Development of Next Generation Antibody Drug Conjugates (ADCs) Against CD276

Summary (1024-character limit)
The National Cancer Institute (NCI) seeks research collaborations and/or licensees for the development of a CD276 antibody drug conjugate (ADC) for the treatment of solid tumors.

NIH Reference Number
E-145-2019

Product Type
- Therapeutics

Keywords
- CD276, Antibody Drug Conjugate, ADC, B7-H3, Monoclonal Antibody, Immunotherapy, St. Croix

Collaboration Opportunity
This invention is available for licensing and co-development.

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Description of Technology
Angiogenesis is the formation of new blood vessels from pre-existing blood vessels. Angiogenesis occurs during normal growth and development (physiological angiogenesis) and during the growth of solid tumors (pathological angiogenesis). CD276, also known as B7-H3, is a cell surface tumor endothelial marker that is highly expressed in the tumor vessels of human lung, breast, colon, endometrial, renal, and ovarian cancer, but not in the angiogenic vessels of normal, healthy tissue. This differential expression makes CD276 an attractive target for cancer treatment due to the ability to selectively target pathological angiogenesis without impacting physiological angiogenesis. In fact, CD276-directed therapeutic antibodies may have a higher degree of specificity for tumor vessels than current antiangiogenic agents that cannot distinguish physiological and pathological angiogenesis. Moreover, CD276 protein is also frequently overexpressed on tumor cells. The ability to target the vasculature as well as tumor cells directly makes CD276 a potentially ideal dual-compartment therapeutic target.

Researchers at the National Cancer Institute (NCI) have created a potent antibody-drug conjugate (ADC) with an improved therapeutic index that selectively reacts with a broad variety of tumor types. The lead
ADC, m276-PBD-SL, targets CD276 for the treatment of cancer. The m276 antibody used to develop this ADC is fully-human and recognizes mouse, non-human primate, and human CD276 with similar affinity – unlike all other CD276 antibodies described to date. This ADC contains mutations to prevent inappropriate interaction of the ADC with endogenous immunoglobulin receptors present on cells of the immune system. These mutations prevent the potentially harmful killing of normal cells and minimize off-target toxicity. The ADC also contains a mutation which allows site-directed conjugation of the payload to the antibody. Payload attachment at this specific site prevents the premature release of the warhead from the antibody, increasing the stability of the ADC in the circulation and preventing non-specific toxicity. This ADC is the only one that combines all these critical features with a potent optimized warhead and an optimally targeted pan anti-cancer fully-human antibody against CD276. These advantages can be leveraged to facilitate preclinical ADC studies and may be a better reflection of what a human clinical response would be, may facilitate GMP scale-up, may facilitate preclinical testing in multiple species using the same clinical-grade product, and may facilitate earlier toxicity assessments due to the multiple cross-species reactivity of the fully-human CD276 antibody.

The National Cancer Institute (NCI) seeks research collaborations and/or licensees for the development of a CD276 antibody drug conjugate (ADC) for the treatment of solid tumors.

**Potential Commercial Applications**
- Therapeutic for various solid cancer including, but not limited to, lung, breast, colon, endometrial, renal, and ovarian cancer

**Competitive Advantages**
- Simultaneously targets both tumor cells and tumor vasculature
- Potentially superior adverse events mitigation over existing anti-angiogenic agents due to the differential expression of CD276 on tumor versus normal vasculature
- Fully human antibodies are less likely to be recognized and cleared by the immune system upon repeated administration
- Cross-reactive with mouse, rat, and monkey CD276 making preclinical studies easier and more informative
- Antibody mutations block inappropriate killing of Fc-receptor-bearing normal cells to minimize off-target toxicity
- The mutation in the Fc domain creates a superior site-directed conjugation attachment site for the drug payload to the warhead by increasing solubility of the ADC and preventing premature shedding of the drug in serum

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**Development Stage**
- Pre-clinical (in vivo)

**NCI Technology Transfer Center**
Patent Status
• **U.S. Provisional:** U.S. Provisional Patent Application Number 62/947,135, Filed 12 Dec 2019

Related Technologies
• E-104-2013
• **E-250-2014 - Fully Human Antibodies and Antibody Drug Conjugates Targeting CD276 (B7-H3) for the Treatment of Cancer**

Therapeutic Area
• Cancer/Neoplasm