12.4.5 Salermide

Lara *et al.* (2009) synthesized salermide (*N*-phenyl-propionamide) (Figure 12.6), which exhibits higher selectivity against SIRT2 than against SIRT1.[125] Similar to sirtinol, which inhibited both SIRT1 and SIRT2, salermide significantly impaired MCF-7 cell proliferation through a p53-dependent mechanism. This dual inhibition of SIRT1 and SIRT2 was essential to achieve MCF-7 cell death.[110] Salermide also upregulated the expression of death receptor 5 and induced apoptosis in NSCLC, BE(2)-C and MiaPaca-2 pancreatic cells, leukemia MOLT4 cells, and MCF-7 cells.[65,126–128] The effect of salermide was more potent in cancerous cells, but not in non-tumorigenic cell lines with low level expression of SIRT1,[126] indicating that SIRT1 is a cancer-related gene that inhibits p53 function.

12.4.6 Indole Derivatives

Napper *et al.* discovered a series of indoles as potent inhibitors that were selective for SIRT1. The most active compound was named EX-527 (Figure 12.7), which inhibited SIRT1 in the nanomolar range with a 500-fold

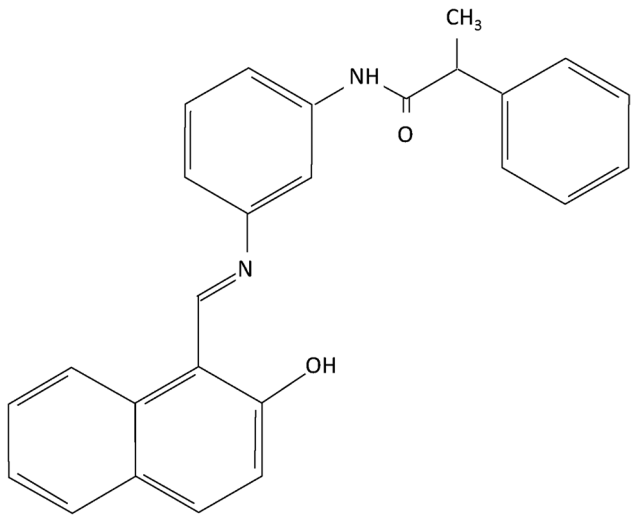

Figure 12.6 Salermide.

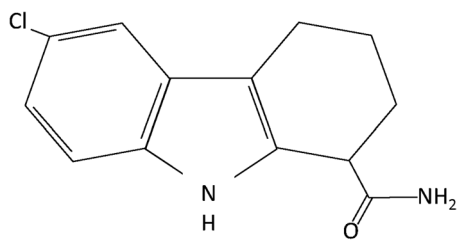

Figure 12.7 Ex-527.