Candel Therapeutics Reports Both Prolonged Median Overall Survival and Long Tail of Survival in Phase 2a Clinical Trial of CAN-2409 in Advanced Non-Small Cell Lung Cancer (NSCLC) Patients Non-Responsive to Immune Checkpoint Inhibitor (ICI) Treatment

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- *Experimental treatment with CAN-2409 was associated with a median overall survival (mOS) of 24.5 months in patients with advanced NSCLC who had an inadequate response to ICI treatment, failed several chemotherapy regimens, and presented with multiple negative prognostic factors at enrollment (90% of the patients had stage IV disease, most patients had low or undetectable PDL-1 expression, > 90% were current or former smokers, and most patients had failed multiple lines of chemotherapy)*

- *mOS of 21.5 months was observed in patients with progressive disease at baseline despite ICI therapy (cohort 2), markedly exceeding mOS which has been reported in published literature for this population with standard of care of docetaxel chemotherapy (mOS of 9.8-11.8 months)*

- *Long tail of survival observed in 37% (15/41) of patients with progressive disease despite ICI treatment at enrollment, who were still alive more than 2 years after CAN-2409 administration at the time of data cutoff (March 3, 2025)*

- *Evidence of a systemic immune response with regression of both injected and uninjected lesions observed in approximately two-thirds of patients with metastatic disease and at least one uninjected tumor (abscopal effect)*

- *Statistically significant improved overall survival in non-squamous NSCLC compared to squamous NSCLC after experimental treatment with CAN-2409, supported by immunological biomarker data; mOS of 25.4 months in per protocol population of patients with non-squamous NSCLC with progressive disease at baseline despite ICI*

- *CAN-2409 continued to exhibit a generally favorable safety and tolerability profile throughout the extended follow-up period, with no new safety signals identified*

NEEDHAM, Mass., March 26, 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 final survival data from a phase 2a clinical trial of CAN-2409 in patients with stage III/IV NSCLC, inadequately responding to ICI treatment. mOS was 24.5 months in 46 evaluable patients receiving 2 courses of CAN-2409 (per protocol population; cohort 1 and 2) and 21.5 months in evaluable patients from cohort 2 (n=41) that presented with progressive disease at baseline, despite ICI treatment. mOS in patients with progressive disease despite ICI treatment, was 9.8-11.8 months in other studies, including those with standard of care of docetaxel chemotherapy, which has a very poor prognosis, did not exceed 12 months in other published studies.[1, 2] This final analysis included extended follow-up data (1 year after the previous data cut) with a median follow up time for the per protocol population of 32.4 months. Data showed a sizable percentage of patients with survival exceeding 24 months, evidence of a long tail of survival, with 37% of patients with progressive disease despite treatment with ICI alive 2 years after CAN-2409 administration.

Biomarker research showed an enhanced immunological and clinical response after CAN-2409 administration in patients with non-squamous histology compared to squamous histology, and improved mOS was observed in this population (25.4 months in patients with progressive disease despite ICI treatment and non-squamous NSCLC, n=33).

“Treatment options are quite limited for patients with unresectable NSCLC who progress on anti-PD-1 therapy,” said Charu Aggarwal, MD, MPH, Leslye Heisler Professor for Lung Cancer Excellence at the University of Pennsylvania’s Perelman School of Medicine and Principal Investigator of the study. “The survival benefit seen in this study is striking, especially when compared to both the current standard of care treatment of docetaxel chemotherapy and other therapies under investigation for this patient group,” she added.

Data Highlights:

Pre-treatment and mid-treatment dropout rates were comparable to those reported in other clinical trials in similar populations of patients with advanced NSCLC.[1, 3] Three patients were enrolled, but did not receive treatment, 22 patients received only one injection of CAN-2409, 51 patients received at least 2 injections of CAN-2409, but 5 patients did not complete treatment. 46 patients received complete treatment (2 courses of CAN-2409 plus prodrug) and were included in the evaluable, per protocol population. The per protocol population was representative of the overall enrolled population in terms of baseline demographics and prognostic factors.

- Survival data:

- In patients with an inadequate response to ICI treatment (Cohort 1+2, n=46), mOS was 24.5 months.
- In patients with progressive disease, despite ICI treatment (Cohort 2, n=41), mOS was 21.5 months, which is markedly longer than the 9.8–11.8 months of survival reported in published literature in a similar patient population receiving standard of care of docetaxel chemotherapy.[1,2]
- 37% of patients exceeding 24 months survival were still alive at the time of the March 3, 2025 data cut.

- Potential precision medicine approach:
  - Patients with non-squamous histology predominated amongst the long-term survivors: 14/15 patients with OS > 24 months and 9/9 patients with OS > 30 months had non-squamous NSCLC.
  - Patients with non-squamous histology exhibited larger changes in T cells, B cells, and dendritic cells after CAN-2409 administration compared to patients with squamous NSCLC.
  - mOS of 25.4 months observed in non-squamous NSCLC patients with progressive disease, despite ICI treatment (n=33).
  - Although a phase 2a open-label experimental medicine clinical trial is not designed for an intention to treat (ITT) analysis, we conducted an exploratory ITT analysis and observed mOS of 16.7 months after CAN-2409 administration in non-squamous NSCLC patients with progressive disease despite ICI treatment (n=53). Recent trials have reported a mOS of 9.9–12.3 months in ICI-refractory, non-squamous NSCLC patients receiving standard of care docetaxel chemotherapy.[1,2]
- Systemic anti-tumor response (abscopal effect) and safety profile:
  - Decrease in size of uninjected tumors was observed in 69% of patients with multiple lesions (n=35), indicating that local injection may induce a systemic anti-tumor immune response (abscopal effect).
  - CAN-2409 maintained its generally favorable safety and tolerability profile throughout the extended follow-up period.

“These updated survival data confirm and strengthen our previously reported findings, demonstrating that CAN-2409 has the potential to extend survival for patients with advanced NSCLC, who have limited treatment options after failing to respond to, or progressing, despite immune checkpoint inhibitor therapy,” said Paul Peter Tak, MD, PhD, FMedSci, President and Chief Executive Officer of Candel. “CAN-2409 may represent an entirely new approach to solid tumor treatment, with its unique mechanism of action and favorable safety profile to date, enabling potentially meaningful improvements in outcomes beyond current standard of care. These compelling results mark a potentially transformative advance in our fight against this aggressive disease.”

“The extension of survival in patients with non-squamous disease is notable even when compared to data that have been reported for other investigational products, such as antibody-drug conjugates, for this patient population,” said W. Garrett Nichols, MD, CMO of Candel. “CAN-2409, in addition to continued ICI treatment, may prolong survival beyond that offered by docetaxel chemotherapy, and has the potential to be better tolerated.”

Based on these positive findings, the Company will advance its development program for CAN-2409 in NSCLC, including preparation and enabling work for a future, potentially registrational, clinical trial in patients with NSCLC with non-squamous histology. The U.S. Food and Drug Administration (FDA) previously granted Fast Track Designation for CAN-2409 plus valacyclovir in combination with ICI treatment for the treatment of 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.

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 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 favorable tolerability profile 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 non-small cell lung cancer (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 standard of care versus 12.5 months in the control group in patients with PDAC, who received only standard of care. 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 primary 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 BLA ready 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 recurrent high-grade glioma. 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.[4] 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.

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