

# Product Information

## Geldanamycin-Biotin

Catalog Number **SML0985**

Storage Temperature –20 °C

CAS RN 1320265-38-0

### Product Description

Molecular Formula: C<sub>55</sub>H<sub>87</sub>N<sub>7</sub>O<sub>17</sub>S

Formula Weight: 1,150.35

Geldanamycin is a benzoquinone ansamycin antitumor antibiotic.<sup>1</sup> Geldanamycin binds specifically to Hsp90 (Heat Shock Protein 90)<sup>2</sup> and to its endoplasmic reticulum homologue GP96.<sup>3</sup> The Hsp90 chaperone is required for the activation of several families of eukaryotic protein kinases and nuclear hormone receptors, many of which are proto-oncogenic and play a prominent role in cancer. The geldanamycin antibiotic has antiproliferative and antitumor effects, as it binds to Hsp90, inhibits the Hsp90-mediated conformational maturation/refolding reaction, and results in the degradation of Hsp90 substrates.<sup>2</sup> Hsp90 also plays a key role in regulating the physiology of cells exposed to environmental stress and thus, geldanamycin interferes with cellular stress response.<sup>4</sup>

Geldanamycin was found to be a potent antibiotic active at nanomolar concentrations against 60 cell lines<sup>1</sup> as well as in mouse tumor models.<sup>5</sup>

It is an inhibitor of proto-oncogenic protein kinases, such as erbB2,<sup>6</sup> EFG receptor tyrosine kinases,<sup>7</sup> and non-receptor tyrosine kinases, such as v-src<sup>8</sup> and Raf-1.<sup>9</sup> In addition, it is a potent inhibitor of the nuclear hormone receptor family including the estrogen and androgen hormone receptors.<sup>10,11</sup> In order to identify geldanamycin-binding proteins, biotinylated geldanamycin and avidin resins are used for affinity purification and isolation of these proteins.<sup>12</sup>

### Precautions and Disclaimer

This product is for R&D use only, not for drug, household, or other uses. Please consult the Safety Data Sheet for information regarding hazards and safe handling practices.

### Preparation Instructions

The product is soluble (3 mg/ml) in methanol, in DMSO (10 mg/ml), and insoluble in water.

### Storage/Stability

It is recommended the product be stored desiccated and protected from light at –20 °C. The product as supplied is stable for 5 years when stored properly.

Solutions in DMSO are stable for at least two weeks when stored at –20 °C. Geldanamycin decomposes in acidic solution.

### Related product

17-(Allylamino)-17-demethoxygeldanamycin (17-AAG), Catalog Number A8476, which is a less toxic analog

### References

1. Supko, J.G. et al., Preclinical pharmacologic evaluation of geldanamycin as an antitumor agent. *Cancer Chemother. Pharmacol.*, **36**, 305-315 (1995).
2. Whitesell, L. et al., Inhibition of heat shock protein HSP90-pp6Ov-src heteroprotein complex formation by benzoquinone ansamycins: Essential role for stress proteins in oncogenic transformation. *Proc. Natl. Acad. Sci. USA*, **91**, 8324-8328 (1994).
3. Chavany C. et al., p185erbB2 binds to GRP94 *in vivo*. Dissociation of the p185erbB2/GRP94 heterocomplex by benzoquinone ansamycins precedes depletion of p185erbB2. *J. Biol. Chem.*, **271**, 4974-4977 (1996).
4. Schneider, C. et al., Pharmacologic shifting of a balance between protein refolding and degradation mediated by Hsp90. *Proc. Natl. Acad. Sci. USA*, **91**, 14536-14541 (1996).
5. Sasaki, K. et al., Growth inhibition of virus transformed cells *in vitro* and antitumor activity *in vivo* of geldanamycin and its derivatives. *J. Antibiot. (Tokyo)*, **32**, 849-851 (1979).
6. Miller, P. et al., Depletion of the erbB-2 gene product p185 by benzoquinoid ansamycins. *Cancer Res.*, **54**, 2724-2730 (1994).

7. Murakami, Y. et al., Accelerated degradation of 160 kDa epidermal growth factor (EGF) receptor precursor by the tyrosine kinase inhibitor herbimycin A in the endoplasmic reticulum of A431 human epidermoid carcinoma cells. *Biochem. J.*, **301**, 63-68 (1994).
8. June, C.H. et al., Inhibition of tyrosine phosphorylation prevents T-cell receptor-mediated signal transduction. *Proc. Natl. Acad. Sci. USA*, **87**, 7722-7726 (1990).
9. Schulte, T.W. et al., Disruption of the Raf-1-Hsp90 Molecular Complex Results in Destabilization of Raf-1 and Loss of Raf-1-Ras Association. *J. Biol. Chem.*, **270**, 24585-88 (1995).
10. Whitesell, L., and Cook, P., Stable and specific binding of heat shock protein 90 by geldanamycin disrupts glucocorticoid receptor function in intact cells. *Mol. Endocrinol.*, **10**, 705-712 (1996).
11. Smith, D.F. et al., Progesterone receptor structure and function altered by geldanamycin, an hsp90-binding agent. *Mol. Cell Biol.*, **15**, 6804-12 (1995).
12. Clevenger, R.C. et al., Biotinylated geldanamycin. *J. Org. Chem.*, **69**, 4375-4380 (2004).

KA,DWF,MAM 05/14-1