Candel Therapeutics Announces Initial Positive Interim Data from Randomized Phase 2 Clinical Trial of CAN-2409 in Non-Metastatic Pancreatic Cancer

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- *Initial positive interim data revealed notable improvements in patients with borderline resectable pancreatic ductal adenorcarcinoma (PDAC) after experimental treatment with CAN-2409*
- *Estimated overall survival rate was 71.4% at 36 months in CAN-2409 treated patients versus 16.7% in the control arm after chemoradiation*
- *In patients with progressive disease, there was both a CA19-9 and a survival response to salvage chemotherapy in the CAN-2409 arm, but not in the control arm.*
- *Dense aggregates of immune cells, including CD8 positive granzyme B positive cytotoxic T cells, dendritic cells, and B cells, were observed in PDAC tissue after CAN-2409 treatment, confirming activation of a robust antitumoral immune response*
- *Safety analysis demonstrated that multiple injections of CAN-2409 were generally well tolerated, with no reported dose-limiting toxicities and no cases of pancreatitis*

NEEDHAM, Mass., Nov. 03, 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 initial positive interim survival and immunological biomarker data from the ongoing randomized phase 2 clinical trial of CAN-2409 plus valacyclovir (prodrug) together with standard of care (SoC) chemoradiation followed by resection for borderline resectable pancreatic ductal adenocarcinoma (PDAC). Data were presented today in a poster session titled '*Neoadjuvant CAN-2409+Prodrug Plus Chemoradiation for Borderline Resectable or Locally Advanced Non-Metastatic Pancreatic Adenocarcinoma (PDAC)* at the 2023 Society for Immunotherapy (SITC) Annual Meeting.

"Given frequent recurrence and short survival with SoC chemotherapy for non-metastatic PDAC, effective new treatment options are urgently needed," said Garrett Nichols, MD, MS, Chief Medical Officer of Candel. "We are encouraged by the improved survival associated with CAN-2409 for the treatment of borderline resectable PDAC, demonstrated for the first time in a randomized clinical trial. CAN-2409 was generally well tolerated without significant additional local or systemic toxicity when added to SoC chemoradiation."

Data Highlights as of August 21, 2023 Data Cutoff, include:

- Prolonged and sustained survival was observed after experimental treatment with CAN-2409 plus prodrug in patients with borderline resectable PDAC (n=13)
  - An estimated survival rate of 71.4% at both 24 and 36 months, observed in patients who received CAN-2409 regimen together with SoC chemoradiation prior to surgery, versus only 16.7% survival at 24 and 36 months in patients with SoC chemoradiation prior to surgery.
  - Importantly, 5 out of 7 patients who received CAN-2409 were still alive at the time of data cut-off, with two patients surviving more than 45 months from enrollment. Only one patient randomized to control SoC chemotherapy remained alive at data cut-off (alive at 43 months).
  - Median overall survival has not yet been reached in patients who received CAN-2409; median overall survival was 12.5 months in the control arm.
  - Disease course was altered after salvage chemotherapy with improved CA19-9 levels and ongoing survival in CAN-2409 arm, but not in control arm.
- Data showed consistent and robust activation of immune response after dosing with CAN-2409
  - In pancreatic tissue of patients treated with CAN-2409 plus prodrug together with SoC (but not SoC alone), dense aggregates of CD8+ granzyme B positive cytotoxic T cells, dendritic cells, and B cells were observed in the tumor microenvironment.
  - Increased levels of soluble granzymes B and H as well as pro-inflammatory cytokines, including IFN-γ, were observed in peripheral blood after CAN-2409 treatment, but not with control treatment.
- CAN-2409 was associated with a favorable tolerability profile
  - Addition of CAN-2409 regimen to SoC was generally well tolerated, with no reported dose-limiting toxicities, including no cases of pancreatitis.

“The failure of immunotherapy to improve outcomes in pancreatic cancer is attributed to the highly immunosuppressive tumor microenvironment, which is largely devoid of immune cells,” said Paul Peter Tak, MD, PhD, FMedSci, President and Chief Executive Officer of Candel. “The immunological changes induced by CAN-2409, as observed in the pancreatic tissue after dosing, suggest that CAN-2409 treatment can convert the immune desert microenvironment and enable the generation of an effective antitumoral response and improve survival.”

Further details from the poster will be available at time of the SITC embargo poster presentation lift on the Candel website at: www.candeltx.com/media

About the Phase 2 Clinical Trial of CAN-2409 in Non-Metastatic Pancreatic Cancer

In its current design, the randomized, open-label phase 2 clinical trial is designed to evaluate the safety, preliminary efficacy, and biologic activity of a 2-3 injection regimen of CAN-2409 plus prodrug (valacyclovir or acyclovir) in patients with borderline resectable pancreatic cancer who are being treated with neoadjuvant chemoradiation or stereotactic body radiation therapy. After amendment in 2022, when enrollment of patients with locally advanced PDAC was discontinued, the clinical trial is exclusively focused on borderline resectable disease. In a previously completed phase 1b clinical trial, a highly significant increase in the number of CD8+ tumor infiltration lymphocytes was demonstrated at the site of the tumor after CAN-2409 treatment.

About Pancreatic Ductal Adenocarcinoma

Pancreatic cancer is a highly lethal malignancy, and is the fourth leading cause of cancer-related death in the United States among both men and women. Based on the National Cancer Institute, Surveillance, Epidemiology and End Results (SEER) database, pancreatic cancer is expected to account for 3.3% of all new cancer cases, with an estimated 64,050 new cases and estimated 50,550 deaths in 2023.[1] Effective therapeutics for pancreatic cancer, including PDAC, which accounts for 90% of all pancreatic carcinomas[2], are urgently needed.

Surgical resection offers the only chance of cure, thus a major therapeutic goal for subjects with non-metastatic disease is to achieve complete tumor resection. Surgical treatment (pancreaticoduodenectomy, also known as the Whipple procedure) or total or distal pancreatectomy (depending on tumor location) is generally the recommended treatment for patients diagnosed with resectable cancer; the addition of adjuvant chemotherapy has been shown to only slightly improve survival rates (20 to 23 months).[2] To this end, there has been increasing use of neoadjuvant chemotherapy and chemoradiation regimens for subjects with borderline resectable pancreatic ductal adenocarcinoma. Neoadjuvant regimens are intended to debulk the tumor, thereby increasing the proportion of patients who may become eligible for surgical resection and achieve complete resection (i.e., resection with negative margins, designated ‘R0 resection’). Unfortunately, even when an R0 resection is initially achieved, cures remain elusive as most patients experience disease recurrence due to residual micrometastatic disease. In a recent meta-analysis of 20 studies representing 283 patients with borderline resectable PDAC, neoadjuvant FOLFIRINOX with or without radiotherapy, median OS was only 22.2 months (95% CI, 18.8 to 25.6 months).[3]

Immunotherapy with PD-1 antibodies with or without CTLA-4 antibodies has been uniformly unsuccessful in patients with PDAC due to the dense stroma that surrounds PDAC tissue and the absence of tumor infiltrating lymphocytes.

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 intratumoral 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 non-small cell lung cancer (NSCLC), borderline resectable pancreatic cancer, and localized, non-metastatic prostate cancer in ongoing clinical trials.

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), borderline resectable 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

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, 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 current and future 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.

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