Candel Therapeutics Reports Encouraging Initial Survival Data from Phase 2 Clinical Trial of CAN-2409 in Non-Small Cell Lung Cancer

Sep 26, 2023

- *Initial data suggests 12-month survival is consistent with an increased tail on the maturing survival curve*
- *Negative or low PD-L1 status appears to be associated with long survival in CAN-2409 treated patients*
- *Biomarker data suggests association between immune cell activation and survival*
- *Topline overall survival data expected in Q2 2024*

NEEDHAM, Mass., Sept. 26, 2023 (GLOBE NEWSWIRE) -- **Candel Therapeutics, Inc.** (Candel or the Company**)** (Nasdaq: CADL)**,** a clinical stage biopharmaceutical company focused on developing viral immunotherapies to help patients fight cancer, today announced updated activity data from its ongoing, open-label, phase 2 clinical trial of CAN-2409 plus valacyclovir in combination with continued immune checkpoint inhibitor (ICI) treatment in patients with non-resectable, stage III/IV non-small cell lung cancer (NSCLC), who have an inadequate response to front line anti-PD(L)1 therapy. These patients historically have had an expected median overall survival of 10-13 months (Reckamp K et al. J Clin Onc 2022;40:2295-2306). The aim of the CAN-2409 immunotherapy antitumor strategy is to raise the tail on the survival curve by increasing the number of long survivors beyond 10-13 months.

In 2022, the Company presented data from this phase 2 clinical trial where patients who received two administrations of CAN-2409 plus prodrug demonstrated: 1) increased infiltration of CD8+ cytotoxic T cells in the tumor microenvironment, systemic expansion of effector T cells and increased soluble granzyme B levels in peripheral blood, 2) favorable changes in the trajectory of tumor progression, 3) decreased tumor size of target lesions in most patients, and 4) reduced size of uninjected tumor lesions (Aggarwal C et al. Abstract #9037 ASCO June 2022 and Aggarwal C et al. Candel Virtual R&D Day, December 2022). These data were further confirmed in the current update.

Highlights as of August 1, 2023 data cutoff, include:

- As of data cutoff (August 1, 2023), 40 patients across Cohort 1 (stable disease at enrollment; n=5) and Cohort 2 (progressive disease at enrollment; n=35) were evaluable, as they received two courses of CAN-2409 + valacyclovir and completed the 12-week treatment window.
- While overall survival is not yet mature, Candel has observed an encouraging number of long survivors, which the Company believes that CAN-2409 may induce a new state of functional immunosurveillance and durable disease control in a subset of the patients.
    - Of the 40 evaluable patients, 15 patients have lived ≥ 12 months; of these, 10 patients have lived > 18 months, of whom 70% (7/10) were alive as of last follow up. All 4 patients (100%) with OS > 24 months were alive at last follow up, with the longest reaching 31.7 months (data cutoff August 1, 2023).
    - An additional 18 out of the 40 evaluable patients are also alive but have not yet reached 12 months of follow up.
- Notably, many patients treated with CAN-2409 have had long survival (≥ 12 months) despite having disease features generally associated with advanced disease and reduced likelihood to benefit from ICI therapy, such as low or negative PD-L1 expression, including:
    - Amongst patients alive ≥ 12 months with known PD-L1 status (14/15), 93% had negative or low PD-L1 score (<1 or between 1-49).
    - Advanced disease with stage IV in 73% (11/15), lymph node involvement in 73% (11/15), pleural effusion in 40% (6/15), bone metastases in 27% (4/15), adrenal metastases in 20% (3/15), brain metastases in 13% (2/15), liver metastases in 7% (1/15), involvement of 3 or more organs in 13% (2/15), and ECOG performance status 1 in 40% (6/15).
- There was a significant increase observed in activated central memory, effector-memory, effector T cells, and NK cells after

CAN-2409 treatment. These include CD8+Ki67+IFNg+ T cells, CD8+ granzyme B+Ki67+ T cells, CD56+CD16+granzyme B+ NK cells, and gd+ T cells. Candel also observed an increase in B memory cells after CAN-2409 treatment.

- Candel observed an increase in effector/cytotoxic T cells and NK cells in peripheral blood after the second CAN-2409 administration associated with improved survival (≥ 12 months).

- Candel continued to observe a favorable safety / tolerability profile after CAN-2409 treatment in NSCLC. There were no dose limiting toxicities or grade 4 or greater treatment related adverse events. Grade 3 treatment related adverse events were reported in < 10% of patients receiving at least one dose of CAN-2409 (safety population), which Candel believes compares favorably to current standard of care options.

- Candel expects to share topline overall survival data for Cohort 2 in the second quarter of 2024, assuming mature data at that time.

“We are very encouraged by the initial survival data, particularly for Cohort 2 which enrolled patients whose disease progressed despite receiving anti-PD(L)1 treatment. This patient population represents a major unmet need, since median survival following progression is typically less than 12 months with available treatments,” said Paul Peter Tak, MD, PhD, FMedSci, President and Chief Executive Officer of Candel. “Importantly, 93% of patients with long survival were low or negative for PD-L1 expression, which we believe confirms the potential of CAN-2409 to convert patients with highly immunosuppressive tumor microenvironments, unresponsive to ICI treatment, into long term survivors. These early data support the promise and potential of CAN-2409 to provide a long-term survival tail in some of the most difficult to treat NSCLC cases.”

Dr. Tak continued, “Our approach is patient-centric. The proposed treatment regimen for CAN-2409 with prodrug is approximately 12 weeks, and patients can continue their anti-PD(L)1 therapy at local treatment centers, reducing treatment burden. The immediate goal is to provide a treatment benefit through disease stabilization via the addition of CAN-2409. The ultimate goal is to extend patient survival with improved quality of life. These data support a survival benefit in individual patients, which continues to be associated with a favorable safety and tolerability profile, particularly when compared to standard of care taxane-based chemotherapy.”

“The latest biomarker research performed by Candel, PACT, CIMAC and the National Cancer Institute further supports and expands previous findings,” said Francesca Barone, MD, PhD, Chief Scientific Officer of Candel. “We demonstrated for the first time the potential of CAN-2409 to engage the humoral arm of the immune system, broadening the scope of the antitumoral immune response. The correlations between early changes in key effector immune populations after CAN-2409 treatment and survival suggest the possibility to use early biological readouts as predictors of clinical response.”

“Although ICIs have transformed initial therapy in NSCLC and extended life for many patients, there still remains a serious unmet need, especially in patients with low levels of PD-L1 expression,” said Charu Aggarwal, MD, MPH, Associate Professor for Lung Cancer Excellence, Perelman School of Medicine, University of Pennsylvania, and Co-Principal Investigator for the phase 2 clinical trial. “Most patients progress following ICI treatment and options after progression are often associated with toxicity and small treatment benefit. The report of today’s initial promising data on survival gives us an insight into the potential of CAN-2409 to produce a sustained anti-tumor immune response and potentially extend the lives of patients living with advanced NSCLC. I look forward to the maturation of these overall survival data and expected readout in Q2 2024.”

About CAN-2409

CAN-2409, Candel’s most advanced viral 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 disease. HSV-tk is an enzyme that locally converts orally administered valacyclovir into a toxic metabolite that kills nearby cancer cells. The intra-tumoral administration results in the release of tumor-specific neoantigens in the microenvironment. At the same time, the adenoviral serotype 5 capsid protein elicits a strong pro-inflammatory signal in the tumor microenvironment. This is designed to create the optimal conditions to induce an individualized and specific CD8+ T cell mediated response against the injected tumor and uninjected distant metastases for broad anti-tumor activity. 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 ICI have previously been shown in several preclinical and clinical settings. Furthermore, more than 950 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 the effects of treatment with CAN-2409 in NSCLC, borderline resectable pancreatic cancer, and localized, non-metastatic prostate cancer in ongoing clinical trials. The U.S. Food and Drug Administration granted Fast Track designation for CAN-2409 plus valacyclovir in combination with pembrolizumab in order to improve survival or delay progression in patients with stage III/IV NSCLC who are resistant to first line anti-PD(L)1 therapy and who do not have activating molecular driver mutations or have progressed on directed molecular therapy.

About Candel Therapeutics

Candel is a clinical stage biopharmaceutical company focused on developing off-the-shelf viral immunotherapies that elicit an individualized, systemic anti-tumor immune response to help patients fight cancer. Candel’s engineered viruses are designed to induce immunogenic cell death through direct viral-mediated cytotoxicity in cancer cells, thus releasing tumor neo-antigens while

creating a pro-inflammatory microenvironment at the site of injection. This leads to in-situ vaccination against the injected tumor and uninjected distant metastases.

Candel has established two clinical stage viral 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 NSCLC (phase 2), pancreatic cancer (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 investigator-sponsored phase 1 clinical trial in recurrent high-grade glioma. In addition, 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.

About the Partnership for Accelerating Cancer Therapies

The biomarker research in the phase 2 clinical trial of CAN-2409 in NSCLC is supported by the Partnership for Accelerating Cancer Therapies (PACT), a project that supports research to identify, develop, and validate robust biomarkers - standardized biological markers of disease and treatment response - to advance new immunotherapy treatments that harness the immune system to attack cancer. PACT is overseen by the Foundation for the National Institutes of Health. The pharmaceutical companies participating that make funding for this project possible are: AbbVie, Amgen, Boehringer Ingelheim, Bristol-Myers Squibb, Celgene Corporation, Genentech, Gilead, GlaxoSmithKline, Janssen/Johnson & Johnson, Novartis, and Pfizer.

National Cancer Institute Support

Scientific and financial support for the CIMAC-CIDC Network is provided through the National Cancer Institute (NCI) Cooperative Agreements: U24CA224319 (to the Icahn School of Medicine at Mount Sinai CIMAC), U24CA224331 (to the Dana-Farber Cancer Institute CIMAC), U24CA224285 (to the MD Anderson Cancer Center CIMAC), and U24CA224309 (to the Stanford University CIMAC).

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 timing and availability of additional data, the possibility to use early biological readouts as predictor of clinical response and expectations regarding the therapeutic benefit of its programs, including the potential for CAN-2409 to extend patient 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; that final data from our pre-clinical studies and completed clinical trials may differ materially from reported interim data from ongoing studies and trials; expectations regarding the therapeutic benefit of the Company's programs; 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, and strategic plans for the Company's business and product candidates, and other risks identified in the Company's SEC filings, 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.

Media Contact
Aljanae Reynolds
Director
Wheelhouse Life Science Advisors
areynolds@wheelhouselsa.com

Investor Contact
Sylvia Wheeler
Principal
Wheelhouse Life Science Advisors
swheeler@wheelhouselsa.com