DBPR901: a Humanized HSP90α Antibody with Anti-Desmoplasia Potency

INDICATIONS:

- ✓ Pancreatic ductal adenocarcinoma
- ✓ Colorectal cancer

PATENTS:

PCT Patent Filed

DEVELOPMENT STATUS:

Drug Candidate

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INVENTION DESCRIPTION

Desmoplasia is a hallmark of many malignancies, which is tightly associated with rapid tumor growth, metastatic occurrence, and refractory therapeutic outcome. A big production of cancer-associated fibroblasts (CAFs) is one of main causes of desmoplasia, and endothelial-mesenchymal transition (EndoMT) of endothelial cells provides a rich source for CAFs. EndoMT-derived CAFs recruit a large amount of myeloid-derived macrophages into tumor, and facilitate polarization of these macrophages toward M2 type. The M2-type macrophages do not only exhibit M2-type markers but also express and secrete a great amount of extracellular HSP90α (eHSP90α) and thus create an eHSP90α-rich tumor microenvironment which facilitates cancer cell spreading and malignant progression. Therefore, eHSP90α and eHSP90α-rich tumor microenvironment can be regarded as novel cancer therapeutic targets.

- ➤ DBPR901 is a humanized anti-HSP90α IgG1 derived from a murine hybridoma through a rational design approach involving protein engineering and relevant assessments of biochemical and physicochemical properties.
- ➤ DBPR901 exhibits its superiority in suppressing cancer cell invasive and spheroid-forming activities in pancreatic ductal adenocarcinoma (PDAC) and colorectal cancer cell lines.
- ➤ In mouse cancer models, use of DBPR901 alone can abolish M2-macrophages and EndoMT-promoted tumor-growth activities of subcutaneously inoculated PDAC cell grafts, and can also effectively block pancreatic ductal K-Ras mutation-caused desmoplastic PDAC development and liver metastasis and thus prolong the survival time of experimental mice. Additionally, DBPR901 can be used in combination with gemcitabine to exhibit more suppressive effect on desmoplastic tumor model in humanized ASID mice.

COMPETITIVE ADVANTAGES OF DBPR901

- ➤ In mice, DBPR901 exhibits a promising anti-cancer activity, and is quite water-soluble but not easy to be excreted out of mouse bodies with a half-life > 18.4 days in blood.
- ➤ DBPR901 is not cytotoxic to retinal pigmented epithelial cells and does not cause mouse splenic enlargement.

MARKET POSITIONING/OPPORTUNITY

Agents targeting cancer desmoplasia are the unmet medical needs for patients to alleviate malignant progression and improve therapeutic efficacy. PDAC is a highly desmoplastic and deadly disease with a 5-year survival rate < 9%. The size of the Global Pancreatic Cancer Therapeutics Market was worth USD 2.41 billion in 2020, and is estimated to be growing at a CAGR of 7.54% to reach USD 3.47 billion by 2025.

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