October 16, 2017

Celsion Announces Publication of the HEAT Study Manuscript in the High Impact Journal, Clinical Cancer Research

80+ Month Overall Survival (HR = 0.63, P_{value} = 0.02) Discussed in the 285 Patient Sub-group Treated with ThermoDox® plus Standardized Radiofrequency Ablation (sRFA)

Ongoing Phase III OPTIMA Study to Confirm Hypothesis that the Combination of Standardized Radiofrequency Ablation Plus ThermoDox® May Substantially Increase Survival of Patients with HCC Compared to sRFA Alone

OPTIMA Study Enrollment Approaching 70%

LAWRENCEVILLE, N.J., Oct. 16, 2017 (GLOBE NEWSWIRE) -- Celsion Corporation (NASDAQ:CLSN) today announced publication of the manuscript, "Phase III HEAT Study Adding Lyso-Thermosensitive Liposomal Doxorubicin to Radiofrequency Ablation in Patients with Unresectable Hepatocellular Carcinoma Lesions," in *Clinical Cancer Research*, a high impact, peer-reviewed medical journal. The article reports on one of the largest controlled studies in hepatocellular carcinoma (HCC). It provides a comprehensive review of ThermoDox®, 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 and includes results from computer simulation studies and includes interesting findings from a *post hoc* subgroup analysis, all of which are consistent with each other and which -- when examined together -- suggest a clearer understanding of a key ThermoDox® 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: ThermoDox, when used in combination with Radiofrequency Ablation (RFA) standardized to a minimum dwell time of 45 minutes (sRFA ≥ 45 min), may increase the overall survival (OS) of patients with HCC. The lead author is Won Young Tak, M.D., Ph.D., Professor Internal Medicine, Gastroenterology & Hepatology, Kyungpook National University Hospital Daegu, Republic of Korea, and there are 22 HEAT Study co-authors along with Nicholas Borys, M.D., Celsion's senior vice president and chief medical officer. The article is available online in the October 2017 issue of the journal, *Clinical Cancer Research, at* http://clincancerres.aacrjournals.org/content/early/2017/10/10/1078-0432.CCR-16-2433.long.

To test and confirm the HEAT Study *post hoc* subgroup analysis, Celsion is conducting 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 researchers, and statistical and regulatory experts, and based on extensive analysis of prior clinical and preclinical studies of ThermoDox® plus standardized RFA, the OPTIMA Study is 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.

Global interest in ThermoDox as a potential treatment option for HCC was recently showcased in the Company sponsored R&D Day held in New York City on October 12, 2017. Lead OPTIMA Study clinical investigators representing various geographical regions (Asia-Pacific and Europe) and multiple medical disciplines (hepatology, interventional radiology and surgery) presented their past and current experiences with ThermoDox for the treatment of primary liver cancer. The final 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 provided an average 58% improvement in OS compared to standardized RFA alone. The Hazard Ratio (HR) 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 years) 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 months for the standardized RFA only group.

"There is clear evidence that the duration of the RFA regimen is critical when treating patients with ThermoDox®, and the totality of the data presented in the newly published article in the peer reviewed journal, *Clinical Cancer Research,* demonstrate that ThermoDox® plus standardized RFA has a strong potential to serve as a curative therapy for patients with liver cancer," said Professor Won Young Tak, M.D., Ph.D., lead investigator in South Korea for the Company's HEAT and

OPTIMA studies. "The OPTIMA Study is designed to validate this approach in an indication where there exists a strong unmet need for effective treatment options."

In August 2017, the OPTIMA Study's Independent Data Monitoring Committee (IDMC), comprised of medical and scientific experts who are responsible for reviewing and evaluating patient safety and efficacy data, completed a planned interim analysis of the first 50% of patients randomized in the trial as of April 2017 and unanimously recommended that the OPTIMA Study continue as planned based on the risk to benefit analysis by the Committee. The OPTIMA Study to date has accumulated data within acceptable safety parameters. The Company announced that enrollment in the OPTIMA Study is approaching 70% of the 550 patients necessary to ensure that its primary end point, overall survival, can be evaluated with statistical significance. The statistical plan for the OPTIMA Study calls for two interim efficacy analyses by the IDMC. The Company currently projects full patient enrollment by mid-2018 and the first pre-planned efficacy analysis after 118 overall survival events by the first quarter of 2019.

"There is an urgent need for new and better treatment options for HCC, the third leading cause of cancer in the world. We believe strongly that ThermoDox® may be an important new approach for the treatment of HCC. We are now fully committed to the OPTIMA Study and to learning more about how this combination therapy of standardized RFA plus ThermoDox® may significantly prolong the survival of, if not cure, patients suffering from this extremely deadly cancer," stated Michael H. Tardugno, Celsion's chairman, president and chief executive officer, in response to the article's publication. "Supported with an independent endorsement by the National Institutes of Health, the OPTIMA Study and ThermoDox® may prove to be the most important oncology research in a generation," Mr. Tardugno added.

On November 29, 2016, the Company announced results from an independent retrospective analysis conducted by the National Institutes of Health on the intent-to-treat population of the 701 patient HEAT Study of ThermoDox® plus optimized RFA for the treatment of primary liver cancer. The NIH analysis, which sought to evaluate the correlation between RFA burn time per tumor volume (min/ml) and clinical outcome, concluded that increased RFA "burn time" per tumor volume significantly improved overall survival (OS) in patients with solitary lesions treated with RFA + ThermoDox® compared to patients treated with RFA alone. The NIH analysis included 437 patients with a single lesion from the Company's HEAT Study, the same patient population being treated in the Company's ongoing Phase III OPTIMA study. The NIH findings are consistent with Celsion's own analysis of the HEAT Study data, which demonstrated that over a 3.5 year period, there was a statistically significant survival benefit consistent with the HEAT Study in patients treated with ThermoDox® plus optimized RFA over the optimized RFA only group.

"We are highly focused on successfully executing the ongoing OPTIMA study," stated Nicholas Borys, Celsion's chief medical officer. "With independent confirmation by the NIH of the relationship between RFA heating time and the significant impact that it has on overall survival when combined with ThermoDox®, OPTIMA Study investigators fully recognize the value of the findings from the HEAT Study, reinforcing their interest and support for our highly de-risked, ongoing global Phase III OPTIMA Study, and to accomplishing our chief goal, the delivery of ThermoDox® as a novel, first-line treatment to HCC patients worldwide."

About the OPTIMA Study

The Phase III OPTIMA Study is expected to enroll up to 550 patients in up to 70 clinical sites in the United States, Europe, China and Asia Pacific, and will evaluate 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 three to seven centimeters, versus optimized RFA alone. The primary endpoint for the trial is Overall Survival, which is supported by post-hoc analysis of data from the Company's 701 patient HEAT Study, where optimized RFA has 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.

ThermoDox® has received U.S. FDA Fast Track Designation and has been granted orphan drug designation for primary liver cancer in both the U.S. and Europe. Further, the U.S. FDA has provided ThermoDox® with a 505(b)(2) registration pathway. Subject to a successful trial, the OPTIMA Study has been designed to support registration in all key primary liver cancer markets. Celsion fully expects to submit registrational applications in the USA, Europe and China. The Company believes that applications will be accepted in South Korea, Taiwan and Vietnam, three other large and important markets for ThermoDox® subject to approval in Europe, China or the USA.

About 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, ThermoDox®, 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 to allow significant accumulation of liposomes at the tumor site at the time of radiofrequency ablation as these liposomes recirculate in the blood stream. The second: When the tumor tissue is heated 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 targets 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 anti-cancer DNA or RNA therapies. For more information on Celsion, visit our website: http://www.celsion.com. (CLSN-LTSL/ThermoDox® CLSN-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.

Celsion Investor Contact

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

Primary Logo

Source: Celsion Corporation

News Provided by Acquire Media