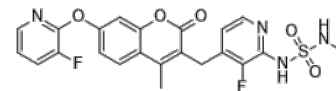


**Product Name** : NST-628  
**Cat. No.** : PC-22122  
**CAS No.** : 3002056-30-3  
**Molecular Formula** : C<sub>22</sub>H<sub>18</sub>F<sub>2</sub>N<sub>4</sub>O<sub>5</sub>S  
**Molecular Weight** : 488.47  
**Target** : Raf  
**Solubility** : 10 mM in DMSO



CAS: 3002056-30-3

## Biological Activity

NST-628 is a potent, brain-penetrant, pan-**RAF-MEK molecular glue**, prevents phosphorylation and activation of MEK by RAF, leading to deep durable inhibition of MEK kinase activity and downstream ERK signaling.

NST-628 engages all isoforms of RAF and prevents the formation of BRAF-CRAF heterodimers, a differentiated mechanism from all current RAF inhibitors.

NST-628 treatment glues ARAF, BRAF, and CRAF with unphosphorylated MEK1, stabilizing an inactive RAF-MEK complex and deeply inhibiting phospho-ERK signaling in MEK1 immunoprecipitation assay.

NST-628 demonstrates efficacy across multiple tumor types with RAS-MAPK alterations, including melanoma, lung, and pancreatic models.

NST-628 is broadly efficacious in models with BRAF Class II/III mutations, KRAS-mutations (G12C, G12D, G12V, G12R, Q61H), and NRAS-mutations (Q61x, G12x) as well as showing anti-proliferative effects in NF1-mutant/deficient models.

NST-628 (3-5 mg/kg QD treatment) led to tumor regressions in HCT116 (KRAS G13D colorectal) and IPC-298 (NRAS Q61L melanoma) xenograft models, 53% and 38% respectively, correlating to inhibition of both phospho-MEK and phospho-ERK in tumors.

NST-628 (3 mg/kg QD) dosing demonstrates broad anti-tumor responses across melanoma, lung, pancreatic, glioma, and ovarian models with patient derive xenograft (PDX) tumors harboring NF1, KRAS G12D/R, BRAF Class II/III, and NRAS Q61x mutations.

## References

Meagan B Ryan, et al. *Mol Cancer Ther* (2023) 22 (12\_Supplement): A088.

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**Caution: Product has not been fully validated for medical applications. Lab Use Only!**

E-mail: tech@probechem.com