BPR5K230: Small Molecule AXL and MERTK Dual Kinase Inhibitor as Anti-tumor and Immunomodulatory Agent

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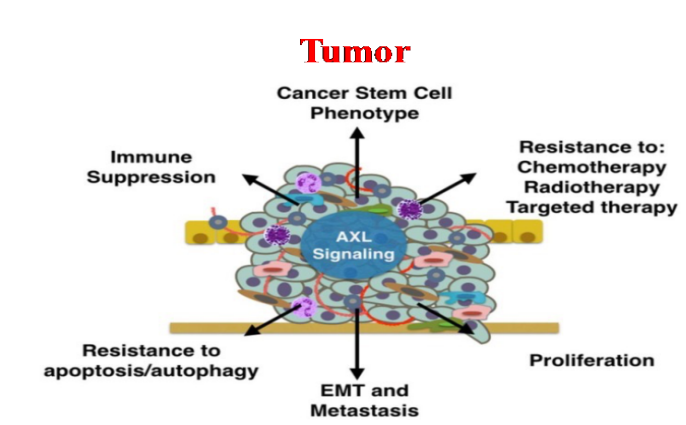
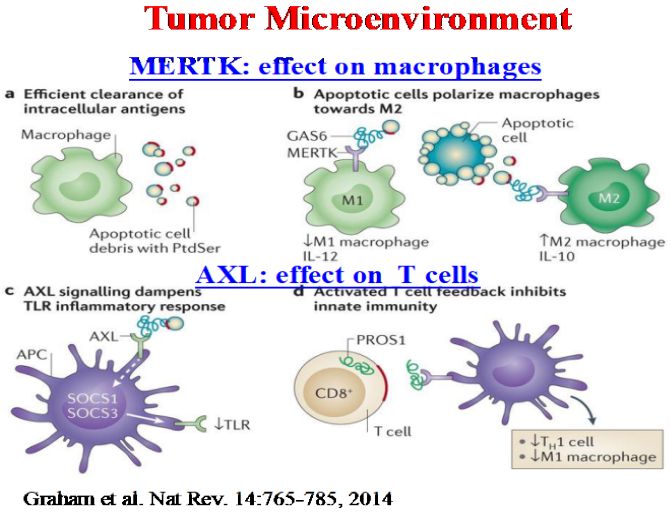
Disease Background and Market Size

AXL and MERTK Signaling in the Tumor and Tumor Microenvironment:

Drivers for Tumor Progression, Metastasis, Treatment Resistance and Immune Suppression



Rankin EB and Giaccia AJ. Cancers 8:103, 2016

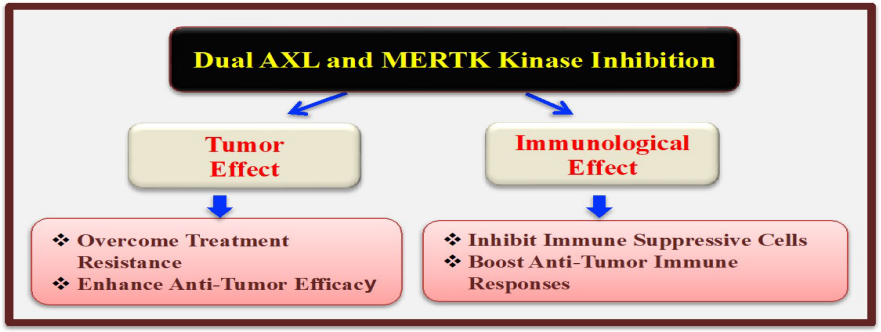


Graham et al. Nat Rev. 14:765-785, 2014

Market Size and Forecast	Therapy Types	Opportunities
2022-2031 Period • Global immuno-oncology market size will be expected to exceed USD261.7 billion by 2031 with a CAGR of 13.6% • Largest market share: North America	• Monoclonal Antibodies • Checkpoint Inhibitors • Immunomodulators • Cancer Vaccines • Cell Therapy • Others	• Increase in R/D infrastructure • Accuracy and newer therapy

Transparency Market Research Rep ID: TMRGL4312, 2022

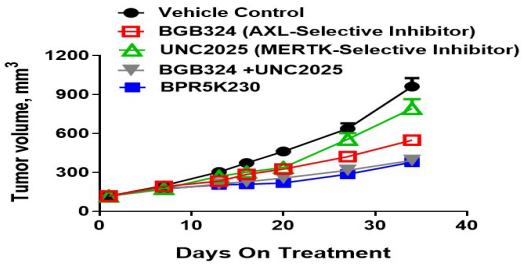
Product Mechanism of Action and Key POC Data



Axl and MERTK Dual Targeted Therapy

MDA-MB231 Human Triple Negative Breast Tumor Model

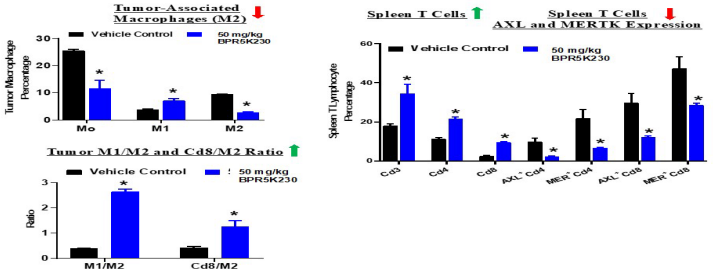
(AXL and MERTK Co-Expression on the Tumor Cells)



Immunomotherapy

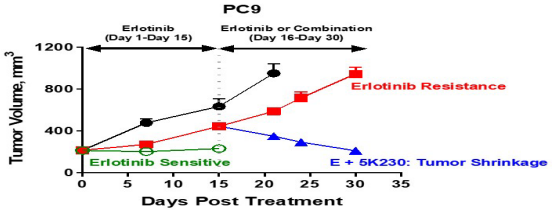
MC38 Murine Colon Tumor

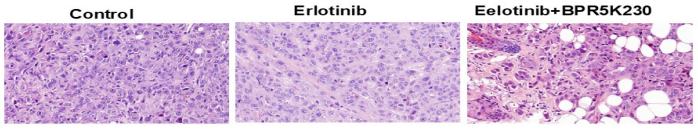
(AXL and MERTK Expression on the Immune Cells)



Overcoming Acquired Drug Resistance

Human EGFR mutated NSCLC Xenograft Tumor Model

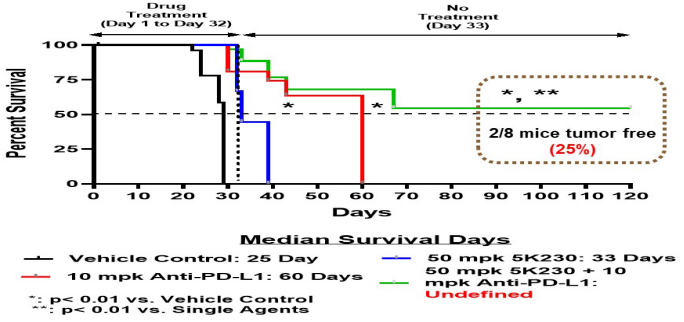




Combination Therapy

EMT6 Murine Triple Negative Breast Tumor

(AXL Expression on the Tumor Cells and AXL and MERTK Expression on the Immune Cells)



Competitor Landscape Analysis

(Target Product Profiles)

Parameters	BPR5K230	Ono-7475
Kinase Inhibitory Activities (IC_{50})	AXL: **7.2** nM, MERTK: **2.7** nM, TYRO3: **24.5** nM	AXL: 2.2 nM, MERTK: 13.9 nM, TYRO3: 5.6 nM
Immunomodulatory Activities (MC38 tumors, % of Vehicle Control)	Tumor M2 macrophage: **30%** Spleen Cd8: **400%**, Spleen Cd4: **200%** Spleen Cd8: AXL: **41%**, MERTK: **60%,** Pd1: **34%** Spleen Cd4: AXL: **24%** , MERTK: **31%**, Pd1: **43%**	NA
Pharmacokinetics (PO, mouse: 10 mg/kg; rat : 1 mg/kg)	**AUC (ng/g*hr)** Mouse = 8,588; Rat = 324 **F (%)** Mouse = **60%**; Rat = **34%**	NA

In Vivo Anti-tumor Efficacy (In combination with anti-tumor antibody therapeutics)	**Single Agent TGI, % of Vehicle Control**
	• MC38 murine colon tumor: **86%**
	• 4T1:murine TNBC **49%**
	• MDA-MB-231 human TNBC: **44%**
	• H1299 human NSCLC: **40%**
	• Hepa1-6 murine liver tumor: **60%**
	Combination, TGI, %
	• MC38 murine colon tumor:
	  • Combination: **52%** vs. anti-PD-L1 mAb
	• EMT-6 murine TNBC:
	  • Combination: **50 %** vs. anti-PD-L1 mAb
	• Erlotinib-resistant PC9 human $EGFR^{MT}$ NSCLC:
	  • 5K230 + erlotinib **induced tumor regression** and **apoptotic cell death**
	Median Survival Days:
	• 4T1 murine TNBC:
	  • Anti-PD-1: 30 days; Combination: **36 days**
	• EMT-6 murine TNBC:
	  • Anti-PD-L1: 60 days; Combination: **Undefined**
		Single Agent TGI, % of Vehicle Control
		• MC38 murine colon tumor: 45%
		• 4T1 murine TNBC: 12%
		• MDA-MB-231 human TNBC: 9%
		• Hepa 1-6 murine liver tumor: 16.7±12%

14-day Repeated Dose Toxicity (ICR mice)	• No significant toxicity @ 10, 30 and 100 mg/kg/day; mild decline in kidney serum biomarker CRE @ 30 and 100 mg/kg	• No significant toxicity @ 100 mg/kg/day; mild decline in kidney serum biomarker CRE 100 mg/kg

Product Summary including IP and publication

Key Features:

- BPR5K230 is a potent, orally bioavailable small molecule AXL and MERTK with anti-tumor and immunomodulatory activities
- BPR5K230 demonstrates single agent anti-tumor effect, prevent lung metastasis and prolongs median survival days in combination with immune checkpoint inhibitors in multiple preclinical murine tumor models
- BPR5K230 is most suitable for patients who fail current therapies and whose tumors and immune cells overexpress AXL and MERTK

Intellectual Properties:

- US patent application

Market Positioning:

- Novel AXL and MERTK dual kinase inhibitors can be positioned in kinase inhibitors markets, targeted cancer therapy market and immuno-oncology market.
- Drug and companion diagnostics (CDx) co-development would identify patients who are likely to benefit from BPR5K230, either alone or in combination with other agents, including chemotherapeutic agents, target agents or immune checkpoint inhibitors.

Business Opportunities:

- License and/or collaboration and sponsored research