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Dendreon's \$70M Investment in Production Capabilities Could Woo Firms without Similar Expertise

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[Dendreon](#) is counting on FDA approval of its prostate cancer fighting therapy, Provenge, with a major investment in new manufacturing facilities near Atlanta. The sites will employ about 300 workers and cost \$70 million. Dendreon has spent more than \$560 million to develop this immunotherapeutic, and the drug is expected to cost patients somewhere between \$30,000 and \$50,000 annually.

Just over two years ago, in May 2007, Dendreon lost over half its value when the FDA delayed approval of its only product, requesting additional clinical data in support of Provenge's efficacy. This April the company presented positive results from a Phase III trial designed based on discussions with the agency. Its stock rose almost 133% to reach \$16.99 in the first day of trading and closed yesterday at \$22.67. Dendreon also secured \$221 million from investors as a result of the Phase III data and indicated that it would use the money to expand its manufacturing capabilities.

The company intends to amend its BLA before the end of this year, and the FDA will have up to six months to review it. If green-lighted Provenge will be the first autologous cell-based cancer therapy to achieve commercialization. The company hopes to initiate a launch in the first half of 2010 from its existing facility in Morris Plains, NJ. It will then ramp up production once the new facilities in Union City, GA, and Seal Beach, CA, are completed.

Provenge's Potential

Provenge may prove that it and other autologous cell-based immunotherapies can eventually become profitable. The therapy has the potential to treat about 100,000 men annually whose cancer has spread beyond the prostate gland and who no longer benefit from conventional therapies. The only currently approved treatment for these patients is sanofi-aventis' Taxotere, which extended median survival by about three months in trials and was associated with substantial toxicity.

Additionally, according to a *Decision Resources* report from July, surveyed oncologists expect to prescribe Provenge for 54% of patients with asymptomatic, hormone-refractory metastatic prostate cancer. Doctors said that "due to the side effects associated with currently available chemotherapy, most oncologists recommend that men who have stopped responding to hormone therapy wait for the development of symptoms before starting chemotherapy."

On April 28 Dendreon reported that its pivotal Phase III study met its primary endpoint of significantly improving overall survival compared to placebo and was safe and well tolerated. Median survival was extended by 4.1

months to 25.8 months, and risk of death was reduced by 22.5% compared to placebo.

To produce Provenge, 2 mL of patient blood is sent to Dendreon about two days prior to each of three scheduled infusions. The company then uses leukapheresis to isolate a mixed cell population that includes antigen-presenting cells (APCs). Finally, the patient's APCs are co-cultured with a recombinant fusion protein containing prostatic acid phosphatase (PAP), a normal prostate tissue protein, and GM-CSF. PAP is an antigen found in high concentrations on prostate tumor cells. Once returned to the patient, the activated APCs stimulate T cells to attack the tumor.

"By doing cell culture ex vivo we have removed the APCs from an environment in which tumors produce immune-suppressing factors, so we can get effective antigen loading and APC activation," explains David Urdal, Ph.D., CSO, director, and svp. "Another important factor is the dose factor—we are treating a large number of cells. By loading the APCs with our antigen cassette, we can infuse 900 million activated cells back into the patient."

Acting on a similar principle, Dendreon's Neuvenge consists of patient APCs activated in vitro with a recombinant fusion protein consisting of sequences from intracellular and extracellular domains of HER2 linked to GM-CSF. "We finished Phase I studies (in HER2-overexpressing metastatic breast cancer) and are planning on moving forward, but we focused all our attention on Provenge," Dr. Urdal states.

"We've not been in a position to push our other pipeline products. Additionally, we have preclinical data with two cancer-associated antigens, CA9 and chorioembryonic antigen, associated with colon kidney and colon cancer, respectively."

Investment in Production Capabilities Could Attract Deals

Another firm developing cell-based cancer treatments is ImmunoCellular Therapeutics, which reported encouraging Phase I results for its ICT-107 when tested in glioblastoma. The treatment comprises patient-derived APCs exposed to six different peptides. According to Manish Singh, Ph.D., president and CEO of [ImmunoCellular Therapeutics](#), three of the peptides are highly expressed on cancer cells in general and three others on cancer stem cells.

The Phase I trial enrolled 19 patients; 16 with newly diagnosed glioblastoma and three with recurrent disease. Seven newly diagnosed patients showed stable disease with a median progression-free survival of 64 weeks; three of these patients had progression-free survival of over two years. The median progression-free survival time of newly diagnosed glioblastoma patients has historically been 30 weeks.

Despite encouraging data, however, ImmunoCellular Therapeutics' primary focus will be on its off-the-shelf cancer immunotherapeutic, ICT-121, consisting of peptides designed to elicit immune responses against cancer stem cells only. Dr. Singh says that ICT-107 is a better fit for a company with a large manufacturing infrastructure that can use the same platform for different indications.

Dendreon, having developed the expertise and invested in the infrastructure to produce autologous, antigen-presenting cell-based vaccines in a number of locations, could find itself with plenty of potential clients with promising tumor antigens and no manufacturing capability.

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