

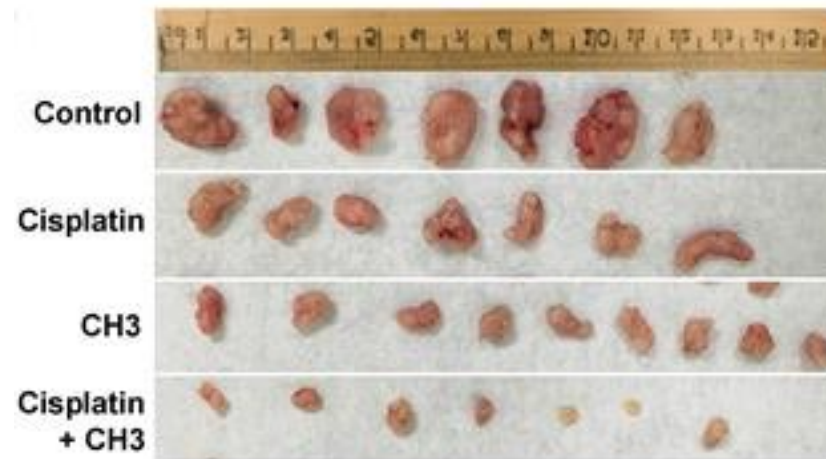
ChemRes Therapeutics

Targeting chemotherapy resistance in cancer

Developed by The George Washington University

Elevator Pitch – Executive Summary

- ▶ Up to 80% of ovarian cancer patients develop resistance towards platinum based chemotherapy drugs which are most commonly used against cancer
- ▶ There is an urgent need for therapeutic agents that overcome such drug resistance
- ▶ **We developed small molecule drugs that overcome platinum drug resistance in vivo and in vitro**
 - ▶ These compounds inhibit Acidic nucleoplasmic DNA-binding protein 1 (And1) or sentrin-specific protease 1 (SEN1) and re-sensitize platinum-resistant cancer cells to platinum drugs



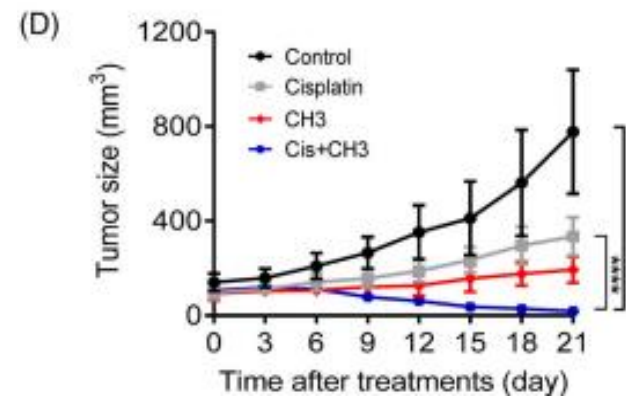
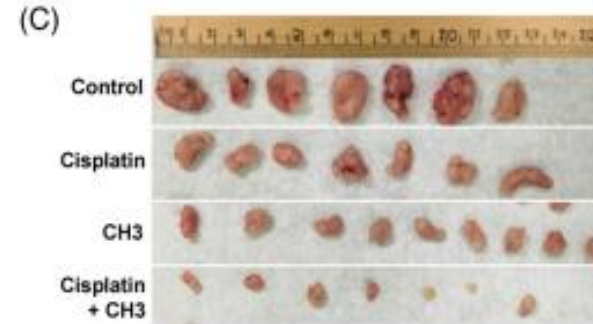
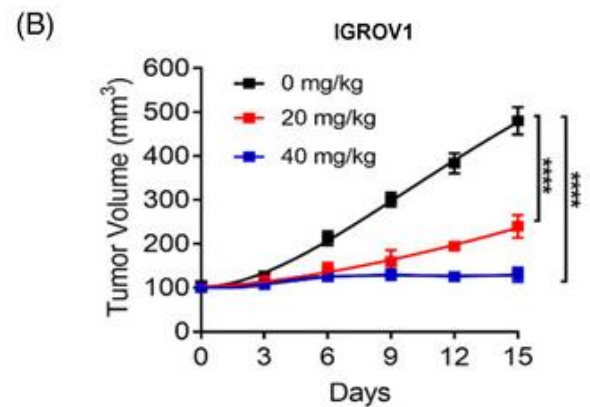
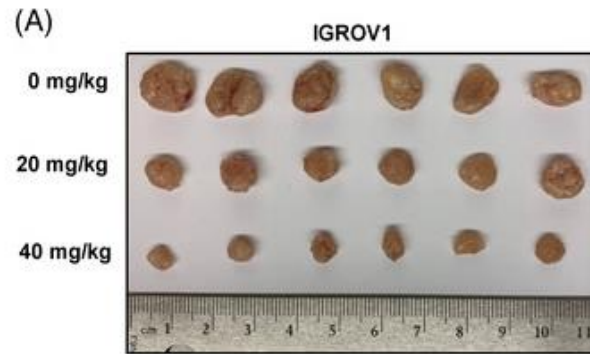
Compound CH3 overcomes cisplatin resistance in mouse ovarian cancer model
(Li et al., Clin Transl Med. 2021)

What is the pain in the market?

- ▶ Ovarian cancer ranks 5 in cancer deaths among women
- ▶ Platinum-based chemotherapy drugs are most widely used against cancer
- ▶ 70-80% of advanced-stage ovarian-cancer patients develop a resistance to platinum-based chemotherapy
- ▶ There is a need for therapeutic agents to overcome platinum drug resistance

Our Solution: compounds inhibiting And-1 protein

- ▶ These compounds inhibit cancer cell growth and overcome platinum drug resistance of Ovarian Cancer *in vitro* and *in vivo*
- ▶ These inhibitors induce And-1 degradation via a proteasome degradation pathway



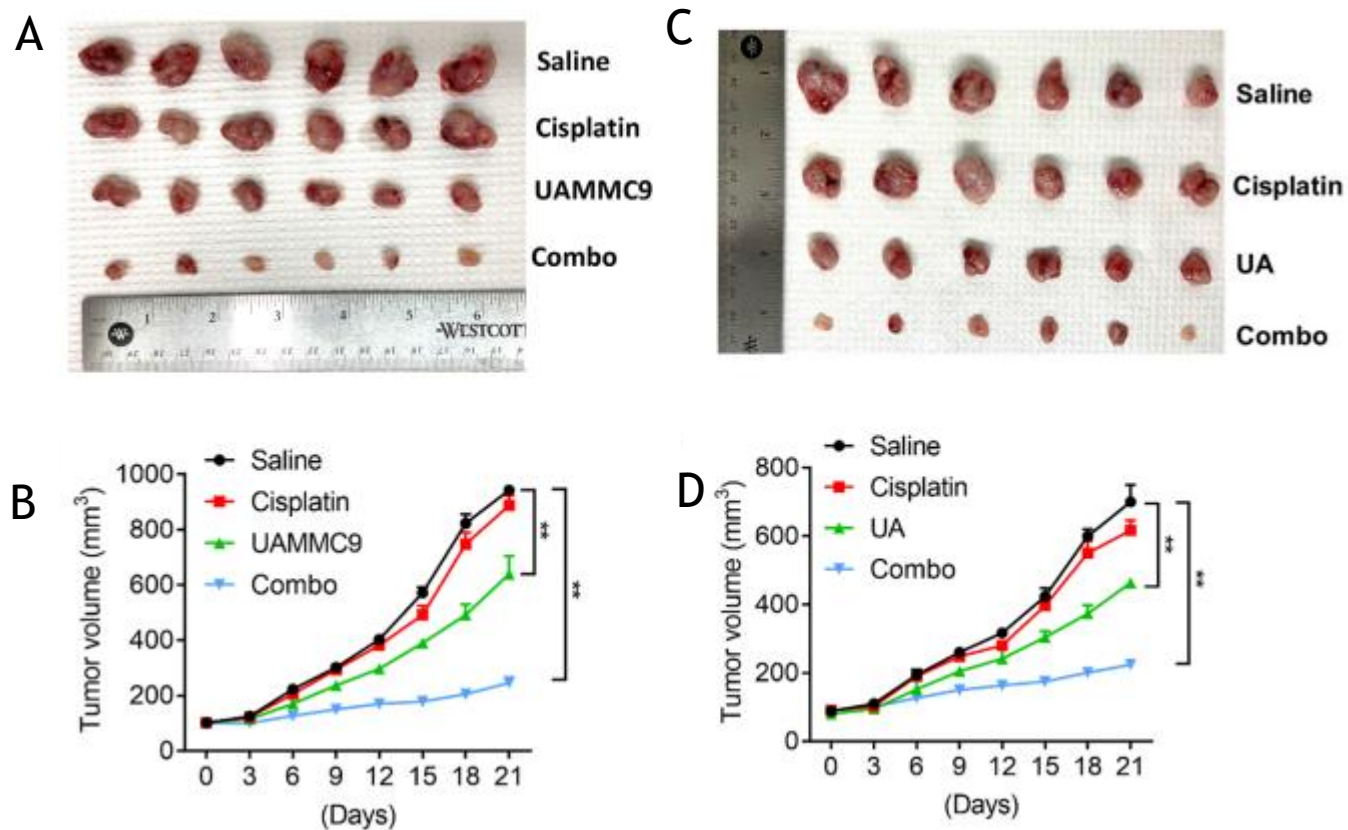
A-B: CH3, an And-1 inhibitor, significantly inhibits tumor growth mouse ovarian cancer model

C-D: CH3 overcomes cisplatin resistance in mouse ovarian cancer model

(Li et al., Clin Transl Med. 2021)

Our Solution: compounds inhibiting SENP1 enzyme

- ▶ Identified ursolic acid as a potent SENP1 inhibitor that overcomes platinum drug resistance in ovarian cancer in vitro and in vivo
- ▶ We developed novel ursolic acid derivatives which also inhibit SENP1 activity



A-B: UAMMC9, a SENP1 inhibitor, significantly inhibits tumor growth mouse ovarian cancer model

C-D: Ursolic acid overcomes cisplatin resistance in mouse ovarian cancer model

(Zhang et al., Clin Transl Med. 2021)

Patent Protection

- ▶ And-1 inhibitors:

- ▶ PCT application number: PCT/US2021/26164, filed on 4/7/2021 – nationalized in US and EU.

- ▶ SENP1 inhibitors:

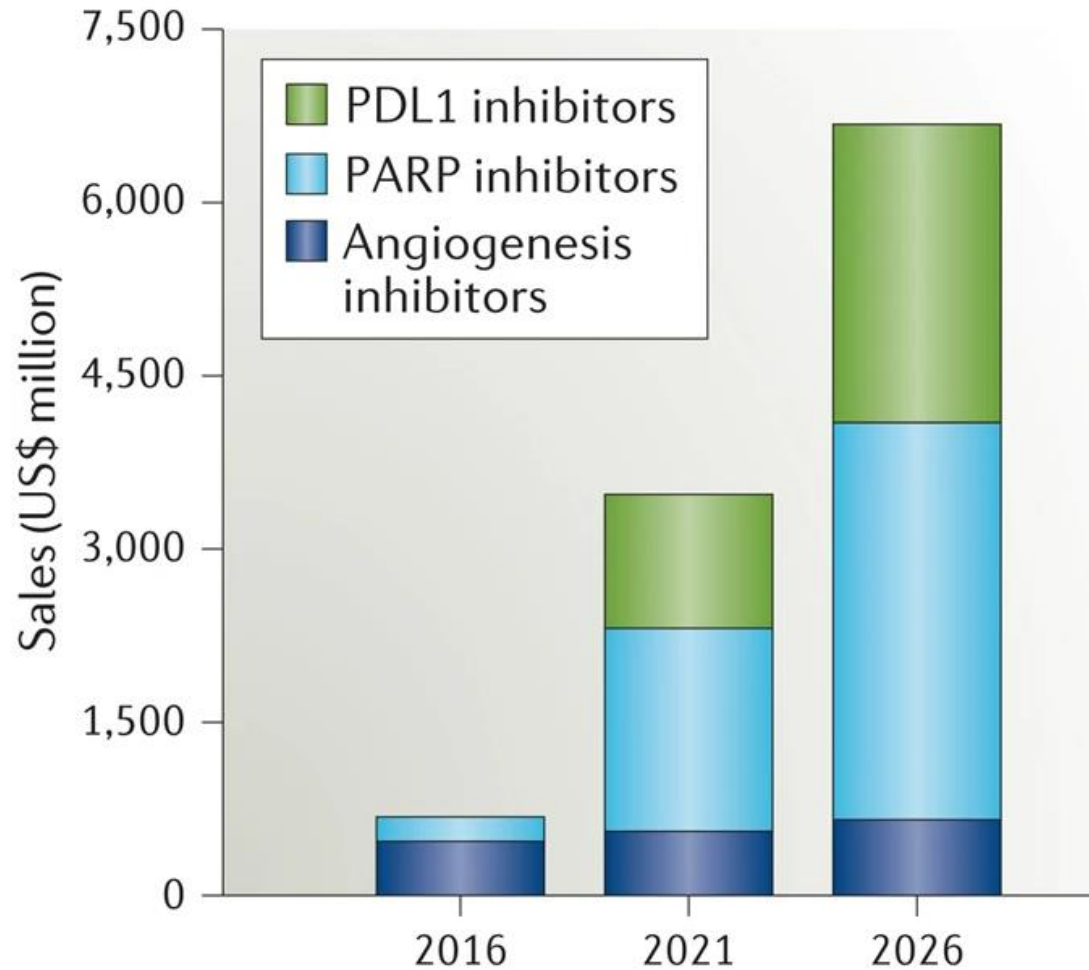
- ▶ PCT application number: PCT/US2021/20866, filed on 3/4/2021 – nationalized in US only.

Market Landscape

- ▶ The global Ovarian Cancer Market was USD 1.54 billion in 2021, and is expected to grow at a 23.8% CAGR between 2022 and 2030
- ▶ In 2022, it is estimated that there will be 19,880 new cases of ovarian cancer and an estimated 12,810 people will die of this disease in the US
- ▶ >60% of patients with ovarian cancer are diagnosed with advanced disease, the main treatment is platinum-based chemotherapy
- ▶ The global Platinum (Pt) Based Cancer Drugs market was valued at USD 1.3 billion in 2018 and is expected to exhibit a CAGR of 4.1% between 2019 and 2026

Market Landscape

Current and forecast future sales of key drug classes for ovarian cancer in the G7 nations (United States, France, Germany, Italy, Spain, United Kingdom and Japan)



Source: Bamford et al., Nature Reviews Drug Discovery, 2017

Competition

- ▶ Combination therapies in trial to address platinum resistance include:

Drugs in combination	Development phase	Clinical trial identifier	Last update posted	Sponsor
Cediranib and Olaparib	Phase 2	NCT02345265	July 5, 2022	National Cancer Institute
Avelumab and chemotherapy	Phase 3	NCT02580058	July 29, 2022	Pfizer
Pembrolizumab and Niraparib	Phase 1/2	NCT02657889	Oct 27, 2021	Tesaro, Inc
Gemcitabine Hydrochloride Alone or With M6620	Phase 2	NCT02595892	Mar 24, 2022	National Cancer Institute
Gemcitabine Hydrochloride With or Without WEE1 Inhibitor MK-1775	Phase 2	NCT02101775	Aug 12, 2022	National Cancer Institute
Mirvetuximab Soravtansine versus chemotherapy	Phase 3	NCT02631876	Oct 14, 2020	ImmunoGen, Inc
Mirvetuximab soravtansine with Bevacizumab	Phase 1/2	NCT02606305	Dec 7, 2021	ImmunoGen, Inc
Batiraxcept /Placebo in combination with Paclitaxel	Phase 3	NCT04729608	July 1, 2022	Aravive, Inc.

Competition

- ▶ New platinum drugs in preclinical/clinical development include:

Drug	Development phase	Clinical trial identifier	Last update posted	Sponsor
Dicycloplatin	Phase 3	NCT05472896	July 25, 2022	Gao-jun Teng
LA-12	Not known	NA	NA	NA
PT-112 (Phosplatin)	Phase1/2	NCT03409458	April 26, 2022	Promontory Therapeutics Inc.
Phenanthriplatin	Preclinical	NA	NA	NA

- ▶ Nanoparticle formulations of platinum drugs in preclinical/clinical development include:

Drug	Development phase	Clinical trial identifier	Last update posted	Sponsor
LiPlaCis (liposomal formulation)	Phase1/2	NCT01861496	February 24, 2022	Allarity Therapeutics
Lipoplatin (liposomal formulation)	Phase 3	EudraCT Number: 2011-003601-25	NA	Regulon AE
ProLindac (polymer formulation)	NA	NCT00415298	January 10, 2014	University of California, San Diego

- ▶ Non-platinum based chemotherapy: 5-fluorouracil, taxanes, and irinotecan

Competition

► Selected therapies in the pipeline for ovarian cancer

Product	Companies	Target or mechanism of action	Development status
Atezolizumab*	Roche/Genentech	PDL1	III
Avelumab*	Pfizer/Merck KGaA	PDL1	III
Micellar paclitaxel	Oasmia Pharmaceuticals	Cytotoxic; cell cycle inhibitor	Preregistration
Lurbinectedin	PharmaMar/Chugai	Cytotoxic; cell cycle inhibitor	III
Veliparib	AbbVie	PARP	III
Trametinib*	Novartis	MEK	II/III
Fosbretabulin	Mateon Therapeutics	Vascular disrupting agent	II/III
Mirvetuximab soravtansine	ImmunoGen	Folate receptor alpha	III
Cediranib	AstraZeneca	VEGFR1-3	III
Gemogenovatumel-T	Gradalis	Tumour cell vaccine	III
AZD1775	AstraZeneca	WEE1	II
Acalabrutinib	AstraZeneca/ Acerta Pharma	BTK	II
Epacadostat	Incyte Corporation	IDO1	I/II
Cabiralizumab	Five Prime Therapeutics	CSF1R	I
Enoblituzumab	MacroGenics	B7-H3/CD276	I

Source: Bamford et al., Nature Reviews Drug Discovery, 2017

Competitive advantage

- ▶ Re-sensitize platinum-resistant cancer cells to platinum drugs
- ▶ No systemic toxicity or side effects observed in mice
- ▶ Overcomes cisplatin resistance in mouse ovarian cancer model
- ▶ Composition of matter intellectual property for new derivatives (AND-1i)

Lead Innovator

Wenge Zhu, PhD

- ▶ Professor of Biochemistry and Molecular Medicine at the George Washington University
- ▶ Research focused in DNA replication, cell cycle, DNA repair, drug discovery and drug resistance in cancer
- ▶ Identified multiple compounds for potential cancer treatment and filed several patents for cancer therapy



What are we looking for?

- ▶ Business mentor
- ▶ Serial entrepreneurs
- ▶ Industry / Market knowledge
- ▶ Investment / Financing
- ▶ Facilities / Strategic Partners