## IRAK4-IN-28

Cat. No.: HY-155132 CAS No.: 2952532-92-0 Molecular Formula:

 $C_{27}H_{31}N_{9}O_{3}$ Molecular Weight: 529.59 IRAK Target:

Pathway: Immunology/Inflammation

Please store the product under the recommended conditions in the Certificate of Storage:

Analysis.

**Product** Data Sheet

## **BIOLOGICAL ACTIVITY**

Description IRAK4-IN-28 (compound 42) is an orally active IRAK4 inhibitor (IC50=8.9 nM). IRAK4-IN-28 has binding affinity for IRAK4 with a Kd of 0.58 nM. IRAK4-IN-28 can be used in the research of inflammation and autoimmune diseases<sup>[1]</sup>.

IC50:8.9 nM (IRAK4) $^{[1]}$ , IC50:>30 nM (hERG) $^{[1]}$ , Kd:0.58 nM (IRAK4) $^{[1]}$ , Kd:140 nM (IRAK1) $^{[1]}$ IC<sub>50</sub> & Target

In Vitro IRAK4-IN-28 (compound 42) has no inhibition on cytochrome P450 enzymes CYP1A2, CYP2D6, CYP3A4, and hERG which means a good safety and 'drug-likeness' properties[1].

IRAK4-IN-28 inhibits CYP2C9, CYP2C19 with IC $_{50}$  of 12  $\mu$ M and 2.7  $\mu$ M, respectively<sup>[1]</sup>.

IRAK4-IN-28 has high plasma protein binding in human and rat (99.8 an 97.2, respectively)<sup>[1]</sup>.

IRAK4-IN-28 (1 h) inhibits the LPS (HY-D1056)-induced TNF-α and IL-6 expression at both mRNA and protein levels in a dosedependent manner<sup>[1]</sup>.

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

Cell Viability Assay<sup>[1]</sup>

| Cell Line:       | iBMDM cell   |
|------------------|--|
| Concentration:   | 0-33 μΜ  |
| Incubation Time: | 1h   |
| Result:          | Reduced mRNA levels and protein levels of TNF- $\alpha$ and IL-6 in mouse iBMDM cells. |

In Vivo IRAK4-IN-28 (compound 42) has favorable pharmacokinetic properties in the SD rat model [1].

IRAK4-IN-28 has orally bioactive with 68% availability<sup>[1]</sup>.

IRAK4-IN-28 (50 or 100 mg/ml, single dose, oral) significantly reduces LPS-induced TNF- $\alpha$  and IL-6 cytokines release in the mouse model<sup>[1]</sup>.

Pharmacokinetic Analysis in male SD Rat Model<sup>[1]</sup>

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Route Dose Clobs Clmax  $V_{ss\_obs}$ AUC<sub>last</sub>  $t_{1/2}$  (h) T<sub>max</sub> (h) F (%)

|                           | (mg/kg) | (mL·h/kg)  | (ng/mL)   | (L/kg)         | (ng·h/mL)        |             |                |          |  |  |
|---------------------------|---------|--|---|----------------|------------------|-------------|----------------|----------|--|--|
| i.v.                      | 2       | 21   | /   | 3.2            | 1520             | 1.8         | /              | /        |  |  |
| p.o.                      | 10      | /  | 1133  | /              | 5196             | /           | 1.7            | 68       |  |  |
| nimal Model:              |         | LPS-stimulated female C57BL/6 mice <sup>[1]</sup>  |   |                |                  |             |                |          |  |  |
| nimal Model:              |         |  | confirmed the accuracy of these methods. They are for reference only. $ \label{lem:LPS-stimulated}  \mbox{LPS-stimulated female C57BL/6 mice} \mbox{ [1]} $ |                |                  |             |                |          |  |  |
|                           |         | 50 or 100 mg/ml, single dose; 1 h prior to 1 mg/kg LPS administration by intraperitoneal injection |   |                |                  |             |                |          |  |  |
| Dosage:                   |         |  | ng/ml, single c   | lose; 1 h prio | r to 1 mg/kg LPS | administrat | ion by intrape | ritoneal |  |  |
| Dosage:<br>Administration | on:     |  |   | lose; 1 h prio | r to 1 mg/kg LPS | administrat | ion by intrape | ritoneal |  |  |

## **REFERENCES**

[1]. Yongjin Hao, et al. Design, synthesis, evaluation and optimization of potent IRAK4 inhibitors alleviating production of inflammatory cytokines in LPS-induced SIRS model. Bioorg Chem. 2023, 137:106584.

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

Tel: 609-228-6898

Fax: 609-228-5909

 $\hbox{E-mail: tech@MedChemExpress.com}$ 

Address: 1 Deer Park Dr, Suite Q, Monmouth Junction, NJ 08852, USA