells. Administered intravenously, LTLD is engineered to allow significant accumulation of liposomes at the tumor site at the time of radiofrequency ablation as these liposomes recirculate in the blood stream. The second: When the tumor tissue is heated to a temperature of 40°C or greater, the heat-sensitive liposome rapidly changes structure and the liposomal membrane selectively dissolves, creating openings that release the chemotherapeutic agent directly into the tumor and into the surrounding vasculature. Drug concentration increases as a function of the accumulation of liposomes at the tumor site, but only where the heat is present. This method targets only the tumor and the area related to tumor invasion, supporting precise drug targeting.

About the OPTIMA Study

The Phase III OPTIMA Study is expected to enroll up to 550 patients in up to 70 clinical sites in the United States, Europe, China and Asia Pacific, and will evaluate ThermoDox® in combination with optimized RFA, which will be standardized to a minimum of 45 minutes across all investigators and clinical sites for treating lesions three to seven centimeters, versus optimized RFA alone. The primary endpoint for the trial is overall survival, which is supported by post-hoc analyses of data from the Company's 701-patient HEAT Study, where optimized RFA has demonstrated the potential to significantly improve survival when combined with ThermoDox®. The statistical plan calls for two interim efficacy analyses by an independent Data Monitoring Committee.

About Celsion Corporation

Celsion is a fully-integrated oncology company focused on developing a portfolio of innovative cancer treatments, including directed chemotherapies, immunotherapies and RNA- or DNA-based therapies. The Company's lead program is ThermoDox®, a proprietary heat-activated liposomal encapsulation of doxorubicin, currently in Phase III development for the treatment of primary liver cancer. The pipeline also includes GEN-1, a DNA-based immunotherapy for the localized treatment of ovarian and brain cancers. Celsion has two platform technologies for the development of novel nucleic acid-based immunotherapies and other anti-cancer DNA or RNA therapies. For more information on Celsion, visit our website: http://www.celsion.com. (CLSN-LTSL/ThermoDox® CLSN-Optima Study/HCC)

About the National Institute for Health Research Oxford Biomedical Research Centre

The National Institute for Health Research Oxford Biomedical Research Centre is based at the Oxford University Hospitals NHS Foundation Trust and run in partnership with the University of Oxford, funded by the National Institute for Health Research (NIHR).

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Celsion wishes to inform readers that forward-looking statements in this release are made pursuant to the "safe harbor" provisions of the Private Securities Litigation Reform Act of 1995. Readers are cautioned that such forward-looking statements involve risks and uncertainties including, without limitation, unforeseen changes in the course of research and development activities and in clinical trials; the uncertainties of and difficulties in analyzing interim clinical data; the significant expense, time, and risk of failure of conducting clinical trials; the need for Celsion to evaluate its future development plans; possible acquisitions or licenses of other technologies, assets or businesses; possible actions by customers, suppliers, competitors, regulatory authorities; and other risks detailed from time to time in Celsion's periodic reports and prospectuses filed with the Securities and Exchange Commission. Celsion assumes no obligation to update or supplement forward-looking statements that become untrue because of subsequent events, new information or otherwise.

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