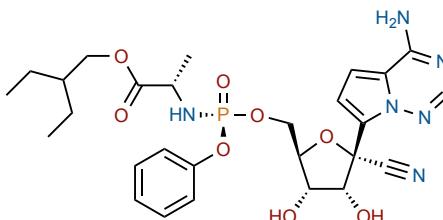


## Remdesivir (GS-5734)



## COVID-19

- Caused by SARS-CoV-2
- April 8: 1.5 million infections and 87,000 deaths
- April 27: 2.99 million infections and 207,000 deaths
- May 15: 4.48 million infections and 304,000 deaths
- SARS-CoV-2 binds more tightly to human receptors than other coronaviruses
- SARS-CoV-2 is an RNA based virus
- RNA replication is a common target for antivirals

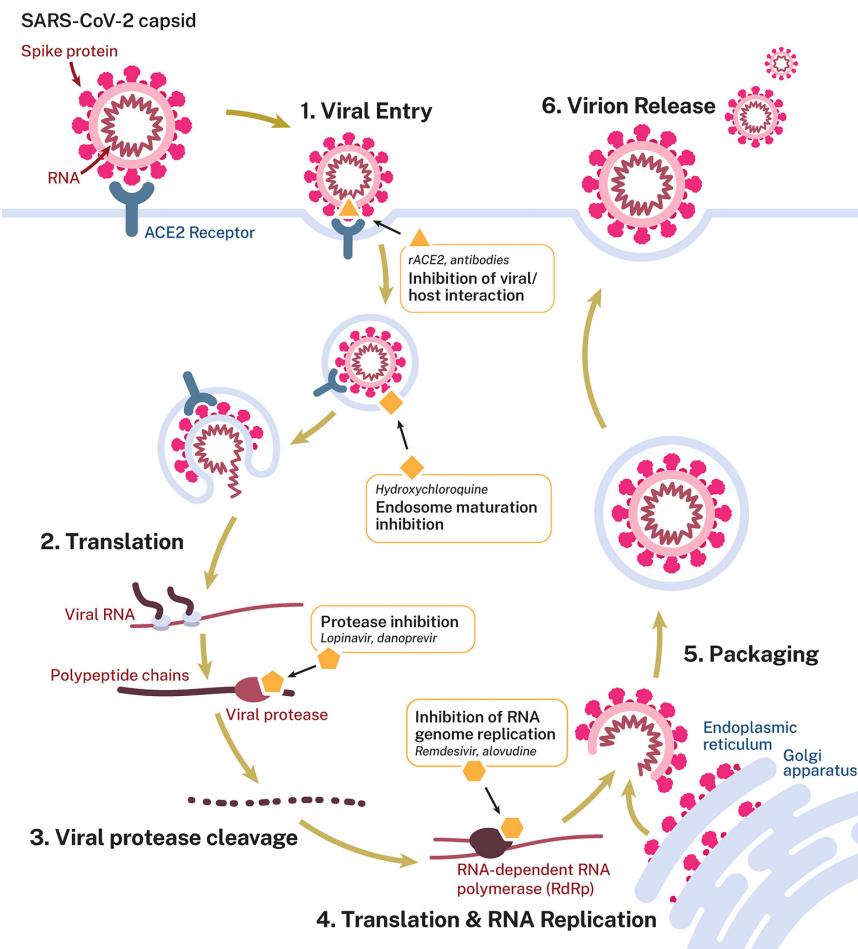
## Remdesivir

- Prodrigue drug that is converted into a monophosphate inside cells
- Active metabolite interferes with RNA-dependent RNA polymerase
- Action as a delayed chain inhibitor evades proofreading

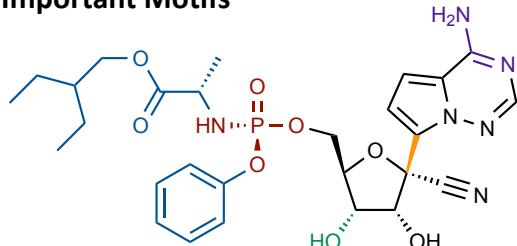
Science, 2020, <https://doi.org/10.1126/science.abc1560>

ACS Cent. Sci. Article ASAP, <https://doi.org/10.1021/acscentsci.0c00489>

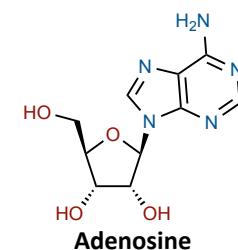
J. Med. Chem. 2017, 60, 1648 <https://doi.org/10.1021/acs.jmedchem.6b01594>



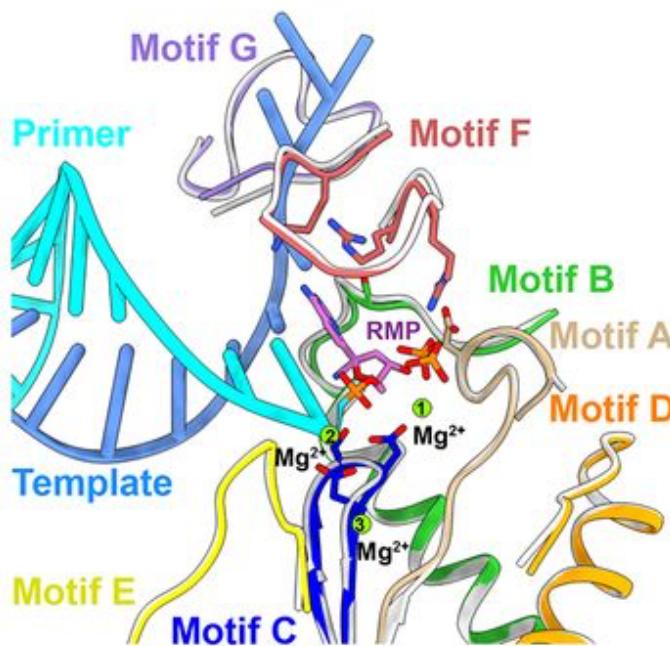
## Important Motifs



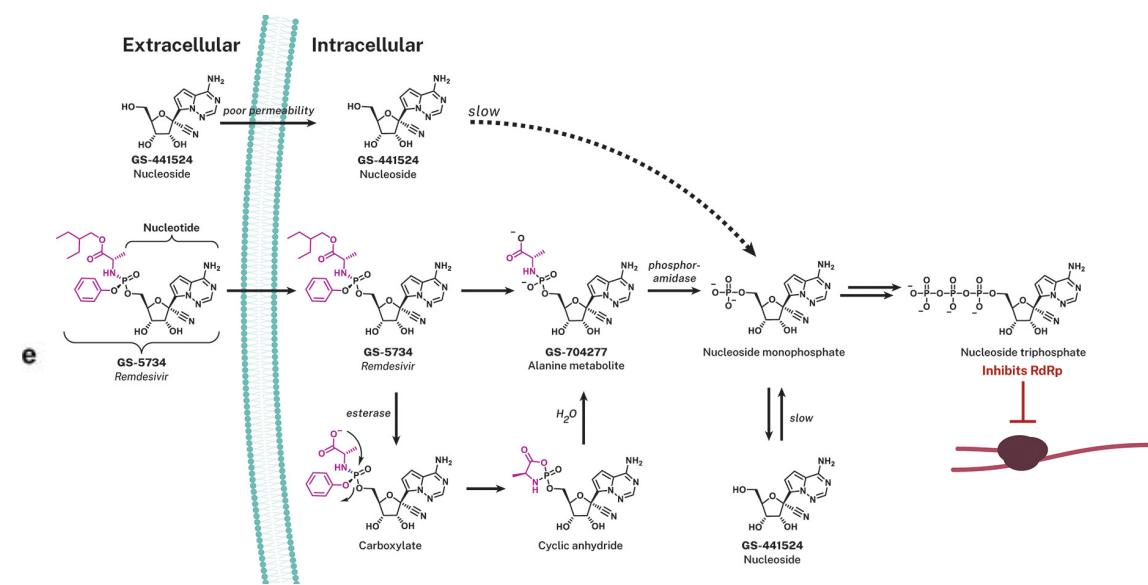
- Increases lipophilicity, allows diffusion through cell walls
- Pre-phosphorylation skips slowest step in active drug generation
- 3' hydroxy allows chain growth after incorporation of Remdesivir
- C-C bond increases stability of drug over natural hemiaminals
- Hydrogen bond donor/acceptor allow for recognition of Remdesivir



## Remdesivir Binding



## Protide to active drug



## Synthesis

