CHD1L Inhibitors for the Treatment of Cancer

Innovations
UNIVERSITY OF COLORADO
ANSCHUTZ MEDICAL CAMPUS

Product

CHD1Li Lead Drug Candidates

Indication

Breast, ovarian, lung, glioma, and GI cancers among others

Value Propositions

- Halt and reverse EMT, a driving force in cancer metastasis
- Synergizes with existing chemotherapies

Market

- Global breast cancer US $16 billion
- Global ovarian cancer US $2.0 billion
- Global pancreatic cancer US $4.1 billion
- Global colorectal cancer US $8.15 billion
- Global lung US $42.2 billion

Intellectual Property

- Patent pending*
- Available for licensing

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Ref# CU5158H

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Background on CU5158H

Since the discovery of Chromodomain Helicase DNA Binding Protein 1 Like (CHD1L, *a.k.a* ALC1) in 2008, it has emerged as an oncogene implicated in the pathology of numerous cancers, including but not limited to: breast, glioma, lung, and gastrointestinal (GI) cancers. In the clinic, CHD1L is associated with metastatic cancer, poor prognosis, and low survival. CHD1L plays a critical role in regulating epithelial-mesenchymal transition (EMT), apoptosis, DNA Repair, and evasion of the immune response. Taken together, CHD1L is a novel molecular target that promotes tumor progression, metastasis, and multi-drug resistance.

Technical Innovation

Dr. Daniel LaBarbera, with a team at the University of Colorado, has discovered, validated, and optimized (through medicinal chemistry) first-in-class CHD1L inhibitor (CHD1Li) lead drug candidates with potential toward an investigational new drug (IND) and clinical translation. CHD1Li display excellent *in vivo* pharmacokinetics, including a plasma half-life of 8 hours in mice that are oral bioavailable with 44-55% (depending on the analog) penetrating the circulatory system after oral administration. CHD1Li are well tolerated in mice at maximum tolerated doses and display no toxicity to mice measured grossly, and no liver toxicity measured by a board-certified veterinary pathologist. Furthermore, CHD1Li are effective antitumor agents alone and in combination with clinical therapies (**Figure**).

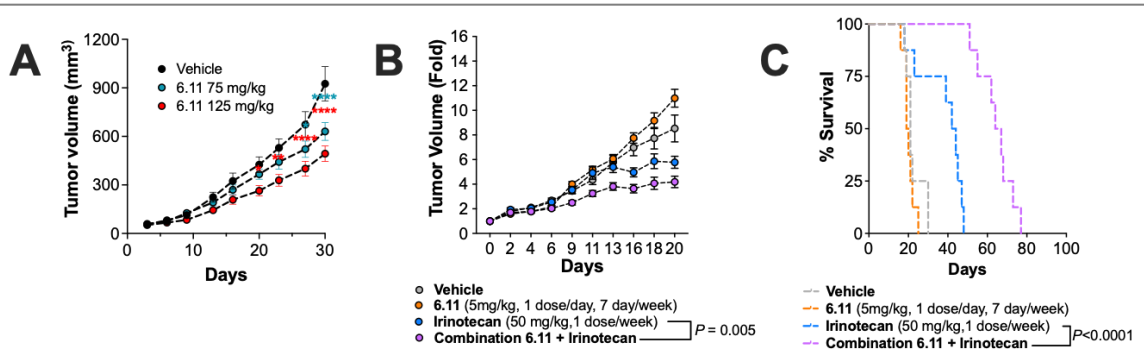

Figure: CHD1Li lead drug 6.11 displays potent antitumor activity alone and in combination with Irinotecan in nude mouse xenografts generated from isolated mesenchymal cell with enhanced tumorigenic and MDR properties. (A) CHD1Li 6.11 displays significant antitumor activity as a single agent at the doses indicated. (B) CHD1Li 6.11 strongly synergizes with irinotecan at low doses of 5 mg/kg, significantly inhibiting tumor growth compared to irinotecan alone. (C) The same combination of 6.11 and irinotecan (purple line) significantly improved survival compared to Irinotecan alone (blue line).

Resources & Documents:

** PCT pending: PCT/US2021/023981—"Small Molecule Inhibitors of Oncogenic CHD1L with Preclinical Activity Against Colorectal Cancer"—Filed March 24th, 2021.*