BIOLOGICAL ACTIVITY:

TES-1025 is a potent and selective human α-amino-β-carboxymuconate-ε-semialdehyde decarboxylase (ACMSD) inhibitor with an IC_{50} of 13±3 nM.

IC_{50} & Target: IC_{50}: 13±3 nM (human ACMSD) \[^{[1]}\]

**In Vitro:** TES-1025 is a low nanomolar human ACMSD inhibitor, which increases NAD^{+} levels in cellular systems \[^{[1]}\].

**In Vivo:** TES-1025 is subjected to in vivo pharmacokinetic studies, following intravenous (IV) and oral (PO) dosings of male CD-1 mice. After the intravenous administration of 0.5 mg/kg, TES-1025 shows low blood clearance, with low volumes of distribution and half-lives (t_{1/2}) of about 5.33 h, although after oral administration at 5 mg/kg, the blood concentration of TES-1025 is quantifiable for up to 8 h. A good systemic exposure is recorded for TES-1025, with a C_{max} of 2570 ng/mL reaches at 2 h after dosing. The greater oral exposure of TES-1025 is further confirmed in the liver and kidneys with AUC_{0-8h} of 19?200 h•ng/mL and 36?600 h•ng/mL, respectively \[^{[1]}\].

PROTOCOL (Extracted from published papers and Only for reference)

**Kinase Assay:** \[^{[1]}\] Recombinant hACMS is expressed in Pichia pastoris and purified. Its enzyme activity is assayed by a coupled spectrophotometric assay. Briefly, in a pre-assay mixture, the ACMS substrate is generated from 10 μM 3-hydroxyanthranilic acid by recombinant 3-hydroxyanthranilate 3,4-dioxigenase from Ralstonia metallidurans. ACMS formation is monitored at 360 nm, and after the reaction is complete, an appropriate amount of ACMSD is added. Activity is calculated from the initial rate of the absorbance decrease subtracted from that of a control reaction mixture in the absence of ACMSD. The effects of the various compounds (e.g., TES-1025) on the enzyme activity are tested by adding the compounds to the assay mixture along with ACMSD. For the IC_{50} evaluations for each compound, a serial dilution from a stock solution prepared in DMSO is tested, maintaining a DMSO concentration in all the reaction mixtures of 1.0%. One unit is defined as the amount of enzyme that consume 1 μmol of ACMS per minute at 37°C \[^{[1]}\].

**Animal Administration:** \[^{[1]}\] Mice

Male CD-1 mice are used. The study is conducted in 3 phases. Phase 1: 18 mice receive an oral administration of TES-1025 at a target dose level of 5 mg/kg. Blood, brain and liver are collected at intervals up to 8 h after dose administration (n=3 animals per each time point). Phase 2: 3 mice receive each an intravenous administration of TES-1025 at a target dose of 0.5 mg/kg. Blood samples are collected from the lateral tail vein at intervals up to 24 h after dose administration. Phase 3: 3 mice receive a single intravenous administration of Elacridar (5 mg/kg) shortly before an oral administration of TES-1025 at a target dose of 5 mg/kg. Blood and brain samples are collected 0.5 h after dose administration. Brain, liver and kidney are collected from all animals of the study \[^{[1]}\].
References:

Caution: Product has not been fully validated for medical applications. For research use only.
Tel: 732-484-9848  Fax: 888-484-5008  E-mail: sales@ChemScene.com
Address: 1 Deer Park Dr, Suite Q, Monmouth Junction, NJ 08852, USA