

## Talacotuzumab

Cat. No.:	HY-P99395
CAS No.:	1826831-79-1
Target:	Interleukin Related
Pathway:	Immunology/Inflammation
Storage:	Please store the product under the recommended conditions in the Certificate of Analysis.

### BIOLOGICAL ACTIVITY

<b>Description</b>	<p>Talacotuzumab (JNJ 56022473; CSL 362) is an IgG1-type fully humanized, CD123-neutralizing monoclonal antibody containing a modified Fc structure. Talacotuzumab has <math>K_D</math>s of 0.43 nM, 188 nM, 46 nM, 16.8 nM for CD123, CD32b/c, CD16-158F, CD16-158V, respectively. Talacotuzumab inhibits IL-3 binding to CD123, antagonizing IL-3 signaling in target cells. Talacotuzumab has mutated the Fc region to increase affinity for CD16 (FcγRIIIa), thereby enhancing antibody-dependent cell-mediated cytotoxicity (ADCC). Talacotuzumab is highly effective in vivo reducing leukemic cell growth in acute myeloid leukemia (AML) xenograft mouse models<sup>[1][2][3][4]</sup>.</p>								
<b>In Vitro</b>	<p>Talacotuzumab (JNJ 56022473; CSL 362) strongly mediates ADCC of TF-1 cells with an <math>ic_{50}</math> of 5 ng/ml (33 pM)<sup>[1]</sup>. Talacotuzumab (1 μg/ml; pretreatment for 24 hours) inhibits TLR7-stimulated (<a href="#">Imiquimod</a>; HY-B0180; 0.5 μM; for 6 days) and TLR9-stimulated (CpG C; 0.5 μM; for 6 days) IFN-α production in both SLE donors and healthy donors plasmacytoid dendritic cells (pDCs) and basophils, whereas TLR4-stimulated (<a href="#">LPS</a>; HY-D1056; 10 μg/ml) production is not significantly reduced. Talacotuzumab inhibits TLR7- and TLR9-induced plasmablast expansion and proliferation by depletion of plasmacytoid dendritic cells (pDCs)<sup>[2]</sup>.</p> <p>MCE has not independently confirmed the accuracy of these methods. They are for reference only.</p>								
<b>In Vivo</b>	<p>Talacotuzumab (JNJ 56022473; CSL 362; 300 μg; ip; thrice weekly for 5 weeks) results in a significant delay in tumor growth compared with an isotype control in acute myeloid leukaemia mice xenografts<sup>[1]</sup>.</p> <p>Talacotuzumab (1, 10, 30 mg/kg; s.c.; single injection) has maximal serum concentrations at 48 hours of ~12, 190, and 380 μg/ml at doses of 1, 10, and 30 mg/kg in naive cynomolgus monkeys, respectively<sup>[2]</sup>.</p> <p>MCE has not independently confirmed the accuracy of these methods. They are for reference only.</p> <table border="1" style="width: 100%; border-collapse: collapse;"> <tr> <td style="width: 30%;">Animal Model:</td> <td>Nonobese diabetic/severe combined immunodeficiency mice injected intravenously AML xenograft cells (AML-5)<sup>[1]</sup></td> </tr> <tr> <td>Dosage:</td> <td>300 μg</td> </tr> <tr> <td>Administration:</td> <td>IP; thrice weekly for 5 weeks</td> </tr> <tr> <td>Result:</td> <td>Resulted in a significant delay in tumor growth compared with an isotype control.</td> </tr> </table>	Animal Model:	Nonobese diabetic/severe combined immunodeficiency mice injected intravenously AML xenograft cells (AML-5) <sup>[1]</sup>	Dosage:	300 μg	Administration:	IP; thrice weekly for 5 weeks	Result:	Resulted in a significant delay in tumor growth compared with an isotype control.
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### REFERENCES

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- [1]. S J Busfield, et al. Targeting of acute myeloid leukemia in vitro and in vivo with an anti-CD123 mAb engineered for optimal ADCC. *Leukemia*. 2014 Nov;28(11):2213-21.
- [2]. Shereen Oon, et al. A cytotoxic anti-IL-3R $\alpha$  antibody targets key cells and cytokines implicated in systemic lupus erythematosus. *JCI Insight*. 2016 May 5;1(6):e86131.
- [3]. Erwin M Lee, et al. Efficacy of an Fc-modified anti-CD123 antibody (CSL362) combined with chemotherapy in xenograft models of acute myelogenous leukemia in immunodeficient mice. *Haematologica*. 2015 Jul;100(7):914-26.
- [4]. L H Xie, et al. CD123 target validation and preclinical evaluation of ADCC activity of anti-CD123 antibody CSL362 in combination with NKs from AML patients in remission. *Blood Cancer J*. 2017 Jun 2;7(6):e567.
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**Caution: Product has not been fully validated for medical applications. For research use only.**

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