

## **SL-49. SMO inhibitors**

The aberrant Hedgehog signaling pathway is implicated in the pathogenesis of several solid and hematologic tumors; moreover, this pathway plays a key role in the maintenance and differentiation of cancer stem cells (CSCs) which are hypothesized to be responsible for the emergence of drug resistance, disease progression, and metastasis. Smoothened (SMO) is a GPCR-like protein that positively regulates Hedgehog signaling and its mutations can lead to unregulated activation of the pathway and eventually to cancer. Several SMO inhibitors are in clinical

development [1,2]. In 2012, first-in-class SMO inhibitor Vismodegib (Genetech) was approved by the US Food and Drug Administration for the treatment of basal-cell carcinoma; in 2015 Sonidegib (Novartis) was approved. Using a proprietary computational algorithm ASINEX has designed a library of small molecules sharing high structural similarity with approved drugs making them an interesting starting point for SMO-oriented drug discovery and research

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Vismodegib	Sonidegib	Taladegib
N N N O N O CN  Glasdegib	BMS-833923	SANT-1
Glasuegib	DIVI3-833323	SANT-1
		N O N O F F F F

## Signature Library 49

Formats	Supplementary Information	
80 compounds per plate	SL#49_SMO inhibitors.sdf	
0.1 mg; 1 mg; 2 mg dry film/powder		
0.1 µmol; 1 µmol DMSO solutions		

## References:

- 1. Nature medicine, 2013, 19, 11, 1410-1422 doi: 10.1038/nm.3389
- 2. OncoTargets and Therapy 2012, 5, 47-58, doi: <a href="https://dx.doi.org/10.2147/OTT.S21957">https://dx.doi.org/10.2147/OTT.S21957</a>

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