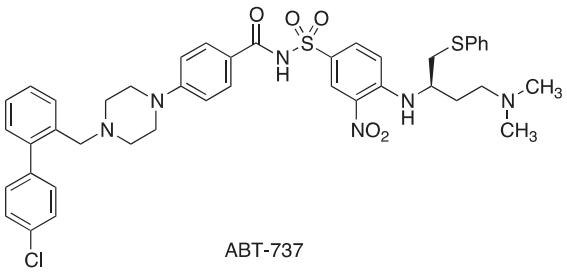
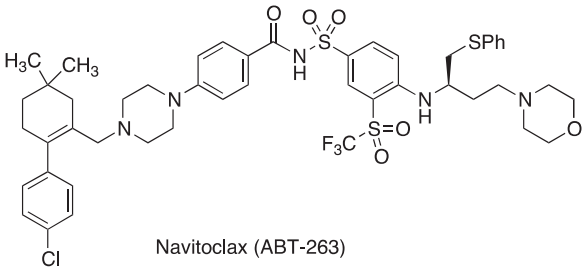
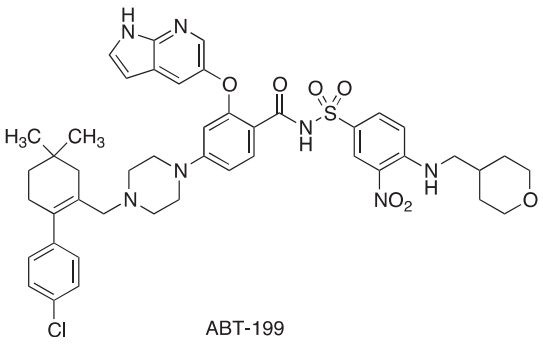
protein. It induced remission in patients with relapsed/refractory CLL and small lymphocytic lymphoma, but clinical assays were suspended after the death of a patient due to tumor lysis syndrome—an effect caused by breakdown products liberated from the sudden death of a large number of leukemia cells.



ABT-737



Navitoclax (ABT-263)



ABT-199

Obatoclax (GX15-070) is another BH3 mimetic in clinical evaluation as a single-agent or combination regimen for the treatment of hematological malignancies and solid tumors[177] that was designed by structural manipulation of bacterial secondary metabolites of the prodigiosin class. Prodigiosin and its analogs, nonylprodigiosin and streotorubin B, are blood red-colored natural products from bacteria such as *Serratia marcescens* or *Streptomyces coelicolor* that have demonstrated potent antimicrobial, antifungal, immunosuppressive, and cytotoxic activities.[178] Streptorubin B was found to be responsible for the activity of a natural extract in a biactivity-guided assay aimed at identifying inhibitors of the interaction of Bcl-2 with the pro-apoptotic protein Bax. Structure–activity studies and further optimization led to obatoclax, one of the first Bcl-2 antagonists to enter clinical trials. Further studies showed that obatoclax is a pan-Bcl-2 inhibitor that blocks BH3-mediated binding of Bax and Bak to their binding partners (Bcl-2, Bcl-xl, Mcl-1, and A1), thereby resulting in pro-apoptotic activity.[179] Additional biological targets have been proposed for this compound.[180]