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Preclinical Discovery of Pearl-101, a First-in-Class Poly(ADP-ribose)-Stabilizing Peptide Therapeutic for BRCA-Mutant Therapy-Resistant Breast Cancer

Pearlsinmires Co., Ltd.

PearlsInMires

ONCOLOGY | **Candidate**

Product Type	rProtein
Indication	BRCA-Mutant Therapy-Resistant Breast Cancer
Target	Poly(ADP-ribose) (PAR)
MoA(Mechanism of Action)	**First-in-Class PAR-Stabilizing Peptide Therapeutic** Pearl-101 is a First-in-Class PAR-stabilizing peptide therapeutic designed to induce Parthanatos in Platinum- and PARP inhibitor-resistant tumors. Unlike PARP/PARG inhibitors, Pearl-101 directly targets the PAR polymer itself to drive irreversible tumor cell death. This differentiated mechanism of action may enable: • Therapeutic activity in Platinum- and PARP inhibitor-resistant tumors • Potential bypass of BRCA reversion-associated resistance • HR-independent anti-tumor activity • Caspase-independent programmed cell death induction (Parthanatos)
Competitiveness	**Ⅰ. First-in-Class PAR-Stabilizing Therapeutic** Directly targets and stabilizes PAR polymer rather than PAR metabolism enzymes **Ⅱ. Designed for Post-PARPi Resistance** Developed specifically for Platinum/PARP inhibitor-resistant BRCA-mutant tumors **III. Differentiated Parthanatos Mechanism** Induces irreversible tumor cell death through PAR accumulation and AIF signaling **IV. Superior Potential vs PARG Inhibitors** Demonstrated differentiated potency and survival benefit in resistant tumor models **Ⅴ. Broad Combination & Expansion Potential** Potential applicability across BRCA/BRCAness tumors and combination settings
Development Stage	Candidate
Route of Administration	Once-weekly intravenous infusion