Celsion Announces Data Lock for First Interim Analysis in OPTIMA Phase III Study of ThermoDox® in Primary Liver Cancer

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Independent Data Monitoring Committee to Meet in October to Evaluate Interim Trial Data

LAWRENCEVILLE, N.J., Aug. 05, 2019 (GLOBE NEWSWIRE) -- Celsion Corporation (NASDAQ: CLSN), an oncology drug-development company, announces the prescribed number of events has been reached for the first prespecified interim analysis of the OPTIMA Phase III Study with ThermoDox® plus RFA (radiofrequency ablation) in patients with hepatocellular carcinoma (HCC), or primary liver cancer. Following preparation of the data, the first interim analysis will be conducted by the Independent Data Monitoring Committee (iDMC). The Company expects the iDMC meeting to occur by mid-October. 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 the meeting. The hazard ratio for success at 128 deaths is 0.63, which represents a 37% reduction in the risk of death compared with RFA alone.

Michael Tardugno, Celsion's chairman, president and chief executive officer, said, "We look forward to receiving the iDMC's recommendation from this first interim analysis of the OPTIMA Study. 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 0.63 and is 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."

The OPTIMA Study was fully enrolled in August 2018 with 556 subjects from 65 clinical sites in 14 countries. The design of the OPTIMA Study is based on the Company's HEAT Study, in which a subgroup analysis of 285 subjects received a single ThermoDox ® administration in combination with a 45 minute or more RFA procedure in patients with a single lesion of 3-7 cm in size. Followed prospectively for 3 years, those patients treated with ThermoDox demonstrated a median survival of more than 7 ½ years and a survival benefit of more than 2 years over the control group. These data were published in the October 2017 issue of the peer-reviewed journal *Clinical Cancer Research,* and are available here.

In December 2018, the iDMC evaluated the safety and data integrity for all 556 patients enrolled in the OPTIMA Study. The last data review demonstrated:

- The OPTIMA patient demographics and risk factors are consistent with what the Company saw in the HEAT Study subgroup and all data quality metrics are meeting expectations.
- Median PFS for the OPTIMA Study had reached 21.2 months as of October 4, 2018. These blinded, data compare favorably to 16.2 months median PFS for the 285 patients in the subgroup of patients treated with RFA > 45 minutes.
- The OPTIMA Study had lost only three patients to follow-up from the initiation of the trial in September 2014.
- Blinded data from the intent-to-treat population showed that overall survival thus far is consistent with the HEAT Study subgroup on which the Study's statistical plan was based.

"Assuming OPTIMA results are similar to the HEAT Study's prospective subgroup, it is possible, although not probable, for the OPTIMA Study to be declared successful at the first interim analysis. Because the probability of success improves with the number of patients evaluated, a second interim analysis, if necessary, is expected to occur at a minimum of 158 events. The second analysis has a hazard ratio for success of 0.70. While we remain optimistic for a positive trial result in October, the likelihood of success is much greater at the second analysis, which is expected to occur in the first half of 2020," added Mr. Tardugno.

About the OPTIMA Study

The Phase III OPTIMA Study enrolled 556 patients at 65 clinical sites in North America, Europe, China and Asia Pacific. The Study is evaluating 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 3-7 cm in size, 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 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 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.

Celsion Investor Contact

Jeffrey W. Church
Executive Vice President and CFO
609-482-2455
jchurch@celsion.com

Or

LHA Investor Relations
Kim Sutton Golodetz
212-838-3777
kgolodetz@lhai.com

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