Waisman Biomanufacturing

Experience cGMP Quality with Waisman Biomanufacturing

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WB Client Signs Technology Licensing Agreement

Long-standing client Aduro BioTech, Inc. (Aduro) announced in May 2014 an exclusive licensing agreement for their novel immunotherapy platform with Janssen Biotech. This immunotherapy is based on live-attenuated double-deleted (LADD) Listeria monocytogenes strains and went through clinical production in our clean room facility. LADD is a platform technology intended for the treatment of a broad range of cancers, such as pancreatic cancer, mesothelioma, non-small cell lung cancer, and glioblastoma. This is just one example of a successful product manufactured by WB through a strategic partnership and gives evidence to our ability to manufacture clinical-grade therapies with licensing potential.

The American Cancer Society estimates the number of new cancer cases in the U.S. will be more than 1.6 million in 2014 alone. New cases of pancreatic cancer have been increasing annually since 2000 and will affect an estimated 46,420 new patients this year. With early detection, the 5-year survival rate is just 24% and is significantly less for cases detected in later stages (2-9%). Current treatments include radiation therapy and chemotherapy but rarely result in a cure. Another devastating form of cancer is non-small cell lung cancer (NSCLC), which accounts for 14% (31,389) of all new lung cancer diagnoses. Current treatments include surgery, radiation therapy, chemotherapy, and targeted therapies. The 5-year survival rate for NSCLC is just 18%. Aduro is offering a new approach to treatment for both of these and many other cancers with their LADD and GVAX therapies. For the millions of individuals and families affected by cancer each year, immunotherapies offer optimism that a cure is near.

Waisman has been a key partner for Aduro as we have developed our LADD technology. Without their process development and manufacturing expertise and capabilities, we would not have been able to achieve the significant clinical progress we have experienced. Carl Ross has managed our program from the outset, and brings tremendous value to us through his depth and breadth of experience. We look forward to continuing our great working relationship as our pipeline grows.

-Justin Skoble, Director, Biodefense and Process Development, Aduro BioTech, Inc.

Our partnership with Aduro began with its predecessor companies including Anza and Cerus. Aduro has been developing several live-attenuated Listeria monocytogenes–based vaccines for a variety of cancer indications. Aduro's recent announcement of a license agreement with Janssen Biotech includes further development and commercialization of certain product candidates based on the LADD platform. This agreement was timely with the recent announcement of successful Phase 2 clinical trial results in pancreatic cancer.

The vaccine platform is based on a normally pathogenic microorganism, L. monocytogenes. Early observations that wild-type Listeria replicated in the cytoplasm of infected cells suggested a means for delivering antigens directly to immune cells responsible for… **(continued on page 2)**

WB Staff Highlight: Carl Ross

For over 10 years Carl Ross, along with a team of highly qualified manufacturing, quality control, and quality assurance specialists, has led the development and manufacture of Aduro's CRS-207 at Waisman Biomanufacturing. His primary team of scientists includes, Janice Boyer (QC), Josh Sotos (QC), Alan Bettermann (manufacturing), and Jaime Bellon (QA) but the group also utilizes the talent and knowledge of other staff scientists as well. The breadth of knowledge on the WB scientific staff includes microbiology, downstream purification, aseptic filling, QC assay development, cellular biology and more, which allows for collaboration and encourages innovation when dealing with a novel product like Aduro's.

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Upcoming Conference Attendance

Cancer Vaccine & Gene Therapy October 6-7, 2014 Malvern, PA	**Bioscience Vision Summit** October 8, 2014 Madison, WI	**Rocktoberfest** October 9, 2014 Madison, WI	**8th Vaccine & ISV Congress** October 26-28, 2014 Philadelphia, PA	**World Stem Cell Summit** December 3-5, 2014 San Antonio, TX
Sponsor! Join WB at this 2nd annual conference and learn how we can advance your development of anti-cancer therapeutics. ngtcancervaccines.com	This networking event brings together local and regional leaders in the Wisconsin biotechnology industry. bioforward.org	Visit us at this annual Fisher Scientific product show at the UW-Madison Stock Pavilion, 9:00am-2:00pm	This vaccine-specific conference brings together researchers, CMO's, and governmental policy, safety and regulation experts. vaccinecongress.com	Attendees will learn about the latest in translational research while building new relationships at small group events. worldstemcellsummit.com

The Significance of Process Development and Quality Control for cGMP

Process Development is critical in transitioning a new drug from research to clinical development, and important to the long-term success of a drug. During this stage, our scientists work at a small scale to optimize upstream and downstream purification protocols to ensure that they are robust and scalable. Critical raw materials, process parameters, and specifications are all documented for future scale-up. The priorities our scientists weigh during this process include, but are not limited to: raw material (RM) risks/cost/availability, manufacturing process scalability, potential regulatory issues, drug storage and delivery, and cost/timeline tradeoffs to bring a product to the clinic.

Expanding our Quality Control lab is essential to further streamlining production runs. Our QC team is actively involved during various steps of the manufacturing process. First, testing is completed at the raw material preparation stage to ensure stability and purity levels. Second, in-process testing is performed at critical process steps during each manufacturing run. Lastly, additional QC testing is completed on bulk drug substance and final drug product to measure identity, purity, and strength prior to release for clinical use. Having an expanded space for RM's and in-process and product testing allows for efficient use of company resources, supporting rapid development of new drugs.

We look forward to fully utilizing this space for current and future projects. If you are moving into translational research stages, we may be able to help with your transition. Contact us to learn more about our capabilities and how our comprehensive services can add short and long-term value for you.

Open House Recap

WB moved into our new Process Development (PD) and Quality Control (QC) laboratory in May. To recognize the addition of this space to our facility, WB hosted an Open House on July 10th. Attendees included WB staff, Waisman Center staff, WB Advisory Board members, and UW Investigators. The focus on this event was to showcase the relationship between WB and UW Investigators and to exemplify the importance of the PD and QC stages in clinical development. This additional space will support the advancement of many current and future projects for our clients.

Thank you, to all who were in attendance!

WB Client Signs Technology Licensing Agreement (cont.)

antigen processing and presentation [(Starks et al., 2004); ref within]. Virulence attenuation was achieved by two mechanisms: actA deletion for cell-cell spread and InlB for cell invasion of non-phagocytic cells (Brockstedt et al., 2004). The attenuated strain is then engineered to deliver a variety of antigens for cancer immunotherapy or vaccination. Waisman has worked closely with Aduro to establish the cell banks and vaccine product for clinical evaluation.

Multiple clinical studies have evaluated the safety and immunogenicity of LADD-based immunotherapies. One such study evaluated CRS-207 in a Phase I study for patients with mesothelin-related malignancies including pancreatic adenocarcinoma. Results showed no dose-limiting toxicity and suggested improved survival (Le et al., 2012). Recently, Aduro presented data at the 2014 American Society of Clinical Oncology meeting (http://alturl.com/wnm9z) on a randomized Phase 2 clinical trial of CRS-207 that achieved survival endpoints in metastatic pancreatic cancer patients. In July 2014, the combination immunotherapy CRS-207 and GVAX Pancreas was granted Breakthrough Therapy Designation by the US FDA for pancreatic cancer treatment (http://alturl.com/fahx6).

Waisman is proud of the partnership with Aduro and the opportunity to contribute to the development of a potential treatment for these devastating forms of cancer.

Reference List

American Cancer Society. Cancer Facts & Figures 2014. Atlanta: American Cancer Society; 2014.

Brockstedt,D.G.et al. (2004). Proc. Natl. Acad. Sci. U. S. A 101, 13832-13837.

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WB Staff Highlight: Carl Ross (cont.)

Commercial products to maintain sterility during downstream processing of microbial products have not always been readily available, which introduced a major hurdle in the early years of CRS-207. Out of necessity, Ross and his team developed viable procedures to ensure the sterility of the CRS-207 cultures and pushed forward in development. Over the past 10 years Ross has lead this project through many successes and challenges, while developing a collaborative relationship with Aduro. Ross feels privileged to lead this project and noted it is *"…exciting to see the progress of CRS-207 through Phase I and II and to see the clinical data showing benefit to patients that have such serious disease. I've spent my career working with early phase clinical products, which often fail in Phase I. I'd like to see a product make it to market before I retire, and this could be the one!"*

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