

# Derivation of lead compound as TRIB2 inhibitor for development of triple negative breast cancer therapy

Genesen Co.,Ltd



ONCOLOGY	Lead
Product Type	Chemical Product(Small molecule)
Indication	Triple Negative Breast Cancer(TNBC)
Target	Tribbles homolog 2 (TRIB2)
MoA(Mechanism of Action)	<p>GSS1 suppresses activation of AKT and YAP as a TRIB2 kinase inhibitor.</p> <p><b>(A)</b> GSE27830: Spearman <math>\rho</math> value &lt;math&gt;&lt; -0.0001&lt;/math&gt;, r value 0.4279; Pearson <math>\rho</math> value &lt;math&gt;&lt; -0.0001&lt;/math&gt;, r value 0.3180. Node Meta: Spearman <math>\rho</math> value 0.0339, r value 0.1084; Pearson <math>\rho</math> value 0.0021, r value 0.1569.</p> <p><b>(B)</b> TRIB2 inhibition of GSS1. Schematic showing GSS1 inhibiting TRIB2, which normally activates AKT and YAP. AKT inhibits FOXO3, and YAP inhibits FOXO3 and TEAD. FOXO3 inhibits proliferation, while TEAD promotes migration and invasion. GSS1 also inhibits C/EBP<math>\alpha</math>, leading to degradation of C/EBP<math>\alpha</math> and subsequent ubiquitination. Overall, this leads to inhibition of tumor cell proliferation, migration, invasion, and metastasis.</p> <p><b>(C)</b> Western blot analysis of GSS1-126 (20nM) treatment over time (0h, 0.5h, 1h, 2h, 24h) compared to siCon and siTRIB2. Blots show levels of TRIB2, p-AKT, p-YAP, and <math>\beta</math>-actin.</p>
Competitiveness	<ul style="list-style-type: none"> <li>• GSS1 is a first-in-class TRIB2 inhibitor without competitor.</li> <li>• GSS1 is a treatment for TNBC with a high unmet need.</li> <li>• GSS1 is a potent anti-cancer drug with selective kinase inhibition and good bioavailability.</li> </ul>
Development Stage	Lead
Route of Administration	Oral