Candel Therapeutics Sets Path to Success: Recent Achievements Pave the Way for a Promising 2024 Propelled by Key Value Drivers and Catalysts

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- Approaching 6 anticipated data readouts across 3 platforms in 2024, including survival data in non-small cell lung cancer (NSCLC) and a potentially registrational phase 3 clinical trial in prostate cancer
- Focusing on strategic key value drivers and catalysts, as a follow up to positive initial clinical and biomarker data in hard-to-treat cancers
- Advancing the immunotherapy field with next-generation investigational therapies at the intersection of advanced analytics, biology and vectorology
- Executing on goal for operational excellence and efficiency, as evidenced by company's recent program prioritization

NEEDHAM, Mass., Feb. 05, 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 highlighted recent successes across the Company's immunotherapy portfolio and provided updates on multiple upcoming milestones.

"Candel is innovating a new frontier in immunotherapy, backed by promising clinical and biomarker data in hard-to-treat indications with six data readouts expected this year," said Paul Peter Tak, MD PhD FMedSci, President and CEO of Candel. "Candel is focused on delivering key value drivers to maximize the impact of its assets and to create substantial value to patients and other stakeholders. In 2023, we received Fast Track Designation from the FDA for CAN-2409, our most advanced product candidate, for both NSCLC and pancreatic cancer. Clinical data from the ongoing phase 1 clinical trial of CAN-3110 in patients with recurrent high-grade glioma have recently been published in Nature, which further supports the scientific and clinical excellence of Candel's programs."

Dr. Tak continued: "Beyond our promising drug candidates that are being tested in the clinic, the novel enLIGHTEN Discovery Platform has already demonstrated the capability to generate experimental candidates, expanding Candel's potential to create value through novel collaborations to develop treatments for diverse types of cancer. We are excited for our upcoming clinical and scientific readouts in 2024."

2024 Anticipated Data Readouts and Key Catalysts:

Candel plans to announce 6 anticipated readouts across its 3 platforms in 2024, which include novel clinical and biomarker data in lung cancer, pancreatic cancer, brain cancer and a potentially registrational phase 3 clinical trial in prostate cancer.

- Phase 2 topline overall survival (OS) data for CAN-2409 in NSCLC expected in Q2 2024
- Phase 2 updated overall survival data for CAN-2409 in borderline resectable pancreatic cancer expected in Q2 2024
- New preclinical data on the second drug candidate from the enLIGHTEN™ Discovery Platform expected by Q3 2024
- Phase 1 data for CAN-3110 in recurrent high-grade glioma expected in 2H 2024 for the multiple injection cohort
- Phase 2 topline data for CAN-2409 in low-to-intermediate-risk, localized, non-metastatic prostate cancer expected in Q4 2024
- Phase 3 topline data for CAN-2409 in localized intermediate/high-risk prostate cancer expected in Q4 2024

These milestones present a compelling opportunity for progress, success and significant differentiation, underscoring the Company's dedication to advancing its therapeutic pipeline.

2023 Accomplishments:

- **Phase 2 clinical trial of CAN-2409 in NSCLC**
  - In September 2023, the Company announced encouraging initial activity and biomarker data from the phase 2 clinical trial of CAN-2409 in NSCLC. Initial data suggests that ongoing 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 an association between immune cell activation after the second injection of CAN-2409 and subsequent survival.
  - U.S. Food and Drug Administration (FDA) granted Fast Track Designation for CAN-2409 plus valacyclovir in combination with pembrolizumab to improve survival or delay progression in patients with Stage III (not candidates for curative intent) or Stage IV non-small cell lung cancer, 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.

- **Phase 2 clinical trial of CAN-2409 in non-metastatic pancreatic cancer**
  - In November 2023, the Company reported initial positive interim clinical activity and biomarker data from a

randomized, controlled clinical trial where a notable increase in survival was observed in patients with borderline resectable pancreatic ductal adenocarcinoma (PDAC) after experimental treatment with CAN-2409. Estimated OS rate at 36 months was 71.4% in patients treated with CAN-2409 plus standard of care chemoradiation followed by resection versus 16.7% in the control arm treated with standard of care chemoradiation followed by resection. 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. Safety analysis demonstrated that multiple injections of CAN-2409 were generally well tolerated, with no reported dose-limiting toxicities and no reported cases of pancreatitis.
    - FDA granted Fast Track Designation for CAN-2409 plus prodrug (valacyclovir) for the treatment of patients with pancreatic ductal adenocarcinoma to improve overall survival.

- **Phase 1 clinical trial of CAN-3110 in high-grade glioma**
    - In October 2023, Candel published results in Nature demonstrating that CAN-3110 was well tolerated with no dose-limiting toxicity reported. The investigators observed a nearly doubling of the expected median (mOS) after a single CAN-3110 injection, achieving a median OS of 12 months, compared to historical reports of less than 6 to 9 months in this therapy-resistant condition. Positive HSV-1 serology was a predictor of response and was associated with improved survival (mOS in this population reached 14 months). Increased infiltrating immune cells in the tumor microenvironment and expansion of the T cell repertoire after treatment were also associated with improved survival, demonstrating the ability of CAN-3110 to elicit both a local and systemic antitumoral response.

- **enLIGHTEN™ Discovery Platform**
    - During the Society for Immunotherapy of Cancer (SITC) 2023 Annual Meeting and the International Oncolytic Virus Conference in November 2023, Candel presented preclinical data from the first experimental candidate from its discovery pipeline: Alpha 201-macro-1, an investigational, locally delivered biological oncolytic therapeutic, designed to interfere with the CD47/SIRP1a pathway, which demonstrated better inhibition of tumor growth when compared to systemic anti-CD47 antibody therapy in a mouse model of breast cancer.

Advancing the Immunotherapy Field

The Company is poised to advance the next generation of viral immunotherapy, leveraging a data-driven approach to create new assets by design and advance development of existing drug candidates, creating new value inflection points.

“The data generated with CAN-3110 in recurrent high-grade glioma represents a significant step forward in the development of groundbreaking therapeutic candidates for this difficult to treat disease,” said Francesca Barone, M.D. PhD, CSO, at Candel Therapeutics. “At the same time, they provide initial proof of concept for the expansion of CAN-3110 in other Nestin positive indications. With the enLIGHTEN Discovery Platform, we are leveraging our internal capabilities in advanced analytics, cancer biology and vectorology to design a new class of multimodal therapeutics that are able to overcome mechanisms of resistance present in the tumor microenvironment. This platform is open for collaborations with external partners.”

Operational Excellence and Efficiency:

- The Company's strategic prioritization of programs highlights Candel Therapeutics' commitment to operational excellence and efficiency. This focus has translated into an extension of Candel runway, while providing the opportunity to generate preclinical data in support of the expansion of CAN-3110 in novel indications, to develop enLIGHTEN for external partnerships, and deliver on the readouts of Candel’s advanced clinical trials.
- This approach positions the Company for sustained success in the current dynamic market for new cancer therapeutics.

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 disease. 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. 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 Company plans to explore the right partnering opportunities for the future development of this asset.

About CAN-3110

CAN-3110 is a first-in-class, replication-competent herpes simplex virus-1 (HSV-1) oncolytic viral immunotherapy candidate designed with dual activity for oncolysis and immune activation in a single therapeutic. Its activity is conditional to the expression of Nestin in cancer cells. CAN-3110 is being evaluated in a phase 1 investigator-sponsored clinical trial in patients with recurrent HGG. In October 2023, the Company announced that Nature published results from this clinical trial. CAN-3110 was well tolerated with no dose-limiting toxicity reported and CAN-3110 plus prodrug was associated with improved survival. Positive HSV-1 serology was a predictor of response and was associated with improved survival. Increased infiltrating immune cells in the tumor microenvironment and expansion of the T cell repertoire after treatment were also associated with improved survival. In the clinical trial, the investigators observed a nearly doubling of the expected median overall survival after a single CAN-3110 injection,

compared to historical reports of less than 6 to 9 months in this therapy-resistant condition. By comparison, survival in the anti-HSV1 positive patients treated with CAN-3110 was more than 14 months. The Company and academic collaborators are currently evaluating the effects of multiple CAN-3110 injections in recurrent HGG, supported by the Break Through Cancer Foundation, and expect initial results in H2 2024.

Candel will also initiate IND-enabling work in a second indication characterized by Nestin expression.

About the enLIGHTEN™ Discovery Platform

The enLIGHTEN™ Discovery Platform is a systematic, iterative herpes simplex virus (HSV)-based discovery platform leveraging human biology and advanced analytics to create new multimodal biological immunotherapies for solid tumors. In October 2022, the Company announced a discovery collaboration with the University of Pennsylvania Center for Cellular Immunotherapies to identify how viral immunotherapy could enhance the efficacy of CAR-T cell therapy in solid tumors. The enLIGHTEN™ Discovery Platform is designed to deconvolute the complexity of the tumor microenvironment to identify druggable properties that correlate with clinical outcomes. These discoveries are rapidly translated into optimized multi-gene payloads of tumor modulators that are tailored for specific indications, disease stage, and rationally designed therapeutic combinations. During the Society for Immunotherapy of Cancer (SITC) 2023 Annual Meeting and the International Oncolytic Virus Conference in November 2023, Candel presented encouraging data on the discovery pipeline, demonstrating the effects of Alpha 201-macro-1, an investigational locally delivered biological oncolytic therapeutic designed to interfere with the CD47/SIRP1a pathway, in a mouse model of breast cancer.

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 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 (HGG). 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 timing and availability of additional data, key data readout milestones, expectations regarding the therapeutic benefit of its programs, including the potential for its programs to extend patient survival; and expectations regarding cash runway and expenditures. 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 our 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, 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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