1.5.1.2.9 Istodax® (Romidepsin)

SAR:

Cyclic macrolactone with:

a- Polyamide

b- Disulfide bond

c- Alkene bond (Minucci and Pelicci 2006).

Mechanism of action:

Romidepsin acts as a prodrug with the disulfide bond undergoing reduction within the cell to release a zinc-binding thiol. The thiol reversibly interacts with a zinc atom in the binding pocket of Zn-dependent histone deacetylase (Shao *et al.*, 2010).

Histone deacetylase HDAC inhibitors are potential treatments for cancer through the ability to restore normal expression of genes, which may result in cell cycle arrest, differentiation, and apoptosis (Witt *et al.*, 2009).

Romidepsin is mainly used in the treatment of cutaneous T-cell lymphoma (Reimer 2010).

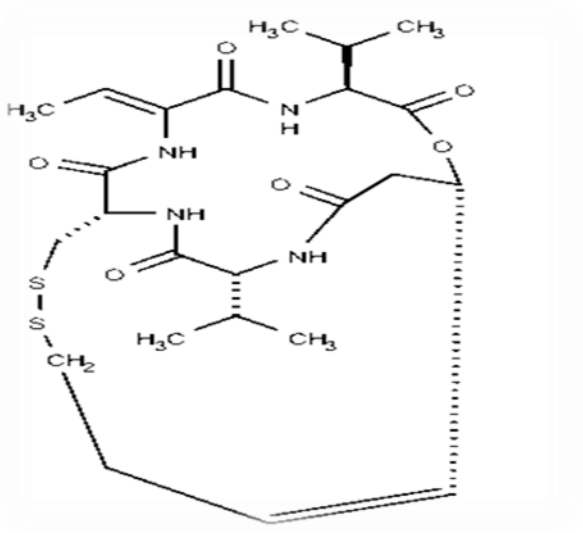

Figure 10: (1S, 4S, 7Z, 10S, 16E, 21R)-7-ethylidene-4,21-diisopropyl-2-oxa-12,13-dithia-5,8,20,23-Tetrazabicyclo{8,7,6}tricos-16-ene-3,6,9,19,22-pentone.