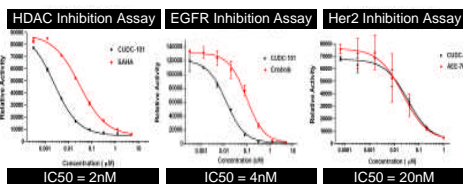


Cheng-Jung Lai, Xu Tao, Le Zhang, Shumei Liu, Yue Liu, Rudi Bao, Hui Qu, Ling Yin, Da-Gong Wang, Brian Zifcak, Hai-Xiao Zhai, Xiong Cai, Changgeng Qian
 Curis Inc., 45 Moulton Street, Cambridge, MA 02138



1. CUDC-101 Specifically and Potently Inhibits HDAC, EGFR and Her2

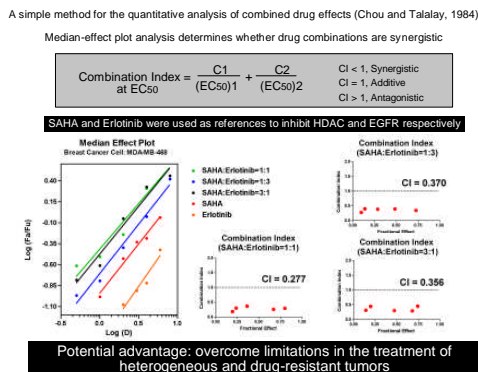


CUDC-101 displays weak or no activities on other 69 kinases tested

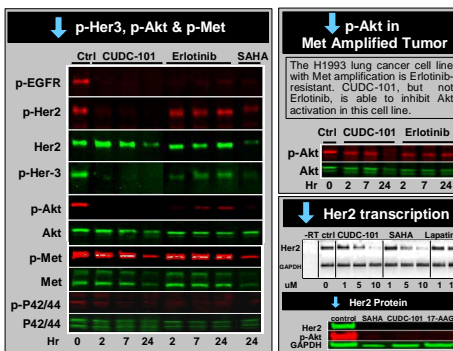
Kinase	KDR	Src	Lyn	Lck	Abl-1	FGFR	FLT3	RET
IC50 (nM)	849	11000	840	5910	2890	3430	1500	3200

CUDC-101 inhibits the Erlotinib resistant EGFR/T790M mutant

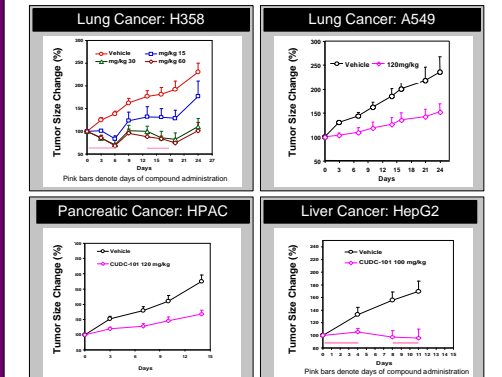
3. Rationale for CUDC-101 Design: Synergism between EGFR & HDAC Inhibition



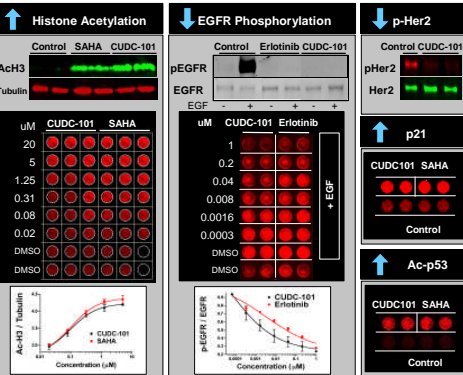
5. Potential Mechanism for Synergism: CUDC-101 Rapidly and Durably Inhibits Her2, Her3, MET and Akt Signaling



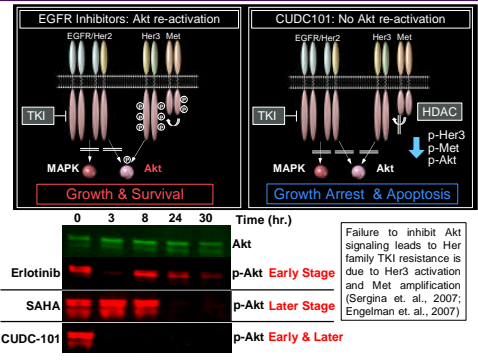
7. CUDC-101 is Efficacious in Xenograft Models of Human Cancer



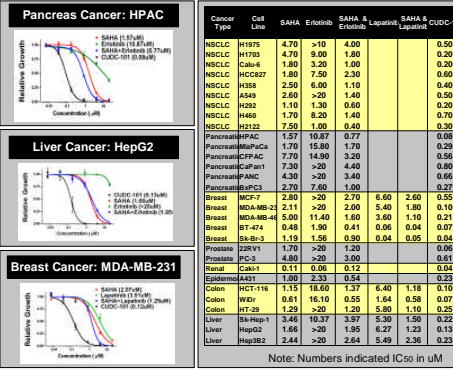
2. CUDC-101 Inhibits HDAC, EGFR and Her2 Pathways in Tumor Cells



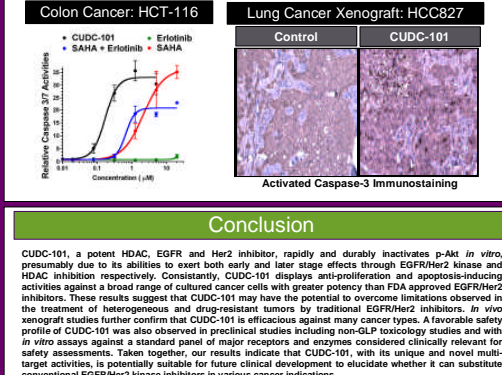
4. Potential Mechanism for Synergism: CUDC-101 Rapidly and Durably Inhibits Her2, Her3, Met and Akt Signaling



6. CUDC-101 Effectively Inhibits Proliferation of Human Cancer Cell Lines



8. CUDC-101 Induces Apoptosis in Cultured Cancer Cells and Xenografts



Conclusion

CUDC-101, a potent HDAC, EGFR and Her2 inhibitor, rapidly and durably inactivates p-Akt *in vitro*, presumably due to its abilities to exert both early and later stage effects through EGFR/Her2 kinase and HDAC inhibition respectively. Consistently, CUDC-101 displays anti-proliferation and apoptosis-inducing activities against a broad range of cultured cancer cells with greater potency than FDA approved EGFR/Her2 inhibitors. These results suggest that CUDC-101 may have the potential to overcome limitations observed in the treatment of heterogeneous and drug-resistant tumors by traditional EGFR/Her2 inhibitors. *In vivo* xenograft studies further confirm that CUDC-101 is efficacious against many cancer types. A favorable safety profile of CUDC-101 was also observed in pre-clinical studies including non-GLP toxicology studies and *in vitro* assays against a standard panel of major receptors and enzymes considered clinically relevant for safety assessments. Taken together, our results indicate that CUDC-101, with its unique and novel multi-target activities, is potentially suitable for future clinical development to elucidate whether it can substitute conventional EGFR/Her2 kinase inhibitors in various cancer indications.