Inhibition of virus replication. Replication inhibitors include remdesivir (GS-5734), favipiravir (T-705), ribavirin, lopinavir and ritonavir. Except for lopinavir and ritonavir, which inhibit 3CLpro, the other three all target RdRp[128,135] (FIG. 5). Remdesivir has shown activity against SARS-CoV-2 in vitro and in vivo [128,136]. A clinical study revealed a lower need for oxygen support in patients with COVID-19 (REF.[137]). Preliminary results of the Adaptive COVID-19 Treatment Trial (ACTT) clinical trial by the National Institute of Allergy and Infectious Diseases (NIAID) reported that remdesivir has shown the recovery time in hospitalized adults with COVID-19 by a couple days compared with placebo, but the difference in mortality was not statistically significant [138]. The FDA has issued an emergency use authorization for remdesivir for the treatment of hospitalized patients with severe COVID-19. It is also the first approved drug by the European Union for treatment of adults and adolescents with pneumonia requiring supplemental oxygen. Several international phase III clinical trials are continuing to evaluate the safety and efficacy of remdesivir for the treatment of COVID-19.

Favipiravir (T-705), which is an antiviral drug developed in Japan to treat influenza, has been approved in China, Russia and India for the treatment of COVID-19. A clinical study in China showed that favipiravir significantly reduced the signs of improved disease signs on chest imaging and shortened the time to viral clearance [139]. A preliminary report in Japan showed rates of clinical improvement at 73.8% and 86.7%, from the use of favipiravir in patients with mild COVID-19 at 7 and 14 days, respectively, and 40.1% and 60.3% in patients with severe COVID-19 at 7 and 14 days.