

# Antivirals for zoonotic viruses: Preparing for the next spill over.

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## Introduction

Zoonotic viruses—those transmitted from animals to humans—pose a persistent and growing threat to global health. From HIV and Ebola to SARS, MERS, and most recently SARS-CoV-2, history has shown that spillover events can trigger devastating pandemics. As human encroachment into wildlife habitats increases and global connectivity accelerates, the frequency of these events is expected to rise. While vaccines are critical for long-term prevention, antivirals offer rapid-response tools to contain outbreaks, treat infections, and reduce mortality. Developing broad-spectrum and targeted antiviral therapeutics for zoonotic viruses is essential to prepare for the next spillover [1].

Zoonotic viruses originate in animal reservoirs—often bats, rodents, birds, or primates—and cross species barriers through direct contact, intermediate hosts, or environmental exposure. Many of these viruses are RNA-based, characterized by high mutation rates and genetic plasticity, which facilitate adaptation to human hosts. Spillovers are often unpredictable, but ecological and epidemiological factors such as deforestation, wildlife trade, and agricultural intensification increase the likelihood of transmission. Once a virus establishes human-to-human transmission, the window for containment narrows. Antivirals can play a crucial role in this early phase, especially when vaccines are unavailable or under development [2].

Several antivirals have been repurposed or developed to treat zoonotic infections, originally developed for Ebola, was repurposed for COVID-19 and showed moderate efficacy in reducing recovery time. A broad-spectrum RNA polymerase inhibitor, has been tested against influenza, Ebola, and SARS-CoV-2. Ribavirin, used for Lassa fever and hantavirus infections, remains a cornerstone for

treating certain hemorrhagic fevers. Monoclonal antibodies, such as REGN-EB3 and mAb114, have shown promise in treating Ebola virus disease. These examples highlight the potential of antiviral platforms to be rapidly adapted for emerging zoonoses. Broad-spectrum antivirals target conserved viral mechanisms, such as RNA-dependent RNA polymerases or proteases, across multiple virus families. This approach offers flexibility in responding to unknown or newly emerged pathogens. For instance, GS-441524, the parent nucleoside of remdesivir, has shown activity against coronaviruses, filoviruses, and paramyxoviruses [3].

Host-targeted antivirals, which modulate cellular pathways essential for viral replication, also offer broad-spectrum potential. Drugs targeting endosomal acidification, lipid metabolism, or interferon signaling can inhibit diverse viruses but require careful balancing to avoid host toxicity. Developing antivirals for zoonotic viruses faces several hurdles: Many zoonotic outbreaks are sporadic or localized, reducing commercial interest. RNA viruses evolve quickly, potentially rendering antivirals ineffective. Studying zoonotic viruses often requires high-containment facilities and specialized models. By the time a virus is identified, it may have already spread widely, limiting the utility of targeted antivirals [4].

Addressing these challenges requires coordinated investment in research, surveillance, and infrastructure. To prepare for future spillovers, researchers are developing modular antiviral platforms that can be quickly adapted: These technologies, combined with high-throughput screening and cloud-based data sharing, can accelerate antiviral discovery and deployment. The One Health approach recognizes the interconnectedness of human, animal, and environmental health. Emergency use authorizations (EUAs) and accelerated approval

pathways have facilitated antiviral deployment during pandemics. However, ethical concerns around access, equity, and informed consent remain. Ensuring that antivirals are available to low-resource settings and vulnerable populations is critical for global health equity [5].

## Conclusion

Zoonotic viruses will continue to challenge global health systems, but antivirals offer a critical line of defense. By investing in broad-spectrum platforms, integrating One Health surveillance, and streamlining regulatory pathways, we can build a resilient antiviral arsenal. Collaborative frameworks involving governments, pharmaceutical companies, and international organizations can streamline regulatory processes while maintaining safety and efficacy standards. The COVID-19 pandemic underscored the importance of having antivirals ready before a spillover occurs. While vaccines took months to develop, antivirals like remdesivir and molnupiravir were deployed early, albeit with mixed results. Preparing for the next spillover is not just a scientific imperative—it is a moral and strategic necessity to protect lives and prevent pandemics.

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