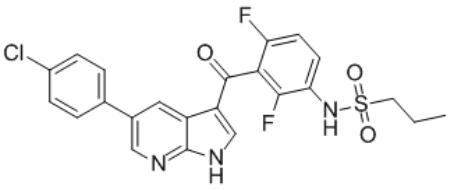
FT-LSB130

Vemurafenib

Product Description

Product Name:	**Vemurafenib** *Syn.*: PLX-4032; RG7204; R7204; RO5185426; PLX4032; HY-12057
Cat No :	LSB130, 10mg LSB131, 50mg LSB132, 100mg LSB133, 200mg LSB1329, 1ml at 10mM Solution in DMSO
CAS No.:	918504-65-1
MWt:	489.92
Formula:	$C_{23}H_{18}ClF_2N_3O_3S$
Purity :	>98%
Solubility:	DMSO: ≥ 45 mg/mL
Bioactivity:	IC50 value: 31 nM(B-RafV600E); 48 nM (c-Raf)[1]
Storage:(L)	Store in a tightly closed container, in a cool and dry place



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Technical and Scientific Information

Biological Activity of Vemurafenib

Vemurafenib (PLX4032, RG7204; RO5185426) is a novel and potent inhibitor of B-RafV600E with IC50 of 31 nM.

Pathways: B-RAF

Target: B-RafV600E

PLX4032 inhibits B-RAFV600E, C-RAF, as well as wildtype B-RAF, with IC50 of 31 nM, 48 nM and 100 nM, respectively. PLX4032 also inhibits several non-RAF kinases, including ACK1, KHS1, and SRMS, with IC50 of 18 nM to 51 nM [1].

In vitro: In melanoma cell lines, the inhibitory effect by PLX4032 depends on B-RAF mutational status, because PLX4032 potently inhibits those harboring B-RAF V600 mutants, including V600E, V600D, V600K, and V600R, but not wildtype or other mutants.
The IC50 values of PLX4032 on these cells, including MALME-3M, Colo829, Colo38, A375, SK-MEL28, and A2058, ranges from 20 nM to 1 μM. In these cells, PLX4032 (0.1 μM to 30 μM) also inhibits the phosphorylation of both MEK1/2 and ERK1/2 [2].

In vivo: PLX4032 is highly effective in the treatment of melanoma, for its ability of inhibiting B-RAFV600E. However, PLX4032 displays limited effect in colon cancer patients that also carrying B-RAFV600E oncoprotein. The reason for this is that, in colon cancer cells, B-RAFV600E inhibition by PLX4032 results in a rapid feedback EGFR activation, which compensates for the PLX4032-inhibited cell proliferation [3].
In B-RAFV600E-mutant mice xenograft models, PLX4032 (6 mg/kg–20 mg/kg) inhibits tumor growth [1]. In mice xenograft models of LOX, Colo829, and A375 cells, PLX4032 (12.5 mg/kg–100 mg/kg) inhibits tumor growth and prolongs mice survival [2].

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Preparing Stock Solutions

	1 mg	5 mg	10 mg
1 mM	1.6250 mL	8.1249 mL	16.2499 mL
5 mM	0.3250 mL	1.6250 mL	3.2500 mL
10 mM	0.1625 mL	0.8125 mL	1.6250 mL

Clinical Information of Vemurafenib

Sponsor Only	Condition	Start Date	End Date	Phase	Last Change Date
Roche Holding AG	Stage IV melanoma	31-OCT-13	31-MAY-16	Phase 4	06-NOV-13
Novartis AG	Stage IV melanoma	30-SEP-13	30-JUN-17	Phase 3	05-NOV-13
Hoffmann-La Roche Inc	Neoplasm	28-FEB-13	31-MAR-18	Phase 4	15-NOV-13
California Stem Cell Inc	Stage IV melanoma	31-MAR-14	30-JUN-17	Phase 3	12-SEP-13
Prometheus Laboratories Inc	Stage IV melanoma	31-AUG-12	01-APR-16	Phase 4	05-NOV-13

References on Vemurafenib

[1]. Bollag G, et al. Clinical efficacy of a RAF inhibitor needs broad target blockade in BRAF-mutant melanoma. Nature, 2010, 467(7315), 596-599.

[2]. Yang H, et al. RG7204 (PLX4032), a selective BRAFV600E inhibitor, displays potent antitumor activity in preclinical melanoma models. Cancer Res, 2010, 70(13), 5518-5527.

[3]. Prahallad A, et al. Unresponsiveness of colon cancer to BRAF(V600E) inhibition through feedback activation of EGFR. Nature, 2012, 483(7387), 100-103.

Specifications

Appearance	White to off-white solid	
Identification	The retention time of the major peak in the chromatogram of standard preparation	
	Mass spectrum of sample corresponds to that of standard preparation	
	1H NMR spectrum of sample corresponds to that of sample corresponds to that in the chromatogram of standard preparation	
Purity by HPLC	NLT 98.0%	
Conclusion:	The product tested complies with the specifications	

Legals

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