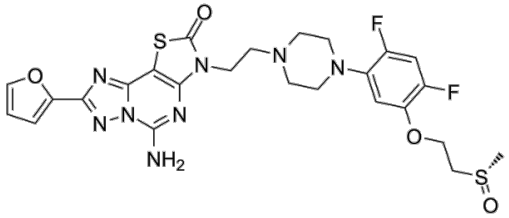
Product Data Sheet

Product Name: Inupadenant
Cat. No.: GC63022

Chemical Properties

Cas. No.	2246607-08-7		
Formula	$C_{25}H_{26}F_2N_8O_4S_2$	M.Wt	604.65
Solubility		Storage	Store at -20°C
General tips	For obtaining a higher solubility , please warm the tube at 37 °C and shake it in the ultrasonic bath for a while.Stock solution can be stored below -20°C for several months.		
Shipping Condition	Evaluation sample solution : ship with blue ice All other available size: ship with RT , or blue ice upon request.		
Structure			



Protocol

Cell experiment [1]:

Cell lines	Peripheral blood cells

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Preparation Method	Peripheral blood cells were stimulated for 45min at 37°C with DMSO as control, or CGS-21680 (5μM) in the presence or in the absence of Inupadenant (10nM). After stimulation, samples were incubated at RT for 10min with PROT1 buffer and immediately transferred at -80°C. Samples were thawed for 10min in a cold water bath (12-14°C) and treated with Thaw/Lyse buffer. Cells were permeabilized with Phosflow Perm II buffer , stained with a solution of Brilliant Staining Buffer and relevant antibodies for 60min, washed twice and resuspended in FACS buffer before acquisition on a LSRFortessa FACS machine.
Reaction Conditions	10nM; 45min
Applications	When peripheral blood was incubated with CGS-21680, approximately 2-fold induction of CREB phosphorylation in CD4+ and CD8+ T cells, as well as in CD19+ B cells were observed. Co-incubation with Inupadenant (10nM) strongly reduced CREB phosphorylation in T and B lymphocytes.

Animal experiment [2]:

Animal models	Immunocompetent syngeneic mice implanted subcutaneously with MCA205 and CT26 cells
Preparation Method	After tumors reached 100-200mm^3 and again at 600-700mm^3, tumor interstitial fluid was collected and adenosine concentration was measured. Subsequently, the antitumor effect of Inupadenant administered orally at 0.6mg/kg with oxaliplatin 10mg/kg or doxorubicin 5mg/kg was evaluated in models with different adenosine concentration levels.
Dosage form	0.6mg/kg/d; p.o.

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Applications	MCA205 tumors displayed the highest adenosine concentration with an average of 33μM while CT26 was considered as intermediate with an average of 6μM . Inupadenant , in combination with chemotherapy, demonstrated similar tumor growth inhibition in both models, regardless of the concentration of adenosine.

References:
[1] Tieppo P, Shehade H, Martinoli C, et al. Inhibition of A2AR alleviates adenosine-mediated suppression of plasma cell differentiation. Front Immunol. 2025;16:1702402.
[2] 34th Annual Meeting & Pre-Conference Programs of the Society for Immunotherapy of Cancer (SITC 2019): part 2 : National Harbor, MD, USA. 10 November 2019. J Immunother Cancer. 2019;7(Suppl 1):283.

Background

Inupadenant is an orally active, highly selective A2A receptor antagonist, which maintains full potency at the high adenosine levels found in tumors, exhibiting strong antitumor activity[1-2]. Inupadenant is not brain-penetrant[1].

In vitro, treatment with 10nM Inupadenant for 45 minutes antagonized A2AR signaling and reduced CREB phosphorylation in T and B lymphocytes[3]. Treatment with 300nM Inupadenant for 3 days restored A2AR-mediated suppression of B cells differentiation to Antibody-Secreting Cells (ASCs), both at the level of PBs and PCs[3]. Inupadenant has an IC_{50} value of 0.73nM against HEK293 cells stably expressing human A2AR(HEK293-hA2AR), an IC_{50} value of 575nM against H293-hA2B, and an IC_{50} value of 192nM against CHO-K1-hA1 [3].

In vivo, Inupadenant (0.6mg/kg/d; p.o.), in combination with chemotherapy, demonstrated tumor growth inhibition in mouse tumor models with subcutaneous implantation of MCA205 or CT26 cells[4].

References:
[1] Laurence Buisseret, et al. Phase 1 trial of the adenosine A2Areceptor antagonist inupadenant (EOS-850): Update on tolerability, and antitumor activity potentially associated with the expression of

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the A2A receptor within the tumor. Journal of Clinical Oncology. Volume 39, Issue 15_suppl.
[2] The A2AR antagonist inupadenant promotes humoral responses in preclinical models. Abstract 48P. Presented at: ESMO Immuno-Oncology Congress 2024; December 2024; Geneva, Switzerland.
[3] Tieppo P, Shehade H, Martinoli C, et al. Inhibition of A2AR alleviates adenosine-mediated suppression of plasma cell differentiation. Front Immunol. 2025;16:1702402.
[4] 34th Annual Meeting & Pre-Conference Programs of the Society for Immunotherapy of Cancer (SITC 2019): part 2 : National Harbor, MD, USA. 10 November 2019. J Immunother Cancer. 2019;7(Suppl 1):283.

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