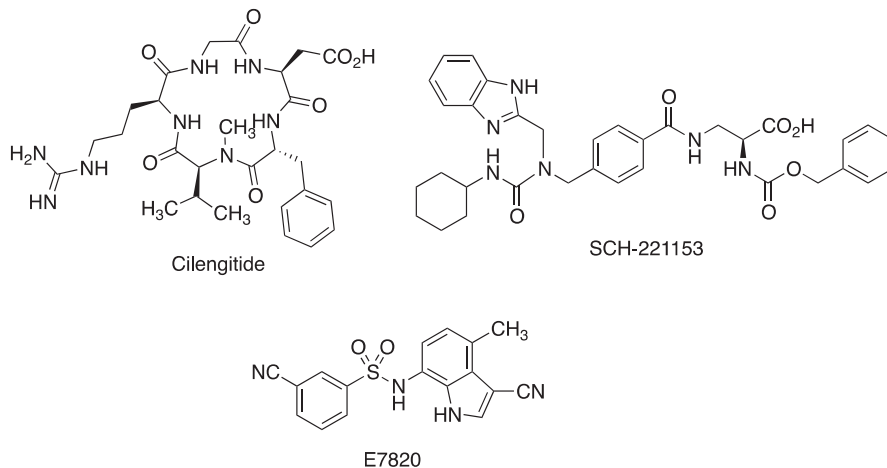
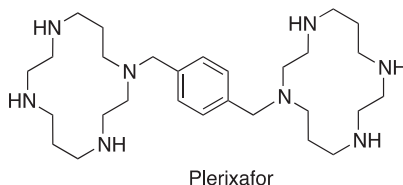


the expression of integrin  $\alpha_2$  subunit on endothelium.<sup>72</sup> After a phase I assay,<sup>73</sup> several phase II studies in patients with advanced malignancies are ongoing.



Peripheral blood stem cell mobilization, which is important as a source of hematopoietic stem cells for autologous transplantation in non-Hodgkin's lymphoma and MM cancer patients, is generally performed using granulocyte colony-stimulating factor (G-CSF), but this technique is ineffective in some patients. The interaction between the stromal-derived factor-1 (SDF-1) and the chemokine receptor CXCR4 (also known as fusin) plays an important role in holding hematopoietic stem cells in the bone marrow; consequently, inhibitors of CXCR4 are able to mobilize hematopoietic stem cells into the bloodstream. The percentage of patients who produce enough stem cells for transplantation increases with the combination of G-CSF with the CXCR4 inhibitor plerixafor (Mozobil<sup>®</sup>), which was approved by the FDA in 2008. Plerixafor has a curious history. It was synthesized in 1987 as part of basic studies on the redox chemistry of dimetallic coordination compounds, but later it was discovered that this compound could have a potential use in the treatment of HIV because it inhibits CXCR4, one of several chemokine receptors that certain strains of HIV uses to infect T-cells. The lack of oral availability and cardiac disturbances prevented the development of plerixafor for this indication, but further studies led to its approval as a subcutaneous injection for the previously mentioned cancer patients.<sup>74</sup>



## 5 ENDOGENOUS INHIBITORS OF ANGIOGENESIS

Some endogenous compounds, including endostatin, angiostatin, thrombospondin-1 (TSP-1), and the platelet-derived factor 4 (PF-4), are angiogenesis inhibitors. Endostatin is an inhibitor of integrin  $\alpha_v\beta_3$  whose activity can be mimicked by short arginine-rich peptides.<sup>75</sup> It is a polypeptide of 184 amino acids