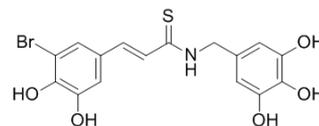


## Data Sheet

|                           |   |
|---------------------------|---|
| <b>Product Name:</b>      | NT157   |
| <b>Cat. No.:</b>          | HY-100037   |
| <b>CAS No.:</b>           | 1384426-12-3  |
| <b>Molecular Formula:</b> | C <sub>16</sub> H <sub>14</sub> BrNO <sub>5</sub> S |
| <b>Molecular Weight:</b>  | 412.26  |
| <b>Target:</b>            | Insulin Receptor                                    |
| <b>Pathway:</b>           | Protein Tyrosine Kinase/RTK                         |
| <b>Solubility:</b>        | DMSO: ≥ 30 mg/mL                                    |



### BIOLOGICAL ACTIVITY:

NT157 is a selective inhibitor of IRS-1/2. IC<sub>50</sub> values at sub-micromolar doses (ranging from 0.3 to 0.8 μM).

IC<sub>50</sub> value: 0.3 to 0.8 μM [1]

Target: Insulin receptor

in vitro: NT157 significantly affects the cells' migratory ability, as confirmed by a wound-healing assay. NT157 induces cytostatic effects, as evidenced by G2/M cell cycle arrest, and does not affect apoptosis. NT157, a novel small-molecule that specifically targets IRS protein, in OS cells. NT157 is a small-molecule inhibitor that induces Ser-phosphorylation and consequently the degradation of IRS-1 and IRS-2. NT157 efficiently affects migration ability of MG-63 and U-2OS OS cells. NT157 treatment induces cell cycle arrest and inhibits IGF system signaling. [1] The density of LNCaP cells grown in FBS was decreased approximately 20% at 1 μM, approximately 70% at 2 μM, and >90% at 5 μM (IC<sub>50</sub>, 1.4 μM). Growth of LNCaP cells is suppressed >60% when cultured in CSS but still exhibited significant density at 2 μM and maximal decreased density at 5 μM. The density of FBS-cultured PC3 cells was similarly decreased by NT157 treatment (40% at 2 μM and > 70% at 5 μM; IC<sub>50</sub>, 2.5 μM). [2]

in vivo: NT157 suppresses growth of LNCaP xenografts following castration. NT157 treatment affects IGF1R and IRS targets in xenografts and significantly delays castration-resistant progression of LNCaP androgen-responsive xenografts when combined with castration. NT157 potentiates docetaxel activity in PC3 xenografts.[2]

### PROTOCOL (Extracted from published papers and Only for reference)

Cell assay (Western blotting) [1] NT157 was dissolved in dimethyl sulfoxide (DMSO) to generate a 10-mM stock solution, which was stored at -80°C. Cells were treated with NT157 (0.3-1.3 μM) for 48 h or left untreated, and cell lysates were prepared and processed. The membranes were incubated overnight with the following primary antibodies: anti-Shc clone PG-797, anti GAPDH, anti-β-actin, anti-phospho-Akt (Ser473) clone 736E11, anti-Akt, anti-ERK, anti-phospho-ERK (Tyr202/Tyr204), anti-IRS-1, anti-IRS-2, and phospho-IRS-1 (Tyr612); anti-rabbit or anti-mouse antibodies conjugated to horseradish peroxidase were used as secondary antibodies. Animal administration [2] For xenograft studies, 2 × 10<sup>6</sup> LNCaP (suspended in 0.1 mL Matrigel) or PC3 cells (suspended in 0.1 mL serum-free DMEM) were inoculated s.c. in the flank of 6- to 8-week-old male athymic nude mice via a 27-gauge needle under isoflurane anesthesia. For LNCaP xenografts, when tumor volume exceeded 200 mm<sup>3</sup>, mice were castrated and randomly selected for treatment with 50 mg/kg NT157 or vehicle (10% 2-HP-beta-CD + 0.67% NaCl/H<sub>2</sub>O) injected i.p. three times per week. Each experimental group consisted of 12 mice. Tumor volume was measured twice weekly (length × width × depth × 0.5432). Data points were expressed as average tumor volume ± SEM. When PC3 tumors reached 100 mm<sup>3</sup>, mice were randomly selected for treatment with 50 mg/kg NT157 or vehicle (10% 2-HP-beta-CD + 0.67% NaCl/H<sub>2</sub>O) injected i.p. three times per week or treated with 10 mg/kg docetaxel injected i.p. three times a week for 1 week or combination of 50 mg/kg NT157 and 10 mg/kg docetaxel as indicated. Experimental groups consisted of 7 mice (vehicle), 9 mice (NT157), 10 mice (docetaxel), and 16 mice (combination). Tumor volume and body weight (BW) were measured once weekly. Data points were expressed as average tumor volume ± SEM.

## References:

- [1]. Garofalo C, et al. Preclinical Effectiveness of Selective Inhibitor of IRS-1/2 NT157 in Osteosarcoma Cell Lines. *Front Endocrinol (Lausanne)*. 2015 May 13; 6:74.
- [2]. Ibuki N, et al. The tyrophostin NT157 suppresses insulin receptor substrates and augments therapeutic response of prostate cancer. *Mol Cancer Ther*. 2014 Dec;13(12):2827-39.

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

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