DBPR22998:A Potent QPCTL (IsoQC) Inhibitor Targeting CD47-SIRPα Axis for Cancer Immunotherapy

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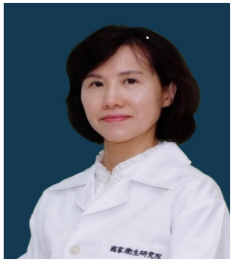

Dr. Chih-Hao Chen
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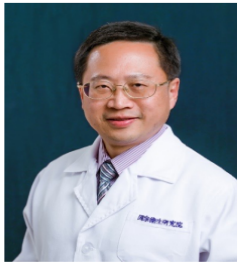

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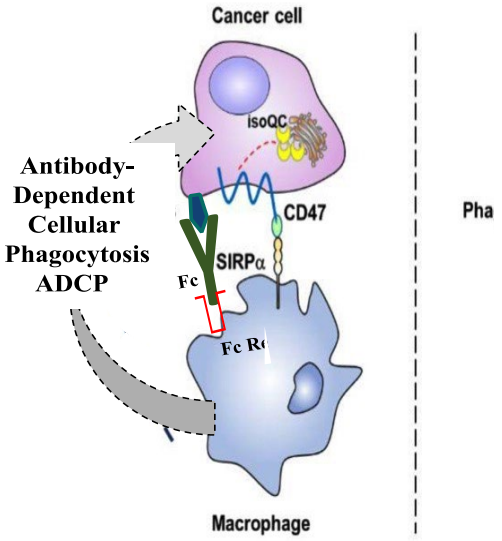
Disease Background and Global CD47 Inhibitors Market Analysis

CD47-SIRPα Signaling: Mask Macrophage to See Cancer Cells

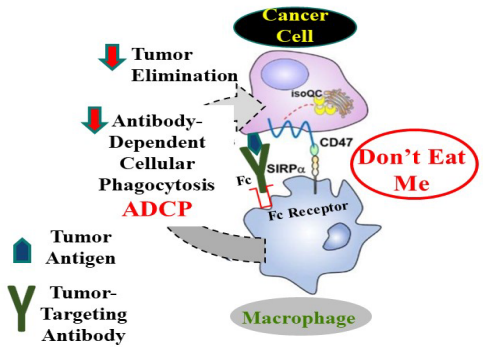


Market Size and Forecast	Drug Types	Highest Phase
2022-2030 Period • Global market size will be expected to surpass US $2 billion with a CAGR of 67% • Largest Region: USA • Combination therapies will be dominated	• Biologics: 74% • Peptides: 24% • Others: 1% • Small Molecules: < 1%	• Phase III: 1 • Phase II/III: 3 • Phase I/II: 7 • Phase I: 20 • IND filed: 2 • Preclinical: 54 • Biological Testing: 211

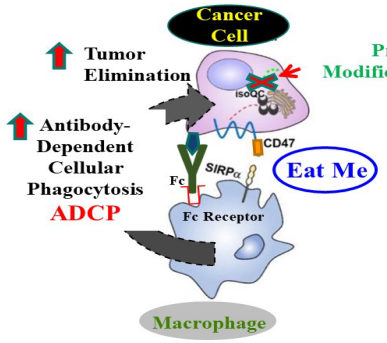
Source: InsightAce Analytic, 2022

Product Mechanism of Action and POC Data

CD47-SIRPα Signaling: Mask Macrophage to See Cancer Cells



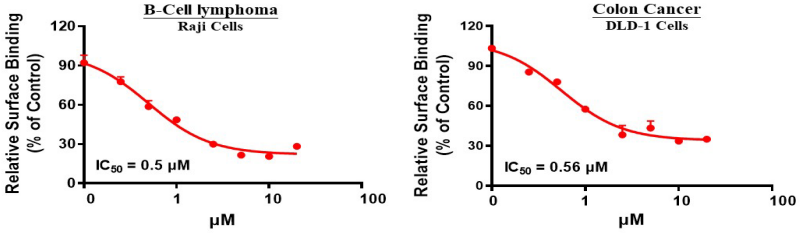
DBPR22998: A Potent IsoQC (QPCTL) Inhibitor Targeting CD47-SIRPα "Don't Eat Me" Signal



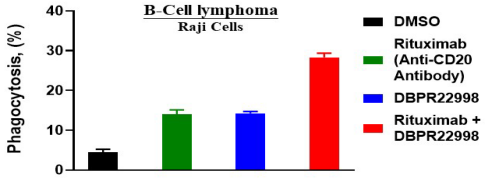
DBPR22998
(Ki= 0.55 nM)
Prevent Post Translational Modification (pGlu) of CD47 Protein

In Vitro Efficacy

DBPR22998 Blocks pGluCD47 And SIRPα-Fc Interaction

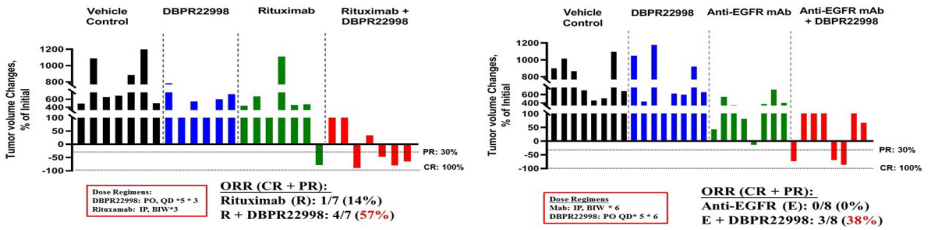


DBPR22998 in Combination with Anti-Tumor Antibody Rituximab Enhances ADCP vs. Rituximab Alone

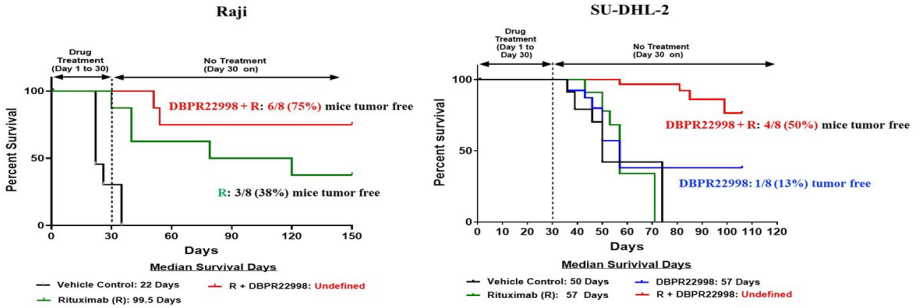


In Vivo Efficacy

DBPR22998 in Combination with Therapeutic Antibody Induces Tumor Regression



DBPR22998 in Combination with Rituximab Prolongs Post Treatment Survival in B-Cell Lymphoma Xenograft Models



Competitor Landscape Analysis
(Target Product Profiles)

Parameters	DBPR22998	Competitor - PQ912
IsoQC Enzymatic assay, Ki	**0.55 nM**	6 nM
CC2C6 Binding to pGluCD47, IC_{50}	**B-Lymphoma Raji**: **1.1** μM; **Ramos**: **0.6** μM **Colon DLD-1**: **0.6** μM **Ovarian SKOV-3**: **0.2** μM (EC_{50}, IC_{50} not reached) **Head/Neck FaDu**: **0.6** μM (EC_{50}, IC_{50} not reached)	**B-Lymphoma Raji**: 6.0 μM; **Ramos**: 2.4 μ M **Colon DLD1**: 3.2 μM **Ovarian SKOV-3**: 0.4 μM (EC_{50} , IC_{50} not reached) **Head/Neck FaDu**: 2 μM (EC_{50}, IC_{50} not reached)
pGluCD47 and SIRPα-Fc Binding, , IC_{50}	**B-Lymphoma Raji**: **0.5** μM **Colon DLD-1**: **0.6** μM	**B-Lymphoma Raji**: 2.9 μM **Colon DLD-1**: 1.3 μM
ADCP (%)	**B-Lymphoma Raji**: Rituximab (R) : 15%; R+ 22998: **28%**	**B-Lymphoma Raji**: Rituximab (R) : 15%; R+ 22998: 19.5%
In Vivo Anti-tumor Efficacy **(In combination with anti-tumor antibody therapeutics)**	• **B-Lymphoma Raji** TGI, % of Control: Rituximab + 22998: **89%**; TGI, % of Rituximab: **72%** Median survival days: Rituximab = 99.5 days R + 100 mpk 22998 = **Undefined (disease-free)** • **Diffused Large B-Lymphoma SU-DHL-2** Median survival days: Rituximab = 57 days R + 100 mpk 22998 = **Undefined (disease-free)** • **Head and Neck FaDu** TGI, % of Control: Anti-EGFR mAb + 22998: **85%**; TGI, % of Anti-EGFR mAb: **46%** • **Murine colon MC38** TGI, % of Control: Anti-PDL1 mAb + 22998: **52%**; TGI, % of Anti-PDL1 mAb: **38%**	• **B-Lymphoma Raji** Median survival days: Rituximab = 99.5 days R + 100 mpk PQ912 = 102.5 days
Pharmacokinetics **(PO, mouse:30 mg/kg; rat: 5 mg/kg)**	**AUC (ng/g*hr)** Mouse = **56,451**; Rat: **3,117** **F (%)** Mouse = 43 ; Rat = 31	**AUC (ng/g*hr)** Mouse = 6,359; Rat: 181 **F (%)** Mouse = 82 ; Rat = 16
14-day Repeated Dose Toxicity in ICR mice	No significant toxicity @ 100 and 300 mg/kg/day Mild toxicity in organ weight change and mild liver enzymes by serum biochemistry analysis @ 500 mg/kg/day No decline in RBC and platelet numbers	NA

Product Summary including IP and publication

Key Features:

- An orally bioavailable small molecule isoQC (QPCTL) inhibitor modulating CD47-SIRPα "Do not eat me" cancer immune checkpoint activities
- Target post translational modification process of CD47 protein synthesis
- Opportunity for combination with anti-tumor antibody therapeutics and immune checkpoint inhibitors (ICIs)

Intellectual Properties:

- US (US10,584,120B2) , China, Taiwan, Japan, Korea, Canada, India and Australia substance patents granted; cancer indication PTC patent applications under review.

Market Positioning:

- Anti-CD47 monoclonal antibodies are the most extensively studies for cancer immunotherapy. As opposed to antibody approaches in clinical development, our small molecule isoQC (QPCTL) inhibitor DBPR22998 is a best-in-class and innovative therapeutic approach for boosting the efficiency of cancer immunotherapy.

Business Opportunities:

- License and/or collaboration and sponsored research