Candel Therapeutics Announces Publication of Phase 1b Clinical Trial Data on the Combination of CAN-2409 and Nivolumab plus Standard of Care in Newly Diagnosed High-Grade Glioma Patients

April 1, 2025

Data published in Neuro-Oncology demonstrate promising safety profile and potential survival benefit when combining CAN-2409 and nivolumab with standard of care

NEEDHAM, Mass., April 01, 2025 (GLOBE NEWSWIRE) -- Candel Therapeutics, Inc. (Candel or the Company) (Nasdaq: CADL), a clinical stage biopharmaceutical company focused on developing multimodal biological immunotherapies to help patients fight cancer, today announced the publication of a manuscript reporting the results of a phase 1b clinical trial exploring safety and tolerability of the combination of CAN-2409 plus prodrug (valacyclovir) and nivolumab, in addition to standard of care (neurosurgery, radiotherapy, and temozolomide), in patients with newly diagnosed high-grade glioma. The study, which includes evidence of clinical activity and extensive biomarker analysis, has been published online in *Neuro-Oncology*, the official journal of the Society for Neuro-Oncology (22 March 2025).

High-grade glioma (primarily glioblastoma) remains one of the most aggressive forms of primary brain cancer, affecting more than 13,000 new patients in the United States annually. Despite optimal therapy with surgery, radiation, temozolomide chemotherapy, and, in some cases, tumor-treating fields, the prognosis remains poor with median survival of approximately 20 months from the time of diagnosis for patients without methylguanine methyltransferase (MGMT) promoter methylation and about 2 years for those with MGMT promoter methylation.[1] Poor survival is associated with paucity of intratumoral T cell infiltrates and a highly immunosuppressive tumor microenvironment. To date, clinical trials of conventional tumor vaccines and checkpoint inhibitors have failed to demonstrate clinical benefit in this indication.

The publication, titled “A multi-institutional phase 1 clinical trial exploring upfront multimodal standard of care and combined immunotherapies for newly diagnosed glioblastoma,” (Wen, P. Y., et al.) demonstrates that the addition of CAN-2409 and nivolumab and standard of care was generally well tolerated and extended survival in a subset of patients with evidence of local and systemic immune activation after experimental treatment. The clinical trial (NCT03576612) enrolled 41 patients, with 35 completing the full treatment regimen, and assayed tumor and blood for genetic and immunological biomarkers before and during treatment.

“The results from this mechanistic clinical trial confirm and extend previous observations in clinical trials that have shown clinical and immunological activity of CAN-2409 across different solid tumors,” said Paul Peter Tak, MD, PhD, FMedSci, President and Chief Executive Officer of Candel. “In this trial, treatment with CAN-2409 plus valacyclovir was associated with discrete longitudinal changes in peripheral cytokines, immune cells, and T cell clone diversity, particularly at early timepoints, after patients had been treated with neurosurgery, radiotherapy, and CAN-2409 plus prodrug, but before combination therapy with nivolumab was initiated. The most noteworthy serial systemic immune changes were observed in a long-term survivor subset of patients. While we are not currently developing CAN-2409 for high-grade glioma, in light of portfolio prioritization (We are developing CAN-3110 in recurrent high-grade glioma (rHGG)), the data support the notion that CAN-2409 may be a pan-solid tumor therapy that could invoke individualized anti-cancer immune response in different indications. CAN-2409 is in late-stage development for localized prostate cancer, borderline resectable pancreatic ductal adenocarcinoma, and non-small cell lung cancer (NSCLC).”

CAN-2409 is an investigational, off-the-shelf, replication-defective adenovirus that delivers the herpes simplex virus thymidine kinase (HSV-tk) gene to tumor cells. CAN-2409, when administered with valacyclovir, is designed to induce immunogenic cell death of tumor cells with exposure of tumor antigens in the context of an activated tumor microenvironment. Together, this regimen is designed to induce an individualized, systemic, specific CD8+ T cell-mediated response against the tumor, based on *in situ* vaccination against a variety of the patient’s own tumor antigens.

“We are excited by the promising results from this phase 1b clinical trial,” said Francesca Barone, MD, PhD, Chief Scientific Officer of Candel. “Our data demonstrates that CAN-2409 has the potential to broaden the T cell receptor repertoire, and foster a more diverse immune response, which has previously been shown in several publications to be associated with improved clinical outcome in high-grade glioma and other solid tumors. The findings are consistent with previous observations in clinical trials after administration of CAN-2409 in NSCLC and other solid tumors, where CAN-2409 administration led to local and systemic immune cell activation, reinforcing the potential to create a “pipeline in a product” across multiple solid tumors.”

Data highlights:

- Median overall survival for the overall patient population was 15.1 months. A subset of patients with methylated MGMT promoter, who underwent gross total tumor resection (n=6), showed particularly encouraging outcomes, with a median overall survival of 30.6 months.

- Baseline tumor immune cell composition was associated with clinical outcomes, with patients with higher levels of B cells, dendritic cells, HLA-DR high macrophage clusters, and memory CD4+ T cells exhibiting improved survival. Conversely, we observed a negative correlation between tissue immunosuppressive monocytes and survival.

- Experimental combination treatment with CAN-2409 plus prodrug and nivolumab induced noteworthy systemic immune activation at weeks 3 and 5 post treatment. This included increased naive and effector T cells, marked reduction in

immunosuppressive TIM3+ NK cells, and changes in cytokine profiles observed at weeks 3 and 5 timepoints that were correlated with subsequent survival.

- Increase in T cell receptor (TCR) density and richness was observed at the week 3 timepoint (after CAN-2409 treatment but before initiation of nivolumab). These changes were associated with improved survival.

- Long-term survivors (more than 30 months) in the population of patients with MGMT methylated tumors who had undergone gross total resection, showed distinct TCR profiles and immune cell patterns compared to short-term survivors. These included enrichment in TCR richness and diversity, supporting the hypothesis that CAN-2409 can release tumor-associated antigens and broaden the antitumoral T cell response, both locally and systemically.

- No dose-limiting toxicities attributable to CAN-2409 were observed and a generally favorable safety and tolerability profile of the combination therapy was reported.

“The increase in TCR density and richness demonstrated early after experimental treatment with CAN-2409 is an important finding in this phase 1b clinical trial,” said E. Antonio Chiocca, MD, PhD, Chair of the Department of Neurosurgery at Brigham and Women’s Hospital, Professor at Harvard Medical School, Candel Scientific Advisor, and co-author of the publication. “Moreover, we observed an association between TCR diversity and long-term survival in patients with a methylated MGMT promoter, who were able to undergo gross total resection of the tumor, supporting the opportunity for implementation of a novel stratification strategy in future clinical trials.”

About CAN-2409

CAN-2409, Candel’s most advanced multimodal biological immunotherapy candidate, is an investigational, off-the-shelf, replication-defective adenovirus engineered to deliver the herpes simplex virus thymidine kinase (HSV-tk) gene to a patient’s specific tumor and induce an individualized, systemic immune response against the tumor. HSV-tk is an enzyme that locally converts orally administered valacyclovir into a toxic nucleotide analogue that kills nearby cancer cells. Together, this regimen is designed to induce an individualized and specific CD8+ T cell-mediated response against the injected tumor and uninjected distant metastases for broad anti-tumor activity, based on in situ vaccination against a variety of tumor antigens. Because of its versatility, CAN-2409 has the potential to treat a broad range of solid tumors. Encouraging monotherapy activity, as well as combination activity with standard of care (SoC) radiotherapy, surgery, chemotherapy, and immune checkpoint inhibitors, have previously been shown in several preclinical and clinical settings. More than 1,000 patients have been dosed with CAN-2409 with a generally favorable tolerability profile reported to date, supporting the potential for combination with other therapeutic strategies.

Candel's clinical development program for CAN-2409 includes completed phase 2a clinical trials in both NSCLC and pancreatic ductal adenocarcinoma (PDAC), as well as a positive pivotal randomized, placebo-controlled phase 3 clinical trial of CAN-2409 in localized, non-metastatic prostate cancer. In December 2024, Candel announced that CAN-2409 achieved its primary endpoint in a phase 3 clinical trial in men with intermediate-to-high-risk, localized prostate cancer, demonstrating statistically significant and clinically meaningful improvement in disease-free survival when added to SoC radiation therapy +/- androgen deprivation therapy.

In the Company’s randomized controlled phase 2a clinical trial of CAN-2409 in borderline resectable PDAC, positive survival data showed notable improvement in estimated median overall survival of 31.4 months after experimental treatment with CAN-2409 plus SoC versus 12.5 months in the control group in patients with PDAC who only received SoC. Median survival post-progression was 21.2 months in patients who received CAN-2409 compared to 6.4 months in the control arm. CAN-2409 plus prodrug has been granted Fast Track Designation by the FDA for the treatment of PDAC, stage III/IV NSCLC in patients who are resistant to first line PD-(L)1 inhibitor therapy and who do not have activating molecular driver mutations or have progressed on directed molecular therapy and localized prostate cancer. The FDA has also granted Orphan Drug Designation to CAN-2409 for the treatment of PDAC. Candel’s pivotal phase 3 clinical trial in newly diagnosed, localized prostate cancer was conducted under a Special Protocol Assessment (SPA) agreed with the FDA.

About Candel Therapeutics

Candel is a clinical stage biopharmaceutical company focused on developing off-the-shelf multimodal biological immunotherapies that elicit an individualized, systemic anti-tumor immune response to help patients fight cancer. CAN-2409 is the lead product candidate from the adenovirus platform. CAN-3110 is the lead product candidate from the HSV platform and is currently in an ongoing phase 1b clinical trial in rHGG. In October 2023, the Company announced that *Nature* published initial results from this ongoing clinical trial: CAN-3110 was well tolerated and the investigators observed nearly two-fold increase in median overall survival compared to historical controls after a single CAN-3110 injection in this therapy-resistant condition.[2] Finally, Candel’s enLIGHTEN™ Discovery Platform is a systematic, iterative HSV-based discovery platform leveraging human biology and advanced analytics to create new viral immunotherapies for solid tumors.

For more information about Candel, visit: www.candeltx.com

Forward-Looking Statements

This press release includes certain disclosures that contain “forward-looking statements,” within the meaning of the Private Securities Litigation Reform Act of 1995, as amended, including, without limitation, express or implied statements regarding the timing and advancement of current and future development programs; including the timing and availability of additional data and key data readout milestones and presentations; expectations regarding early biological readouts as predictor of clinical response; and expectations regarding the therapeutic benefit of the Company’s programs, including the ability of CAN-2409 to treat a broad range of solid tumors and improve disease-free survival, overall survival, and post-progression survival. The words “may,” “will,” “could,” “would,” “should,” “expect,” “plan,” “anticipate,” “intend,” “believe,” “estimate,” “predict,” “project,” “potential,” “continue,” “target” and similar expressions are intended to identify forward-looking statements, although not all forward-looking statements contain these identifying words. Any forward-looking statements in this press release are based on management’s current expectations and beliefs and are subject to a number of risks, uncertainties and important factors that may cause actual events or results to differ materially from those expressed or implied by any forward-looking statements contained in this press release, including, without limitation, those risks and uncertainties related to the

timing and advancement of development programs; expectations regarding the therapeutic benefit of the Company's programs; that final data from the Company's pre-clinical studies and completed clinical trials may differ materially from reported interim data from ongoing studies and trials; the Company's ability to efficiently discover and develop product candidates; the Company's ability to obtain and maintain regulatory approval of product candidates; the Company's ability to maintain its intellectual property; the implementation of the Company's business model, including strategic plans for the Company's business and product candidates; and other risks identified in the Company's filings with the U.S. Securities and Exchange Commission (SEC) including the Company's most recent Annual Report on Form 10-K filed with the SEC and any subsequent filings with the SEC. The Company cautions you not to place undue reliance on any forward-looking statements, which speak only as of the date they are made. The Company disclaims any obligation to publicly update or revise any such statements to reflect any change in expectations or in events, conditions, or circumstances on which any such statements may be based, or that may affect the likelihood that actual results will differ from those set forth in the forward-looking statements. Any forward-looking statements contained in this press release represent the Company's views only as of the date hereof and should not be relied upon as representing its views as of any subsequent date.

Investor Contact:
Theodore Jenkins
VP, Investor Relations and Business Development
Candel Therapeutics, Inc.
tjenkins@candeltx.com

Media Contact:
Ben Shannon
ICR Healthcare
CandelPR@icrhealthcare.com

_____

1 Stupp R et al. *JAMA.* 2017; 318(23):2306-2316.

2 Ling AL, et al. Nature. 2023;623(7985):157-166.