Celsion Corporation to Continue Following Patients in Phase III OPTIMA Study for Overall Survival

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Ongoing Analysis of Unblinded Study Data Suggests Data Maturity May be at Issue

Cohort of 26 Consecutive Patient Deaths Differs Substantially from Predicted Behavior and from the Balance of the Trial

LAWRENCEVILLE, N.J., Aug. 04, 2020 (GLOBE NEWSWIRE) -- Celsion Corporation (NASDAQ: CLSN), an oncology focused drug-development company, today provided an update on its ongoing review of unblinded data from the second pre-planned interim analysis of the global Phase III OPTIMA Study of ThermoDox® in combination with radiofrequency ablation (RFA) for the treatment of hepatocellular carcinoma (HCC), or primary liver cancer. The Company announces it will continue following patients for overall survival (OS), noting that the unexpected and marginally crossed futility boundary, suggested by the Kaplan-Meier analysis at the second interim analysis on July 9, 2020, may be associated with a data maturity issue. The Company further notes that 26 consecutive patient deaths represented exclusively in the second analysis behave far differently from the balance of the patients who have died as of this date.

Removing the 26 consecutive patient deaths, which occurred between September 2019 and March 2020, from the pre-planned interim analysis suggests that the OPTIMA Study OS pattern is similar to the prospective HEAT Study subgroup upon which the OPTIMA Study is based, at the approximate comparable point in time. In addition, subsequent to the second interim analysis there were eight patient deaths in a 3:1 ratio of control arm to treatment arm patients, which further supports a concern for data maturity.

Celsion further noted that OPTIMA Study investigators in China and Vietnam, who enrolled 37% of the subjects, joined the study approximately 12 and 18 months, respectively, after the trial was initiated. The Kaplan-Meier curves for both geographies demonstrate a potential data maturity issue when compared with the behavior of the HEAT Study subgroup and other OPTIMA Study testing site regions. The China sites, in particular, show a negative Kaplan-Meier curve, yet with a 56% improvement in the treatment arm in the median time to death. The Vietnamese sites show a marginal Kaplan-Meier benefit, yet with a 45% improvement in the median time to death. The Company believes that this dichotomy must be reconciled, most probably with longer follow up, before it can determine the study's direction.

Additionally, Celsion has sent the trial data, including Chemistry, Manufacturing and Controls data, to the National Institutes of Health (NIH) for independent analysis. All computed tomography (CT) scans are being prepared and will be sent for NIH's evaluation of progression-free survival (PFS). Depending on the trends noted during the OS follow-up period, Celsion may choose to discontinue the Study at any time.

On July 13, 2020 Celsion announced that the independent Data Monitoring Committee (DMC) recommended that Celsion should consider stopping the OPTIMA Study. Finding that the pre-specified boundary for stopping the trial for futility of 0.900 was marginally crossed with an actual value of 0.903, the DMC left the final decision up to the Company as the p-value of 0.524 for this analysis provided uncertainty.

"Last month's DMC recommendation to consider discontinuation of the OPTIMA Study based on the 2 nd interim data was never anticipated, nor was it supported by the science, independent clinical evaluation of the HEAT Study subgroup or prospective preclinical research conducted by Celsion and our consultants to support the OPTIMA Study. We believe, therefore, that Celsion is obligated to undertake this rigorous evaluation of the data and the trial's recruitment trends," stated Michael H. Tardugno, Celsion's chairman, president and chief executive officer. "While the trial outcome as predicted by the second interim analysis may not change, and as unlikely as it may be, in the event we see substantial clinical benefit while continuing to monitor patients, we will carefully review our options with the 14 regulatory agencies that have allowed the OPTIMA Study to be conducted. We appreciate the ongoing support and confidence from our research Investigators and clinical advisors."

The OPTIMA Study is a global, randomized, double-blind, placebo-controlled clinical trial assessing the efficacy of ThermoDox® in combination with RFA, which was standardized to a minimum of 45 minutes for treating patients with a lesion 3-7 cm in size, versus standardized RFA alone. The OPTIMA Study enrolled 554 patients at 65 clinical sites in North America, Europe, China and Asia Pacific. In addition to the primary overall survival endpoint, progression-free survival, time to disease progression and safety are key secondary endpoints.

The statistical plan for the OPTIMA Study included two interim efficacy analyses by the DMC. The first interim analysis was announced in November 2019 following data lock in August 2019 after the prescribed minimum number of 128 patient events (deaths) was reached, and the second interim analysis was conducted in July 2020 following data lock in April 2020 after the prescribed minimum number of 158 events was reached.

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 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 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 subject to tumor invasion, supporting more precise drug targeting.

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.

Forward-looking Statements

Forward-looking statements in this news 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 or regulatory authorities; and other risks detailed from time to time in the Celsion's periodic filings 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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