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

Development of Antitumor AXL Kinase Inhibitor

Institute of Pharmaceutics
Development Center for Biotechnology

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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.

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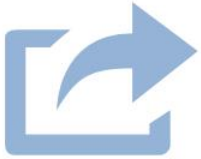


20+ out licensed assets and 5 Spin offs under **out-licensing** and **co-development** model.

Project Team

T **Project leader (pharmacologist)**
Chu-Bin Liao, Ph.D.

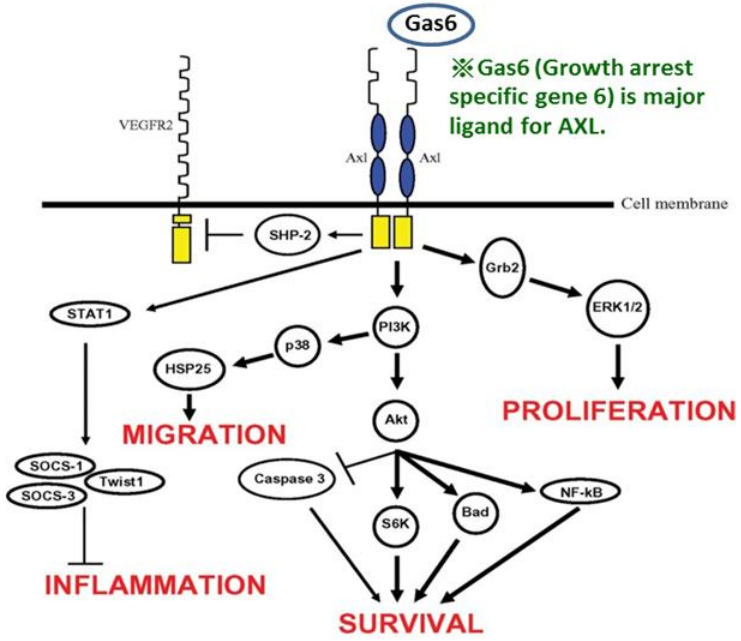
E **Chemistry leader**
Shih-Chieh Yen, Ph.D

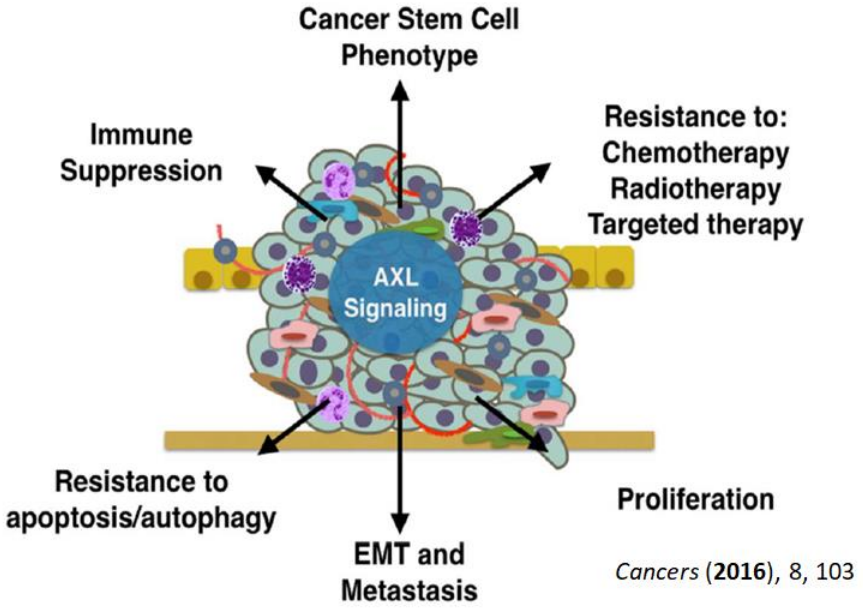
A **DMPK leader**
Yih-Chiao Tsai, Ph.D.

M ***In vivo* pharmacology leader**
Pei-Yi Tsai, Ph.D

Targeting AXL in Human Malignancy

- AXL is a member of the TAM (Tyro3, Axl, Mer) RTK subfamily.
- Up-regulation of AXL is associated with poor prognosis in several cancers.
- Overexpression, but not mutation, of AXL promotes tumor progression.





Cancers (**2016**), 8, 103

AXL overexpression drives wide-ranging processes, including enhanced tumor proliferation, resistance to chemotherapeutic and targeted agents, epithelial to mesenchymal transition (EMT), and decreased antitumor immune response.

Targeting AXL for cancer treatment as well as cancer immunotherapy

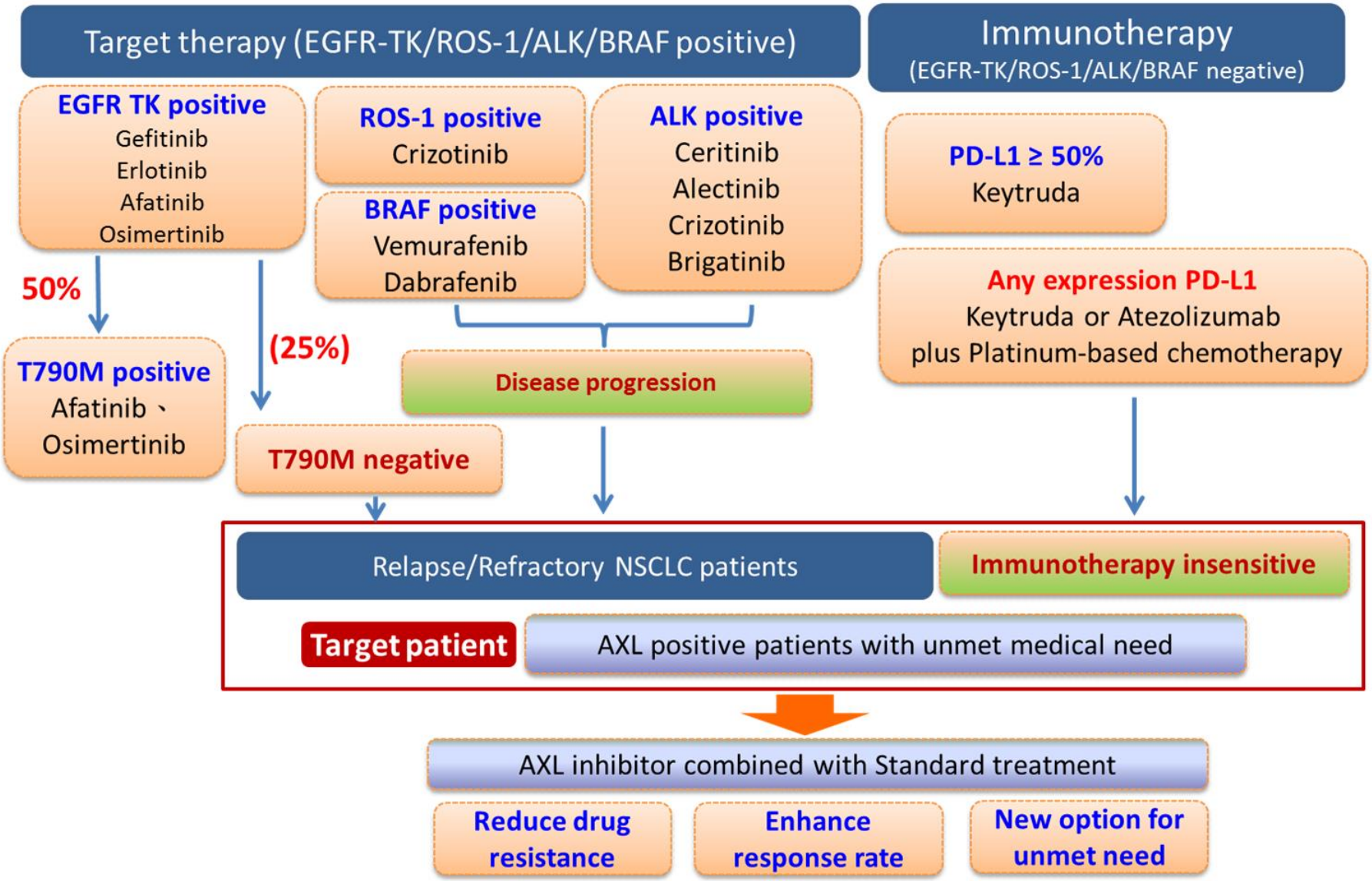
Current Clinical Trials of Selective AXL Inhibitors

◎To date, no selective AXL inhibitor gains approval

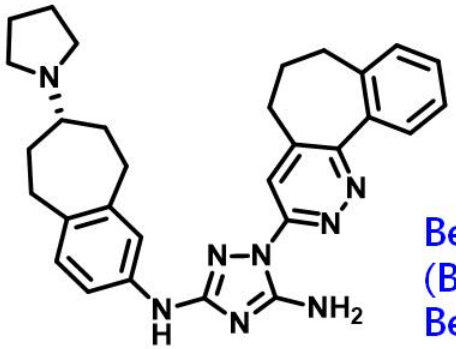
Drug/Phase	Clinical trial reference number	Indication	Status	Intervention
BGB324 Phase II	NCT03184558 (Start :2017.07.26 Complete:2018.08.30)	TNBC (Inflammatory Breast Cancer Stage IV)	Completed	BGB324 (400mg on days 1-3, and 200mg there after) in combination with pembrolizumab (200mg every 3 weeks).
BGB324 Phase II	NCT03184571 (Start :2017.10.17)	NSCLC (NSCLC Stage IV)	Recruiting	
BGB324 Phase I/II	NCT02872259 (Start :2017.02.13)	Melanoma	Recruiting	BGB324 (200mg once daily) in combination with pembrolizumab (2mg/kg every 3 weeks).
BGB324 Phase Ib/II	NCT03649321 (Start :2019.01.03)	Cancer of Pancreas	Recruiting	BGB324 200 mg oral daily, plus chemotherapy.
BGB324 Phase II	NCT03824080 (Start :2018.12.20)	AML	Recruiting	Daily dosing of 200mg for each 28 days cycle.
DS1205 Phase I	NCT03255083 (Start:2019.04.10)	NSCLC (EGFR-Mutant)	Recruiting	DS-1205c (twice daily: 200 mg, 400 mg, 600 mg, 800 mg) in combination with osimertinib (80 mg daily)
DS1205 Phase I	NCT03599518 (Start:2018.10.09)	NSCLC (EGFR-Mutant)	Recruiting	DS-1205c (twice daily: 200 mg, 400 mg, 600 mg, 800 mg) in combination with gefitinib (250 mg daily)

Combine with standard treatment was current trend for AXL inhibitor development

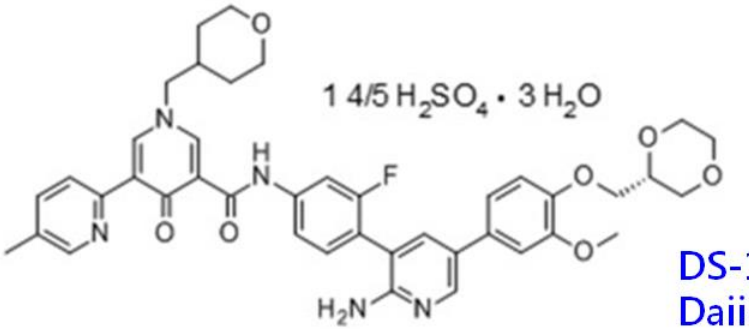
Target Patient Population — Advanced NSCLC



Highlight of Project

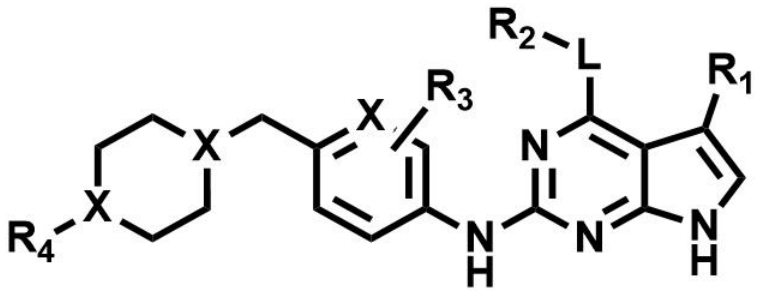


Bemcentinib
(BGB324 , R428)
BerGenBio



DS-1205b
Daiichi Sankyo

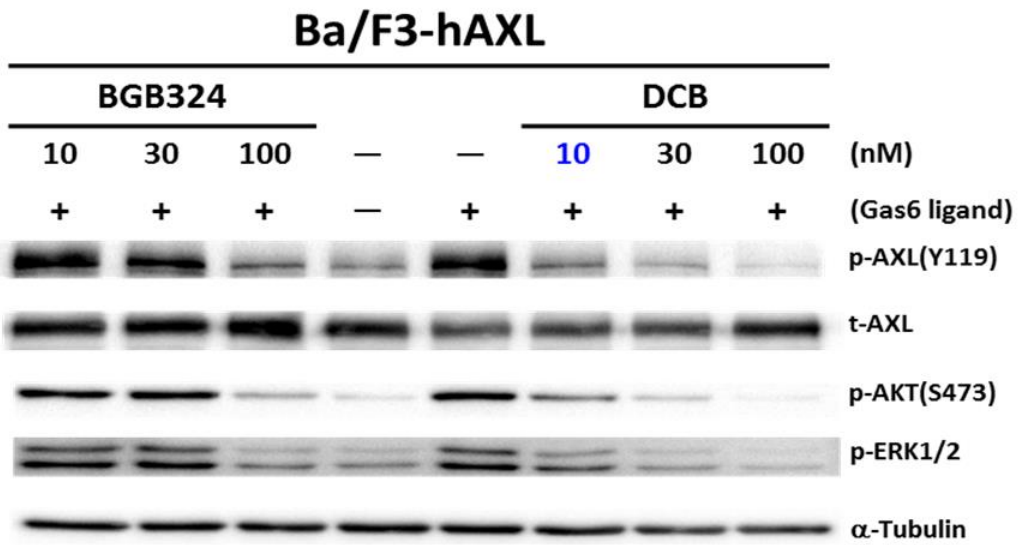
- **Clear structure activity relationship**
- **New chemical series with patentability and high potency against AXL kinase (IC_{50}< 10 nM)**

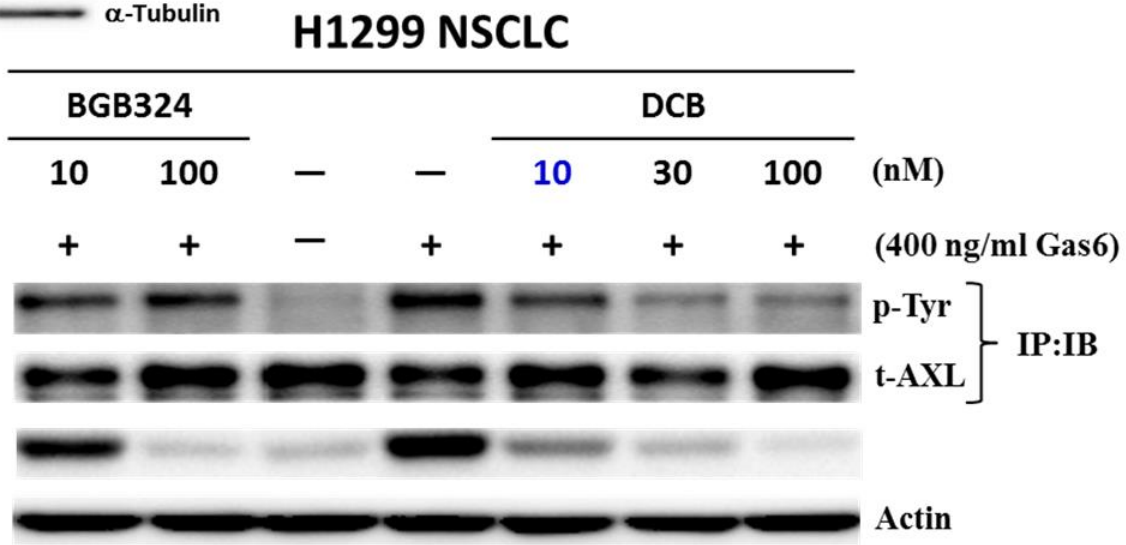


DCB pre-candidate	
Kinase	Mean IC_{50} (nM)
AXL	2
VEGFR2	94
MET	250

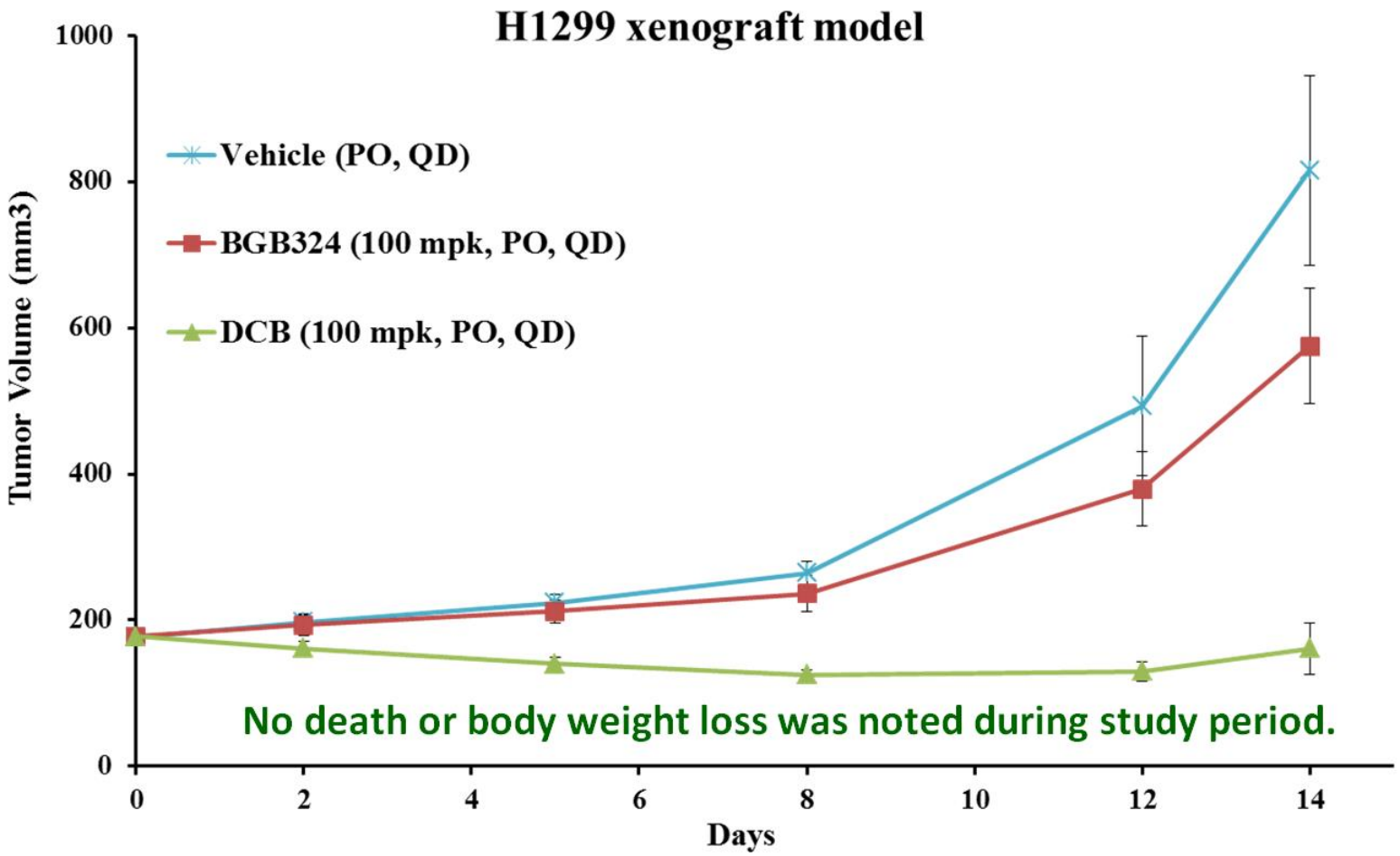
- DCB chemical series distinguished from known AXL inhibitors.
- Regular PCT application was filed on Dec. 26, 2018.

Cellular Potency of DCB Pre-candidate Is Superior to Benchmark BGB324





DCB Pre-candidate Is Orally Active



DCB' s Pre-candidate alone exhibits Superior antitumor activity to BGB324

IP/Dev Status

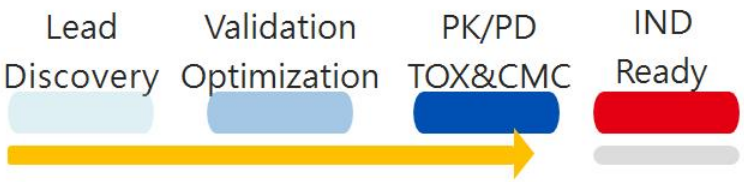
IP

TW(107147559) and PCT(PCT/US2018/067532) Patents Applied in December 2018.

Partnership

Exclusive License

Development status



Summary and Contact

- AXL inhibitor is a novel medication for cancer treatment as well as cancer immunotherapy. **To date, no selective AXL inhibitor gains approval.**
- The chemical structure of DCB pre-candidate is distinguished from known AXL inhibitors. **The regular patent has been applied.**
- **The general *in vitro* potencies of DCB pre-candidate is superior to reference compound BGB324**, which is currently in phase II clinical trial for treating lung cancer.
- DCB pre-candidate has acceptable PK property and orally antitumor activity. **Single agent of DCB pre-candidate exhibits superior antitumor activity to BGB324**.

BD Contact

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Thank you for your attention