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Preface

We find ourselves in the midst of another coronavirus outbreak—with this outbreak causing a global pandemic. Readiness on the vaccine front is in a far better place than during previous outbreaks. However, options on the therapeutic front remain limited. It is still not possible to predict the emergence of viruses capable of founding an epidemic, a fact that has been reconfirmed many times over the past few decades. Since the emergence of the West Nile virus in 1999, the world has endured one viral outbreak after another. Such events cause significant morbidity and mortality on a global scale. The sudden, rapid, global spread of coronavirus disease in 2019 (COVID-19) represents yet another example. While the world is ever poised for an influenza virus pandemic, readiness on a global scale for such an event is likely on par with our readiness for severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2). Particularly noteworthy is that scientists and clinicians in the United States were bracing themselves for an outbreak of enterovirus D68 (EV-D68): an infection associated with acute flaccid myelitis in young children. Instead, they were faced with SARS-CoV-2. The only way to change course and enhance global readiness no matter the virus is to create an arsenal of broad-spectrum/pan-virus-family antiviral therapeutics. Viral enzymes represent our best options for the development of antiviral therapeutics to address the widest swath of both known and unknown viruses. A major obstacle to achieving this goal is the dearth of young scientists with an interest in the nitty-gritty of the biochemistry and biophysics governing the function and inhibition of viral enzymes. This two-part volume, published as Volume 49 Part A and Volume 50 Part B, has been assembled to share the state of the art in the study of viral enzymes and their inhibitors, with the hope of inspiring a new generation of investigators to pick up the baton, and finally carry us across the finish line and into an era where pandemic preparedness is no longer the concern that it is today. Part A presents a mechanistic view of viral replication and inhibition from a detailed kinetic, structural, and single-molecule perspective. Part B presents a view of specific viral polymerase systems and clinically relevant pan-viral enzyme targets.

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