

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	PI3K δ & CSF1R																																			
Mechanism of Action	Immune activation by reduction of Treg and TAM in tumor microenvironment																																			
Competitiveness	<ul style="list-style-type: none"> - High potency for CSF1R and PI3Kδ - High selectivity for PI3Kδ among PI3K subtypes (α, β, γ) - Good kinase inhibition profile 																																			
Development Stage	Lead																																			
Route of Administration	Oral																																			
Key Data	<p>- IC₅₀ values of the representative compounds</p> <table border="1"> <thead> <tr> <th rowspan="2"></th> <th colspan="5">IC₅₀ (nM)</th> </tr> <tr> <th>PI3Kα</th> <th>PI3Kβ</th> <th>PI3Kγ</th> <th>PI3Kδ</th> <th>CSF1R</th> </tr> </thead> <tbody> <tr> <td>MPD 001</td> <td>61</td> <td>>1000</td> <td>164</td> <td>4</td> <td>43</td> </tr> <tr> <td>MPD 022</td> <td>>1000</td> <td>>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> </tbody> </table> <p>- MC38 syngeneic mouse tumor model</p> <p>Tumor volume</p> <p>Legend: Vehicle (blue), 50mg/kg PLX3397 (red), 50mg/kg MKPD 022 (BID) (green)</p> <p>Y-axis: Tumor volume (mm³)</p> <p>X-axis: Days post-treatment (0, 4, 7)</p> <p>Day 7</p> <p>Y-axis: Tumor volume (mm³)</p> <p>X-axis: Vehicle, 50mg/kg PLX3397, 50mg/kg MKPD 022 (BID)</p>		IC ₅₀ (nM)					PI3K α	PI3K β	PI3K γ	PI3K δ	CSF1R	MPD 001	61	>1000	164	4	43	MPD 022	>1000	>1000	941	21	4	PI-103	4	-	60	10	-	Staurosporin	-	-	-	-	1.5
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IP	Patent pending																																			