Celsion Announces Publication of Results of National Institutes of Health (NIH) Analysis of ThermoDox® in Journal of Vascular and Interventional Radiology

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NIH's Independent Analysis of Celsion's Phase III HEAT Study Confirms Increasing Radiofrequency Ablation (RFA) Heating Time + ThermoDox ® Improves Overall Survival with Significance in Patients with Primary Liver Cancer

NIH Analysis Supports the OPTIMA Study Design, Celsion's Fully Enrolled Global Phase III Study of ThermoDox ® to Treat Primary Liver Cancer; First Pre-Planned Efficacy Analysis of the Phase III OPTIMA Study Planned for October 2019

LAWRENCEVILLE, N.J., Aug. 13, 2019 (GLOBE NEWSWIRE) -- Celsion Corporation (NASDAQ: CLSN), an oncology drug development company, today announced that results from an independent analysis of the Company's ThermoDox ® HEAT Study conducted by the National Institutes of Health (NIH) were published in the peer-reviewed publication,*Journal of Vascular and Interventional Radiology (JVIR)*. ThermoDox® is Celsion's heat-activated liposomal formulation of doxorubicin currently in Phase III development for the treatment of primary liver cancer, also known as hepatocellular carcinoma (HCC). The analysis was conducted by the intramural research program of the NIH and the NIH Center for Interventional Oncology (CIO), with the full data set from the Company's HEAT Study. The analysis evaluated the full data set to determine if there was a correlation between baseline tumor volume and radiofrequency ablation (RFA) heating time (minutes/tumor volume in milliliters), with or without ThermoDox® treatment, for patients with HCC. The NIH analysis was conducted under the direction of Dr. Bradford Wood, MD, Director, NIH Center for Interventional Oncology and Chief, NIH Clinical Center Interventional Radiology.

The article titled, "*RFA Duration Per Tumor Volume May Correlate With Overall Survival in Solitary Hepatocellular Carcinoma Patients Treated With RFA Plus Lyso-thermosensitive Liposomal Doxorubicin*," discussed the NIH analysis of results from 437 patients in the HEAT Study (all patients with a single lesion representing 62.4% of the study population). The key finding was that increased RFA heating time per tumor volume significantly improved overall survival (OS) in patients with single-lesion HCC who were treated with RFA plus ThermoDox®, compared to patients treated with RFA alone. A one-unit increase in RFA duration per tumor volume was shown to result in about a 20% improvement in OS for patients administered ThermoDox®, compared to RFA alone. The authors conclude that increasing RFA heating time in combination with ThermoDox® significantly improves OS and establishes an improvement of over two years versus the control arm when the heating time per milliliter of tumor is greater than 2.5 minutes. This finding is consistent with the Company's own results, which defined the optimized RFA procedure as a 45-minute treatment for tumors with a diameter of 3 centimeters. Thus, the NIH analysis lends support to the hypothesis underpinning the OPTIMA Study, Celsion's fully enrolled, on-going Phase III trial in newly diagnosed HCC patients.

On August 5, 2019, the Company announced the prescribed number of events has been reached for the first pre-planned interim analysis of the OPTIMA Phase III Study with ThermoDox® plus RFA in patients with HCC. Following preparation of the data, the first interim analysis will be conducted by the Independent Data Monitoring Committee (iDMC). This timeline is consistent with the Company's stated expectations and is necessary to provide a full and comprehensive data set that may represent the potential for a successful trial outcome. Celsion expects to announce iDMC recommendations as soon as possible after their meeting in October. In accordance with the statistical plan, this initial interim analysis has a target of 118 events, or 60% of the total number required for the final analysis. At the time of the data cutoff, the Company received reports of 128 events. The hazard ratio for success at 128 events is approximately 0.637, which represents an approximate 36.3% reduction in the risk of death, consistent with the 0.65 hazard ratio that was observed in the prospective HEAT Study subgroup, which demonstrated a 2-year overall survival advantage and a median time to death of more than 7 ½ years.

"We believe the NIH analysis of Celsion's HEAT Study validates the importance of combining the proper dose of heat with ThermoDox ®," said Nicholas Borys, M.D., Celsion's executive vice president and chief medical officer. "The independent analysis by the NIH augments our own analyses which demonstrated a significant, two-year survival benefit for patients with intermediate-size lesions who are given ThermoDox® along with the newly standardized, extended course of RFA and further support our belief that ThermoDox® has the potential to be an important treatment for many cancers."

"The dependency of OS on a well-executed RFA procedure was theorized in a prospective review of the data from the HEAT Study," said Khursheed Anwer, PhD, Celsion's executive vice president and chief science officer. "Time dependency, once established in prospective large animal models and computational studies, was applied to the HEAT Study population. A 285-patient well-balanced subgroup meeting the time-dependent criteria of a minimum of 45-minute ablation established in our preclinical work was identified. These patients were then evaluated for over two and one-half years. The results were remarkable, with an OS benefit of more than two years for patients receiving ThermoDox® plus optimized RFA, compared to optimized RFA alone. It is reassuring that NIH's independent work corroborates our own findings."

The NIH analysis utilized a specialized image and ablation parameter analysis to determine the burn time per tumor volume for each solitary tumor treated in Celsion's HEAT Study and then statistically evaluated the relationship between tumor volumes and the RFA duration on patient survival. The results indicated a highly significant quadratic relationship between tumor volume, RFA treatment time, and overall survival. Indeed, the NIH analysis underscores the value of the HEAT Study in establishing a standard approach to planning and conducting RFA treatments based on tumor volumes.

"The findings from the NIH analysis now published in the *Journal of Vascular and Interventional Radiology* provide independent confirmation of conclusions drawn from our own HEAT Study analysis suggesting that ThermoDox® treatment with standardized RFA dwell time can result in greater localized doxorubicin concentrations for improved survival outcomes in patients with intermediate-size liver lesions," said Michael Tardugno, Celsion's chairman, president and chief executive officer. "The reaffirmation of the importance of standardized RFA heating time with ThermoDox ® treatment by

the NIH scientists, and the rigor of the scientific approach confirmed by the *JVIR* peer-review process, provide us with an added level of confidence in the design and execution of our ongoing OPTIMA Study, which is based on the learnings from the HEAT Study. We look forward to seeing the first interim data from OPTIMA during the second half of 2019."

About ThermoDox®

Celsion's most advanced program is a heat-mediated 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. ThermoDox® is positioned for use with multiple heating technologies and has the potential to treat of a broad range of cancers including metastatic liver, recurrent chest wall (RCW) breast cancer and non-muscle invading bladder cancers.

Celsion's LTLD technology leverages two mechanisms of tumor biology to deliver higher concentrations of drug directly to the tumor site. In the first mechanism, 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, ThermoDox® is engineered with a half-life to allow significant accumulation of liposomes at the tumor site as these liposomes recirculate in the blood stream. In the second mechanism, when an external heating device heats tumor tissue to a temperature of 40°C or greater, the heat-sensitive liposome rapidly changes structure and the liposomal membrane selectively dissolves, creating openings that can release a 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 damages only the tumor and the area related to tumor invasion, supporting more precise drug targeting.

About the OPTIMA Study

The Phase III OPTIMA Study has enrolled 556 patients in over 60 clinical sites in the United States, Europe, China and Asia Pacific, and will evaluate ThermoDox® in combination with optimized RFA, which was 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. The OPTIMA Study is a follow-on study supplemented by *post-hoc* analyses of data from the Company's 701-patient HEAT Study in which optimized RFA demonstrated the potential to significantly improve survival when combined with ThermoDox®. The OPTIMA Study's 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 and in development for other cancer indications. The Company's product pipeline also includes GEN-1, a DNA-based immunotherapy for the localized treatment of ovarian cancer. Celsion has two platform technologies for the development of novel nucleic acid-based immunotherapies and other anti-cancer DNA or RNA therapies.

The Company has a Cooperative Research and Development Agreement (CRADA) with the NIH. Any reference to NIH should not be viewed as an endorsement of Celsion, its products or services. For more information on Celsion, visit our website: http://www.celsion.com (LTSL/ThermoDox®, HEAT Study/HCC, OPTIMA Study/HCC).

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, particularly in small subgroups that are not statistically significant; FDA and regulatory uncertainties and risks; 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 the 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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