BREAKTHROUGH PROGRAM

Cylomox

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Startup Brief

Cancer vaccines are developing in to the "next big thing" in immunotherapy. (1) The novel FlowVax cancer vaccine immunotherapy allows cancers to be treated by teaching the patient's immune system to attack only tumor cells, leaving healthy cells undamaged. The patented FlowVax platform used tiny beads called microspheres, the same size as white blood cells, to deliver manufactured tumor markers that killer T-cells learn to attack after the FlowVax microspheres are naturally processed by the patient's immune system. This results in fewer side effects. FlowVax can be given as a single injection causing killer T-cells to attack cancer cells which display the tumor marker survivin (BIRC5) which is not present on normal cells but is expressed by many different types of cancers including breast cancer, colon cancer, brain cancer, prostate cancer, skin cancer, lung cancer, uterus cancer and others (2). For example, FlowVax has been shown in a peer reviewed publication to slow tumor growth of a very aggressive breast cancer in an animal model. (3) FlowVax is synthetic, is not made from animal products, and can be given as a single injection without requiring an intravenous infusion. This three-year proposal takes FlowVax to approval for first-in-man human testing for patients with breast cancer, colon cancer, and a deadly brain cancer called glioblastoma. Experienced teams from Saudi Arabia and the United States will work closely together to manufacture FlowVax doses in the US and Saudi Arabia, conduct animal safety testing, and to secure US and Saudi regulatory approval to proceed with human testing. These results will help obtain funding from other sources to conduct larger clinical studies to secure regulatory approval for Phase 1 / 2 / 3 testing leading to the sale and distribution.

Problem

Checkpoint inhibitor immunotherapy using drugs like pembrolizumab has improved cancer treatment over traditional chemotherapy by broadly activating the immune system using checkpoint inhibitors causing cancer cells to be killed. This broad activation produces side effects as the activated killer T-cells also attack healthy cells causing complications such as diabetes, arthritis and kidney damage. Another immunotherapy approach called CAR-T modifies the patient's T-cells in a laboratory and puts the modified cells back into the patient. This technique can be very effective but is expensive and causes side effects as the body reacts to the modified T-cells which can cause a severe inflammatory response called cytokine storm that can be deadly.

The highest revenue pharmaceutical in the world is pembrolizumab (Keytruda) which can generally only treat tumors that express PD-L1. The fact that pembrolizumab often relies on the presence of PD-L1 for effectiveness is well recognized. For example, indication for using pembrolizumab in metastatic triple negative breast cancer requires PD-L1 expression while the non-metastatic indication does not. Pembrolizumab is also indicated for metastatic head and neck squamous cell cancer, esophageal or gastroesophageal junction tumors, and cervical cancers and other tumors that express PD-L1. For many cancers, the majority of tumors do not express PD-L1 and are therefore not addressable by Keytruda (Figure 1).

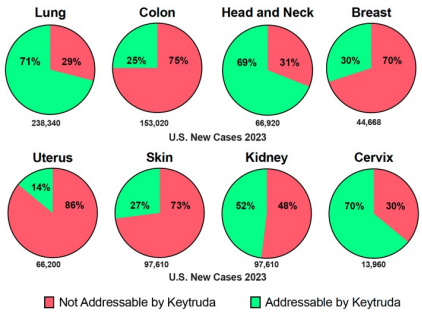

Figure 1. The leading immunotherapy in the world, pembrolizumab (Keytruda), is largely ineffective against cancers that do not produce PD-L1. FlowVax targeting survivin decreased tumor growth rate in an aggressive triple negative cell line that did not produce PD-L1. This represents a large opportunity for FlowVax to be used in patients whose cancers do not produce PD-L1.

Solution

Preclinical data for FlowVax has shown it to be safe and able to treat an aggressive breast cancer tumor in mice that does not express PD-L1. FlowVax therefore is positioned to treat tumors which do not express PD-L1 and are therefore not addressable by Keytruda. Given that for some cancers approved for treatment by Keytruda, most patients have tumors that do not express PD-L1, FlowVax is well positioned to be the preferred alternative for those patients.

Value Proposition

Using the conservative assumptions outlined below, FlowVax can be very successful in the immunotherapy marketplace:

- 1 approval / year over 8 years:
- Breast, colon, lung, head & neck, skin, uterus, kidney, and cervix cancer
- Total addressable market (TAM) set as only cases not addressable by Keytruda
- (actual TAM includes cases addressable by Keytruda as well)
- 15% of TAM patients treated
- 21,000 patients/year at year 8
- $75K revenue per patient treated (estimated to be the same as for Merck's Keytruda)
- **$24B USD total revenue by year 8 post first cancer indication approval**

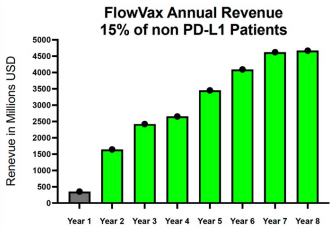

Figure 2. Making the assumptions that FlowVax is only used for 15% of non PD-L1 producing tumors and that only one new indication is approved per year, and that the revenue generated per patent treated is the same as that for pembrolizumab. In this model, $24B USD total revenue is generated by year 8.

About the research

(1) Harris, P.E., Rubsamen, R. New Vaccine Therapy for Triple-Negative Breast Cancer. Curr Breast Cancer Rep 16, 288–301 (2024)
(2) Wright S, Burkholtz S, Zelinsky C, Wittman C, Carback R. Harris P, Blankenberg T, Herst C, Rubsamen RM. Survivin Expression in Luminal Breast Cancer and Adjacent Normal Tissue for Immuno-Oncology Applications. Int. J. Mol. Sci. 2023, 24, 11827
(3) Burkholz SR, Herst CV, Carback RT, Harris PE, Rubsamen RM. Survivin (BIRC5) Pepitide Vaccine in the 4T1 Murine Mammary Tumor Model: A Potential Neoadjuvant T Cell Immunotherapy for Triple Negative Breast Cancer: A Preliminary Study. Vaccines 2023 11(3)