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Tarlatamab

Cat. No.:	HY-P99575
CAS No.:	2307488-83-9
Target:	Notch
Pathway:	Neuronal Signaling; Stem Cell/Wnt
Storage:	Please store the product under the recommended conditions in the Certificate of Analysis.

BIOLOGICAL ACTIVITY

Description	<p>Tarlatamab (AMG-757) is a bispecific T-cell engager (BiTE) antibody targeting delta-like ligand 3 (DLL3). DLL3 is a target that is selectively expressed in small-cell lung cancer (SCLC) tumors, but with minimal normal tissue expression. Tarlatamab has the K_Ds of 0.64 nM and 0.50 nM for human and nonhuman primate (NHP) DLL3, respectively. Tarlatamab has the K_Ds of 14.9 nM and 12 nM for human and NHP CD3, respectively. Tarlatamab is a first-in-class HLE BiTE immuno-oncology therapy targeting DLL3 and has the potential for SCLC research^[1].</p>								
In Vitro	<p>Tarlatamab (AMG-757; 0-10 nM; 48 hours) has potent, specific cytotoxic activity against DLL3-expressing SCLC cell lines in vitro^[1].</p> <p>Tarlatamab (0-10 nM; 4-72 h) increased granzyme B levels and cytotoxicity over time, with maximal signal observed at 48 hours. Markers of T-cell activation or inflammation, CD69, CD71, PD-1, and PD-L1 (37-39) were upregulated^[1].</p> <p>MCE has not independently confirmed the accuracy of these methods. They are for reference only.</p> <p>Cell Viability Assay^[1]</p> <table border="1"> <tr> <td>Cell Line:</td> <td>SCLC cell lines (DMS 79, NCI-H2171, NCI-H889, SHP-77, NCI-H211, COR-L279)</td> </tr> <tr> <td>Concentration:</td> <td>0-10 nM</td> </tr> <tr> <td>Incubation Time:</td> <td>48 hours</td> </tr> <tr> <td>Result:</td> <td>AMG 757 effectively engaged human T cells to kill SCLC cell lines, including those with very low DLL3 expression levels.</td> </tr> </table>	Cell Line:	SCLC cell lines (DMS 79, NCI-H2171, NCI-H889, SHP-77, NCI-H211, COR-L279)	Concentration:	0-10 nM	Incubation Time:	48 hours	Result:	AMG 757 effectively engaged human T cells to kill SCLC cell lines, including those with very low DLL3 expression levels.
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In Vivo	<p>Tarlatamab (AMG-757; 3 mg/kg; IP; once weekly for 3 weeks) drives tumor regression in mouse models of SCLC^[1].</p> <p>Tarlatamab (IP; 12 µg/kg; single dose) has a mean half-life of 234 hours (9.8 days), a mean clearance of 0.487 mL/hour/kg and a steady-state volume of distribution of 146 mL/kg in nonhuman primates (NHPs)^[1].</p> <p>MCE has not independently confirmed the accuracy of these methods. They are for reference only.</p> <table border="1"> <tr> <td>Animal Model:</td> <td>Female NOD.Cg-Prkdcscidll2rgtm1Sug/JicTac (NOG) mice with patient-derived SCLC tumor fragments (LXFS 1129 and LXFS 538)^[1]</td> </tr> <tr> <td>Dosage:</td> <td>3 mg/kg</td> </tr> <tr> <td>Administration:</td> <td>IP; once weekly for 3 weeks</td> </tr> </table>	Animal Model:	Female NOD.Cg-Prkdcscidll2rgtm1Sug/JicTac (NOG) mice with patient-derived SCLC tumor fragments (LXFS 1129 and LXFS 538) ^[1]	Dosage:	3 mg/kg	Administration:	IP; once weekly for 3 weeks		
Animal Model:	Female NOD.Cg-Prkdcscidll2rgtm1Sug/JicTac (NOG) mice with patient-derived SCLC tumor fragments (LXFS 1129 and LXFS 538) ^[1]								
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Administration:	IP; once weekly for 3 weeks								

Result:	Led to 83% tumor regression and an overall significant reduction in tumor volume compared with that in mice which received a control HLE BiTE molecule in the LXFS 1129 model. Induced 98% tumor regression in the LXFS 538 model.
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REFERENCES

[1]. Michael J Giffin, et al. AMG 757, a Half-Life Extended, DLL3-Targeted Bispecific T-Cell Engager, Shows High Potency and Sensitivity in Preclinical Models of Small-Cell Lung Cancer. Clin Cancer Res. 2021 Mar 1;27(5):1526-1537.

Caution: Product has not been fully validated for medical applications. For research use only.

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