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Celsion Announces the Potentially Curative Approach to Treatment of Primary Liver Cancer - The Focus of Hepatic Oncology Peer-Reviewed Article

Ongoing Phase III Trial to Confirm Hypothesis That The Combination of Standardized Radio Frequency Ablation (sRFA) Plus Lyso-Thermosensitive Liposomal Doxorubicin (LTLD) May Substantially Increase Survival of Patients with HCC Compared to sRFA Alone

LAWRENCEVILLE, N.J., June 21, 2016 (GLOBE NEWSWIRE) -- Celsion Corporation (NASDAQ:CLSN) today announced publication of the article, *"RFA plus lyso-thermosensitive liposomal doxorubicin: In search of the optimal approach to cure intermediate-size hepatocellular carcinoma,"* in *Hepatic Oncology*, a peer-reviewed medical journal. The article provides a comprehensive overview of the clinical evaluation conducted to date of lyso-thermosensitive liposomal doxorubicin (LTLD), Celsion's proprietary heat-activated liposomal encapsulation of doxorubicin, for the treatment of primary liver cancer, also known as hepatocellular carcinoma or HCC. The article details learnings from the Company's 701 patient HEAT Study, a computational modeling study, an experimental animal study and the HEAT Study *post hoc* subgroup analysis, all of which are consistent with each other and which -- when examined together -- suggest a clearer understanding of a key LTLD heat-based mechanism of action: the longer the target tissue is heated, the greater the doxorubicin tissue concentration. Additionally, the article explores a new hypothesis prompted by these findings: LTLD, when used in combination with Radio Frequency Ablation (RFA) standardized to a minimum dwell time of 45 minutes (sRFA $\geq$ 45 min), may increase the overall survival (OS) of patients with HCC. Written by Riccardo Lencioni, MD and Dania Cioni, MD of the Sylvester Comprehensive Cancer Center, University of Miami Miller School of Medicine in Miami, Florida, the article is published in the June 10, 2016 issue of the journal, *Hepatic Oncology*.

"There is an urgent need for new and better treatment options for HCC, the sixth most common cancer in the world, and the third most common cause of death from malignant disease," noted Michael H. Tardugno, Celsion's chairman, president and chief executive officer, in response to the article's publication. "We believe strongly that ThermoDox® may be an important new approach to the treatment of HCC. We are also now committed to learning more about how an LTLD regimen may prolong the survival of patients suffering from this extremely deadly cancer," Mr. Tardugno added.

Interest in ThermoDox® as a potential treatment option for HCC increased markedly among liver cancer experts worldwide following the announcement by Celsion in July 2015 of the latest OS analysis of the HEAT Study *post hoc* subgroup. According to this announcement, this most current OS analysis demonstrated that in a large, well bounded, subgroup of patients (n=285 patients, 41% of the previous 701 patient HEAT Study), treatment with a combination of ThermoDox® and standardized RFA (defined as Radio Frequency Ablation standardized to a minimum of 45 minutes or sRFA $\geq$ 45 min) provided an average 58% improvement in OS compared to standardized RFA alone. The Hazard Ratio (HR) at this analysis is 0.63 (95% CI 0.43 - 0.93) with a p-value of 0.0198. In this large subgroup, median OS for the ThermoDox® plus standardized RFA group translates into a 25.4 month (more than 2.1 year) survival benefit over the standardized RFA only group - totaling approximately 80 months (6-1/2 years, which is considered a curative treatment for HCC) for the ThermoDox® plus standardized RFA group versus 53.6 months for the standardized RFA only group.

> Note: As discussed in the *Hepatic Oncology* article, the hypothesis tested in the HEAT Study was that ThermoDox® would produce a therapeutic doxorubicin tumor concentration when combined with the normal practice of RFA, thereby expanding the 'treatment zone' and targeting any micro-metastases outside the so-called 'ablation zone.' The criterion for RFA use in the HEAT Study was limited to ablation of each target lesion plus a 360° 1-cm margin, however; it included no attempt to manage RFA approach or RFA dwell time, despite the essential role of heat in the LTLD mechanism of action.

To test and confirm this most current HEAT Study *post hoc* subgroup analysis, Celsion initiated the Phase III OPTIMA study, a global, pivotal, double-blind, placebo-controlled clinical trial (Clinical Trials.gov NCT021126560). Developed in consultation with leading primary liver cancer, statistical and regulatory experts, and based on extensive analysis of prior clinical and preclinical studies of ThermoDox® plus standardized RFA, the OPTIMA study is now evaluating ThermoDox® in combination with RFA standardized to a minimum of 45 minutes across all investigators and sites for treating lesions 3 to 7 centimeters, versus standardized RFA alone.

"We are highly focused on successfully executing the ongoing OPTIMA study, the only global study in HCC," Mr. Tardugno stated. "We look forward to sharing our progress with the scientific community as we continue to advance this program, and

to accomplishing our chief goal, the delivery of ThermoDox® as a novel, first-line treatment to HCC patients worldwide."

The OPTIMA Study

OPTIMA, a pivotal, double-blind, placebo-controlled Phase III clinical trial, is expected to enroll up to 550 patients at up to 75 sites in the North America, Europe, China and Asia Pacific. As of June 2016, the study has been successfully enrolling patients at more than 50 clinical sites in 13 different countries in North America, Europe and Asia Pacific. In December 2015, Celsion announced that it had received a Clinical Trial Application (CTA) approval from the China Food and Drug Administration (CFDA) to conduct the OPTIMA Study at up to 20 additional clinical sites in China, the country where approximately 50% of the 850,000 new cases of primary liver cancer are diagnosed each year and where the Company aims to enroll more than 200 patients in the China territory, the minimum number required by the CFDA to file a New Drug Application (NDA), assuming positive clinical results.

The primary endpoint for the OPTIMA Study is overall survival (OS). The statistical plan calls for two interim efficacy analyses by an independent Data Monitoring Committee (iDMC). The design of the OPTIMA Study is supported by the retrospective analysis of a large subgroup of 285 patients in the Company's previous 701 patient HEAT Study in primary liver cancer. The study is also designed to establish a clear path to approval in major liver cancer markets worldwide, with results from the OPTIMA Study, if successful, providing the basis for a global registration filing and marketing approval.

About LTLD (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, LTLD, 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 with a half-life to allow significant accumulation of liposomes at the tumor site as these liposomes recirculate in the blood stream. The second: When an external heating device heats the 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 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 damages only the tumor and the area related to tumor invasion, supporting 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 Phase II development for the treatment of recurrent chest wall breast 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 anticancer DNA or RNA therapies, including TheraPlas™ and TheraSilence™. For more information on Celsion, visit our website: http://www.celsion.com. (CLSN-TD CLSN-HS CLSN-OS)

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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