Dual-function Molecular Glue-Like STING Antagonist

Drug Introduction

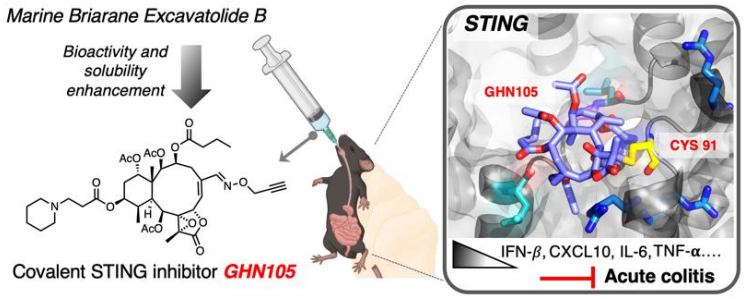
- Site-specific, orally bioavailable novel STING inhibitor and degrader.
- It shows high specificity, safety, and strong potential in treating STING-associated disorders.

Drug Mechanism

- **Covalent**: It forms a strong, irreversible (or long-lasting) bond with the Cys91 residue. This provides sustained suppression of STING activity, which is beneficial for chronic autoimmune conditions.
- **Orally Bioavailable**: This is a critical feature that differentiates our asset from earlier experimental STING antagonists (which were often injectable).

Key Business Takeaways

- *First-in-class, orally-bioavailable, site-specific* covalent STING inhibitor and degrader.
- Reduces the production of not only interferons but also other pro-inflammatory cytokines (e.g., TNF-α, IL-6) in vivo.
- This broad anti-inflammatory effect is beneficial for a wide range of autoimmune and inflammatory diseases where STING is overactive, such as systemic lupus erythematosus (SLE), Sjögren's syndrome, and dermatomyositis, and STING-Associated Vasculopathy with onset in Infancy (SAVI).



Drug Comparison

- Our dual-function STING modulator outperforms H151 and LB244 in bioactivities in human PBMC and exerts great PK/PD correlation in vivo.

In Vivo Experimental / Preclinical Data

- Orally administered of our STING modulator reversed pathological features in a delayed treatment acute colitis mouse model and exhibited *in vivo* on-target engagement of STING.
- It also potentiates significant recovery of body weight, colon length, epithelial architecture and marked reduction of immune cells infiltration in the acute colitis.

Intellectual Properties

- TWI872830, US and PCT pending.

Publications

- Orally bioavailable and site-selective covalent STING inhibitor derived from a macrocyclic marine diterpenoid. Journal of Medicinal Chemistry. 2025 Mar 13;68(5):5471-5487.

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