

## Finding Solutions that Help a Unique Monoclonal Antibody Advance the Fight Against Metastatic Breast Cancer

**April 2017 -- Plantation, Florida** -- An important, seminal study was recently published in *Cancer Biotherapy and Radiopharmaceuticals*, a peer-reviewed journal ([Revskeya, E, et al. Vol 32 \(2\); 57-65](#)), on the work that Goodwin Biotechnology did in conjunction with Panacea Pharmaceuticals on a radiolabeled antibody conjugate that was evaluated for imaging and possible treatment of metastatic breast cancer. This radiolabeled antibody conjugate targets Human Aspartyl (Asparaginy)  $\beta$ -Hydroxylase or HAAH, which is overexpressed in a variety of cancers, and has proven to be a promising reagent for the development of imaging and possible therapeutic agents for the treatment of metastatic breast cancer.

“HAAH has emerged as a promising biomarker of cancer cells,” said Steven A. Fuller, PhD, Chief Operating Officer at Panacea Pharmaceuticals, Inc. “HAAH is an oncofetal antigen that modulates NOTCH signaling pathways during embryogenesis where it plays a role in cell growth, movement, and cell-to-cell interaction in tissues during formation. At the time of birth, the gene is silenced and HAAH is internalized into the internal cellular compartments such as the endoplasmic reticulum. However, in cancer tissue in adults, HAAH is overexpressed and translocated on the tumor cell surface, rendering it a specific antigen for tumor cells. This surface localization is uniquely associated with cancer and is related to cancer cell growth, cell motility, and invasiveness. HAAH is prevalent on more than 20 different cancer cells, but is not recognized by the immune system due to immune tolerance.”

“At Panacea Pharmaceuticals, we developed a fully humanized, IgG1 monoclonal antibody, PAN-622, to target HAAH,” continued Dr. Fuller. “This is a unique mAb that has been shown to internalize into tumor cells and serve as a vehicle for the delivery of cytotoxic moieties. However, we first wanted to demonstrate the ability of the conjugate to specifically target the cancer cells *in vivo*. We selected metastatic breast cancer because, despite advances in treatment, it remains in third place in the list of cancers killing the highest number of American women and men.”

“When Dr. Fuller and his colleagues from Panacea Pharmaceuticals approached us with this project, we were intrigued,” noted Muctarr Sesay, PhD, Chief Scientific Officer at Goodwin Biotechnology, Inc. “Our initial efforts were focused on the classical random conjugation of the ‘naked’ antibody that Panacea Pharmaceuticals supplied and comparing DOTA and CHX-A’ chelators as the linkers. Unfortunately, increased levels of conjugation with these resulted in a loss of binding capacity to both recombinant HAAH protein and tumor cells. As a result, it didn’t meet the requirements for a viable conjugate.”

“When we first evaluated the random conjugation results, we were seriously considering going back to the drawing board and developing a new antibody,” said Hossein Ghanbari, PhD, Chairman & CEO/CSO of Panacea Pharmaceuticals, Inc. “Finding a solution to this significant challenge could save us years of development work and a significant amount of money.”

“We then suggested a proprietary, site-directed approach via a partial reduction of the disulfide bond at the hinge region of the antibody,” continued Dr. Sesay. “PAN-622 was conjugated to several ligands, DOTA and DTPA, to enable subsequent radiolabeling. The immunoreactivity was evaluated by an HAAH-specific enzyme linked immunoabsorbent assay and binding to the HAAH-positive cells. Based on the positive results of these *in vitro* studies, the DTPA-PAN-622 was selected to investigate biodistribution in

healthy CD-1 female mice and 4T1 mammary tumor-bearing BALB/c mice. For this facet of the project, we recommended Dr. Kate Dadachova because we had worked with her for radiolabeling of conjugates for over 10 years.”

“Radiolabeling of a conjugate has proven to be quite valuable for diagnostic studies and for monitoring disease,” noted Ekaterina (Kate) Dadachova, PhD, Fedoruk Chair in Radiopharmacy, Professor, College of Pharmacy and Nutrition at the University of Saskatchewan. “In addition, Radioimmunotherapy (RIT) permits a high dose of therapeutic radiation to cancer cells while minimizing the exposure of normal cells. This approach has been investigated for several decades, and the cumulative advances in cancer biology antibody engineering and radiochemistry in the past decade have markedly enhanced the ability of RIT to produce durable remissions of multiple cancer types.”

“The site-directed conjugation of DTPA-Mal chelator to the PAN-622 mAb was done and labeled with <sup>111</sup>In with 93% efficiency,” explained Dr. Dadachova. “These conjugates showed structural integrity by size exclusion HPLC and nonreducing SDS-PAGE and preserved their immunoreactivity toward HAAH as per ELISA and cell binding. In our murine model, the <sup>111</sup>In-DTPA-PAN-622 mAb concentrated on the primary tumors and to some degree in lung metastases. Further, the pilot therapy study with <sup>213</sup>Bi-DTPA-PAN-622 demonstrated a significant effect on the primary tumor. The pathological investigation revealed that the weight of the primary tumors was significantly ( $p=0.04$ ) less in <sup>213</sup>Bi-DTPA-PAN-622-treated mice than in the untreated cohort, although the number of metastases in the lungs of both groups was practically the same. ( $p=0.08$ ) In addition, there was some uptake in the heads of all mice and it was hypothesized that it might be due to metastases in the skull, but it is unclear whether this observation is significant and it warrants further investigation.”

“As importantly, the radiolabeled conjugate cleared rapidly from the circulation with less than 1% ID/gram remaining in the blood at 96 hours post injection,” continued Dr. Dadachova. “The processing and excretion of the conjugate followed the hepatobiliary route, which is typical for radiolabeled conjugates.”

“We are quite excited with the results of this Pilot study,” continued Dr. Fuller. “Since HAAH is overexpressed in other cancers, the use of radiolabeled PAN-622 will be explored in other tumor types as well. Further, we are also currently collaborating with Goodwin Biotechnology to investigate the potential for adding a cytotoxic anti-cancer payload to PAN-622 to see how it performs in treating these diseases.”

“This is just another example of the value that Goodwin Biotechnology brings to the field of healthcare that has huge upside potential for contributing to the quality of life for the patients and families impacted by this insidious disease,” added Karl Pinto, Chief Executive Officer at Goodwin Biotechnology, Inc. “Our staff of highly skilled scientists are energized when we face challenges, and by working together in partnership with our clients, we strive to develop viable solutions. It is equally rewarding when a project reaches a significant milestone on a cutting-edge product candidate such as this. With over 15 years of bioconjugation experience, we’ve accumulated significant expertise and experience in developing robust processes and we’ve been able to contribute to a number of scientific advancements in this field and it is exhilarating to be on the forefront in contributing to these medical advances.”

For more information about the study, please [click here](#).

**About Goodwin Biotechnology, Inc.**

**Goodwin Biotechnology** is a uniquely qualified CDMO that offers a Single Source Solution™ for our clients from cell line development, exploratory proof of concept projects through process development and cGMP contract manufacturing of monoclonal antibodies, recombinant proteins, vaccines, and Biologic Drug Conjugates including Antibody Drug Conjugates (ADCs) for early and late stage clinical trials. By working with Goodwin Biotechnology, clients can enhance the value of their product candidates with clear development and manufacturing strategies, as well as a road map to meet the appropriate quality requirements from the milligram and gram range to kilogram quantities as the product candidates move along the clinical development pathway in a cost-effective, timely, and cGMP compliant manner to enhance patients' lives. With over 24 years of experience as an independent integrated contract manufacturer, Goodwin Biotechnology has worked as a strategic partner with companies of all sizes from small university spin-offs to major research institutes, government agencies and large, established and multi-national biopharmaceutical companies. Based on the impressive track record, Goodwin Biotechnology has been awarded **Frost & Sullivan's Customer Value and Leadership Award for Best Practices in Mammalian Contract Manufacturing!** In addition, Goodwin Biotechnology was awarded 'Best in Sector: Biopharmaceutical Contract Development & Manufacturing' at *Acquisition International* magazine's 2015 Sector Performance Awards. Most recently, Goodwin Biotechnology received *Global Health & Pharma's* 2016 award for **Best for BioProcess Development & cGMP Manufacturing**. [Click here](#) to view the press releases! Additional information may be found at <http://www.GoodwinBio.com>.

**About Panacea Pharmaceuticals, Inc.**

**Panacea Pharmaceuticals, Inc.** was founded in 1999 to discover, develop, and commercialize novel therapeutic and diagnostic products for oncology and diseases of the central nervous system. Since its inception, the Company's primary approach to cancer treatment has been immunotherapy and development of companion diagnostics for comprehensive patient management. The Company's lead drug product candidate is a nanoparticle-based therapeutic cancer vaccine that targets a novel patented tumor marker, Human Aspartyl (Asparaginyl) beta-Hydroxylase (HAAH). The company relies on a close collaboration with Brown University where teams of researchers are continuing advances on the Company's core technologies. For more information, visit the company's Web site at [www.panaceapharma.com](http://www.panaceapharma.com).

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