

# Discovery of Small-Molecule Immunotherapeutics Dual-Targeting TAM and Treg in the Tumor Microenvironment

Chung-Ang University/College of Pharmacy

Disease Area	Cancer																																																												
Product Type	Small molecule																																																												
Indication	Melanoma and lung cancer																																																												
Target	PI3Kδ & CSF1R																																																												
Mechanism of Action	Immune activation by reduction of Treg and TAM in tumor microenvironment																																																												
Competitiveness	<div><div><div>- High potency for CSF1R and PI3Kδ</div><div>- High selectivity for PI3Kδ among PI3K subtypes (α, β, γ)</div><div>- Good kinase inhibition profile</div></div></div>																																																												
Development Stage	Lead																																																												
Route of Administration	Oral																																																												
Key Data	<div><div><div>- IC<sub>50</sub> values of the representative compounds</div><table><tr><th></th><th colspan="5">IC<sub>50</sub> (nM)</th></tr><tr><th></th><th>PI3Kα</th><th>PI3Kβ</th><th>PI3Kγ</th><th>PI3Kδ</th><th>CSF1R</th></tr><tr><td>MPD 001</td><td>61</td><td>&gt;1000</td><td>164</td><td>4</td><td>43</td></tr><tr><td>MPD 022</td><td>&gt;1000</td><td>&gt;1000</td><td>941</td><td>21</td><td>4</td></tr><tr><td>PI-103</td><td>4</td><td>-</td><td>60</td><td>10</td><td>-</td></tr><tr><td>Staurosporin</td><td>-</td><td>-</td><td>-</td><td>-</td><td>1.5</td></tr></table></div><div><div>- MC38 syngeneic mouse tumor model</div><div><div><div>Tumor volume</div><table><caption>Tumor volume (mm³) over time</caption><tr><th>Days post-treatment</th><th>Vehicle</th><th>50mg/kg PLX3397</th><th>50mg/kg MKPD 022 (BID)</th></tr><tr><td>0</td><td>100</td><td>100</td><td>100</td></tr><tr><td>4</td><td>300</td><td>280</td><td>180*</td></tr><tr><td>7</td><td>680</td><td>450*</td><td>300**</td></tr></table></div><div><div>Day 7</div><table><caption>Tumor volume (mm³) at Day 7</caption><tr><th>Group</th><th>Tumor volume (mm³)</th></tr><tr><td>Vehicle</td><td>~700</td></tr><tr><td>50mg/kg PLX3397</td><td>~450*</td></tr><tr><td>50mg/kg MKPD 022 (BID)</td><td>~300**</td></tr></table></div></div></div></div>		IC <sub>50</sub> (nM)						PI3Kα	PI3Kβ	PI3Kγ	PI3Kδ	CSF1R	MPD 001	61	>1000	164	4	43	MPD 022	>1000	>1000	941	21	4	PI-103	4	-	60	10	-	Staurosporin	-	-	-	-	1.5	Days post-treatment	Vehicle	50mg/kg PLX3397	50mg/kg MKPD 022 (BID)	0	100	100	100	4	300	280	180*	7	680	450*	300**	Group	Tumor volume (mm³)	Vehicle	~700	50mg/kg PLX3397	~450*	50mg/kg MKPD 022 (BID)	~300**
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