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Cinrebafusp alfa

Cat. No.:	HY-P99605
CAS No.:	2218515-90-1
Target:	EGFR; TNF Receptor
Pathway:	JAK/STAT Signaling; Protein Tyrosine Kinase/RTK; Apoptosis
Storage:	Please store the product under the recommended conditions in the Certificate of Analysis.

BIOLOGICAL ACTIVITY

Description

Cinrebafusp alfa (PRS 343) is a high affinity CD137/HER2 bispecfic anticalin-based drug. Cinrebafusp alfa binds to recombinant human HER2 (K_d=0.3 nM) and human monomeric CD137 (4-1BB; K_d=5 nM). Cinrebafusp alfa facilitates T-cell costimulation by tumor-localized, HER2-dependent 4-1BB clustering and activation, further enhancing T-cell receptor-mediated activity and leading to tumor destruction. Cinrebafusp alfa has the potential for HER2+ solid tumors research[1][2].

IC_{50} & Target

4-1BB	HER2
5 nM (Kd)	0.3 nM (Kd)

In Vitro

Cinrebafusp alfa (PRS 343) binds HER2-expressing MCF-7 cells with an EC_{50} of 7.4 nmol/L and binds to CHO cells transfected with human 4-1BB with an EC_{50} of 6.2 nmol/L in a FACS assay[1].

MCE has not independently confirmed the accuracy of these methods. They are for reference only.

In Vivo

Cinrebafusp alfa (PRS 343; 0.2-10 mg/kg; IV; once weekly; for 20 day) leads to tumor growth inhibition and has a dose-dependent increase of tumor-infiltrating lymphocytes in a humanized mouse model engrafted with HER2-positive SK-OV-3 tumor cells[1].

Cinrebafusp alfa (10 mg/kg; IV; single dose) has the terminal elimination half-life of >14 days in male CD-1 mice. Cinrebafusp alfa (3 mg/kg; IV; single dose) has the terminal elimination half-life approximately 4 days in male cynomolgus monkeys[1].

MCE has not independently confirmed the accuracy of these methods. They are for reference only.

Animal Model:	SK-OV-3 ovarian cancer model in human PBMC-reconstituted NOG female mice, ages 5-7 weeks[1]
Dosage:	0.2, 1, 5, 10 mg/kg
Administration:	IV; once weekly; for 20 day
Result:	Displayed dose-dependent antitumor efficacy with doses ranging from 4 μg to 100 μg (approximately 0.2 mg/kg to 5 mg/kg), while the 200-μg dose (approximately 10 mg/kg) did not further enhance tumor regression. Led to a significant increase in human CD45+ lymphocytes in tumor tissue.

Animal Model:	Male CD-1 mice[1]

Dosage:	10 mg/kg (Pharmacokinetic Analysis)
Administration:	IV; single dose
Result:	Had the terminal elimination half-life of >14 days.

REFERENCES

[1]. Marlon J Hinner, et al. Tumor-Localized Costimulatory T-Cell Engagement by the 4-1BB/HER2 Bispecific Antibody-Anticalin Fusion PRS-343. Clin Cancer Res. 2019 Oct 1;25(19):5878-5889.

[2]. G. Ku, et al. 525O A phase I dose escalation study of PRS-343, a HER2/4-1BB bispecific molecule, in patients with HER2-positive malignancies. ABSTRACT ONLY, VOLUME 31, SUPPLEMENT 4, S462-S463, SEPTEMBER 01, 2020.

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