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Discovery of novel anti-CD33 antibody-enabled GSPT1 degraders for treatment of relapsed and refractory AML

Therapex Co., Ltd.

ONCOLOGY | **Candidate**

Product Type	Antibody-Drug Conjugate
Indication	Acute myeloid leukemia
Target	GSPT1
MoA(Mechanism of Action)	Antibody-Drug Conjugate(ADC) is generated to conjugate with CD33 antibody and GSPT1 molecular glue(MG) via linker. Upon binding to the CD33 antigen, the ADC is internalized within leukemia cells and GSPT1 MG is released from the conjugate via hydrolysis in the lysosome. The released GSPT1 MG rapidly induced the degradation of GSPT1, impaired translation termination and robust cytotoxic activity including TP53-mutated AML cells.
Competitiveness	- Therapex' ADC shows potent and sustained degradability against GSPT1 superior to competitor ADC (ORM-6151) - Therapex' ADC significantly induces anti-leukemic activity with picomolar GI50 value in TP53 or FLT3 mutated AML cell lines, and spares CD33-negative leukemia cell line and human PBMC with >100 folds in vitro TI value - Single 1 mg/kg dose of Therapex' ADC leads to completely regress tumor in subcutaneously MV4-11(*FLT3* m+) and HL-60(*TP53* m+) engrafted mice models - There is no tumor regrowth in Therapex' ADC treated-group till day on 42, whereas ORM-6151-treated group drastically develops tumor regrowth on Day 22 after regression
Development Stage	Lead
Route of Administration	intravenous injection (IV)

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