Innovations
UNIVERSITY OF COLORADO
ANSCHUTZ MEDICAL CAMPUS

Hypoxia-Activated PROTAC Coupled AMPK Inhibitor

Product

Selective AMPK Inhibitor Coupled with PROTAC

Indication

Acute Myeloid Leukemia

Value Propositions

- Compounds may help eliminate cancer stem cells or sensitize them to chemotherapy
- Selective AMPK inhibition
- Cancer cell death through ubiquitin pathway

Market

- $922 Million- US AML Market in 2020 (11.9% CAGR through 2029)
- $2.8 Billion- Expected US AML Market Size by 2029

Intellectual Property

- PCT pending*
- Available for licensing

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Ref# CU5200H

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Background on CU5200H

Cancer stem cells have been attributed to cancer recurrence and drug resistance. Studies suggest AMP-activated protein kinase (AMPK) is critical in maintaining cancer stem cells (CSCs), and that AMPK inhibition may eliminate CSCs or sensitize them to cytotoxic chemotherapy.

Acute myeloid leukemia (AML) is the most common acute leukemia in adults. Despite advances in the treatment of AML, only 20–30% of patients achieve long-term disease-free survival and treatment options for relapsed AML are extremely limited. The recurrence of AML has been attributed to leukemic stem cells (LSCs), and efforts are now focused on targeting this drug resistant population of cells to cure AML.

Technical Innovation

Dr. Reigan has developed two selective inhibitors of AMPK coupled to a hypoxia-activated PROteolysis TArgeting Chimera (PROTAC) moiety. Studies out of the University of Colorado show that AMPK is preferentially activated in LSCs and is critical for their viability. The novel therapeutics treats AML by selectively inhibiting AMPK located in LSCs (these cells tend to reside in hypoxic microenvironments) and then targeting those cells for destruction using the ubiquitin system. This treatment may eliminate LSCs or sensitize them to conventional therapy. Dr. Reigan is currently investigating the efficacy of these AMPK inhibitors alone and in combination with cytarabine or venetoclax in primary AML cells and using in-vivo tumor xenograft models. These novel targeted compounds are a next generation series based on core small molecule leads disclosed in CU4954H.

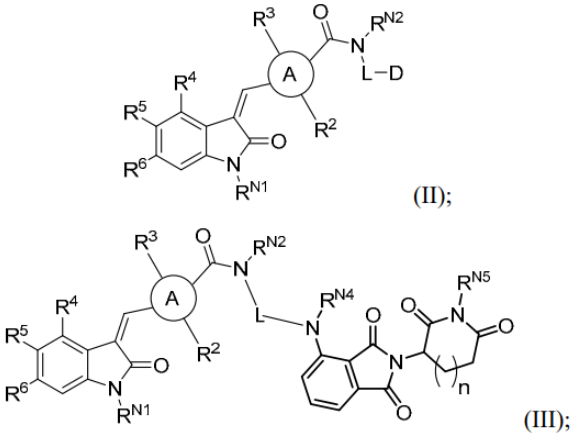

Figure: Diagram depicting (II) the basic chemical structure of the therapeutic with an AMPK inhibiting moiety, a linking moiety, and a PROTAC degrading moiety and (III) showing an example of the PROTAC moiety.

PCT Pending: PCT/US21/40113— "Conjugates of AMPK Inhibitors and PROTAC Degraders and Related Uses"- Filed July 1st, 2021.