BPR5K163 Small Molecule AXL and MERTK Dual Tyrosine Kinase Inhibitor as Anti-Tumor and Immunomodulatory Agent

INDICATIONS:

- ✓ AXL and MERTK over-expression solid tumors
- ✓ Tumors relapsed or resistant to chemotherapy, molecular targeted agents or immune checkpoint inhibitors

PATENTS:

US provisional patent application

DEVELOPMENT STATUS:

Lead optimization to candidate

CONTACT:

Pey-Yea Yang
Chief of Administration,
Institute of Biotechnology and Pharmaceutical Research, National Health Research Institutes
No. 35, Keyan Rd.
Miaoli County 35053
Taiwan, R.O.C.
Tel: 886-37-206-166 ext. 35705
peyyea@nhri.edu.tw

INVENTION DESCRIPTION

TAM (TYRO3, AXL and MERTK) receptor tyrosine kinases play important roles in innate immune homeostasis. Both AXL and MERTK are drivers for tumor progression, metastasis, drug resistance and immune evasion. Thus, dual AXL and MERTK inhibition in the tumor and tumor immune microenvironment would reduce tumor growth and survival, reverse treatment resistance and create more robust anti-tumor immune responses. Utilizing our proprietary small molecule tyrosine kinase inhibitors compound library, we identified BPR5K163 with potent AXL and MERTK kinase inhibitory activities and selectivity over TYRO3. BPR5K163 exhibited good oral bioavailability and *in vivo* anti-tumor efficacy, alone or in combination with immune checkpoint inhibitors in preclinical tumor models. In an AXL and MERTK overexpression human triple negative breast cancer model, BPR5K163 produced greater anti-tumor efficacy than either AXL or MERTK mono-targeted agent alone. In a murine colon tumor model, DBPR5K 163 demonstrated immunomodulatory activities by decreasing M2 tumor-associated macrophages (TAM) and increasing cytotoxic T cells in the tumor microenvironment.

COMPETITIVE ADVANTAGES OF BPR5K163

- ➤ Dual AXL and MERTK kinase inhibitors have advantages over AXL and MERTK-selective agents for their broader clinical indications, preventing treatment resistance and reducing overlapping/multiple side effects caused by mono-target agents.
- ➤ Efficacious as a single agent and in combination with immune checkpoint inhibitor in preclinical tumor models (tumor growth inhibition, TGI >=50%).
- ➤ Greater anti-tumor efficacy than either AXL or MERTK mono-target agent alone in preclinical tumor models.
- ➤ Demonstrate immunomodulatory activities in syngeneic colon tumor model.

MARKET POSITIONING/OPPORTUNITY

- ➤ BPR5K163 with anti-tumor and immune modulatory activities would expect to drive global kinase inhibitors markets, targeted cancer therapy market and immuno-oncology market.
- ➤ Drug and companion diagnostics (CDx) co-development would identify patients who are likely to benefit from BPR5K163, alone or in combination with other agents, including chemotherapeutic agents, target agents or immune checkpoint inhibitors.

August 20, 2021