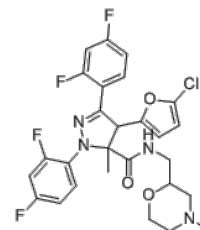


**Product Name** : RSC-1255  
**Cat. No.** : PC-49554  
**CAS No.** : 2171015-78-2  
**Molecular Formula** : C<sub>27</sub>H<sub>25</sub>ClF<sub>4</sub>N<sub>4</sub>O<sub>3</sub>  
**Molecular Weight** : 564.966  
**Target** : Ras  
**Solubility** : 10 mM in DMSO



## Biological Activity

RSC-1255 (KRAS inhibitor 249C, V-ATPase inhibitor) is a Ras-mutant selective cytotoxic agent with nanomolar potency against a spectrum of **Ras-mutant** cancer cells (A549 (KRASG12S), IC<sub>50</sub>=73 nM), binds to **V-ATPase** (K<sub>d</sub>=23 nM) and inhibits its activity.

249C (RSC-1255) shows inhibition of viability in both Ras- and Raf-mutant cells with IC<sub>50</sub> of 73 nM, 60 nM and 22 nM for A549 (KRASG12S), LOX IMVI (BRAFV600E), and MelJuso (HRASG13D and NRASQ61L), respectively.

249C (RSC-1255) blocks lysosomal acidification and autophagy progression. blocked ATP hydrolysis of intact mammalian V-ATPase purified from pig kidneys (but not yeast).

249C (RSC-1255) differentially inhibits fibroblasts bearing mutations in KRAS and BRAF via inhibition of lysosomal pH, V-ATPase activity, and macropinocytosis.

249C (RSC-1255) preferentially kills mouse embryonic fibroblasts bearing specific KRAS mutations with IC<sub>50</sub> values: KRAS WT (1.25 μM); G13D (0.07 μM); G12V (0.15 μM); G12S (0.23 μM); G12D (0.3 μM); Q61L (0.31 μM); G12C (0.44 μM); Q61R (0.55 μM); and for BRAFV600E (0.11 μM).

249C (RSC-1255) inhibits macropinocytosis in a KRAS-mutant-dependent manner in MEFs expressing KRAS/BRAF mutants (KRASG13D, KRASG12V, and BRAFV600E), but less so in MEFs expressing KRAS WT.

249C (RSC-1255) treatment (10 mg/kg, twice a day, i.p.) inhibits in vivo growth of mutant KRAS (KRASG12S) in mouse xenograft models and shows pharmacodynamic safety.

## References

Bhairavi Tolani, et al. *Nat Biotechnol.* 2022 Dec;40(12):1834-1844.

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

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