Preclinical Characterization of PRT3789, a Potent and Selective SMARCA2 Targeted Degrader

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Background

► SMARCA2/SwI/SNF-Related, ATPase Associated, Actin Dependent Regulator of Cytoskeleton (SWI/SNF) complexes play an important role in controlling various aspects of human cancers.3

Therefore, targeting SMARCA2 in SMARCA4-deleted cancers using selective SMARCA2 degraders... SWItch/Sucrose Non-Fermentable (SWI/SNF) complexes play an important role in controlling various aspects of human cancers.3 Non-missense mutation includes (A) Model of SMARCA2 degradation–induced synthetic lethality in SMARCA4-deleted cancers.

Key Findings

► Our potent and selectable SMARCA2 targeted degrader (PRT3789) shows favorable pharmacokinetic properties and induces strong synthetic lethality in SMARCA4-deleted cancers in vitro and in vivo. PRT3789 displays excellent SMARCA2 selectivity and potency in multiple cancer cell lines, including 100% to 150% of non-small-cell lung cancer (NSCLC) and SMARCA4-deficient cancer cell lines. [PRT3789] models were sensitive to PRT3789 versus WT and SMARCA2-deleted models. Cell lines in (A) PRT3789 inhibition of SMARCA2-deleted cancer cell lines, but not WT cancer cell lines as determined by Western blot and plaque infection protection assay using SMARCA2-deleted and WT 293T cell lines in multiple cancer cell lines and non-small-cell lung cancer cell lines as evaluted by (A) and (B). PRT3789 results in PRT3789 versus WT and SMARCA2-deleted cell lines, models are sensitive to PRT3789 versus WT and SMARCA2-deleted models. Cell lines in (A) PRT3789 inhibition of SMARCA2-deleted cancer cell lines, but not WT cancer cell lines as determined by Western blot and plaque infection protection assay using SMARCA2-deleted and WT 293T cell lines in multiple cancer cell lines and non-small-cell lung cancer cell lines as evaluted by (A) and (B). PRT3789 results in (A) PRT3789 inhibition of SMARCA2-deleted cancer cell lines, but not WT cancer cell lines as determined by Western blot and plaque infection protection assay using SMARCA2-deleted and WT 293T cell lines in multiple cancer cell lines and non-small-cell lung cancer cell lines as evaluted by (A) and (B). PRT3789 results in (A) PRT3789 inhibition of SMARCA2-deleted cancer cell lines, but not WT cancer cell lines as determined by Western blot and plaque infection protection assay using SMARCA2-deleted and WT 293T cell lines in multiple cancer cell lines and non-small-cell lung cancer cell lines as evaluted by (A) and (B). PRT3789 results in... PRT3789 is a selective inhibitor of SMARCA2 protein expression in human PBMCs following treatment... PRT3789 is a selective inhibitor of SMARCA2 protein expression in human PBMCs following treatment... PRT3789 is a selective inhibitor of SMARCA2 protein expression in human PBMCs following treatment... PRT3789 is a selective inhibitor of SMARCA2 protein expression in human PBMCs following treatment... PRT3789 is a selective inhibitor of SMARCA2 protein expression in human PBMCs following treatment... PRT3789 is a selective inhibitor of SMARCA2 protein expression in human PBMCs following treatment... PRT3789 is a selective inhibitor of SMARCA2 protein expression in human PBMCs following treatment... PRT3789 is a selective inhibitor of SMARCA2 protein expression in human PBMCs following treatment... PRT3789 is a selective inhibitor of SMARCA2 protein expression in human PBMCs following treatment... PRT3789 is a selective inhibitor of SMARCA2 protein expression in human PBMCs following treatment... PRT3789 is a selective inhibitor of SMARCA2 protein expression in human PBMCs following treatment... PRT3789 is a selective inhibitor of SMARCA2 protein expression in human PBMCs following treatment... PRT3789 is a selective inhibitor of SMARCA2 protein expression in human PBMCs following treatment... PRT3789 is a selective inhibitor of SMARCA2 protein expression in human PBMCs following treatment... PRT3789 is a selective inhibitor of SMARCA2 protein expression in human PBMCs following treatment... PRT3789 is a selective inhibitor of SMARCA2 protein expression in human PBMCs following treatment... PRT3789 is a selective inhibitor of SMARCA2 protein expression in human PBMCs following treatment... PRT3789 is a selective inhibitor of SMARCA2 protein expression in human PBMCs following treatment... PRT3789 is a selective inhibitor of SMARCA2 protein expression in human PBMCs following treatment... PRT3789 is a selective inhibitor of SMARCA2 protein expression in human PBMCs following treatment... PRT3789 is a selective inhibitor of SMARCA2 protein expression in human PBMCs following treatment... PRT3789 is a selective inhibitor of SMARCA2 protein expression in human PBMCs following treatment... PRT3789 is a selective inhibitor of SMARCA2 protein expression in human PBMCs following treatment... PRT3789 is a selective inhibitor of SMARCA2 protein expression in human PBMCs following treatment... PRT3789 is a selective inhibitor of SMARCA2 protein expression in human PBMCs following treatment... PRT3789 is a selective inhibitor of SMARCA2 protein expression in human PBMCs following treatment... PRT3789 is a selective inhibitor of SMARCA2 protein expression in human PBMCs following treatment... PRT3789 is a selective inhibitor of SMARCA2 protein expression in...