Candel Therapeutics Reports Prolonged Overall Survival in Phase 2 Clinical Trial of CAN-2409 for Advanced Non-Small Cell Lung Cancer (NSCLC) in Patients Non-Responsive to Immune Checkpoint Inhibitor (ICI) Treatment at 2024 ASCO Annual Meeting

May 23, 2024

- *Median overall survival of 20.6 months was observed following two administrations of CAN-2409 + valacyclovir in NSCLC patients with progressive disease despite immune checkpoint inhibitor therapy compared to published results of median overall survival of 11.6 months observed with standard of care docetaxel-based chemotherapy in a similar patient population*

- *CAN-2409 treatment resulted in activation of the systemic immune response after two administrations of CAN-2409, including increased numbers of circulating cytotoxic and memory T cells associated with subsequent prolonged survival, and a beneficial effect on both injected and uninjected tumors (abscopal response)*

- *As of the data cut-off date, CAN-2409 treatment in NSCLC continued to exhibit a favorable safety and tolerability profile*

NEEDHAM, Mass., May 23, 2024 (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 topline overall survival data from its phase 2 clinical trial of CAN-2409, a multimodal biological immunotherapy candidate, plus valacyclovir (prodrug), together with standard of care (SoC) immune checkpoint inhibitor (ICI) therapy in patients with Stage III/IV non-small cell lung cancer (NSCLC) inadequately responding to ICI (anti-PD-(L)1) therapy. The data will be presented at the 2024 American Society of Clinical Oncology (ASCO) Annual Meeting, to be held in Chicago, May 31 to June 4, 2024, by Charu Aggarwal, MD, MPH, FASCO, Leslye M. Heisler Associate Professor for Lung Cancer Excellence at the Perelman School of Medicine, University of Pennsylvania and Co-Principal Investigator of the clinical trial.

Highlights of the presentation include: 1) median overall survival (mOS) of 20.6 months achieved in patients with progressive disease despite ICI treatment after two administrations of CAN-2409 plus prodrug; for context, in a 2022 publication of a clinical trial in a similar patient population, mOS in the control arm that received SoC docetaxel-based chemotherapy was 11.6 months; improved survival was observed across both PD-(L)1 positive and PD-(L)1 negative tumors; 2) beneficial effect on both injected and uninjected tumors in more than 70% of the patients with metastatic disease and at least one uninjected tumor; and 3) a significant increase in circulating CD8+ cytotoxic and CD4+ effector and central memory T cells and increased soluble granzyme B levels in peripheral blood after the second ('booster') injection of CAN-2409, associated with subsequent prolonged survival (in each case, as of an April 1 data cut-off). Together, these data continue to support the emerging differentiated profile of CAN-2409 in this difficult-to-treat condition.

"The results from our phase 2 trial in NSCLC continue to support the tremendous promise of CAN-2409 across multiple solid tumors. We are particularly encouraged by the overall survival observed in the patients whose disease had progressed despite receiving prior anti-PD-(L)1 treatment. Improved overall survival is, ultimately, what matters to patients and to the regulators," said Paul Peter Tak, MD, PhD, FMedSci, President and Chief Executive Officer of Candel. "These results, together with our recently reported overall survival data in a randomized clinical trial in pancreatic cancer, add to the growing body of evidence supporting the notion that CAN-2409 treatment may convert progressive cancer into stable disease associated with survival benefit in advanced cancers with high unmet medical needs."

Previously, the Company received FDA Fast Track Designation for CAN-2409 in NSCLC and pancreatic cancer as well as orphan drug designation in pancreatic cancer.

"Current therapeutic options for advanced NSCLC patients whose disease progresses despite ICI treatment are limited; they are characterized by poor tolerability and limited clinical benefit," said Charu Aggarwal, MD, MPH, FASCO. "The data reported today suggest that CAN-2409 can reactivate these patients' exhausted immune systems, including those with low PD-(L)1 expression. This systemic anti-tumor immune response translated to a durable response; increased numbers of circulating cytotoxic and memory T cells were associated with subsequent prolonged survival. I look forward to the continued development of CAN-2409 in NSCLC as a promising approach in an area of unmet therapeutic need."

ASCO presentation highlights:

- The open label phase 2 clinical trial evaluated the efficacy and safety of the combination of CAN-2409 plus prodrug (valacyclovir) and continued, unaltered ICI therapy in patients with an inadequate response to ICI after at least 18 weeks of treatment. The objective of the analysis presented at ASCO was to explore whether experimental treatment with CAN-2409 plus prodrug could improve mOS in patients treated with two injections.

- 46 patients received two administrations of CAN-2409 plus prodrug and were evaluable per protocol.

Cohort 1	Stable Disease at Study Entry	n=5

Cohort 2	Progressive Disease at Study Entry	n=41

- Demographic characteristics of the safety population:

Age	**Years**
Median (Range)	67 (43-88)
Sex	**n (%)**
Female	32 (44)
Male	41 (56)
PD-(L)1 Expression	**n (%)**
<1%	35 (48)
1-49%	15 (21)
≥ 50%	19 (26)
Unknown	4 (5)
Histology	**n (%)**
Squamous	16 (22)
Non-Squamous	57 (78)
Treatment regimen at enrollment	**n (%)**
Single ICI	50 (68)
ICI plus pemetrexed	23 (32)

- We confirmed previously released data on the ability of CAN-2409 to control disease, with a disease control rate of 100% in cohort 1 and 70% in cohort 2 patients.

- As of April 1, 2024, mOS of 22.0 months was observed across all 46 patients who had an inadequate response to ICI (both cohorts 1 and 2).

  In patients with progressive disease despite ICI treatment (cohort 2), a mOS of 20.6 months was observed. A 2022 publication of a clinical trial in a similar patient population reported mOS of 11.6 months for SoC docetaxel-based chemotherapy.[1]

- Improved mOS was observed in both PD-(L)1 negative and PD-(L)1 positive tumors in patients with progressive disease (n=37 patients in cohort 2 for which PD-(L)1 status at baseline was available).

PD-(L)1 Subgroup	Number of Patients	mOS (months)
Negative (<1%)	16	24.5 (7.0, NA)
Positive (>=1%)	21	20.6 (5.5, NA)

- 71.4% of patients with metastatic disease and at least one uninjected tumor (n=35) experienced a beneficial effect on both injected and uninjected tumors, indicating a systemic anti-tumor immune response. When using a threshold of >5% decrease, more than 60.0% of patients showed an abscopal response.

- Increased numbers of circulating CD8+ cytotoxic and CD4+ effector and central memory T cells as well as elevated levels of soluble granzymes B and H after the second CAN-2409 injection were associated with subsequent prolonged survival, underpinning the systemic immune response elicited by CAN-2409 treatment.

- Treatment with CAN-2409 in NSCLC continued to exhibit a favorable safety and tolerability profile. Bronchoscopic delivery of CAN-2409 is an extension of existing care for patients with NSCLC. As of April 1, 2024, there were no dose-limiting toxicities or grade 4 or higher treatment-related adverse events (TRAEs); the majority of TRAEs were grade 1 or 2, and there were three grade 3 TRAEs (one pyrexia, two pneumonitis).

Details on the CAN-2409 ASCO abstract are as follows:

- **Poster Presentation Title:** Overall survival after treatment with CAN-2409 plus valacyclovir in combination with continued ICI in patients with stage III/IV NSCLC with inadequate response to ICI

- **Presenter:** Charu Aggarwal, MD, MPH, FASCO, Leslye M. Heisler Associate Professor for Lung Cancer Excellence, Perelman School of Medicine, University of Pennsylvania

- **Session Title:** Poster Session – Lung Cancer – Non-Small Cell Metastatic
- **Session Date/Time:** Monday, June 3, 2024; 1:30 PM – 4:30 PM CT
- **Location:** Hall A, McCormick Place Convention Center, Chicago, IL

About CAN-2409

CAN-2409, Candel's most advanced multimodal biological immunotherapy candidate, is an investigational, off-the-shelf, replication-defective adenovirus designed 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 metabolite 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 without inordinate concern of overlapping adverse events.

Currently, Candel is evaluating CAN-2409 in NSCLC, borderline resectable PDAC, and localized, non-metastatic prostate cancer in ongoing clinical trials. CAN-2409 plus prodrug (valacyclovir) has been granted Fast Track Designation by the U.S. Food and Drug Administration (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. Candel's pivotal phase 3 clinical trial in prostate cancer is being conducted under a Special Protocol Assessment with the FDA. The FDA has also granted Orphan Drug Designation to CAN-2409 for the treatment of PDAC.

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. Candel has established two clinical stage multimodal biological immunotherapy platforms based on novel, genetically, modified adenovirus and herpes simplex virus (HSV) gene constructs, respectively. CAN-2409 is the lead product candidate from the adenovirus platform and is currently in ongoing clinical trials in non-small cell lung cancer (NSCLC) (phase 2), borderline resectable PDAC (phase 2), and localized, non-metastatic prostate cancer (phase 2 and phase 3). 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 (rHGG). 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 development programs, including the expectations regarding the therapeutic benefit of the Company's programs, including the potential to use CAN-2409 across multiple solid tumors and the potential for CAN-2409 to extend patient survival in pancreatic cancer. 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; the Company's ability to continue as a going concern; expectations regarding the therapeutics 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 Quarterly Report on Form 10-Q filed with the SEC, and 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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[1] Reckamp KL, et al. J Clin Oncol. 2022;40(21):2295-2306.