Addressing cancer through tumor-specific targeting

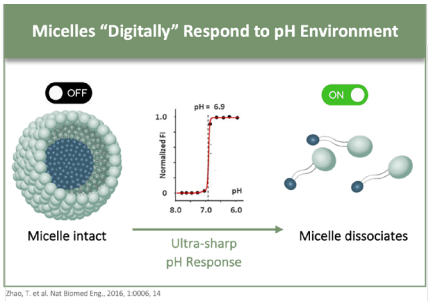
The Holy Grail of Cancer Identification and Treatment: A Universal Biomarker That Allows Precise Tumor Cell Targeting

Efficacy of cancer treatments today are hampered by the difficulty in accurately visualizing and specifically targeting cancer cells. In cancer resection surgery, surgeons lack accurate tools to identify all cancerous lesions, and cancer treatments have poor therapeutic windows as a result of off-target effects in normal tissues. Attempts to selectively impact cancer cells by targeting cell surface molecules with antibodies and other methods have improved, but not eliminated these challenges.

Since the 1930's, however, it has been known that all cancer cells have a universal trait that sets them apart from normal cells – a relatively acidic pH tumor microenvironment (TME). Based on this, OncoNano employs an ultra pH-sensitive technology that, for the first time, promises to enable selective tumor targeting across tumor types for surgery and treatment. In addition, the pH-sensitive micelle technology can be applied to specifically access tumors by leveraging the low endosomal pH environment within dendritic cells in lymph nodes and the TME.

OncoNano ON-BOARD and OMNI Platforms – Ultra pH-Sensitive Polymer-Based Micelles

OncoNano has developed a library of proprietary, tunable, ultra pH-sensitive polymer-based micelles to selectively identify and target cancerous tumors. ON-BOARD micelles can be chemically modified with a fluorescent dye for use as imaging agents to guide surgical resection or encapsulate a wide variety of chemo- and immunotherapeutic payloads. The ON-BOARD micelles are selectively activated in the acidic TME where they dissociate and release their payload. The ON-BOARD micelle dissociation occurs over a very narrow pH window (~0.2 pH units) resulting in an "on-off" property that enables highly selective tumor targeting over normal tissues. OMNI micelles enable delivery of a payload to target dendritic cells within the TME but also feature the ability to take part in the generation of an immune response by activating Stimulator of Interferon Genes (STING) applicable to treatment of multiple tumor types.



Zhao, T. et al. Nat Biomed Eng., 2016, 1:0006, 14

OncoNano Micelle ON-BOARD and OMNI Technology Platforms

PHASE 2

ON-BOARD Platform
Pegsitacianine
Fluorescent nanoprobe for real-time surgical imaging

PRECLINICAL

ON-BOARD Platform
ONM-400
Therapeutic payload delivery

PRECLINICAL

OMNI Platform
ONM-501
Polyvalent STING activation

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Cancer Intervention Programs

Pegsitacianine Fluorescent Nanoprobe for Precision Guided Surgery

Current phase 2 clinical programs in head and neck tumors, peritoneal metastases, and lung cancer

Results to Date:

- In Phase 1 studies in breast, head and neck, esophageal and colorectal tumors, pegsitacianine detected 100% of tumors identified by standard of care and importantly, identified tumors in an additional 30% of patients missed by standard of care.
- In clinical studies conducted to date, pegsitacianine has shown no dose limiting toxicities and favorable ongoing performance metrics.
- Real time imaging provides meaningful practice efficiencies, including shortened surgical times and decreased histopathology requirements.
- Results indicate the potential to establish a large, new market in image-guided surgery across multiple tumor types.
- Received Fast Track Designation from the US FDA.

Potential Clinical Benefits/Implementations

- Real time imaging provides better visualization of the primary tumor, leading to enhanced surgical planning.
- Image-guided surgery produces more efficient surgeries by better detecting disease that was left behind while simultaneously conserving normal tissue and reducing collateral impact.
- Better detection of disease that was left behind and/or previously not diagnosed reduces the need for repeat surgery.

Therapeutic Platforms/Programs

ONM-501 STING Activation

Status: Preclinical

Results to Date:

- STING activation demonstrated *in vivo* – a critical mechanism of T-cell activation and immune response.
- ONM-501 utilizes the ultra pH sensitive micelle technology to achieve targeted delivery of STING-activating OMNI PC7A polymers and a cGAMP payload to resident dendritic cells that are key to instigating an immune response within the tumor site.
- The OMNI PC7A polymers stabilize and congregate STING proteins, producing a sustained activation of the STING immune response pathway following and in synergy with initial burst activation of STING by cGAMP.
- Preclinical studies of ONM-501 show curable outcomes in multiple tumor models in combination with an anti-PD-1 monoclonal antibody.
- ONM-501 has shown robust antitumor efficacy in primary, distal and metastatic cancers with long-term memory effect.
- Low systemic cytokine profiles, suggesting very limited off-target delivery of payload.
- Phase 1 trial anticipated to begin in 2H 2022

ONM-400

Status: Preclinical

Results to Date:

- The ONM-400 program involves the delivery of an undisclosed immuno-therapy as a novel cancer treatment.
- Preclinical studies demonstrate the ability to tailor micelles to encapsulate or conjugate a wide variety of cancer therapeutics including cytokines, small molecules and monoclonal antibodies to improve the therapeutic index.
- Pegsitacianine is proving tumor-specific tissue delivery concept of the ON-BOARD program.
- Progressing towards IND submission in 1H 2023