DBPR728: A Novel Aurora Kinase Inhibitor Targeting SCLC with MYC Amplification

A Precision Medicine for Cancers Genetically Addicted to MYC

INDICATIONS:

- ✓ Small cell lung cancer with *MYC* amplification
- ✓ Cancers with null expression in TP53 and RB1, and acquired MYC amplification
- ✓ Neuroblastoma

DEVELOPMENT STATUS:

candidate determination/ preclinical stage

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

Small cell lung cancer (SCLC) accounts for approximately 15% of all lung cancers, leading to ~30,000 deaths each year in the United States. SCLC patients often present with metastasis at time of diagnosis, excluding surgery as a treatment option. While patients show high response rate to standard chemotherapy such as cisplatin/etoposide, they soon develop drug resistance and disease progression. Therefore, new therapeutic strategies are urgently needed for SCLC.

DBPR728 is an orally bioavailable novel Aurora kinase inhibitor which was selected based on its potency to reduce levels of MYC oncoproteins. DBPR728 efficiently induced cell apoptosis and inhibited proliferation of several SCLC cell lines with IC_{50} < 300 nM. Head-to-head comparison of DBPR728 with the phase II investigational drug MLN8237 demonstrated superiority of DBPR728 on the regression (>80% at 100 mpk QD 5 days/wk for 2 weeks) of SCLC xenografted tumors (NCI-H446 and NCI-H69) in mice. The xenografted NCI-H446 tumors treated with DBPR728 remained stable for more than 30 days after the last dosage. Furthermore, oral administration of DBPR728 at 300 mpk QW showed similar tumor regression potency to the dosage of 100 mpk QD 5 days/wk for 2 weeks. No significant body weight loss was observed in animals treated with either 100 mpk or 200 mpk DBPR728 for 14 consecutive days. A PCT international patent treaty has been filed for this technology.

COMPETITIVE ADVANTAGES OF DBPR728

- ➤ Deregulation of *MYC*-family oncogenes is frequently associated with poor prognosis and unfavorable patient survival. DBPR728 was designed based on its potency to reduce levels of cMYC/MYCN oncoproteins in addition to its inhibitory activity to Aurora kinases.
- ➤ DBPR728 is superior to MLN8237 in inducing degradation of cMYC/MYCN oncoproteins in SCLC cell lines; suggesting the potential of DBPR728 as a therapeutic agent for *MYC*-amplified SCLC.
- ➤ Amplification of *cMYC* or *MYCN* oncogenes can serve as a biomarker for selection of patients who are potentially responsive to BRP6K728.

MARKET POSITIONING/OPPORTUNITY

There is no effective therapeutics for treating SCLC. A drug candidate may thus be clinically developed promptly. In addition to SCLC, amplification of *MYC* paralogs are observed in 28% of the samples across 33 cancers of The Cancer Genome Atlas. The disease indications of DBPR728 may be expanded based on the unambiguous genomic features of the cancers including mutations in *TP53* and *RB1*, and *MYC* amplification.

Sep. 27, 2021