

DEVELOPMENT OF REMDESIVIR



Remdesivir was invented by Gilead building on more than a decade of our research. Over that time, our research scientists have explored the compound for multiple potential uses to help address urgent and unmet medical needs around the world, including Ebola, SARS, Marburg, MERS and most recently COVID-19. Our antiviral expertise is the result of more than 30 years of research and the investment of billions of dollars in research and development. Gilead's antiviral work reflects its commitment to collaborating with the global health community and advancing potential treatments that may help in the global response to public health emergencies.

Remdesivir is an investigational new drug created by Gilead. The research that led to remdesivir began **as early as 2009**, with research programs under way in hepatitis C (HCV) and respiratory syncytial virus (RSV). We continued to explore various uses for remdesivir following its discovery, **including antiviral profiling in 2013 and early 2014** that suggested the potential for remdesivir to have broad spectrum antiviral activity.

Gilead's ground-breaking research has led to an expansive library of compounds invented by Gilead that includes remdesivir. This archive of molecules can be accessed and tested against new viruses as they emerge. Our chemists continually work to invent new compounds, and Gilead has invested resources and time over decades so that even when a molecule initially seems unpromising, it may yet one day save lives.

By working in collaboration with both academic institutions and U.S. government agencies, we have been able to bring together disease experts to help expand knowledge of the antiviral profile of remdesivir against emerging viruses, including Ebola, SARS, Marburg, and MERS through *in vitro* studies and *in vivo* studies in animal models. Testing of remdesivir against the virus that causes COVID-19 is ongoing.

Ebola

In 2014, when the Ebola outbreak was spreading in West Africa, Gilead scientists believed that antiviral compounds that were designed for HCV and RSV might also have the potential to be active against emerging viruses including Ebola. Gilead worked with the U.S. government to confirm remdesivir's preclinical activity against Ebola.

- Gilead worked with **the U.S. CDC and the U.S. Army Medical Research Institute for Infectious Diseases (USAMRIID)** respectively to test collections of Gilead's antiviral molecules and confirmed remdesivir was active against Ebola and other viral pathogens representing potential global health threats.
- **In July 2015, Gilead filed an investigational new drug (IND) application and in August 2015 initiated its own Phase 1 studies** evaluating the safety and pharmacokinetics of remdesivir in healthy volunteers. These studies enabled the progression of remdesivir into clinical trials. At the same time, Gilead further optimized the formulation of remdesivir and scaled up the manufacturing process.
- **At the end of the 2014-2016 Ebola outbreaks in West Africa and again during the outbreak in 2018, Gilead provided remdesivir for the treatment of a small number of patients with Ebola infection under a compassionate use protocol.**
- Gilead provided study drug and input on the design and conduct for **two human clinical trials with remdesivir in Ebola disease** initiated by **the U.S. government.** In 2016, NIH **initiated a study of remdesivir** in Ebola survivors. In 2018, NIH began a study of remdesivir and other investigational treatments in patients with Ebola disease in the Democratic Republic of the Congo. Based on an interim review of the data, the remdesivir arm of this trial was discontinued, as two other investigational treatments in the trial were associated with greater survival.

REMDESIVIR IS AN INVESTIGATIONAL PRODUCT AND HAS NOT BEEN APPROVED ANYWHERE GLOBALLY. THE SAFETY AND EFFICACY OF REMDESIVIR FOR ANY USE HAVE NOT BEEN DETERMINED.

Coronaviruses

In parallel with our research and development efforts in Ebola, in late 2014, Gilead entered into collaborations with other institutions to study remdesivir against coronaviruses, including SARS and MERS. The studies confirmed remdesivir was active against these coronaviruses in *in vitro* laboratory tests and *in vivo* preclinical animal models.

- **Gilead entered into a collaboration with University of North Carolina (UNC) and Vanderbilt University to study the activity of remdesivir against SARS and MERS** in *in vitro* and in mouse models. Gilead provided study drug and input on the design for these studies and helped to interpret the study results.
- UNC and Vanderbilt conducted this research as part of a broader consortium of U.S. universities led by the University of Alabama at Birmingham (UAB) and funded by NIH grant money. **The NIH grant was given to the consortium in 2014 to support the discovery of new compounds against coronaviruses, among other projects.**
- **In 2016-2018, Gilead provided study drug and input on the design and conduct for studies of remdesivir in a non-human primate model of MERS infection conducted by the NIH. Gilead also contributed its expertise to help interpret the study results.**
- **Despite positive preclinical data**, remdesivir could not be advanced into clinical development for SARS and MERS, due to the lack of adequate numbers of potential study participants. The number of clinical MERS infections was limited, with almost exclusive localization in the Kingdom of Saudi Arabia, and there were no SARS infections.

Gilead invented remdesivir after decades of research. The speed with which remdesivir has moved into clinical development for COVID-19 reflects the pressing need for treatment options and our commitment to respond to this public health threat with the highest urgency.

COVID-19

In January 2020, when a new pneumonia-like illness in China was identified as a coronavirus, **Gilead moved quickly to determine whether remdesivir could play a role** in responding to the growing public health threat that subsequently became known as COVID-19. Gilead's preclinical data suggested that testing remdesivir against COVID-19 should take place immediately.

- Gilead's team of virologists quickly generated the preclinical data to characterize remdesivir's activity against the new COVID-19 virus and to determine the potential benefit of further testing.
- **In January 2020, Gilead provided remdesivir to the China CDC** to test the compound against isolates of the virus that causes COVID-19 through their independent antiviral assays. Gilead provided remdesivir to U.S. academic institutions in February 2020 for similar testing. Results are expected soon.
- **In February 2020, Gilead began supporting multiple clinical trials** to evaluate the safety and efficacy of remdesivir as a potential treatment for COVID-19.
- Gilead donated study drug and provided scientific input for **two clinical trials coordinated by the China-Japan Friendship Hospital in China, which began enrolling patients in early to mid- February.**
- Gilead donated drugs and provided scientific input for a **NIAID-initiated global clinical trial of remdesivir in late February**, including the first site to enroll patients in the United States.
- **In late February, Gilead initiated its own two Phase 3 studies of remdesivir**, which will enroll patients in countries globally with high numbers of diagnosed COVID-19 cases. These studies began enrolling patients in March 2020 and will evaluate two dosing durations of remdesivir.
- Gilead has provided input on the design of both WHO's global Solidarity trial and the INSERM-sponsored DisCoVeRy trial in Europe. These trials have already initiated and will expand to additional countries over the coming months. Gilead has committed to providing remdesivir to support these studies, which will be conducted in more than 70 countries worldwide.
- **In anticipation of potential future needs, we have accelerated manufacturing timelines to increase our available supply as rapidly as possible.** We are doing this before knowing whether remdesivir will be determined to be safe and effective to treat patients with COVID-19.