Celsion Announces Publication of Research on Fluorescence Imaging of ThermoDox® Uptake in International Journal of Hyperthermia

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Independent Analysis Confirms Increasing Heating Time + ThermoDox® Improves Tumor Uptake of Drug, which may be visualized by real-time fluorescence imaging

Study Confirms that ThermoDox® Can Deliver Doxorubicin in Unprecedented Concentrations Directly into a Targeted Tumor

Comments on Common Stock Purchase Agreement with Aspire Capital Fund, LLC.

LAWRENCEVILLE, N.J., Nov. 14, 2019 (GLOBE NEWSWIRE) -- Celsion Corporation (NASDAQ: CLSN), an oncology drug development company, today announced that results from an independent study of a lyso-thermosensitive liposomal doxorubicin (LTLD) was published in the peer-reviewed publication, *International Journal of Hyperthermia* showing that real-time fluorescence imaging can visualize uptake of LTLD during delivery, and can predict tumor drug uptake in response to heat. ThermoDox® is Celsion's heat-activated liposomal formulation of doxorubicin currently in Phase III development for the treatment of primary liver cancer, also known as hepatocellular carcinoma (HCC). These data clearly show that high concentrations of tumor fighting doxorubicin can be delivered at unprecedented levels to tumors using ThermoDox® and targeted heat. This helps explain why the Phase III HEAT Study subgroup data is so impressive.

The study, titled, "Real-time fluorescence imaging for visualization and drug uptake prediction during drug delivery by thermosensitive liposomes," may be found here.

Authors were:

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- Bradford J. Wood, Center for Interventional Oncology, Radiology and Imaging Sciences, Clinical Center, National Institutes of Health
- Dieter Haemmerich, Department of Pediatrics, Medical University of South Carolina and Department of Bioengineering, Clemson University

Both Dr. Wood and Dr. Haemmerich have worked extensively with Celsion on ThermoDox. Dr. Wood was the lead investigator on the NIH team that evaluated the Company's HEAT Study data and published an article in *Journal of Vascular and Interventional Radiology* in August 2019 on an analysis of results from 437 patients, which found a correlation between baseline tumor volume and radiofrequency ablation (RFA) heating time. Dr. Haemmerich performed important computational modeling experiments that showed higher drug concentrations with increased heating time at 15, 30, 45 and 60 minutes.

This group used a LTSL-Dox to perform their experiments and confirmed several characteristics of the compound and its delivery mechanism that support the use of ThermoDox plus radiofrequency ablation in the treatment of HCC, as visualized by fluorescent imaging. Researchers used a custom designed hyperthermal (HT) probe to heat the tumors in nude mice carrying Lewis lung carcinoma. Key findings were as follows:

- Fluorescence Intensity Tumor Region of Interest (ROI) of heated tumors was enhanced:
  - 4.6-fold (at 15 mins)
  - 9.3-fold (at 30 mins)
  - 13.2-fold (at 60 mins)

- Tumor doxorubicin concentration of heated tumors was enhanced:
  - 1.9-fold (at 15 mins)
  - 2.9-fold (at 30 mins)
  - 5.2-fold (at 60 mins)

- Fluorescence intensity of LTSL-Dox increased by:
  - 6% when heated to 40°C
  - 11% when heated to 43°C

- There was a good correlation between fluorescence of tumor and tumor drug uptake

- Heat duration predicted tumor drug uptake (drug concentration) (p=0.02)

Commenting on the study, Dr. Haemmerich said, “This study provides visual proof of the power of heating LTSL-Dox and its ability to target tumors with increased concentration of doxorubicin delivered by a thermally sensitive liposomal formulation. Following infusion of LTSL-Dox, we found that the duration of hyperthermia dictated the tumor drug uptake, with each additional minute of hyperthermia enhancing drug uptake by 0.31 ug/g. We also demonstrated that fluorescence intensity was predictive of tumor drug concentrations, which may enable methods for real-time monitoring of drug uptake in patients in the future.”

“This study appears to support previously announced findings published by researchers at the NIH based on ThermoDox® and the HEAT study. There, in a prospective subgroup of 285 patients where RFA was applied for more than 45 minutes, a clinical benefit greater than two years was found for patients treated with ThermoDox® plus RFA, compared to RFA alone. These analyses in combination with our published study summarized above lend support to the hypothesis underpinning the OPTIMA Study, Celsion’s Phase III study in newly diagnosed HCC patients,” Dr. Haemmerich concluded.

Celsion also noted that this study confirms two previously completed studies as summarized below:

- An independent computational model developed by Dr. Haemmerich’s group at the Medical University of South Carolina. The results unequivocally indicate that longer RFA heating times correlate with significant increases in doxorubicin concentration around the RFA treated tissue.

- A prospective preclinical study in 22 pigs conducted at Colorado State University Animal Cancer Center using two different manufacturers of RFA and human equivalent doses of ThermoDox® that clearly support the relationship between increased heating duration and doxorubicin concentrations.

Common Stock Purchase Agreement

Separately, Celsion is commenting on its Common Stock Purchase Agreement with Aspire Capital Fund, LLC. On October 28, 2019 Celsion entered into a new Common Stock Purchase Agreement with Aspire Capital Fund, LLC. whereby Aspire is committed to purchase an aggregate of $10 million of shares of the Company’s common stock over a two-year period. Celsion filed a Form S-1 to register up to 4.5 million shares under this facility, which replaces an earlier agreement. The sale of these securities is at the discretion of Celsion alone. Given market conditions, the Company has little or no intention of using this facility at this time. Celsion reiterates its past comments regarding its strong balance sheet, and notes that based on its previously disclosed cash position at June 30, 2019, it believes that it has a cash runway well into 2021.

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 (RCW) 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 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 more precise drug targeting.

About the OPTIMA Study

The Phase III OPTIMA Study has enrolled 556 patients in over 60 clinical sites in the United States, Europe, China and Asia Pacific, and will evaluate ThermoDox® in combination with optimized RFA, which was 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. The OPTIMA Study is a follow-on study supplemented by *post-hoc* analyses of data from the Company's 701-patient HEAT Study in which optimized RFA demonstrated the potential to significantly improve survival when combined with ThermoDox®. The OPTIMA Study’s statistical plan calls for two interim efficacy analyses by an independent Data Monitoring Committee.

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.

The Company has a Cooperative Research and Development Agreement (CRADA) with the NIH. Any reference to NIH should not be viewed as an

endorsement of Celsion, its products or services. For more information on Celsion, visit our website: http://www.celsion.com (LTSL/ThermoDox®, HEAT Study/HCC, 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.

ThermoDox® is a registered trademark of Celsion Corporation.

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