DEVELOPMENT OF VEKLURY®

GILEAD
Creating Possible

Veklury® (remdesivir) was invented by Gilead building on decades of our antiviral research. It is the first and only FDA-approved antiviral treatment for patients with COVID-19 in the United States. Gilead research scientists have explored the compound for multiple potential uses to help address urgent and unmet medical needs around the world,including Nipah, respiratory syncytial virus (RSV), Ebola, SARS, Marburg, MERS and most recently SARS-CoV-2, the virus that causes COVID-19. Our antiviral work reflects our commitment to collaborating with the global health community and advancing potential treatments that may help in the global response to public health emergencies.

The research that led to the invention of Veklury began as early as 2009, with research programs under way for hepatitis C virus (HCV) and RSV. This research was exclusively funded by Gilead. Following the invention of Veklury we continued to explore various uses for the compound, including identifying its activity against coronaviruses in 2013 and confirming its antiviral activity against various viruses, including RSV, SARS, MERS, Marburg and Ebola.

By working in collaboration with both academic institutions and U.S. government agencies, we have been able to bring together disease experts to help strengthen knowledge of the antiviral profile of Veklury against emerging viruses, including Ebola, SARS, Marburg and MERS through *in vitro* studies and *in vivo* studies in animal models.

COVID-19

When a new pneumonia-like illness in China was identified as a coronavirus in January 2020, **Gilead moved quickly to determine whether Veklury could play a role** in responding to what has become known as COVID-19. There is now a robust data set from three randomized, controlled, Phase 3 clinical trials evaluating the safety and efficacy of Veklury as a treatment for COVID-19.

- Gilead's team of virologists quickly generated the preclinical data to characterize Veklury's activity against the new virus that causes COVID-19 and to determine the potential benefit of further testing.
- **In January 2020, Gilead provided Veklury 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.
- **In February 2020, Gilead began supporting multiple clinical trials** to evaluate the safety and efficacy of Veklury 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 2020. Both trials were stopped early due to low enrollment.
- In late February 2020, Gilead donated study drug and provided scientific input on three **global clinical trials initiated by the National Institute of Allergy and Infectious Diseases (NIAID)** evaluating the safety and efficacy of Veklury. The *New England Journal of Medicine* published findings from the randomized, double-blind, placebo-controlled ACTT-1 trial in November 2020. The ACTT-2 and ACTT-3 trials are evaluating Veklury in combination with the anti-inflammatory drug baricitinib compared with Veklury alone and Veklury in combination with interferon beta-1a, respectively.
- In late February 2020, Gilead initiated **the open-label Phase 3 SIMPLE trials of two dosing durations of Veklury**, which enrolled patients in countries globally with high numbers of diagnosed COVID-19 cases. Full results from the studies were published in the *New England Journal of Medicine* and the *Journal of the American Medical Association*.
- In May 2020, we announced **a collaboration with Roche on the REMDACTA trial of Veklury in combination with tocilizumab**, an IL-6 inhibitor.
- In June 2020, Gilead initiated a Phase 2/3 clinical trial (CARAVAN) evaluating Veklury in **pediatric patients** with COVID-19.
- In October 2020, Veklury was approved by the U.S. Food and Drug Administration for adults and pediatric patients (12 years of age and older and weighing at least 40 kg) for the treatment of COVID-19 requiring hospitalization. Veklury should only be administered in a hospital or in a healthcare setting capable of providing acute care comparable to inpatient hospital care.
- Veklury is approved or authorized for temporary use in ~50 countries worldwide and generic remdesivir, manufactured by our licensees, is provided to 127 middle- and low-income countries.
- Gilead is exploring novel oral antivirals for the treatment of non-hospitalized COVID-19 patients and we continue to study Veklury as a potential treatment in hospitalized populations with specific unmet needs, including people with renal impairment, children and pregnant women.

Veklury is contraindicated in patients who are allergic to Veklury or any of its components. Please see the full Prescribing Information for Veklury available at **www.gilead.com** for additional information.

Ebola

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

- Gilead worked with **the U.S. Centers for Disease Control and Prevention and the U.S. Army Medical Research Institute for Infectious Diseases** respectively to test specific molecules selected by Gilead's scientists and confirmed remdesivir was active against Ebola, which represented a global health threat.
- **In July 2015, Gilead filed an investigational new drug 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 not approved anywhere globally for the treatment of Ebola virus infection.

Coronaviruses

Gilead also conducted its own, privately funded research of Veklury's antiviral activity against coronaviruses. Gilead exclusively funded the research that initially identified remdesivir's activity against coronaviruses. After confirming remdesivir's activity against coronaviruses, starting in 2014, Gilead entered into collaborations with other institutions to further confirm remdesivir against coronaviruses, including SARS and MERS. The studies also 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 confirm 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 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 NIAID. 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 Veklury after more than a decade of research. The speed and rigor with which Veklury has moved in 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.