

Candel Aims High In Next Stage Of Cancer Immunotherapy Mission



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► By Eleanor Malone

EMERGING COMPANY PROFILE:

Candel Therapeutics, formerly known as Advantagene, has hired a new leadership team and is aiming for a Phase III data read-out in prostate cancer in 2023.



The prostate cancer vaccine pipeline is littered with casualties – from the commercial failure of Dendreon Corporation’s approved Provenge (sipuleucel-T) to the late-stage clinical failure of Bavarian Nordic AVS’s Prostavac (rilimogene galvacirepvec) monotherapy and CureVac BV’s mRNA-based CV9104. And time and again, while cancer vaccines across a range of tumor types have shown

promise in stimulating an immune response, they have subsequently failed to show clinical improvement in key endpoints that matter to patients, like overall survival.

Nevertheless, an immense investment in immunotherapy R&D, particularly in oncology, continues to support a populous ecosystem of cancer vaccine developers. Furthermore, there are hopes that combination treatments, for example pairing a cancer vaccine with a checkpoint inhibitor, will eventually bear fruit.

One such development company is **Candel Therapeutics**, formerly known as Advantagene, Inc., which has progressed through three venture financing rounds since 2016 to net \$65.4m, on top of funding from public institutions such as the National Institutes of Health (NIH).



It has recruited a new executive team as it positions for “a new phase of growth” after being led for decades by its scientific founder, Estuardo Aguilar-Cordova. With active development programs across the clinical spectrum up to and including Phase III, and having tested its candidates in more than 700 patients, Candel is “ready to bring to the next level,” Paul Peter Tak, newly appointed president and CEO, told *Scrip*.

Tak, former head of immunology at GlaxoSmithKline plc and more recently president and CEO of Flagship Pioneering start-up Kintai Therapeutics, Inc., was brought in to lead the company earlier this year. He has spent the past few months assembling a leadership team. He spoke to *Scrip* about his new mission: to advance Candel’s candidates through late-stage development and put in place a strategy “to bring medicines to patients and bring value to investors.”

Tak described the company as a “diamond in the rough” which had developed its oncolytic virus therapy for diverse solid tumors “quietly and in a very modest and cost-effective way into Phase II and III.”

Candel has built a pipeline around its Gene Mediated Cytotoxic Immunotherapy, in which a modified adenovirus is injected directly into a tumor to deliver the herpes simplex thymidine kinase (TK) gene, at the same time as the patient is orally given the prodrug valacyclovir, which TK phosphorylates, inducing tumor cell death and the release of tumor-associated antigens that enable the patient’s immune system to identify and destroy cancer cells.

“We have the data *in vivo* in humans to show that if we inject the oncolytic virus into the tumor, which is a relatively easy procedure, it leads to increased expression of markers of proliferation and activation of CD8-positive T-cells, not only at the site of the tumor but also in the peripheral blood. Which means that it leads to systemic immune response.”



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Paul Peter Tak

The company’s most advanced program is a Phase III trial under FDA special protocol assessment in intermediate to high-risk localized prostate cancer, for which data are expected in 2023. A second Phase II trial in prostate cancer patients under active surveillance – or ‘watch and wait’ – is under way, as are additional Phase I and II studies in non-small lung cancer, glioblastoma and pancreatic cancer. Candel is also collaborating with Bristol Myers Squibb Company to investigate the use of the oncolytic virus therapy alongside the latter’s PD-1 checkpoint inhibitor Opdivo (nivolumab) in glioblastoma.

Separately, the company has a second, herpes simplex virus-based oncolytic discovery platform, rQNestin34.5, which has delivered an initial candidate into Phase I trials for recurrent glioblastoma. That study will complete in 2021, Tak noted.

Meanwhile, Candel is building its own manufacturing capability at its site in Needham, near Boston, MA, which represents “a very strong competitive advantage: you’re not dependent on slots being free for your product to be manufactured.”

Funding For Growth

“Depending on funding, there are real opportunities to expand into other indications and we have preliminary evidence [our approach] may work in other types of tumors,” he said. “I’m sure we will start to talk to investors shortly.”

Additional funding would potentially help accelerate current development programs too, he said. It could also enable more investment in discovery, to create new candidates based on the HSV platform.

Another area for potential exploration is to expand collaborative activity beyond that with BMS. "We have data suggesting that we may change the tumor micro-environment in such a way that we convert non-responders to checkpoint inhibitors into responders, because our treatment leads to up-regulation of PD-1 and CTLA-4."

"The reality is that most cancer patients are not achieving long-term remission or cure. So there is a huge unmet need, and I believe we will probably need multi-modular approaches to achieve the goal of stable remission," Tak said. "We've shown in experimental models and in patients that our approach can be combined with surgery, chemotherapy and radiotherapy – so it's an adjuvant or a neo-adjuvant depending on the context to improve the outcomes in patients. We are one of the few companies that is already in Phase III with an oncolytic virus, with evidence that we can induce cell death, change the immune system and improve both biomarker signals like PSA levels and emerging clinical signals."

He also highlighted the company's "relatively large safety database," noting that the treatments have been "well tolerated" and "derisked to a certain extent because we have already dosed more than 700 patients."

As for a strategic plan, "I like optionality. Pharmaceutical companies can be very good at development, and collaboration or partnership with pharma companies would open up the opportunity to accelerate some of the programs. I will definitely start to talk to pharmaceutical companies," Tak said, while acknowledging the possibility of a number of alternative exits for the company in the longer term, be it an acquisition or initial public offering. "Everything is on the table."

New Leadership

As Tak takes over, Aguilar-Cordova has taken on the role of chief scientific officer, while Tak has brought in fresh blood for other leadership positions. Nathan Caffo, formerly chief business officer at ALX Oncology, Inc. (which went

CANDEL THERAPEUTICS AT A GLANCE

Founded: 2003 (In 2019 the company operated as Advantagene, Inc. doing business as Candel Therapeutics. As of 1 December 2020, the company's name is Candel Therapeutics)

Location: Needham, Massachusetts

Employees: ~40

R&D Focus: oncolytic virus-based immunotherapy for solid tumors

Management Team: President and CEO, Paul Peter Tak; CSO and founder, Estuardo Aguilar-Cordova; Chief Medical Officer, Laura Aguilar; CFO, John Canepa; Chief Business Officer, Nathan Caffo; Chief Regulatory Officer, Susan Stewart

Financing: \$65.4m in series A, B and C in 2016 and 2019

Investors: PBM Capital Group, Northpond Ventures, Sands Capital Ventures, H7 Holdings, Level One Partners

public in July 2020) and before that president and CEO of Presage Biosciences, another oncology-focused firm, which secured equity investment from the likes of Celgene Corporation and Takeda Pharmaceutical Co. Ltd., has joined as chief business officer. Joining as chief financial officer is John Canepa, who also helped steer his previous firm (Frequency Therapeutics) to IPO and was previously involved in the sale of companies to strategic and financial buyers. Susan Stewart, a veteran of biopharma regulatory affairs, including previous stints at Abbott and Genzyme Corporation, joins as chief regulatory officer.

The message is clear: the next chapter for Candel is getting its products to patients, and ultimately delivering a return to investors.

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