## Preclinical Development of LEM-S403 Targeting Tumor MicroenvironmentImmune Modulation of Immune Checkpoint Inhibitor Non-Responsive Solid Tumor



ONCOLOGY	Non-Clinical
Product Type	Dual-acting RNA with DegradaBALL
Indication	Patients with locally advanced or metastatic solid tumors refractory to standard therapies (including immune checkpoint inhibitors) with injectable (sub)cutaneous lesions or lymph nodes
Target	1) TLR9 (Toll-Like Receptor 9) 2) IDO1 (Indoleamine 2,3-Dioxygenase 1)
MoA(Mechanism of Action)	<ol> <li>TLR9 agonist (CpG-ODN) → Type 1 Interferons Induction → Immune- boosting</li> <li>IDO1 inhibition (siIDO1) → improvement in tumor microenvironment ⇒ Turn "Cold Tumor" into "Hot Tumor"</li> <li>Based on the mechanism of promoting immune activation and attacking the TME, synergistic effects can be produced when Co-administered with immune checkpoint inhibitors (anti-PD-1 Ab or anti-CTLA-4 Ab)</li> </ol>
Competitiveness	<ul> <li>First in Class (Dual-acting RNA with DegradaBALL DDS platform technology)</li> <li>1) Enhance stability and efficiency of Dual-acting RNA in vivo</li> <li>2) Prevent Treg cell development using DegradaBALL</li> <li>3) Reduce systemic adverse effects of combinational IO strategy using DegradaBALL</li> <li>4) Improve immune response rate to immune checkpoint inhibitors</li> <li>5) DegradaBALL improve dual-acting RNA-induced abscopal effect through manipulation of DCs</li> </ul>
Development Stage	Non-Clinical (GLP-Tox study completed)
Route of Administration	LEM-S403 (intralesional Injection) + Immune checkpoint inhibitors (systemic)

