Antitumor Activity of CUDC-907, a Single Small Molecule Inhibitor That Targets Both PI3K and HDAC, in Hematologic Cancer Models

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Rationale for a Single Molecule Targeting Hematological Cancers and Design

- Both HDAC and PI3K are validated targets in hematological cancers.
- HDAC inhibition may overcome signaling pathway up-regulation following PI3K blockade by single target PI3K inhibitors.
- Therefore, inhibiting both targets achieves synergistic anti-tumor effects.

CUDC-907 Potency Against PI3K Isoforms and HDAC Subtypes

- Enzymatic activity against PI3K isoforms (IC50, nM)
- Enzymatic activity against HDAC subtypes (IC50, nM)

MOA: CUDC-907 Disrupts Signaling Networks in Hematologic Cancer Cells

CUDC-907 Potently Inhibits Proliferation of Hematological Cancer Cell Lines in Vitro

- Cancer Type
- Cell Line
- CUDC-907
- Dox
- IC50 (μM)

CUDC-907 is Orally Bio-Available in Preclinical Animal Studies

- Parameters
- Male
- Female
- Mouse
- Doq
- Time (h)

CUDC-907 Dose-Dependently Disrupts Signaling Networks, Induces Apoptosis in NHL Tumor Xenografts

- Parameters
- Male
- Female
- Mouse
- Doq
- Time (h)

Conclusions

- CUDC-907 is a dual inhibitor of HDAC and PI3K which inhibits PI3K-AKT as well as other vital signaling pathways, and induces apoptosis in cancer cells via epigenetic modification.
- CUDC-907 displays greater anti-proliferation potency against human hematologic cancer cell lines than reference compounds.
- CUDC-907 is orally bioavailable in animals, and displays antitumor activity (with a favorable safety profile) in efficacy studies in hematologic cancer models.
- CUDC-907 disrupts cancer signaling networks, which therefore may overcome limitations of other PI3K-mTOR or HDAC single target inhibitors.
- CUDC-907 was selected as a candidate for clinical development.