**Product Data Sheet**

### Chemical Properties

**Product Name:** Dabrafenib (GSK2118436)

**Cas No.:** 1195765-45-7

**M.Wt:** 519.56

**Formula:** C23H20F3N5O2S2

**Synonyms:** N/A

**Chemical Name:** N-[3-[5-(2-aminopyrimidin-4-yl)-2-tert-butyl-1,3-thiazol-4-yl]-2-fluorophenyl]-2,6-difluorobenzenesulfonamide

**Canonical SMILES:** CC(C)(C)C1=NC(=C(S1)C2=NC(=NC=C2)N)C3=C(C(=CC=C3)NS(=O)(=O)C4=C(C(CC=C4F)F)F

**Solubility:** $\geq 26$mg/mL in DMSO, $\geq 2.59$ mg/mL in EtOH with ultrasonic and warming, $<2.58$ mg/mL in H$_2$O

**Storage:** Store at $-20^\circ$C

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

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

### Biological Activity

**Targets:** MAPK Signaling

**Pathways:** Raf

**Description:**

Dabrafenib is a specific inhibitor of BRAF V600 mutants with IC50 values of 0.5nM, 0.6nM and 1.9nM against V600E, V600K and V600D, respectively [1].

BRAF plays a central role in regulating MAPK signaling pathway which regulates cell growth, division and differentiation. The V600E mutation of BRAF increases the kinase activity and is
involved in metastatic melanomas. Dabrafenib is an ATP-competitive and reversible inhibitor of BRAF mutants. It potently inhibits BRAFV600E, BRAFV600K and BRAFV600D with IC50 values of 0.5nM, 0.6nM and 1.9nM, respectively. Dabrafenib is currently approved by FDA and is widely used in cancer patients harboring BRAF mutations. It is reported that treatment of dabrafenib shrinks the overall size of brain metastases in patients. It also has an impressive 60% response rate for melanomas outside of the brain. Dabrafenib provides a significant survival benefit in patients with metastatic melanoma [1, 2].

Reference:

Protocol

Cell experiment:

Cell lines
B-RafV600E-driven melanoma lines, SKMEL28 and A375P F11, and colorectal carcinoma cells Colo205, HT29 cells

Preparation method
The solubility of this compound in DMSO is > 10 mM. General tips for obtaining a higher concentration: Please warm the tube at 37 °C for 10 minutes and/or shake it in the ultrasonic bath for a while. Stock solution can be stored below -20 °C for several months.

Reacting conditions

Applications
Dabrafenib effectively inhibited cell proliferation of B-RafV600E-driven melanoma lines, SKMEL28 and A375P F11 (IC50 = 3 and 8 nM, respectively), and colorectal carcinoma cells Colo205 (IC50 = 7 nM). Moreover, dabrafenib selectively inhibited RIP3 and inhibited RIP3-mediated necroptosis for HT29 cells.

Animal experiment [3]:

Animal models
CD1 nu/nu mice bearing A375P F11 (B-RafV600E) tumors model

Dosage form
0.1, 1, 10, and 100 mg/kg, oral administration, once daily for 14 days or 300 mg/kg, 100 mg/kg dabrafenib (p.o.).

Applications
Dabrafenib dose-dependently inhibited tumor growth and reduced pERK levels in A375P F11 (B-RafV600E) human melanoma tissue in vivo. Additionally, dabrafenib alleviated acetaminophen-induced
liver injury in mice.

Other notes
Please test the solubility of all compounds indoor, and the actual solubility may slightly differ with the theoretical value. This is caused by an experimental system error and it is normal.

Reference:

Product Citations

Caution
FOR RESEARCH PURPOSES ONLY.

NOT FOR HUMAN, VETERINARY DIAGNOSTIC OR THERAPEUTIC USE.

Specific storage and handling information for each product is indicated on the product datasheet. Most ApexBio products are stable under the recommended conditions. Products are sometimes shipped at a temperature that differs from the recommended storage temperature. Shortterm storage of many products are stable in the short-term at temperatures that differ from that required for long-term storage. We ensure that the product is shipped under conditions that will maintain the quality of the reagents. Upon receipt of the product, follow the storage recommendations on the product data sheet.
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