Results of Celsion's OVATION 1 Study with GEN-1 in Patients with Advanced Ovarian Cancer Published in the Journal of Clinical Cancer Research

July 29, 2021

Data show dose-dependent suppression of immune-suppressive agents

GEN-1 stimulates the immune system through the production of CD4 and CD8 cells

Chemotherapy Response Score tripled in the two highest doses of GEN-1 and is double that of chemotherapy alone

LAWRENCEVILLE, N.J., July 29, 2021 (GLOBE NEWSWIRE) -- Celsion Corporation (NASDAQ: CLSN), a clinical-stage company focused on DNA-based immunotherapy and next-generation vaccines, today announced the publication of data from its Phase 1b OVATION 1 Study with GEN-1 in combination with neoadjuvant chemotherapy (NACT) in patients with advanced ovarian cancer in *Clinical Cancer Research,* a journal of the American Association for Cancer Research. The study, authored by Premel H. Thaker, *et al.* is titled "GEN-1 in Combination with Neoadjuvant Chemotherapy for Patients with Advanced Epithelial Ovarian Cancer: A Phase I Dose-Escalation Study." The publication is available here.

GEN-1 is a DNA-based interleukin-12 (IL-12) immunotherapy currently in Phase I/II clinical development for the localized treatment of advanced ovarian cancer (the OVATION 2 Study). GEN-1 is an immunotherapy that produces safe and durable local levels of IL-12, a pluripotent cytokine associated with the stimulation of innate and adaptive immune response against cancer. The GEN-1 nanoparticle comprises a DNA plasmid encoding IL-12 gene and a synthetic polymer facilitating plasmid delivery vector. Premal H. Thaker, M.D., M.S., Professor of Gynecologic Oncology and Director of Gynecologic Oncology Clinical Research at the Washington University School of Medicine at Washington University Medical Center in St. Louis, is the study chair for the OVATION program.

The OVATION 1 Study enrolled 18 patients with newly diagnosed stage IIIC and IV epithelial ovarian cancer in a standard 3+3 dose-escalation design testing four GEN-1 doses (36 mg/m^2, 47 mg/m^2, 61 mg/m^2 and 79mg/m^2) in combination with NACT (carboplatin-paclitaxel). There were 15 patients evaluable for safety, and 14 underwent interval debulking and were evaluable for Response Evaluation Criteria in Solid Tumors (RECIST).

As previously reported, there were no dose-limiting toxicities. As shown in the chart below, in the two highest doses of GEN-1 the objective response rate was 100% and the R0 resection rate was 88%. Newly published data show the chemotherapy response score (CRS), which is analyzed in this paper for the first time, was 50% in the two highest doses of GEN-1, compared with 28% from a major publication evaluating CRS scoring. The chemotherapy response score is a three-tier standardized scoring system for histological tumor regression into complete/near complete (CRS 3), partial (CRS 2) and no/minimal (CRS 1) response based on omental examination. Like R0 resection rates, CRS 3 response is believed to be a predictor of progression-free survival.

Clinical Responses: Tumor Response, Surgical Outcome, Pathological Response and Chemotherapy Response Score with NAC/GEN-1 escalating doses

Radiographic Response		**Total (n)**	**Cohort 1 36 mg/m^2**	**Cohort 2 47 mg/m^2**	**Cohort 3 61 mg/m^2**	**Cohort 4 79 mg/m^2**
Tumor Response	CR	2	1	0	0	1
	PR	10	0	3	3	4
	SD	2	2	0	0	0
Objective Response Rate			**67%**		**100%**	
Surgical Outcome	R0	9	2	0	2	5
	R1	3	1	2	0	0
	R2	2	0	1	1	0
R0 Resection Rate			**33%**		**88%**	
Pathological Response	cPR	1	1	0	0	0
	Micro	8	1	2	1	4
	Macro	5	1	1	2	1
cPR/Micro Rate			**60%**		**63%**	
Chemotherapy Response Score	CRS 3	5	1	0	2	2
	CRS 2	5	2	1	0	2
	CRS 1	4	0	2	1	1
CRS 3 Rate			**17%**		**50%**	

Commenting on the abstract, Dr. Thaker said, "My colleagues and I are very encouraged by the data generated from the OVATION 1 Study, which is

informing the ongoing Phase I/II OVATION 2 Study. Importantly, the repeated durable increase in IL-12 and IFN-γ levels at the tumor site for an eight-week treatment period provides for a pharmacologic remodeling of the tumor microenvironment. These immunomodulatory effects of GEN-1 may result in an increased sensitivity of tumor microenvironment to other anticancer agents including cytotoxic drugs and immunotherapies such as checkpoint inhibitors and adaptive T cell therapies. The OVATION 2 Study of concurrent GEN-1 at a dose of 100 mg/m^2 weekly for up to 17 doses administered during chemotherapy is actively recruiting."

Translational Responses: IL-12 and IFN-γ Levels, Response to Immune-Suppressive Agents; Ratio of CD8+ cells to Immune Suppressive Agents

Results from translational studies show the following:

- A dose-dependent increase in immunostimulatory cytokines IL-12 and its downstream cytokine IFN-γ in ascitic fluid. The anticancer effects of these cytokines are widely recognized in human malignancies.
- The proportion of myeloid dendritic cells in the peritoneal fluid trended higher (3.1-fold) accompanied by a similar 3.0-fold rise in CD8+ cells.
- GEN-1 appeared to reduce four immunosuppressive signals (Foxp3, IDO1, PD-1 and PD-L1) within the tumor microenvironment, a trend not seen with NAC therapy alone.
- GEN-1 also appeared to stimulate the body's immune system through the production of CD4 and CD8 cells.
- GEN-1 gene therapy was associated with an apparent increase in the cytotoxic state of T cells within the tumor microenvironment as indicated by the increases in the ratios of CD8+/CD4+ and CD8+/Treg cells. Indeed, higher CD8+/CD4+ T cell and CD8+/Treg ratios are considered prognostic for prolonged survival.

Junko Matsuzaki, Ph.D., Director of the Immune Analysis Facility at Roswell Park Comprehensive Cancer Center in Buffalo, N.Y. and a study author, said, "The results from our translational studies show the activation of a multitude of immune responses following GEN-1 + NAC treatment. The multifactorial nature of GEN-1 immune response built on a durable local production of IL-12 may be activating the innate and adaptive immune system creating a unique microenvironment potentially favorable to anti-tumor responses and also conducive to other therapeutic drugs that may be suboptimal as single agents due to the highly immunosuppressive tumor microenvironment in ovarian cancer. The peritoneal cavity of advanced ovarian cancer patients contains the primary tumor environment and is an attractive target for a regional approach to immune modulation."

Nicholas Borys, M.D., Chief Medical Officer of Celsion, said, "We are delighted that our OVATION 1 Study has been published in the *Journal of Clinical Cancer Research.* As patients with advanced ovarian cancer have a poor prognosis, these data are particularly encouraging. We believe this publication will create additional awareness of the work we are doing to treat these patients and provide them with new hope. While we know that R0 resection scores are important to survival and that GEN-1 has exhibited impressive R0 scores, its ability to improve CRS is also compelling. Adding GEN-1 to standard neoadjuvant chemotherapy is safe, appears to be clinically active with translational data suggesting a positive impact on the tumor microenvironment."

About the *Journal of Clinical Cancer Research*

The *Journal of Clinical Cancer Research* is a publication of the American Association for Cancer Research. It publishes innovative clinical and translational cancer research studies that bridge the laboratory and the clinic. The *Journal* is especially interested in clinical trials evaluating new treatments, accompanied by research on pharmacology, and molecular alterations or biomarkers that predict response or resistance to treatment. The *Journal* also prioritizes laboratory and animal studies of new drugs and molecule-targeted agents with the potential to lead to clinical trials, and studies of targetable mechanisms of oncogenesis, progression of the malignant phenotype and metastatic disease.

About Epithelial Ovarian Cancer

Epithelial ovarian cancer (EOC) is the 5th deadliest malignancy among women in the United States. There are approximately 22,000 new cases of ovarian cancer every year and the majority (approximately 70%) are diagnosed in advanced stages III and IV. EOC is characterized by dissemination of tumor in the peritoneal cavity with a high risk of recurrence (75%, stage III and IV) after surgery and chemotherapy. Since the 5-year survival rates of patients with stages III and IV disease at diagnosis are poor (41% and 20%, respectively), there remains a need for a therapy that not only reduces the recurrence rate but also improves overall survival. The peritoneal cavity of advanced ovarian cancer patients contains the primary tumor environment and is an attractive target for regional approach to immune modulation.

About Celsion Corporation

Celsion is a fully integrated, clinical stage biotechnology company focused on advancing a portfolio of innovative cancer treatments, including immunotherapies and DNA-based therapies; and a platform for the development of nucleic acid vaccines currently focused on SARS-CoV2. The company's product pipeline includes GEN-1, a DNA-based immunotherapy for the localized treatment of ovarian cancer. ThermoDox ®, a proprietary heat-activated liposomal encapsulation of doxorubicin, is under investigator-sponsored development for several cancer indications. Celsion also has two platform technologies for the development of novel nucleic acid-based immunotherapies and other anti-cancer DNA or RNA therapies. Both are novel synthetic, non-viral vectors with demonstrated capability in nucleic acid cellular transfection. For more information on Celsion, visit www.celsion.com.

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, statements relating to the offering and the use of proceeds therefrom, 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.

CONTACTS:

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

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

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