

# Derivation of new modality ‘Next Generation TPD’ leading materials targeting new target SOX2

EPD Biotherapeutics Inc.

Disease Area	Cancers																																																																														
Product Type	Gene therapy (mRNA)																																																																														
Indication	Lung cancers (Squamous Cell Lung Carcinoma, Squamous Cell Lung Carcinoma)																																																																														
Target	SOX2 (Sex-determining region Y-box 2)																																																																														
Mechanism of Action	Targeted SOX2 degradation via UPS																																																																														
Competitiveness	<p>1) Pre-existing protein degradation: In the case of siRNA, it is not possible to affect the existing SOX2 proteins already expressed before drug administration. However, EPD’s EPDeg™ platform is expected to show faster and more effective treatment efficacy because it can degrade the existing SOX2 proteins immediately after drug administration.</p> <p>2) Undruggable target degradation: EPDeg™ platform is possible to degrade even most of the undruggable target proteins such as a transcription factors that can not be bonded with small molecule based PROTACs.</p>																																																																														
Development Stage	Hit																																																																														
Route of Administration	I.V.																																																																														
Key Data	<p>1) Discovering three types of nanobodies that bind to target protein SOX2 and not to similar target SOX1 and SOX3 (about 1 to 2 nM KD)</p> <p>2) All three next-generation TPDs showed the SOX2 protein degradation as pM levels of DC50 and the cancer cell growth inhibition as pM levels of GI50 in multiple cancer cell lines.</p> <p>3) Confirming the superior and rapid efficacy of our next-generation TPDs compared to SOX2 siRNA by treatment of our next-generation TPDs and SOX2 siRNA into cancer cell lines at the same concentration and measure SOX2 protein level changes and cancer cell growth inhibition</p> <div><div><p>A549 SOX2 protein level</p><table><caption>A549 SOX2 protein level</caption><tr><th>log[Drug], nM</th><th>SOX2 bioPROTAC</th><th>SOX2 siRNA</th></tr><tr><td>-1.8</td><td>0.62</td><td>0.68</td></tr><tr><td>-1.2</td><td>0.38</td><td>0.58</td></tr><tr><td>-0.5</td><td>0.22</td><td>0.50</td></tr><tr><td>0.0</td><td>0.12</td><td>0.55</td></tr><tr><td>0.5</td><td>0.20</td><td>0.45</td></tr><tr><td>1.0</td><td>0.15</td><td>0.35</td></tr></table></div><div><p>A549 Cell growth</p><table><caption>A549 Cell growth</caption><tr><th>log[Drug], nM</th><th>SOX2 bioPROTAC</th><th>SOX2 siRNA</th></tr><tr><td>-1.8</td><td>100</td><td>100</td></tr><tr><td>-1.2</td><td>100</td><td>100</td></tr><tr><td>-0.5</td><td>100</td><td>100</td></tr><tr><td>0.0</td><td>35</td><td>95</td></tr><tr><td>0.5</td><td>25</td><td>88</td></tr><tr><td>1.0</td><td>25</td><td>62</td></tr></table></div></div> <p>4) Confirmation of the possibility of improving the therapeutic efficacy when administered in combination with standard therapeutic agents</p> <p>5) EPD’s next-generation TPDs shows powerful tumor growth inhibition in the A549 xenograft model via intravenous injection.</p> <div><div><p>A549</p><table><caption>A549 Tumor Volume</caption><tr><th>Day</th><th>Control</th><th>2 mpk i.v. Q1W x 3</th></tr><tr><td>0</td><td>600</td><td>600</td></tr><tr><td>4</td><td>750</td><td>650</td></tr><tr><td>8</td><td>950</td><td>700</td></tr><tr><td>12</td><td>1100</td><td>750</td></tr><tr><td>14</td><td>1250</td><td>800</td></tr></table></div><div><p>A549</p><table><caption>A549 Body Weight</caption><tr><th>Day</th><th>Control</th><th>2 mpk i.v. Q1W x 3</th></tr><tr><td>0</td><td>24.0</td><td>24.0</td></tr><tr><td>4</td><td>24.5</td><td>24.0</td></tr><tr><td>8</td><td>24.0</td><td>24.0</td></tr><tr><td>12</td><td>24.5</td><td>24.0</td></tr><tr><td>14</td><td>25.0</td><td>24.5</td></tr></table></div></div>	log[Drug], nM	SOX2 bioPROTAC	SOX2 siRNA	-1.8	0.62	0.68	-1.2	0.38	0.58	-0.5	0.22	0.50	0.0	0.12	0.55	0.5	0.20	0.45	1.0	0.15	0.35	log[Drug], nM	SOX2 bioPROTAC	SOX2 siRNA	-1.8	100	100	-1.2	100	100	-0.5	100	100	0.0	35	95	0.5	25	88	1.0	25	62	Day	Control	2 mpk i.v. Q1W x 3	0	600	600	4	750	650	8	950	700	12	1100	750	14	1250	800	Day	Control	2 mpk i.v. Q1W x 3	0	24.0	24.0	4	24.5	24.0	8	24.0	24.0	12	24.5	24.0	14	25.0	24.5
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