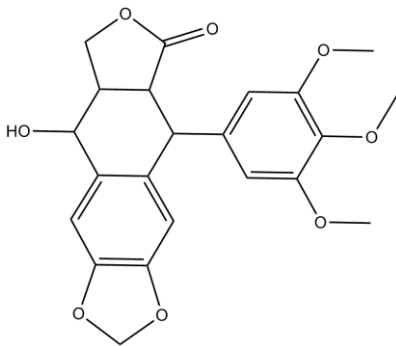


## Product Data Sheet

### Chemical Properties

<b>Product Name:</b>	AXL1717	
<b>Cas No.:</b>	477-47-4	
<b>M.Wt:</b>	414.41	
<b>Formula:</b>	C22H22O8	
<b>Synonyms:</b>	Picropodophyllotoxin; Picropodophyllin; PPP; AXL-1717; AXL 1717	
<b>Chemical Name:</b>	(5R,5aR,8aS,9R)-5-hydroxy-9-(3,4,5-trimethoxyphenyl)-5a,6,8a,9-tetrahydro-5H-[2]benzofuro[5,6-f][1,3]benzodioxol-8-one	
<b>Canonical SMILES:</b>	<chem>COC1=CC(=CC(=C1OC)OC)C2C3C(COC3=O)C(C4=CC5=C(C=C24)OC5)O</chem>	
<b>Solubility:</b>	≥20.7mg/mL in DMSO	
<b>Storage:</b>	Store at -20°C	
<b>General tips:</b>	For obtaining a higher solubility, please warm the tube at 37° C and shake it in the ultrasonic bath for a while. Stock solution can be stored below -20° C for several months.	
<b>Shopping Condition:</b>	Evaluation sample solution : ship with blue ice All other available size: ship with RT, or blue ice upon request	

### Biological Activity

**Targets :** Tyrosine Kinase

**Pathways:** IGF1R

**Description:**

AXL1717 (Picropodophyllotoxin) is a selective inhibitor of IGF-1R with IC50 value ranges from 0.24-0.33 μM [1].

IGF-1R (type 1 insulin-like growth factor receptor) is a transmembrane receptor that activated by

IGF-1 and plays an important role in cell growth and anabolic effects in adults. It has been reported that over-expression of IGF-1R is correlated with a variety of cancers and its inhibitors has been revealed to anti-cancer in clinical study [1] [2].

AXL 1717 is a potent IGF-1RTK inhibitor and has ability to inhibit tumor cells combined with HDAC inhibitor LBH589. When tested with 4 human myeloma cells (RPMI 8226, Karpas707, LP-1, and OPM-2) and 1 murine cell (5T33MM), AXL1717 treatment markedly decreased cell survival in a dose-dependent manner, arrested cell cycle in G2-M phase and induced cell apoptosis by inhibiting IGF-1RTK [1]. In four colon carcinoma cell lines (HT-29, HCT-116, DLD-1 and CaCO-2), AXL1717 treatment showed high ability to inhibit cell proliferation and migration in a dose-dependent manner [2].

In mouse model with 5TMM subcutaneous xenograft, administration of AXL 1717 (1.5 mg/d) resulted in a prolonged survival in combination with LBH (2.5 mg/kg/d) compared with control group [1].

AXL1717 has been tested to treat non-small cell lung cancer patients in a Phase I/II clinically [3].

### **Reference:**

[1].Lemaire, M., et al., *The HDAC inhibitor LBH589 enhances the antimyeloma effects of the IGF-1RTK inhibitor picropodophyllin. Clin Cancer Res, 2012. 18(8): p. 2230-9.*

[2].Feng, X., et al., *Multiple antitumor effects of picropodophyllin in colon carcinoma cell lines: clinical implications. Int J Oncol, 2012. 40(4): p. 1251-8.*

[3].Ekman, S., et al., *Clinical Phase I study with an Insulin-like Growth Factor-1 receptor inhibitor: experiences in patients with squamous non-small cell lung carcinoma. Acta Oncol, 2011. 50(3): p. 441-7.*

## **Protocol**

### **Cell experiment:**

Cell lines	Melanoma cells, sarcoma cells, P6 cells, OPM-2 and RPMI-8226 cells
Preparation method	The solubility of this compound in DMSO > 20.7 mg/mL. 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	AXL1717 (0.05-0.5 µM, 48 h) dose-dependently inhibited cell growth, and induced apoptosis in cultured melanoma cells (FM 55 and SK-MEL-28), sarcoma cells (RD-ES), and the mouse cell line P6 (overexpressing IGF-1R). In P6 cells, AXL1717 (0.025-1 µM) efficiently inhibited IGF-1-stimulated IGF-1R, as well as Akt (serine 473) and Erk1/2 phosphorylation. AXL1717 (1 µM) synergistically enhanced the anti-myeloma activity of ABT-737. In OPM-2 and RPMI-8226 cells, AXL1717 (125-500 nM) synergistically enhanced ABT-737 and ABT-199 mediated apoptosis. AXL1717 (1 µM) inhibited DNA synthesis, chemotaxis, and VEGF secretion of

5T33MM cells.

### Animal experiment [3]:

Animal models	SCID mice xenografted with human ES-1, BE, and PC3; 5T33MM murine model;
Dosage form	Intraperitoneal injection, 20 mg/kg/12 h, 8–14 days
Applications	In SCID mice xenografted with human ES-1, BE, and PC3, AXL1717 (20 mg/kg/12 h, i.p.) resulted in complete tumor regression. In 5T33MM murine model, AXL1717 (1.5 mg/kg, oral administration) showed a strong and significant reduction in BM plasmacytosis and serum M-protein levels. The combination of ABT-737 and AXL1717 (20 mg/kg, twice a day, intraperitoneally) did significantly and strongly prolong the overall survival. AXL1717 inhibited angiogenesis and prolonged the overall survival.
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:

- [1]. Girnita A, Girnita L, del Prete F, et al. Cyclolignans as inhibitors of the insulin-like growth factor-1 receptor and malignant cell growth[J]. *Cancer research*, 2004, 64(1): 236-242.
- [2]. Bieghs L, Lub S, Fostier K, et al. The IGF-1 receptor inhibitor picropodophyllin potentiates the anti-myeloma activity of a BH3-mimetic[J]. *Oncotarget*, 2014, 5(22): 11193.
- [3]. Menu E, Jernberg-Wiklund H, Stromberg T, et al. Inhibiting the IGF-1 receptor tyrosine kinase with the cyclolignan PPP: an in vitro and in vivo study in the 5T33MM mouse model[J]. *Blood*, 2006, 107(2): 655-660.

## 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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**APEX BIO Technology**

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