

## Product Data Sheet

Product Name: GDC-0077 (RG6114)

Cat. No.: GC32710

### Chemical Properties

Cas. No. 2060571-02-8

SMILES C[C@@H](C(N)=O)NC1=CC=C(C2=NC(N3[C@H](C(F)F)COC3=O)=CN2CCO4)C4=C1

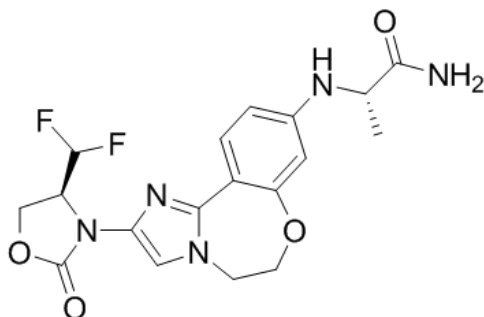
Formula  $C_{18}H_{19}F_2N_5O_4$  M.Wt 407.37

Solubility DMSO :  $\geq 180$  mg/mL (441.86 mM) Storage Store at  $-20^{\circ}\text{C}$

General tips For obtaining a higher solubility , please warm the tube at  $37^{\circ}\text{C}$  and shake it in the ultrasonic bath for a while. Stock solution can be stored below  $-20^{\circ}\text{C}$  for several months.

Shipping Condition Evaluation sample solution : ship with blue ice All other available size: ship with RT , or blue ice upon request.

Structure



### Protocol

#### Cell experiment [1]:

Cell lines *PIK3CA*-mutant cell lines

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

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Preparation Method Twelve-well plates were seeded with 10,000 to 20,000 cells/well in a volume of 1 mL and incubated at 37°C under 5% CO<sub>2</sub> for 24 hours. Compounds (DMSO, 0.3µM GDC-0077, 0.3µM cobimetinib, or a combination of the two drugs) were added the next day at indicated concentration for 2 to 3 weeks. The medium was replaced weekly with fresh medium containing the drugs. Then the medium was aspirated and 100µL of 0.5% crystal violet was added for 15 minutes. The dye was discarded and the cells were washed with PBS for 5 to 10 minutes five times. PBS was then aspirated and the cells were imaged using GelCount.

Reaction Conditions 0.3µM, 2 to 3 weeks

Applications GDC-0077 significantly inhibited proliferation in *PIK3CA*-mutant cell lines compared to the control.

### Animal experiment [2]:

Animal models *PIK3CA*-mutated breast cancer mouse model

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|--------------------|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| Preparation Method | <p>HCC1954 tumor cells (<math>5 \times 10^6</math>) were inoculated in the 2/3 mammary fat pads of female NCR nude mice, whereas WHIM20 and HCI-003 tumors (<math>50\text{mm}^3</math>) were engrafted in 2/3 mammary fat pads in female NOD-SCID gamma mice. Tumor Volume (<math>\text{mm}^3</math>) = <math>(\text{Length} \times \text{Width}^2) \times 0.5</math>. Mice for efficacy studies were distributed into 8 to 10 mice/group with a mean tumor volume of 200 to <math>250\text{mm}^3</math> at the initiation of dosing. Tumor growth inhibition as a percentage of vehicle control (%TGI) was calculated as the percentage of the AUC (Area Under the Curve) for the respective dose group per day in relation to the vehicle, using the following formula: <math>\%TGI = 100 \times (1 - \text{AUC}_{\text{dose}}/\text{AUC}_{\text{vehicle}})</math>. The PI3K inhibitors tasisib, GDC-0941, GDC-0077, and BYL719 were formulated in methylcellulose Tween vehicle consisting of 0.5% (w/v) methylcellulose, 0.2% (w/v) polysorbate 80 (Tween-80) and dosed orally by gavage daily. Tumor sizes and mouse body weights were recorded twice weekly, and mice with tumor volume exceeding <math>2,000\text{mm}^3</math> or body weight loss of 20% of starting weight were promptly euthanized.</p> |
| Dosage form        | 25mg/kg/day, 25 days, i.g.                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        |
| Applications       | GDC-0077 markedly enhanced the antitumor efficacy of the palbociclib-fulvestrant combination, elevating the mean tumor growth inhibition (TGI) from 71% to 106%.                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                  |

### References:

- [1] Song K W, Ong C C, Lin E, et al. KRAS codon-specific mutations differentially toggle PI3K pathway signaling and alter sensitivity to inavolisib (GDC-0077)[J]. Molecular Cancer Therapeutics, 2025, 24(12): 1890-1901.
- [2] Song K W, Edgar K A, Hanan E J, et al. RTK-dependent inducible degradation of mutant PI3K $\alpha$  drives GDC-0077 (Inavolisib) efficacy[J]. Cancer discovery, 2022, 12(1): 204-219.

### Background

GDC-0077 (RG6114) is a potent and selective PI3K $\alpha$  inhibitor with an IC<sub>50</sub> of 0.038nM. GDC-0077 is

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> 300-fold more selective for PI3K $\alpha$  over the other class I PI3K isoforms ( $\beta$ ,  $\delta$ , and  $\gamma$ ) and > 2000-fold more selective over PIK family members. GDC-0077 binds to the ATP binding site of PI3K and inhibits the phosphorylation of PIP2 to PIP3<sup>[1]</sup>. GDC-0077 achieves precise targeting of *PIK3CA*-mutated tumors through a dual-action mechanism: selectively inhibiting PI3K $\alpha$  activity and inducing the degradation of mutant p110 $\alpha$  protein<sup>[2]</sup>. GDC-0077 is commonly used in the study of breast cancer.

GDC-0077 (0.3 $\mu$ M, 2 to 3 weeks) significantly inhibited proliferation in PIK3CA-mutant cell lines compared to the control. GDC-0077 combined with cobimetinib showed an increased cytotoxic response in four of five colorectal cancer cell lines<sup>[3]</sup>.

GDC-0077 (25mg/kg/day, 25 days, i.g.) markedly enhanced the antitumor efficacy of the palbociclib-fulvestrant combination, elevating the mean tumor growth inhibition (TGI) from 71% to 106%<sup>[4]</sup>.

### References:

- [1] Hong R, Edgar K, Song K, et al. Abstract PD4-14: GDC-0077 is a selective PI3K $\alpha$  inhibitor that demonstrates robust efficacy in PIK3CA mutant breast cancer models as a single agent and in combination with standard of care therapies[J]. Cancer research, 2018, 78(4\_Supplement): PD4-14-PD4-14.
- [2] Zhu R, Zhang H, Zhang F. Mechanistic optimization of inavolisib combined with CDK4/6 inhibitors in the treatment of PIK3CA-mutated breast tumors[J]. Frontiers in Immunology, 2025, 16: 1693927.
- [3] Song K W, Ong C C, Lin E, et al. KRAS codon-specific mutations differentially toggle PI3K pathway signaling and alter sensitivity to inavolisib (GDC-0077)[J]. Molecular Cancer Therapeutics, 2025, 24(12): 1890-1901.
- [4] Song K W, Edgar K A, Hanan E J, et al. RTK-dependent inducible degradation of mutant PI3K $\alpha$  drives GDC-0077 (Inavolisib) efficacy[J]. Cancer discovery, 2022, 12(1): 204-219.

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