Human noroviruses are a leading cause of gastroenteritis worldwide, yet there are no licensed antivirals. There is an urgent need for norovirus therapeutics, particularly for chronic infections in immunocompromised individuals, but also a potential need for prophylactic use in epidemics. Continued research has led to the identification of compounds that inhibit norovirus replication in vitro and, at least in some cases, are also effective in vivo against murine norovirus. Progress has included classical approaches targeting viral proteins and harnessing the antiviral action of interferon, strategies targeting essential host cell factors, and novel strategies exploiting the high mutation rate of noroviruses.