財團法人生物技術開發中心
Development Center for Biotechnology

Anti-MSLN ADC against cancer

Institute of Pharmaceutics
Development Center for Biotechnology

Presenter : Shih-Hsien Chuang Ph.D.
Mr. Tony Chung

OOOO/OO/OO Updated

Development Center for Biotechnology, DCB

400+

RD/BD professionals serving as the innovation hub for early drug development.

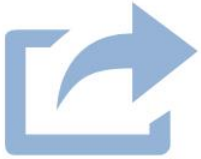
36

Founded in 1984, non-profit RD institution subsidized by the Ministry of Economic Affairs of Taiwan.

1200+

The premium drug development entity and connected with **1200+ biotech** of TW.

25



20+ out licensed assets and 5 Spin offs under **out-licensing** and **co-development** model.

Project Team

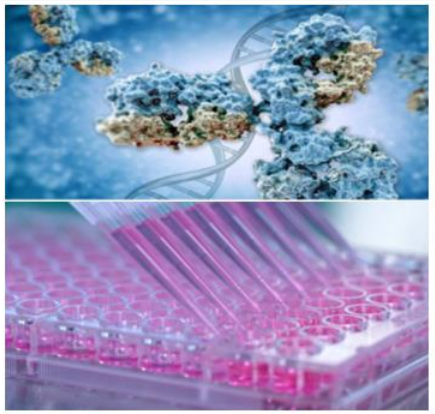
T
E
A
M

Project leader

Simon Shih-Hsien Chuang, Ph.D
Yi-Jen Chen, Ph.D.
Synthetic Chemistry & Conjugation

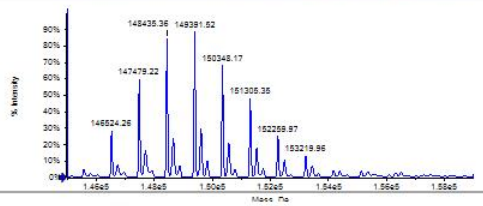
Biology

Shih-Chong Tsai, Ph.D.
Monoclonal Antibody
Ying-Shuan E. Lee, Ph.D.
Cytotoxicity
Chuan Lung Hsu, Ph.D.
Binding & Internalization



DMPK

Tzungjie Yang, Ph.D.
LC/MS Characterization



In vivo Pharmacology

Mei-Ling Hou, Ph.D
Animal Models

Mesothelin: Target for Cancer Treatment

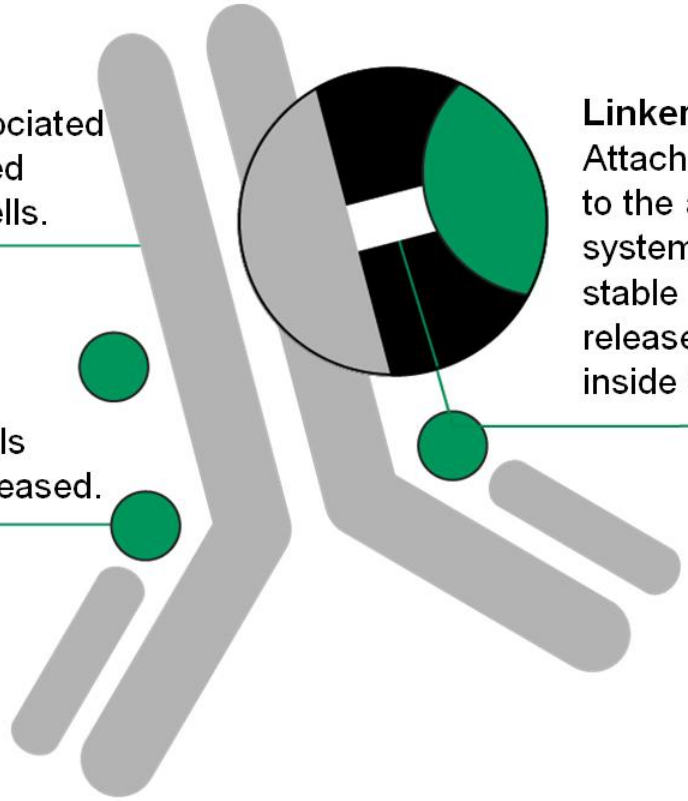
- Mesothelin is a differentiation antigen overexpressed in many solid tumors.
- Its operational tumor selectivity has been clinically proven.
- Anti-MSLN ADC is a potential format against MSLN positive tumors.

Tumor Type	No of patients with MSLN+	Percentage
Mesothelioma (Epithelioid)	248 of 261	95%
Pancreatic adenocarcinoma	303 of 357	85%
Epithelial ovarian cancer	346 of 494	70%
NSCLC (adenocarcinoma)	1082 of 1686	64%
Gastric cancer	312 of 666	47%
Biliary cancer (extrahepatic)	93 of 98	95%
Endometrial cancer	34 of 58	59%
Triple-negative breast cancer	33 of 50	66%

Antibody-Drug Conjugate (ADC)

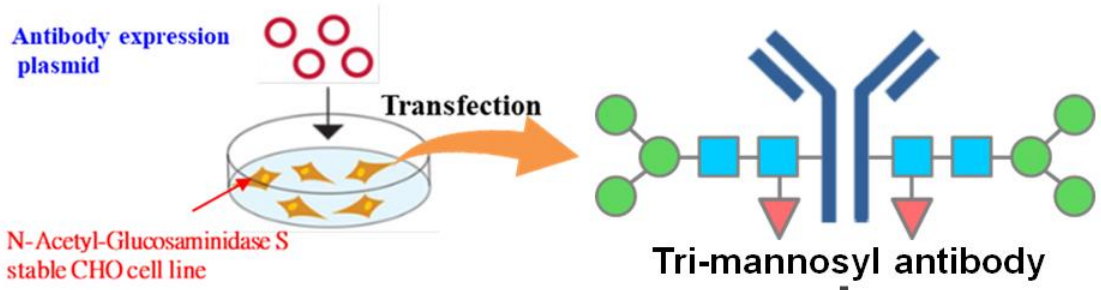
Antibody
Specific for a tumor-associated antigen that has restricted expression on normal cells.

Cytotoxic agent
Designed to kill target cells when internalized and released.



Linker
Attaches the cytotoxic agent to the antibody. Newer linker systems are designed to be stable in circulation and release the cytotoxic agent inside targeted cells.

Tri-mannosyl ADC Platform



GnT-I : N-Acetyl glucosamin transferase I
GnT-II : N-Acetyl glucosamin transferase II
UDP-GlcNAz : Azido-N-acetylglucosamine

One-step : DAR4 with homogenous payload

Sequential : DAR4 with Dual payloads

GnT-I and GnT-II

UDP-GlcNAz

GnT-I

Payloads A

UDP-GlcNAz

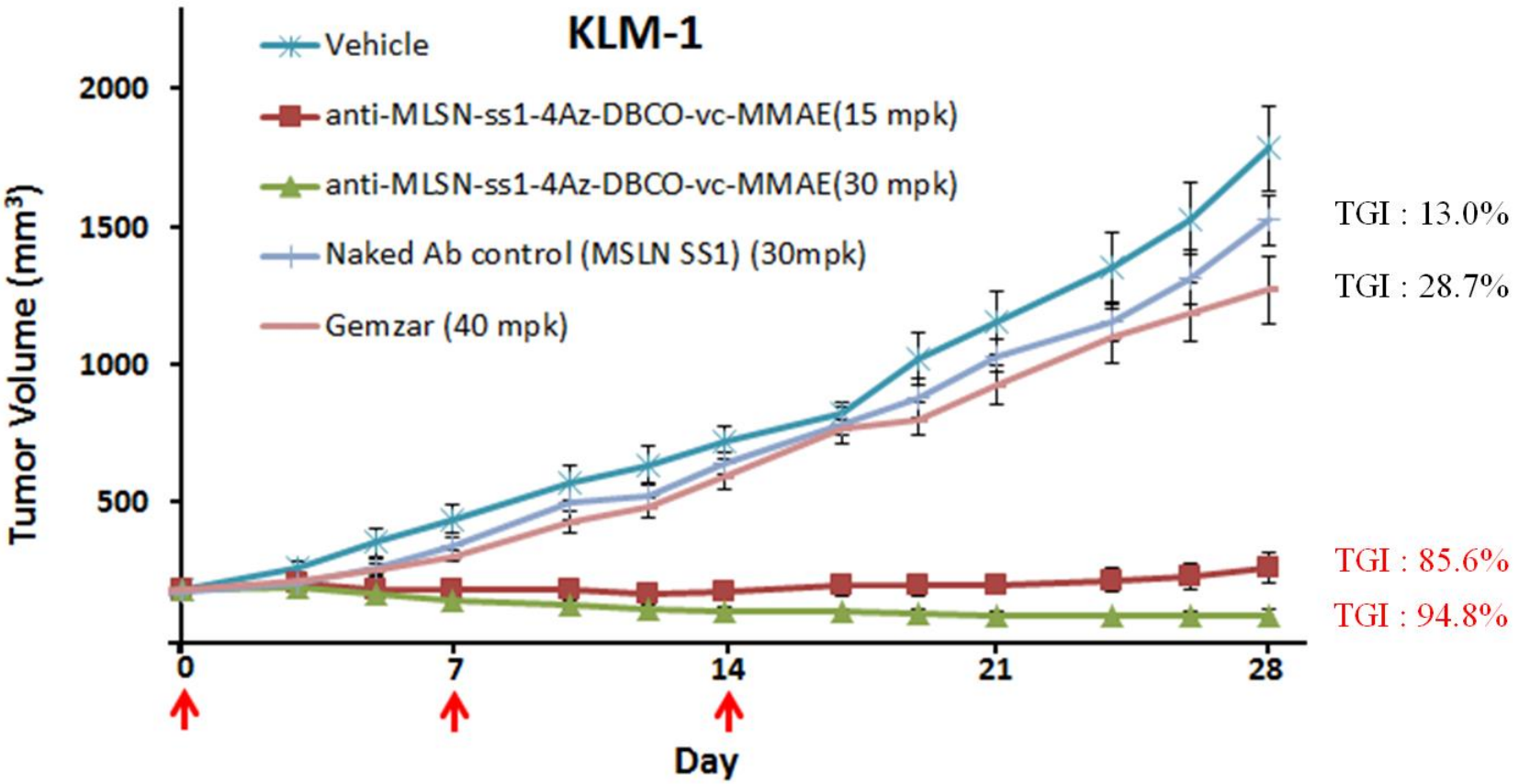
GnT-II

Payloads B

DAR= 4

DAR= 2 + 2

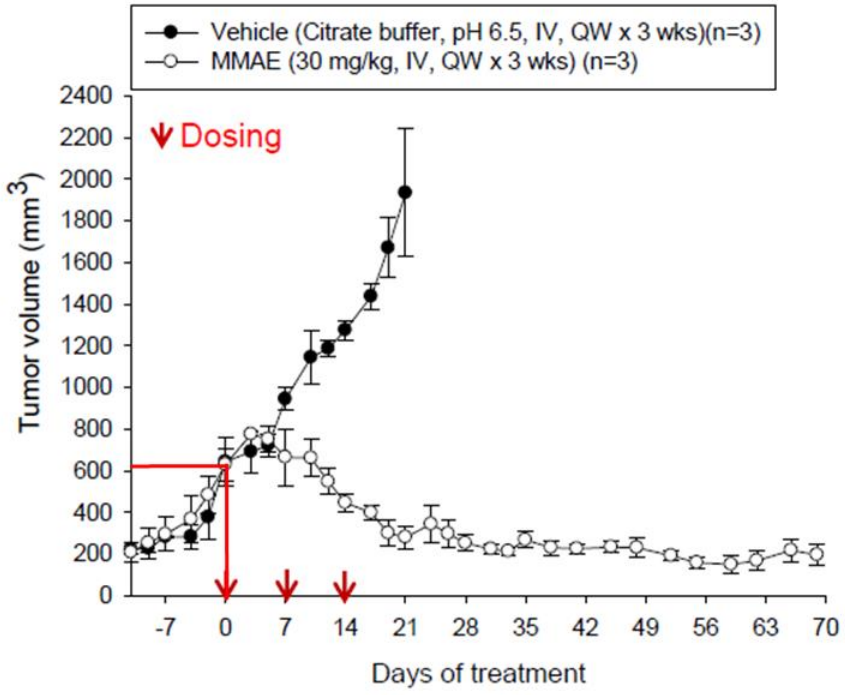
Anti-MSLN ADC Show Great Potency in Pancreatic Cancer Model



Trimannosyl anti-MSLN ADCs showed great antitumor activity in 15 mpk and 30 mpk without any death or body weight loss.

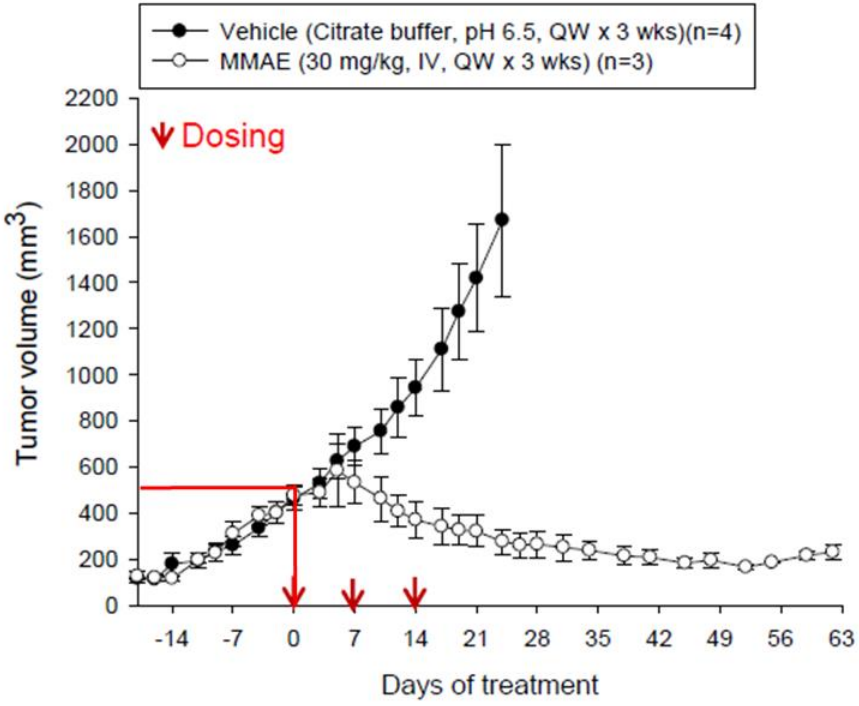
Anti-MSLN ADC Effective on Large Tumor

> 600 mm^3



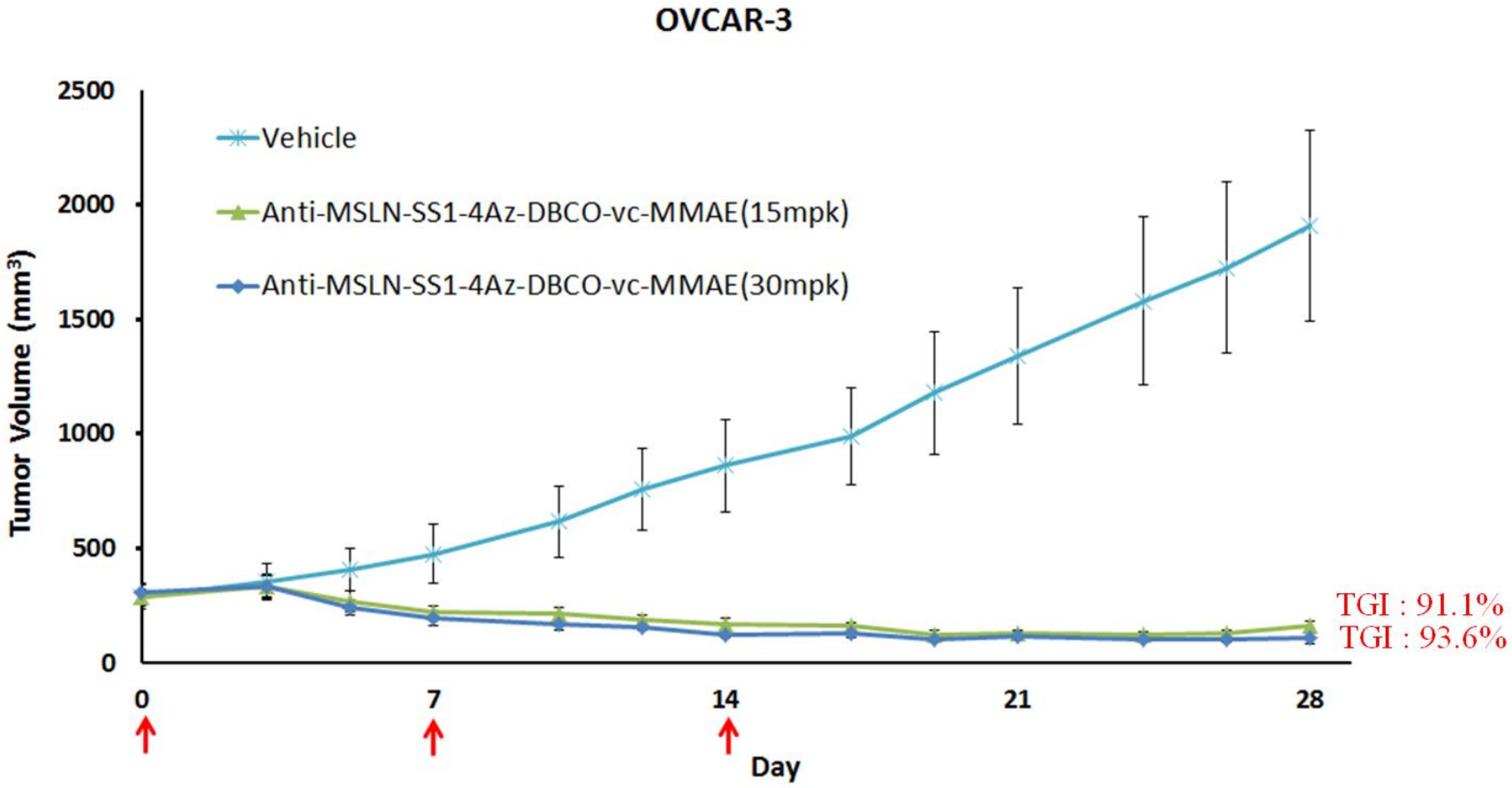
	TGI % (1-T/C)									
Treatment	D0	D3	D5	D7	D10	D12	D14	D17	D19	D21
MMAE (30 mpk)	0	-17	-4	32	42	55	66	73	83	86

> 500 mm^3



	TGI % (1-T/C)										
Treatment	D0	D3	D5	D7	D10	D12	D14	D17	D19	D21	D24
MMAE (30 mpk)	0	11	13	27	42	55	63	71	75	79	84

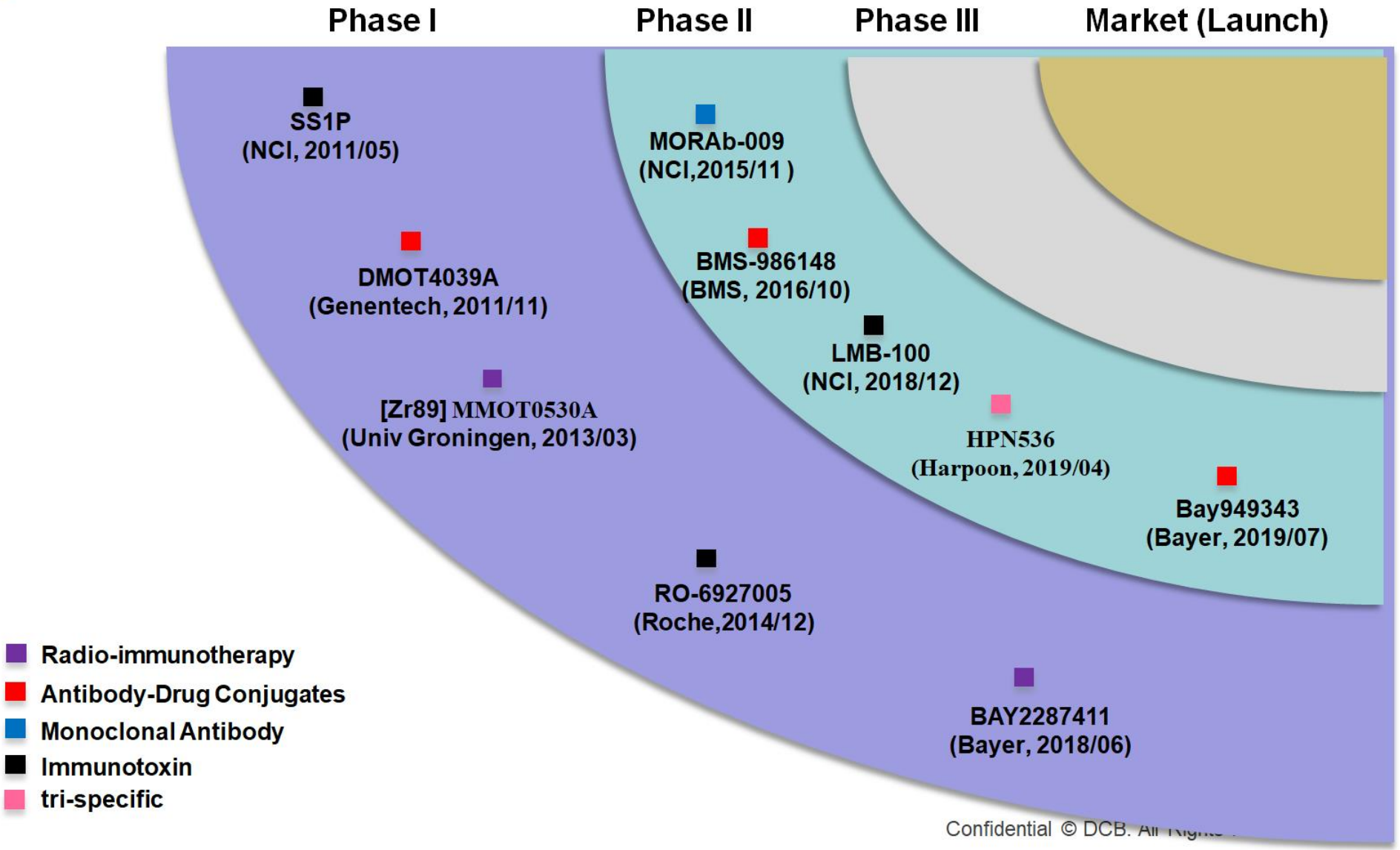
Anti-MSLN ADC Show Great Potency in Ovarian Cancer Model



- Trimannosyl anti-MSLN ADCs showed great antitumor activity in 15 mpk and 30 mpk without any death or body weight loss.

Competitive Landscape of MSLN Products

There are many formats of MSLN related biologics in the clinical trial.



IP Protection over Anti-MSLN ADC

IP

- **Tri-mannosyl conjugation platform**

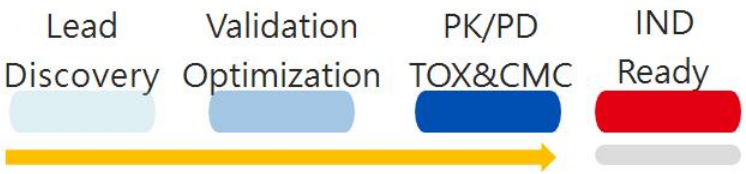
  PCT/US2017/068872 and TW application number: 106146600
- **Anti-MSLN ADC**

  Provisional patent was applied.

Partnership

- Exclusive License
- Co-development
- Other Ways of Partnership

Development status



Summary and Contact

DCB's anti-MSLN ADC

- DCB's anti-MSLN ADC showed great tumor growth inhibition (>90%) in KLM-1 and OVCAR-3 animal model without body weight loss.
- DCB's anti-MSLN ADC also showed great efficacy in large tumor model (>500 mm^3).
- Our own proprietary technology, trimannosyl conjugation, was applied in DCB's anti-MSLN ADC.
- DCB's anti-MSLN ADC showed uniform DAR (4), high affinity, good cytotoxicity.

BD Contact

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Thank you for your attention