

EXECUTIVE SUMMARY

HB Therapeutics, Inc. is a biotech specialized in targeted protein degradation (TPD) for discovery of small-molecule glue degraders of targeted oncoproteins for cancer therapy. Leveraging its expertise in ubiquitin biology and medicinal chemistry, the company has developed a comprehensive TPD platform that enables us to discover small molecule glue degraders that harness natural endogenous ubiquitination process of targeted oncoproteins in various type of cancer. The platform starts with design of genetically engineered cancer cell models to identify hit molecules that destroy the oncogenic drivers in the cancer. The advanced CRISPR-Cas9 technology reveal natural, endogenous E3 ligase complex that mediate the degradation of oncoproteins while Cryo-EM provides the structural basis of molecule glues and guidance for drug design. Machine learning and AI-powered design speed up hit/lead optimization and identification of the candidates for clinical development as the first-in-class anticancer drugs.

This TPD platform has led to the discovery of the first small molecule degraders of small ubiquitin-like modifier-1 (SUMO1) and its endogenous cullin 1 (CUL1) ubiquitin E3 ligase complex that mediates degraders-induced ubiquitination and degradation of SUMO1 in cancer but not normal cells. AI-powered hit to lead optimization has identified potent and orally bioavailable compounds as clinical candidates. Studies of patient derived xenografts (PDXs) have demonstrated the therapeutic efficacy of candidates through oral administration in treatment of advanced stage III and IV metastatic colon cancer. The candidates are at the stage for investigative new drug (IND)-enabling studies and FDA approved phase I clinical trials. This comprehensive TPD platform has enabled our robust drug discovery pipeline of small molecule degraders of the oncoproteins including KRAS mutants, programmed death ligand 1 (PDL-1), and androgen receptor (AR). These small molecule degraders are currently under development as the first-in-class anticancer drugs for targeted therapy of colon, pancreatic, prostate and lung cancer.