Celsion Reports that Sufficient Events Have Been Reached for the Second Interim Analysis of the Phase III OPTIMA Study of ThermoDox® in Primary Liver Cancer

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Independent Data Monitoring Committee is Expected to Meet in July 2020 to Evaluate Overall Survival Data

LAWRENCEVILLE, N.J., April 15, 2020 (GLOBE NEWSWIRE) -- Celsion Corporation (NASDAQ: CLSN), an oncology drug-development company, announces that the prescribed minimum number of events of 158 patient deaths has been reached for the second pre-specified 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 Independent Data Monitoring Committee (iDMC) is expected to meet in July to conduct the second interim analysis. Celsion expects to announce iDMC recommendations as soon as possible after the meeting.

The hazard ratio for success at 158 deaths is 0.70, which represents a 30% reduction in the risk of death compared with RFA alone. This compares favorably with the hazard ratio of 0.65 observed in the prospective HEAT Study subgroup upon which the OPTIMA Study is based.

Michael Tardugno, Celsion's chairman, president and chief executive officer, said, "We look forward to receiving the iDMC's recommendation from this data analysis, and are quite optimistic for a positive outcome. Regardless, we believe that the OPTIMA Study is ultimately well-positioned for success. If a final analysis is necessary, it will be based on 197 patient deaths where the hazard ratio for success of 0.75 represents a significantly lower hurdle than the hazard ratio that was observed in the prospective HEAT Study subgroup. We base our confidence on published pre-clinical data supporting the OPTIMA Study, the National Institutes of Health's independent analysis of and support for the Study's hypothesis, and the OPTIMA Study's current timeline for disease progression and patient death, both tracking in line with the prospective HEAT Study subgroup. The prospective subgroup demonstrated a remarkable 7 ½ years plus survival when treated with ThermoDox® plus RFA. A successful study has "blockbuster" revenue potential and more importantly, will be transformational for patients with HCC, with over 750,000 incidence annually, the largest unmet need in oncology."

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 prospective subgroup analysis of 285 subjects received a single ThermoDox ® administration in combination with a 45 minute or longer 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 November 2019, Celsion announced the iDMC evaluation of the safety and data integrity for all 556 patients enrolled in the OPTIMA Study in its first pre-planned interim analysis following 128 events, which occurred in August 2019. During that review the iDMC unanimously recommended that the OPTIMA Study continue as planned. That data review demonstrated:

- The OPTIMA Study patient demographics and risk factors are consistent with what the Company observed in the HEAT Study subgroup with all data quality metrics meeting expectations.
- Median PFS for the OPTIMA Study reached 17 months as of August 2019. These blinded data compare favorably with 16 months median PFS for the 285 patients in the HEAT Study subgroup of patients treated with RFA >45 minutes and followed prospectively for overall survival.
- Median OS for the OPTIMA Study had not been reached as of August 5, 2019; however, median OS appears to be consistent with the HEAT Study subgroup of patients treated with RFA >45 minutes and followed prospectively for overall survival.

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.

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