



March 2021

BIOMEDICAL RESEARCH

Information on Federal Contributions to Remdesivir

GAO@100 Highlights

Highlights of [GAO-21-272](#), a report to congressional addressees

Why GAO Did This Study

Remdesivir is an antiviral drug patented and manufactured by Gilead. Along with its parent compound, remdesivir was originally developed to treat viral hepatitis and a viral respiratory infection. Remdesivir was later studied for antiviral activity against multiple viruses. It was the first drug approved by the FDA to treat COVID-19. Public interest organizations have raised questions about the extent of federal support for the development of remdesivir.

Federal support can benefit the public by creating new inventions and may result in certain intellectual property rights, including patents, for the federal government. Multiple federal agencies support biomedical research and development, which can directly or indirectly contribute to the development of new drugs like remdesivir. These federal agencies include NIH—the largest public funder of biomedical research in the world—as well as CDC and DOD.

GAO was asked to review federal contributions to the development of remdesivir. This report examines: (1) scientific and funding contributions provided by CDC, DOD, and NIH for the development of remdesivir, and (2) agencies' patent rights related to those contributions. GAO reviewed relevant laws and regulations; reviewed documentation from CDC, DOD, and NIH; and interviewed officials and scientists from the agencies and two universities. We also obtained information from and interviewed representatives of Gilead.

CDC, DOD, NIH, and Gilead provided technical comments, which we incorporated as appropriate.

View [GAO-21-272](#). For more information, contact Candice N. Wright, 202-512-6888, WrightC@gao.gov

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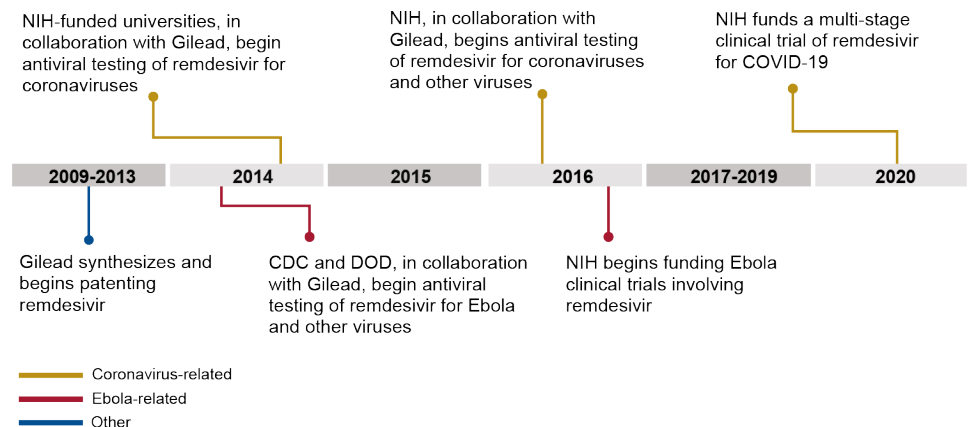
Information on Federal Contributions to Remdesivir

What GAO Found

Between 2013 and 2020, the Centers for Disease Control and Prevention (CDC), the Department of Defense (DOD), and the National Institutes of Health (NIH) conducted and funded preclinical research collaborations with Gilead Sciences, Inc. (Gilead) that helped to demonstrate remdesivir's antiviral properties against multiple viruses. NIH also funded three clinical trials. (See figure for examples of federal support.) Between 2009 and 2013, Gilead had synthesized the remdesivir compound, conducted and funded preclinical research that first identified and confirmed the antiviral activity of remdesivir and its parent compound against coronaviruses and other viruses, and had begun patenting the compounds. As of December 2020, federal funding for preclinical studies and clinical trials involving remdesivir totaled about \$162 million, as follows:

- \$0.7 million for CDC's preclinical research;
- \$39.7 million for DOD's preclinical research;
- \$11.9 million for preclinical research conducted by NIH and NIH-funded universities; and
- \$109.2 million for NIH-funded clinical trials.

Figure: Examples of Federal Involvement in the Development of Remdesivir, 2013-2020



Source: GAO analysis of information from the Centers for Disease Control and Prevention (CDC), Department of Defense (DOD), Gilead Sciences (Gilead), and the National Institutes of Health (NIH). | GAO-21-272

Federally supported remdesivir research conducted by CDC, DOD, NIH, and NIH-funded universities has not resulted in government patent rights, because, according to agency and university officials, federal contributions to the research did not generate new inventions. In addition, Gilead entered research collaborations with federal agencies and universities with a portfolio of existing patents and patent applications, including for the remdesivir compound, which would have left little room for the agencies to generate their own patents. For example, DOD officials told us that when DOD scientists performed antiviral testing of remdesivir against Ebola virus, they used standard tests and screening methods and did not come up with new tests or methods.

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Abbreviations

CDC	Centers for Disease Control and Prevention
COVID-19	Coronavirus Disease 2019
DOD	Department of Defense
FDA	Food and Drug Administration
Gilead	Gilead Sciences, Inc.
HHS	Department of Health and Human Services
MRDC	U.S. Army Medical Research and Development Command
NIAID	National Institute of Allergy and Infectious Diseases
NIH	National Institutes of Health
R&D	research and development
USAMRIID	U.S. Army Medical Research Institute of Infectious Diseases

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March 31, 2021

Congressional Addressees

Multiple federal agencies support biomedical research and development (R&D), which can directly or indirectly contribute to the development of new drugs. Preeminent among them is the National Institutes of Health (NIH), an agency in the Department of Health and Human Services (HHS). NIH is the largest public funder of biomedical research in the world, with \$35 billion obligated in fiscal year 2018. The Centers for Disease Control and Prevention (CDC), another HHS agency, and the Department of Defense (DOD) also play active roles in biomedical R&D. The federal government's support includes research funding for universities, R&D conducted in-house at federal laboratories, and research collaborations that involve federal laboratories, universities, and pharmaceutical companies.

Generally, federally funded inventions generated by grantees and contractors are subject to a government use license.¹ The federal government's intellectual property rights may also include ownership or co-ownership of patented inventions resulting from discoveries made in research collaborations with universities and industry. These ownership rights could enable the federal government to use the inventions for public benefit or collect royalties from industry.²

Remdesivir is an antiviral drug patented and manufactured by Gilead Sciences, Inc. (Gilead), a U.S. pharmaceutical company with expertise in antiviral drug development, which owns a large library of compounds that

¹Under the Bayh-Dole Act, a government use license generally provides the federal government with a nonexclusive, nontransferable, irrevocable, paid-up license to practice (use) the invention or have the invention practiced throughout the world by or on behalf of the federal government. See 35 U.S.C. § 202(c)(4). This government use license may not be available for funding agreements not subject to the Bayh-Dole Act.

²A patent is an exclusive right granted for a fixed period of time to an inventor, which can be assigned to (owned by) other entities. A patent owner can prevent others from making, using, selling, or offering for sale the patented invention in the United States, or importing it into the United States without authorization. A patent owner can license or assign the patent rights.

target viral pathogens.³ Originally developed by Gilead as a candidate to treat viral hepatitis and respiratory syncytial virus infection, remdesivir was later studied for antiviral activity against multiple virus families, including coronaviruses.⁴

In the spring of 2020, remdesivir was the first drug shown to shorten recovery time in hospitalized Coronavirus Disease 2019 (COVID-19) patients and subsequently became the first drug to be approved by the Food and Drug Administration (FDA) as a COVID-19 treatment.⁵ FDA granted an emergency use authorization on May 1, 2020, and approval on October 22, 2020, for using remdesivir to treat COVID-19.⁶

Policymakers, state authorities, and public interest advocates have raised concerns about access to remdesivir in the United States.⁷

³According to Gilead, the company's other areas of expertise are hematology, oncology, and inflammatory diseases; in February 2021 it had more than 25 products on the U.S. market, of which 17 were antiviral drugs.

⁴Viral hepatitis is an infection that causes liver inflammation and damage. Several different viruses, including hepatitis A, B, and C viruses, cause hepatitis. Respiratory syncytial virus infection is caused by a common respiratory virus that usually causes mild, cold-like symptoms, but can be serious, especially for infants and older adults. Coronaviruses, named for the crown-like spikes on their surfaces, are a family of viruses that are common in people and many different species of animals.

⁵According to CDC, COVID-19 is a new disease, caused by a novel coronavirus known as SARS-CoV-2 that has not previously been seen in humans.

⁶Under section 564 of the Federal Food, Drug, and Cosmetic Act, the FDA Commissioner may allow unapproved medical products or unapproved uses of approved medical products to be used in an emergency to diagnose, treat, or prevent serious or life-threatening diseases or conditions caused by chemical, biological, radiological, and nuclear threat agents when there are no adequate, approved, and available alternatives. Following the initial May 1, 2020, emergency use authorization granted to treat hospitalized adult and pediatric patients with severe COVID-19 disease, FDA broadened the authorization's scope to include hospitalized COVID-19 patients, irrespective of the severity of the disease, on August 28, 2020. On October 22, 2020, FDA approved remdesivir for the treatment of COVID-19 in adults and pediatric patients (12 years of age and over weighing at least 40 kg) requiring hospitalization. The emergency use authorization for remdesivir remains in effect for other pediatric patients not covered by the approval.

⁷On June 29, 2020, Gilead announced that it would charge \$2,340 for a five-day course for all governments in the developed world, including the U.S. government's Medicaid program and the Department of Veterans Affairs, and \$3,120 (or 33 percent more) for private U.S. insurers. At present, remdesivir is administered intravenously in a hospital setting. According to Gilead, it is developing inhalable, subcutaneous, and oral forms of remdesivir, which may affect the drug's pricing and could involve additional patents and separate FDA review and approval.

You asked us to review federal contributions to the development of remdesivir and intellectual property rights associated with them. This report examines: (1) scientific and funding contributions provided by federal agencies for the development of remdesivir, and (2) federal agencies' patent rights related to those contributions. For both objectives, we reviewed relevant laws and regulations, and documentation from CDC, DOD, and NIH. We also interviewed officials and scientists from CDC, DOD, NIH, the University of North Carolina at Chapel Hill, and Vanderbilt University. We met with representatives from Gilead and obtained information about remdesivir development and patents from the company. (See app. I for more details about our scope and methodology.)

We conducted this performance audit from August 2020 to March 2021 in accordance with generally accepted government auditing standards. Those standards require that we plan and perform the audit to obtain sufficient, appropriate evidence to provide a reasonable basis for our findings and conclusions based on our audit objectives. We believe that the evidence obtained provides a reasonable basis for our findings and conclusions based on our audit objectives.

Background

Drug Development

The development and approval of a new drug is a long and costly process that can take 15 or more years and can involve multiple public and private entities that fund and conduct R&D.⁸ Typically, this process consists of the following stages:

- **Basic research.** Scientific investigation of the molecular, cellular, or biological mechanisms of a disease that lays the foundation for the development of new drugs;
- **Drug discovery.** Screening of thousands of compounds in the laboratory to identify promising candidates to treat the disease;

⁸The cost of developing a new drug is a subject of debate. A study published in 2016 estimated the cost of developing a new drug at more than \$2.5 billion; see J.A. DiMasi, H.G. Grabowski, and R.W. Hansen, "Innovation in the Pharmaceutical Industry: New Estimates of R&D Costs." *Journal of Health Economics*, vol. 47 (2016). A more recent study estimated the cost at \$1.3 billion; see O.J. Wouters, M. McKee, and J. Luyten, "Estimated Research and Development Investment Needed to Bring a New Medicine to Market, 2009-2018," *Journal of the American Medical Association*, vol. 323, no. 9 (2020).

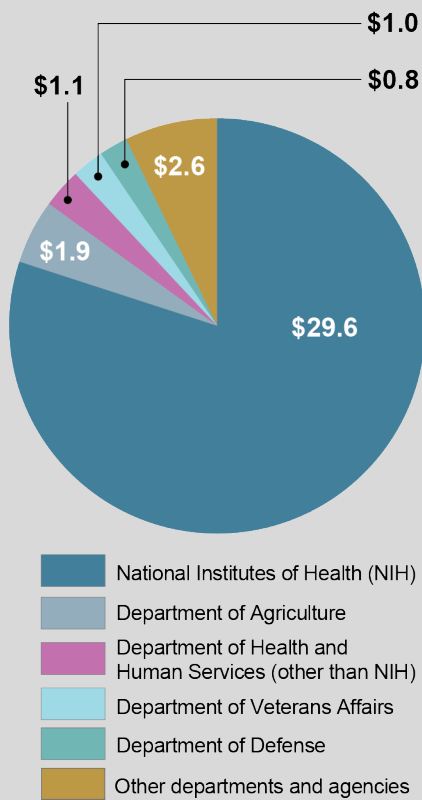
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- **Preclinical research.** Laboratory and animal testing to further narrow the list of compounds and answer basic questions about safety and proof of concept;
 - **Clinical trials.** Testing of the drug in human volunteers for safety and efficacy that is conducted in phases;⁹ and
 - **Review and approval.** FDA conducts a regulatory review before approving, or declining to approve, the drug for marketing and sales in the United States.

During this process, many new drug candidates fail to advance to the next stage or to gain FDA approval. Often, drug candidates and drugs that already have FDA approval are studied for new therapeutic uses. Because such work builds upon previous R&D efforts, new candidate therapies could be ready for clinical trials quickly, speeding their review by FDA. Gilead originally invented and developed remdesivir as a candidate for treating viral hepatitis and respiratory syncytial virus infection; however, it was never approved for either disease. Remdesivir was subsequently investigated for its antiviral potential for several other viruses, as discussed in this report, before FDA approved it as a COVID-19 treatment in October 2020.

⁹Clinical trials are usually conducted in phases that build on one another. Phase I trials of a new drug are usually the first that involve human volunteers and are done to find the highest dose of the new treatment that can be given safely without causing severe side effects. If a new treatment is found to be safe in phase I clinical trials, a phase II clinical trial is conducted to investigate its efficacy against a disease. Phase III clinical trials compare the safety and efficacy of the new treatment against the current standard treatment or a placebo. Phase IV clinical trials study the side effects caused over time by a new treatment after it has been approved and is on the market.

Public Funding for Biomedical R&D

Federal Obligations for Research in Life Sciences, Fiscal Year 2018 (in billions of dollars)



Source: GAO analysis of National Science Foundation data. | GAO-21-272

Federal funding for life sciences, which include biological and medical sciences, accounts for about 29 percent of federally supported R&D. According to the most recent data from the National Science Foundation, the federal government obligated \$129 billion for R&D, including \$37 billion for life sciences, in fiscal year 2018 (see sidebar).¹⁰ NIH is the largest source of support; it directs funding to universities and supports research performed by government scientists at NIH laboratories. At NIH, the National Institute of Allergy and Infectious Diseases (NIAID) is the leading institution for carrying out and supporting research on infectious diseases caused by viral pathogens.

Other agencies—such as CDC, DOD, and the Department of Veterans Affairs—also support biomedical R&D. CDC, which leads outbreak and emergency responses domestically and abroad, has several laboratories across the United States that perform biomedical R&D and public health research. At DOD, several components support biomedical R&D, including the Joint Program Executive Office for Chemical, Biological, Radiological and Nuclear Defense and the U.S. Army Medical Research and Development Command (MRDC). DOD’s lead laboratory for biomedical defense research is the U.S. Army Medical Research Institute of Infectious Diseases (USAMRIID), which is subordinate to MRDC.

Another significant contribution that the federal government makes to biomedical R&D is specialized facilities. For example, some federal laboratories contain biohazard containment systems that are uncommon outside the federal government. These facilities enable federal scientists to study the world’s most dangerous pathogens, including Ebola and other viruses.¹¹

¹⁰National Science Foundation, *Survey of Federal Funds for Research and Development, Fiscal Years 2018–19*, <https://ncesdata.nsf.gov/fedfunds/2018/>, accessed Feb. 23, 2021.

¹¹Ebola virus is one of several filoviruses that cause a deadly hemorrhagic fever in humans and nonhuman primates, such as monkeys, gorillas, and chimpanzees, with occasional outbreaks that occur primarily on the African continent. According to CDC, people can get the disease through direct contact with an infected animal, or a sick or dead person infected with Ebola virus.

How Remdesivir Works

Remdesivir, also known as GS-5734 and approved by the Food and Drug Administration under the brand name Veklury, is an antiviral drug. Remdesivir is a pharmacologically inactive compound. Once absorbed by the patient's body, it is converted into its pharmacologically active parent compound GS-441524. The parent compound's structure is similar to the molecular building blocks of DNA and RNA; such compounds are known as nucleoside analogs. When a virus incorporates the nucleoside analog molecule, viral replication is disrupted, and the virus can no longer multiply.

Source: GAO | GAO-21-272

A recent paper seeks to quantify the relationship between NIH-funded basic research and the development of remdesivir and other drugs with similar chemical structure (see sidebar).¹² According to the paper, two bodies of foundational research enabled the development of drugs like remdesivir: studies of nucleoside analogs, drugs with remdesivir's parent chemical structure, and studies of RNA-dependent RNA polymerase, remdesivir's biological target. It estimates that NIH provided \$6.5 billion from 2000 through 2019 to support these two bodies of basic research. According to officials from NIAID we spoke with, the paper's interpretation of the remdesivir-enabling foundational research is broad, and the estimate includes research for other drugs with similar targets and mechanisms of action as remdesivir. They also told us that NIAID did not have its own estimate of NIH funding for basic research that enabled the development of remdesivir.

Patent Rights for Inventions Developed with Federal Support

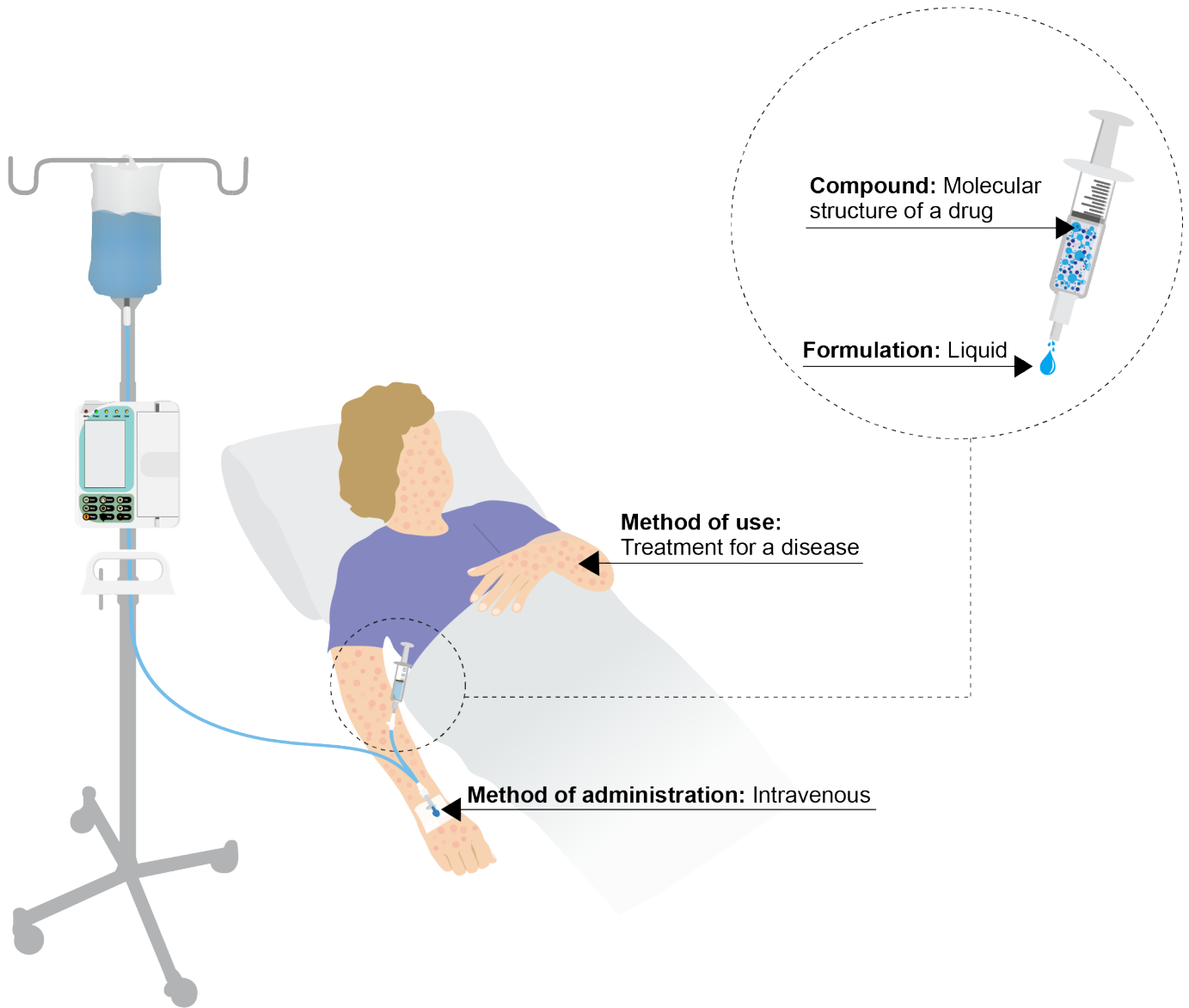
If an inventor invents or discovers a new chemical compound, the inventor may seek a patent claiming the invention.¹³ An inventor can also patent a group of distinct chemical compounds. Also patentable are drug formulations, methods of using a drug to treat a particular disease, methods and technologies to administer or manufacture a drug, as well as methods and technologies that test for and diagnose diseases, if they meet certain patentability requirements. See figure 1 for examples of pharmaceutical patents.¹⁴

¹²E.G. Cleary et al., "Foundational Research and NIH Funding Enabling Emergency Use Authorization of Remdesivir for COVID-19," *medRxiv*. Pre-print version, posted July 6, 2020, doi: <https://doi.org/10.1101/2020.07.01.20144576>. The study had not been peer-reviewed as of March 2021. An earlier study by some of the same authors observed that while estimates exist for the commercial development of new drugs, the public sector contribution to new drugs is less well quantified; E.G. Cleary et al., "Contribution of NIH Funding to New Drug Approvals 2010-2016," *PNAS*, vol. 115, no. 10 (2018).

¹³See generally 35 U.S.C. § 101.

¹⁴Under U.S. patent law, any person who "invents or discovers any new and useful process, machine, manufacture, or composition of matter" may apply for a patent on the invention with the U.S. Patent and Trademark Office (USPTO). If the USPTO patent examiner concludes that the claimed invention is novel, nonobvious, useful, directed at patentable subject matter, and adequately disclosed and claimed, USPTO will issue a patent. Patents typically expire 20 years after the initial patent application is filed.

Figure 1: Examples of Pharmaceutical Patents



Source: GAO. | GAO-21-272

When an invention is conceived and reduced to practice by a company that has received federal support for that invention, any resulting patent rights are owned jointly or separately by the U.S. government or the

company, depending on the nature of federal involvement in the invention.¹⁵ The federal government uses different types of agreements to support R&D conducted by nonfederal entities, such as universities or pharmaceutical companies, and collaborations with such entities. Some agreements, including contracts, grants, cooperative agreements, and “other transaction” authority agreements involve the transfer of federal funding to nonfederal entities.¹⁶ Other agreements, such as cooperative research and development agreements and material transfer agreements, do not.¹⁷

Federal Agencies Made Contributions to Remdesivir Preclinical Research and Clinical Trials

Beginning in 2013, CDC, DOD, and NIH supported and conducted preclinical research collaborations with Gilead that helped to demonstrate remdesivir’s broad-spectrum antiviral properties against multiple viruses, including coronaviruses and Ebola. Later, data from NIH-supported clinical trials helped to advance remdesivir to clinical use once the COVID-19 pandemic reached the United States. Federal funding for these remdesivir preclinical studies and clinical trials totaled \$161.5 million.

¹⁵The federal government’s general policy for federally owned inventions, under the Stevenson-Wydler Technology Innovation Act and the Federal Technology Transfer Act of 1986, is to encourage commercialization by licensing federally owned patent rights to private parties—a process called “technology transfer.”

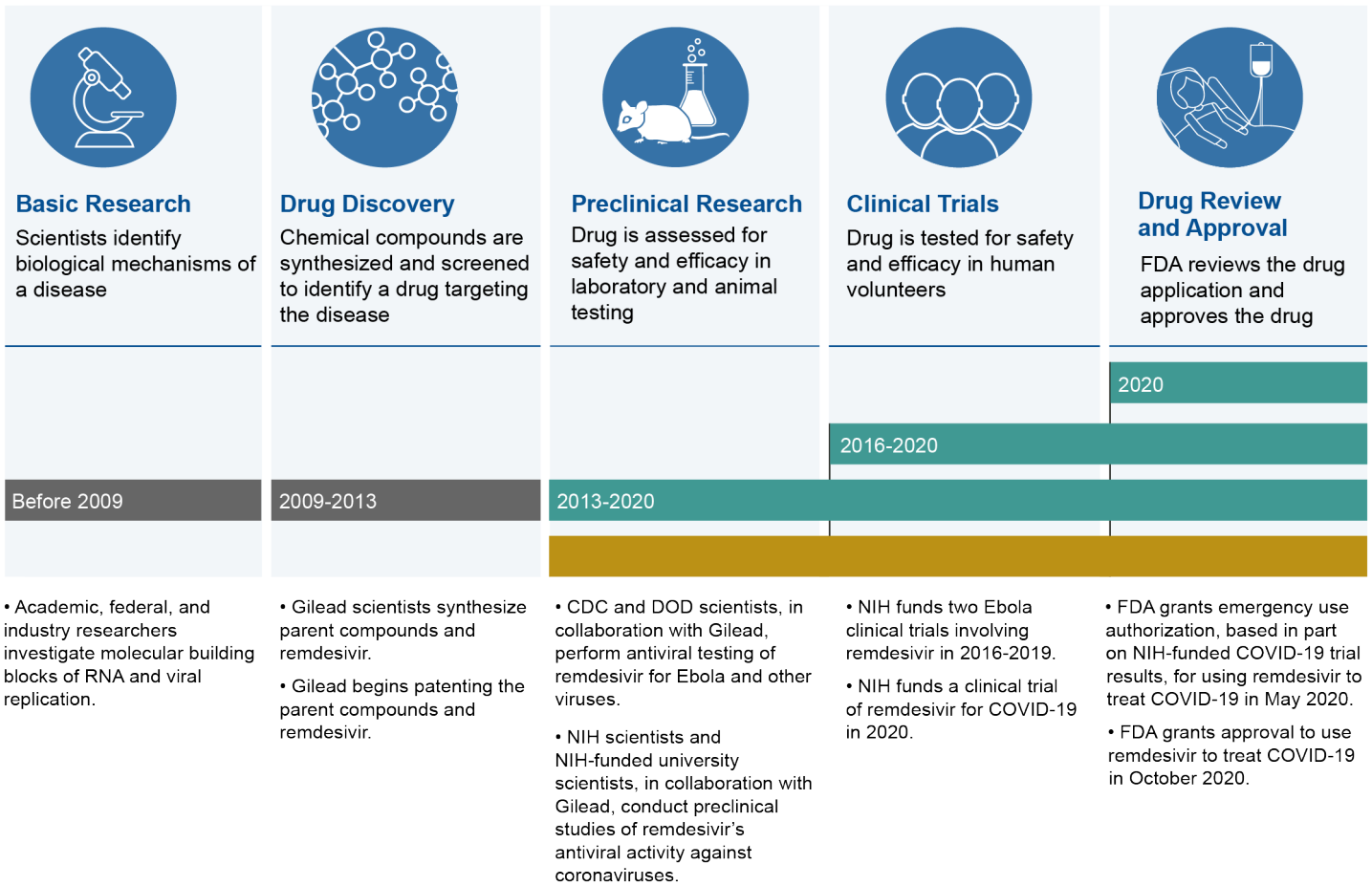
¹⁶A federal agency can use a contract under the Federal Acquisition Regulation to procure and pay for property or services, including research services, from a private company. It can use a grant to fund university-based research or a cooperative agreement to fund a complex or targeted research study conducted by a university consortium. Some agencies, including DOD and NIH, have the authority to enter into “other transaction” authority agreements. “Other transactions” may be exempt from many statutory provisions and procurement regulations, such as the Bayh-Dole provision granting a government use license for federally funded inventions. See 35 U.S.C. § 202(c)(4).

¹⁷A federal laboratory can use a cooperative research and development agreement to provide personnel, services, facilities, or other resources, while the nonfederal collaborator (a company or academic institution) provides funds, personnel, services, facilities, or other resources toward a specific R&D project. A material transfer agreement can be used to transfer a specialized or experimental material between a federal laboratory and another party for commercial evaluation, testing, or other uses.

CDC, DOD, and NIH
Helped to Advance the
Knowledge of
Remdesivir's Antiviral
Activity against
Coronaviruses, Ebola
Virus, and Other
Pathogens

The federal government began supporting Gilead's preclinical remdesivir-related research in 2013 (see fig.2), when Gilead provided three compounds, including remdesivir's parent compound, to CDC for antiviral screening. CDC, DOD, and NIH began supporting research focusing on remdesivir itself in 2014. By that time, Gilead had invented the compound; the company first synthesized the parent compound in March 2009. The company isolated the remdesivir compound in 2013. According to Gilead, between 2009 and 2013, the company conducted and funded preclinical research that first identified and confirmed the antiviral activity of remdesivir and its parent compound against coronaviruses and other viruses. Gilead also began patenting the compounds during this period.

Figure 2: Timeline of Select Events and Federal Contributions to the Development of Remdesivir



Not reviewed by GAO for this report.

Reviewed by GAO for this report.

Following invention, Gilead conducted its own remdesivir research and clinical trials, initiated collaborations with federal agencies, and made substantial contributions to the research performed in those collaborations.

Source: GAO analysis of information from the Centers for Disease Control and Prevention (CDC), Department of Defense (DOD), Food and Drug Administration (FDA), Gilead Sciences (Gilead), and the National Institutes of Health (NIH). | GAO-21-272

Preclinical Research

When Gilead initiated preclinical research collaborations with CDC in 2013 and with DOD's USAMRIID in 2014, Gilead scientists selected

compounds for testing against emerging viruses.¹⁸ CDC and USAMRIID scientists investigated remdesivir for antiviral activity against Ebola and other pathogens. These collaborations took place at the time of several outbreaks of Ebola virus disease affecting multiple countries.¹⁹ According to CDC and USAMRIID scientists we interviewed, most of their research took place at these agencies' Biosafety Level 4 facilities, because it involved very dangerous pathogens.²⁰

CDC began its research collaboration with Gilead in 2013 by screening three Gilead-owned compounds, including remdesivir's parent compound GS-441524, for antiviral activity against Nipah or Hendra viruses.²¹ According to Gilead, the company selected the compounds based on its proprietary knowledge about the compounds' antiviral profiles and requested that CDC evaluate them for antiviral activity against multiple viruses. In 2014, as an Ebola virus disease outbreak was taking place in West Africa, CDC scientists at the National Center for Emerging and Zoonotic Infectious Diseases proposed to test the parent compound GS-441524 against Ebola and found that it exhibited antiviral activity against the virus.²² Later, the collaboration expanded to screening 73 Gilead-owned compounds, which included remdesivir. As described in one of the first scientific publications about remdesivir, CDC scientists designed and executed the initial antiviral testing of remdesivir in cell cultures for

¹⁸Gilead initially provided the compounds to CDC and USAMRIID blinded, meaning that only Gilead knew what the compounds were.

¹⁹Multiple outbreaks of Ebola virus disease occurred between 2012 and 2020, according to CDC. The 2014-2016 outbreak, which generated the largest number of infections and deaths, spread from Africa to Europe and the United States.

²⁰Biosafety Level 4 is the highest level of biosafety precaution.

²¹Nipah and Hendra are related viruses that spread between animals and people. According to CDC, Nipah virus kills about 75 percent of people it infects.

²²Gilead provided the compounds blinded, meaning that CDC scientists did not know what the compounds were at the time.

efficacy against Ebola virus.²³ CDC scientists also evaluated remdesivir's antiviral properties against other virus families.²⁴

At DOD, USAMRIID's collaboration with Gilead, which began in 2014, involved the screening of more than 1,000 Gilead-owned compounds for antiviral activity against multiple viruses. USAMRIID scientists told us that, as the research progressed, they collaborated closely with Gilead scientists to advance multiple promising compounds, including remdesivir, from testing in cell cultures to nonhuman primate testing with live Ebola virus. USAMRIID research demonstrated remdesivir's activity against Ebola in primates and generated data that could support further investigation of remdesivir as an Ebola treatment for humans. Similar to research conducted by CDC scientists, USAMRIID scientists also tested remdesivir for activity against other viruses.²⁵

NIH support for remdesivir research involved funding for extramural research at universities beginning in 2014 as well as conducting its own intramural research beginning in 2016.²⁶ Most of the preclinical remdesivir research funded and conducted by NIH focused on coronaviruses. According to Gilead, the company had already determined that remdesivir's parent compound and remdesivir itself were active against some coronaviruses by the time NIH began supporting remdesivir coronavirus research: research conducted or funded by Gilead demonstrated that remdesivir's parent compound and remdesivir were active against the severe acute respiratory syndrome-associated

²³Travis K. Warren et al., "Therapeutic Efficacy of the Small Molecule GS-5734 against Ebola Virus in Rhesus Monkeys," *Nature*, vol. 531 (2016). The article was co-authored by scientists from multiple organizations, including CDC, Gilead, and USAMRIID. Before publication, initial results were reported in an October 2015 presentation at the joint annual meeting (IDWeek) of the Infectious Diseases Society of America, Society for Healthcare Epidemiology of America, HIV Medical Association, Pediatric Infectious Diseases Society, and Society of Infectious Diseases Pharmacists.

²⁴These virus families included other filoviruses (Ebola is a filovirus), paramyxoviruses, arenaviruses, and flaviviruses, among others. According to Gilead, the company had funded similar screenings of its compounds prior to the collaboration with CDC.

²⁵These viruses included Chikungunya, Rift Valley fever virus, and the Middle East respiratory syndrome coronavirus (MERS-CoV). In addition, according to DOD officials, as of January 2021, USAMRIID was planning to investigate remdesivir's potential against Marburg virus, which, similar to Ebola, causes a hemorrhagic fever.

²⁶Federally funded R&D performed at universities, medical centers, hospitals, and other research institutions is known as extramural; R&D conducted by federal agencies at their own laboratories and facilities is known as intramural.

coronavirus (SARS-CoV) in 2012 and the Middle East respiratory syndrome coronavirus (MERS-CoV) in 2013.

NIH-funded university-based remdesivir preclinical research was conducted by scientists at the University of North Carolina at Chapel Hill and Vanderbilt University in collaboration with Gilead scientists.²⁷ The research confirmed remdesivir's antiviral potential against known coronaviruses and demonstrated that it could be active against new coronaviruses.²⁸ Research performed by NIH scientists at NIAID's Laboratory of Virology between 2016 and 2020 involved preclinical testing of remdesivir in nonhuman primate models of coronavirus infection and disease and necessitated use of specialized facilities for handling dangerous pathogens.

Clinical Trials and FDA Approval

NIH supported three clinical trials involving remdesivir—two for Ebola virus disease in 2016-2019 and a COVID-19 trial in 2020:

- **Ebola trials known as PREVAIL IV and PALM.** After remdesivir showed promise against Ebola virus in preclinical studies, it was tested for safety and efficacy in Ebola clinical trials without becoming an FDA-approved treatment. The PREVAIL IV and PALM trials helped to generate safety and efficacy data for using remdesivir in human patients.²⁹ Before these trials, Gilead initiated its own phase I trials to evaluate the safety and chemical behavior of remdesivir in humans.³⁰ Although the PALM trial showed that remdesivir was less efficacious against Ebola virus disease than another treatment, the two trials helped to establish that remdesivir was safe to use in human patients

²⁷The research was conducted as part of a university consortium research project led by the University of Alabama at Birmingham. In addition to coronaviruses, the project investigated three other virus families.

²⁸See, for example, T.P. Sheahan et al., "Broad-Spectrum Antiviral GS-5734 Inhibits both Epidemic and Zoonotic Coronaviruses," *Science Translational Medicine*, vol. 9, no. 396 (2017).

²⁹The Partnership for Research on Ebola Virus in Liberia IV (PREVAIL IV) trial was a phase II trial. The Pamoja Tulinde Maisha (PALM), translated as "together save lives," was a phase II and phase III trial. Prior to PREVAIL IV and PALM, Gilead had funded or conducted several phase I trials.

³⁰According to Gilead, the phase I safety and chemical behavior (known as pharmacokinetics) studies in humans were considerably expanded in 2016 and then again in 2019 to include an assessment of additional remdesivir formulations, doses, and duration of treatment.

and generated additional safety data that could be reviewed by FDA.³¹

- **The Adaptive COVID-19 Treatment Trial (ACTT).** This multi-stage trial was initiated in February 2020.³² ACTT is an ongoing phase III trial, which was preceded by phase I and II trials involving remdesivir, including Gilead-funded trials as well as PREVAIL IV and PALM that established its safety for human use. Preliminary results of ACTT's first stage released in April 2020 showed that remdesivir shortened recovery time in hospitalized patients with severe COVID-19. Based in part on those results, FDA granted an emergency use authorization on May 1, 2020, for using remdesivir to treat such patients.³³ FDA also cited the trial's data, along with data from trials conducted by Gilead, in its approval of remdesivir granted on October 22, 2020.³⁴

Federal Funding Supported Remdesivir Preclinical Research and Clinical Trials

Federal agencies contributed \$161.5 million to remdesivir R&D from 2013 through 2020. As of December 31, 2020, CDC had provided \$0.7 million and DOD had provided \$39.7 million to support research on Ebola and other viruses, and NIH had provided \$121.1 million to support coronavirus-focused preclinical research and three clinical trials that involved remdesivir. Table 1 summarizes the funding information for CDC, DOD, and NIH. (These agencies are continuing to fund and conduct remdesivir research; see app. II for more details about each agency's funding for remdesivir research and agreements to provide funding). In addition to funding, the three agencies made an important contribution by providing federal Biosafety Level 4 facilities for testing remdesivir against dangerous pathogens such as Ebola virus.

³¹According to Gilead, because Ebola (a filovirus that is spread via body fluids) and coronaviruses (spread via respiratory droplets) are very different, research into the efficacy of remdesivir against Ebola virus disease was of limited utility in assessing the drug's efficacy for treating COVID-19.

³²As of January 2021, there were four stages of ACTT; the last stage began in November 2020. All four stages of the trial involved remdesivir.

³³FDA cited efficacy data from three COVID-19 trials in its emergency use authorization—ACTT and two trials conducted by Gilead—noting that ACTT had generated the most robust clinical data.

³⁴The preliminary and final results of ACTT's first stage were published in *The New England Journal of Medicine*. For final results, see J.H. Beigel et al., "Remdesivir for the Treatment of Covid-19—Final Report," *The New England Journal of Medicine*, vol. 383, no. 19 (2020).

Table 1: CDC, DOD, and NIH Funding for Remdesivir Preclinical Research and Clinical Trials, 2013-2020

Type of research	Amount by agency (in millions \$)			Totals
	CDC	DOD	NIH	
Preclinical research	0.7	39.7	11.9	52.3
Clinical trials	—	—	109.2	109.2
Total	0.7	39.7	121.1	161.5

Source: GAO analysis of documents and information from the Centers for Disease Control and Prevention (CDC), Department of Defense (DOD), and National Institutes of Health (NIH). | GAO-21-272

Note: The amounts in the table reflect funding for intramural and extramural research as of Dec. 31, 2020.

According to Gilead representatives, Gilead did not rely on any federal contributions in conducting its own research that led to the invention of remdesivir and invested \$786 million in remdesivir R&D from 2000 through December 2020.³⁵ Gilead representatives also told us that the company made substantial contributions to the research performed in the collaborations with federally funded scientists, which was corroborated in our interviews with others. For example, principal investigators of the NIH-funded coronavirus research told us that scientists at Vanderbilt University and the University of North Carolina at Chapel Hill worked in close collaboration with Gilead scientists. A principal investigator also noted that Gilead had dedicated substantial resources and maintained a coronavirus research team for several years prior to the COVID-19 pandemic when few others were interested in studying coronaviruses.

³⁵Gilead estimated its overall investment in remdesivir, as of December 2020, at \$1.3 billion. According to the company, of the \$786 million in R&D costs, Gilead spent \$215 million on the discovery and development of remdesivir prior to 2020, of which \$175 million is attributable specifically to R&D costs and \$40 million to costs of supplying remdesivir for use in NIH clinical trials and other clinical and research settings. Gilead told us that in addition to the R&D costs the company spent \$147 million to supply remdesivir for use in clinical and research settings and \$318 million to expand remdesivir manufacturing and distribution capabilities, as of December 2020.

Federal Researchers Did Not Disclose New Inventions Related to Remdesivir and Research Did Not Result in Government Patent Rights

Intellectual property provisions in agreements negotiated with Gilead generally would have allowed the agencies to pursue patents, had the remdesivir research supported and conducted by CDC, DOD, and NIH resulted in new inventions.³⁶ However, remdesivir research supported or conducted by CDC, DOD, and NIH has not resulted in government patent rights, because, according to agency and university officials, the federal contributions to the research did not generate new patentable discoveries, and Gilead already had existing patents on remdesivir. According to DOD and NIH officials, while the federally supported remdesivir research did not result in patent rights for the federal government, it helped to deliver a needed drug to the public.

Some scholars and public interest advocates have suggested that CDC or DOD scientists may be co-inventors on some of Gilead's remdesivir patents.³⁷ The suggestions were based in part on contributions to remdesivir research on Ebola as described in published scientific studies that CDC and USAMRIID scientists co-authored with Gilead scientists.³⁸ The CDC, DOD, NIH, and university officials we interviewed stated that federal and university scientists who conducted remdesivir research did not file invention disclosures, which would have been a precursor to filing a patent.³⁹ Further, according to DOD, NIH, and universities, their

³⁶See app. III for more details about the intellectual property provisions of the agencies' agreements with Gilead.

³⁷See J. Hughes and A. Rai, "Acknowledging the Public Role in Private Drug Development: Lessons from Remdesivir," *STAT* (May 8, 2020); J. Krellenstein and C.J. Morten, "The U.S. Government's Apparent Co-Ownership of Patents Protecting Remdesivir," The PrEP4All Collaboration and New York University School of Law (May 20, 2020); C. Rowland, "Taxpayers Paid to Develop Remdesivir but Will Have No Say when Gilead Sets the Price," *Washington Post* (May 26, 2020); and E. Silverman, "A Payoff for U.S. Taxpayers? CDC May Have Claims on Remdesivir Patents Held by Gilead," *STAT* (Dec. 7, 2020).

³⁸The standards for co-inventorship are different from those for co-authorship. Co-authorship, which is determined by each publication and can vary, generally includes those who contributed to the research. Co-inventorship requires contribution to the conception of the invention.

³⁹An invention disclosure—a form in which scientists document their inventions—is the initial step in the process that federal agencies and universities use for managing their intellectual property. Technology transfer and intellectual property law staff review invention disclosures and consider whether the invention is patentable. They also consider whether patenting the invention is likely to result in a successful commercialization or other practical application before deciding whether to pursue a patent in the United States and other countries.

scientists were not co-inventors of patented remdesivir discoveries for reasons outlined below:

- According to MRDC officials at DOD, USAMRIID scientists had not submitted any invention disclosures from their remdesivir research. Further, MRDC conducted an inventorship analysis in the spring of 2020 in response to questions raised by intellectual property scholars and public advocates cited above about the government’s possible co-inventorship of remdesivir. MRDC determined that scientific work performed by USAMRIID scientists did not rise to the level of co-inventor status on any of Gilead’s remdesivir patents. MRDC officials told us that they reached this determination based on the following factors: (1) Gilead invented the remdesivir compound and determined that it had antiviral activity against hepatitis C virus prior to the company’s collaboration with DOD; (2) Gilead entered into its collaboration with DOD with rights to all remdesivir and other compounds it provided, and told USAMRIID scientists what the compounds should be screened for; and (3) when USAMRIID scientists performed antiviral testing of remdesivir against Ebola virus, they used standard tests and screening methods and did not come up with new types of tests or screenings.⁴⁰
- According to NIH officials, NIH scientists did not submit invention disclosures from their coronavirus-focused remdesivir research, and invention disclosures were unlikely to emerge because Gilead had already determined that remdesivir exhibited antiviral activity against coronaviruses before NIH began its research. NIH officials told us that, given these circumstances, NIH did not conduct an inventorship analysis.
- The principal investigators of NIH-funded coronavirus research projects told us that they did not consider filing invention disclosures because their research did not involve making any modifications to remdesivir or its parent compounds. The principal investigators stated that they viewed such modifications as the threshold for filing such disclosures.

⁴⁰MRDC officials further elaborated that the tests and screening methods used by USAMRIID scientists in their remdesivir research collaborations with Gilead were known and established. According to these officials, for inventorship criteria to be met, a USAMRIID scientist would have had to deviate significantly from the statements of work in agreements with Gilead. The officials stated that USAMRIID scientists did not contribute toward the conception of remdesivir or using remdesivir to treat Ebola or any other viruses.

DOD and NIH officials also told us that Gilead's prior remdesivir research and intellectual property portfolio left few opportunities for federally supported scientists to make new patentable discoveries:

- Gilead entered the research collaborations with the federal agencies and universities with its portfolio of existing patents and patent applications, including for the remdesivir compound. NIH officials stated that Gilead began patenting methods of using remdesivir to treat coronavirus infections in 2015, that is, before NIH scientists began their remdesivir research focusing on coronaviruses in 2016. The company continued to expand its portfolio during collaborations with federally supported scientists. For example, Gilead applied for an Ebola-related remdesivir patent during its research collaborations with CDC and DOD's USAMRIID. Separate from federally supported collaborations Gilead conducted its own remdesivir research and, according to Gilead, patented inventions resulting from that research, such as various formulations of remdesivir.⁴¹ As of December 2020, Gilead owned 16 U.S. patents, including six that claimed the molecular structure of remdesivir and parent compounds, and submitted eight remdesivir-related patent applications, according to the company. Gilead representatives stated that the company's scientists are the sole inventors of the discoveries claimed in those 16 remdesivir patents. (For more information about Gilead's remdesivir patents, see app. IV.)
- DOD and NIH officials told us that even if federal scientists had submitted invention disclosures for new methods of using remdesivir, Gilead's remdesivir compound patents would have reduced the value of method-of-use patents to the federal government. According to DOD and NIH officials, a remdesivir method-of-use patent would be of low economic value because the federal government did not own the compound patents and would have had to license those patents from Gilead if it wanted to commercialize the method of use or license it to another company. DOD officials also told us that such follow-on patents would be hard to obtain and enforce.

With respect to CDC, officials told us that their scientists had not filed invention disclosures from their remdesivir research that began in 2014. CDC scientists told us that at the time of their research they were focused on determining if remdesivir had the potential to become an effective treatment for Ebola virus disease in response to ongoing Ebola outbreaks

⁴¹Larson, Nate. Compositions Comprising an RNA Polymerase Inhibitor and Cyclodextrin for Treating Viral Infections. U.S. Patent 10,675,296, filed July 11, 2017, and issued June 9, 2020.

in Africa, without immediate consideration of the intellectual property implications. According to officials, as of March 2021, it was unlikely that CDC would conduct an inventorship analysis or pursue intellectual property rights given Gilead's background intellectual property and the limited potential for CDC to license any such rights.⁴²

Agency Comments and Third-Party Views

We provided a draft of this report to CDC, DOD, NIH, and Gilead. They provided technical comments, which we incorporated as appropriate.

We are sending copies of this report to the appropriate congressional committees, the Secretary of Health and Human Services, the Secretary of Defense, Chief Executive Officer of Gilead, and other interested parties. In addition, the report is available at no charge on the GAO website at <http://www.gao.gov>.

If you or your staff have questions about this report, please contact me at (202) 512-6888 or WrightC@gao.gov. Contact points for our Offices of Congressional Relations and Public Affairs may be found on the last page of this report. Key contributors to this report are listed in appendix V.



Candice N. Wright
Acting Director
Science, Technology Assessment, and Analytics

⁴²CDC officials further explained that generally the agency undertakes an inventorship analysis if there is disagreement among the involved parties about who the inventors should be, or if there is knowledge of an invention for which another party had filed a patent application and for which CDC scientists may be inventors, among other factors.

List of Addressees

The Honorable Patrick Leahy
Chairman
The Honorable Richard Shelby
Vice Chairman
Committee on Appropriations
United States Senate

The Honorable Ron Wyden
Chairman
The Honorable Mike Crapo
Ranking Member
Committee on Finance
United States Senate

The Honorable Patty Murray
Chair
The Honorable Richard Burr
Ranking Member
Committee on Health, Education,
Labor, and Pensions
United States Senate

The Honorable Gary C. Peters
Chair
The Honorable Rob Portman
Ranking Member
Committee on Homeland Security
and Governmental Affairs
United States Senate

The Honorable Debbie Stabenow
Chair
Subcommittee on Health Care
Committee on Finance
United States Senate

List of Addressees Continued

The Honorable Rosa L. DeLauro
Chairwoman

The Honorable Kay Granger
Ranking Member
Committee on Appropriations
House of Representatives

The Honorable Frank Pallone, Jr.
Chairman

The Honorable Cathy McMorris Rodgers
Republican Leader
Committee on Energy and Commerce
House of Representatives

The Honorable Bennie G. Thompson
Chairman

The Honorable John Katko
Ranking Member
Committee on Homeland Security
House of Representatives

The Honorable Carolyn B. Maloney
Chairwoman

The Honorable James Comer
Ranking Member
Committee on Oversight and Reform
House of Representatives

The Honorable Richard Neal
Chair

The Honorable Kevin Brady
Republican Leader
Committee on Ways and Means
House of Representatives

Appendix I: Objectives, Scope, and Methodology

We reviewed federal contributions to the development of the antiviral drug remdesivir and intellectual property rights associated with them. Specifically, this report examines: (1) scientific and funding contributions provided by the Centers for Disease Control and Prevention (CDC), Department of Defense (DOD), and National Institutes of Health (NIH) for the development of remdesivir, and (2) these agencies' patent rights related to those contributions.

To address these objectives, we reviewed relevant statutes and regulations, and documentation from CDC, DOD, and NIH. We interviewed officials and scientists from CDC, DOD, NIH, the University of North Carolina at Chapel Hill, and Vanderbilt University. We obtained information from and interviewed representatives of Gilead Sciences, Inc. (Gilead), the pharmaceutical company that manufactures remdesivir. We also interviewed intellectual property scholars and public interest organization representatives.

To examine the agencies' scientific and funding contributions, we obtained funding information for extramural and intramural remdesivir research and agreements CDC, DOD, and NIH used to support this research for the period 2013 through 2020. We analyzed the sections of the agreements that described study plans, the parties' responsibilities, and budgets. To assess the reliability of the agencies' funding information, we interviewed knowledgeable agency officials about how that information was generated and compared the funding estimates the agencies provided with the funding in the agreements, where appropriate. We determined that the agencies' funding information was reliable for the purposes of this report. We reviewed publicly available regulatory information from the Food and Drug Administration (FDA) regarding remdesivir's emergency use authorization and approval. We also conducted a literature search to identify published remdesivir research. A GAO research librarian searched various research databases—including ProQuest and Scopus, among others—to identify scholarly and peer-reviewed publications about remdesivir published as of October 30, 2020. Our search terms included “remdesivir” and “GS-5734.”

To examine patent rights related to CDC, DOD, and NIH scientific and funding contributions, we analyzed the agreements used by the agencies to support remdesivir research. The agencies identified 24 such agreements in effect since 2013: 13 of them were between one of the three federal agencies and Gilead; the other 11 were between one of the

agencies and a university.¹ We reviewed intellectual property provisions in the 13 agreements between the federal government and Gilead to determine whether each agreement contained (1) general intellectual property provisions that recognize an agency's existing intellectual property rights and ability to patent inventions; (2) provisions for subject inventions granting the government patent or license rights to inventions made by an agency's scientists, Gilead's scientists, or both; (3) provisions for government licensing rights to Gilead's existing patents or patentable inventions resulting from the research; and (4) provisions for government rights to technical, scientific, or regulatory data.

Gilead provided a list of its remdesivir-related patents issued and applications submitted to the U.S. Patent and Trademark Office as of December 31, 2020. We reviewed FDA's Orange Book to identify Gilead's patents for Veklury, the brand name under which Gilead obtained an FDA approval for remdesivir to treat COVID-19.²

We conducted this performance audit from August 2020 to March 2021 in accordance with generally accepted government auditing standards. Those standards require that we plan and perform the audit to obtain sufficient, appropriate evidence to provide a reasonable basis for our findings and conclusions based on our audit objectives. We believe that the evidence obtained provides a reasonable basis for our findings and conclusions based on our audit objectives.

¹Of the 24 agreements, 22 took effect during the period from 2013 through Dec. 31, 2020, and 2 agreements between NIH and two universities are taking effect in 2021.

²FDA's publication *Approved Drug Products with Therapeutic Equivalence Evaluations* (commonly known as the Orange Book) identifies drug products approved on the basis of safety and effectiveness under the Federal Food, Drug, and Cosmetic Act and patents associated with them: <https://www.accessdata.fda.gov/scripts/cder/ob/index.cfm>, accessed Nov. 30, 2020.

Appendix II: Federal Agreements and Funding for Remdesivir Research

This appendix provides information about Centers for Disease Control and Prevention (CDC), Department of Defense (DOD), and National Institutes of Health (NIH) agreements and funding for remdesivir research. These agencies signed multiple agreements with Gilead Sciences, Inc. (Gilead) and other entities, with some agreements involving the transfer of federal funding. CDC, DOD, and NIH also conducted intramural remdesivir research and provided information for associated costs, which are obligations or expenditures.

CDC Agreements and Funding for Remdesivir Research

CDC identified five material transfer agreements related to its remdesivir research (table 2), including three agreements between CDC and Gilead. Each of the five agreements involved the transfer of materials between the partner organizations for research purposes and did not involve the transfer of federal funding. CDC is continuing to conduct remdesivir research. CDC estimated the cost of its intramural remdesivir research associated with these agreements from 2013 through December 31, 2020, at \$726,000, which included staff salary time, laboratory equipment, supplies, maintenance agreements, and cost sharing of agency laboratory spaces.

Table 2: CDC Agreements and Funding for Remdesivir Research as of Dec. 31, 2020

Agreement type and research description	Effective date	CDC partner	CDC role	Funding (in millions \$)
Material transfer agreement NCEZID-V126727 Preclinical studies of multiple compounds for antiviral activity against several virus families	2/22/2013	Gilead Sciences	Recipient of compounds from Gilead Sciences	— ^a
Material transfer agreement D-389-16 Characterization of the mechanism of action of remdesivir for treatment of Ebola virus infection	5/24/2016	Gilead Sciences	Provider of materials to Gilead Sciences	— ^a
Material transfer agreement D-929-18 Assessment of the combination of monoclonal antibodies with remdesivir in cell cultures for evidence of additive or synergistic antiviral effect	10/16/2018	Uniformed Services University of the Health Sciences (USU)	Recipient of monoclonal antibodies from the USU	— ^a
Material transfer agreement D-541-20 Development of colorimetric and chromatographic assays for testing to identify counterfeits and poor quality product	9/9/2020	Gilead Sciences	Recipient of compounds from Gilead Sciences	— ^a

**Appendix II: Federal Agreements and Funding
for Remdesivir Research**

Agreement type and research description	Effective date	CDC partner	CDC role	Funding (in millions \$)
Material transfer agreement D-684-20 Testing of remdesivir analog compounds and their ability to block viral replication of SARS-CoV-2 and hemorrhagic fever viruses in infected tissue culture cells ^b	10/7/2020	University of California at San Diego (UCSD)	Recipient of compounds from UCSD	— ^a
Total				0.7^a

Source: GAO analysis of documents and funding information from the Centers for Disease Control and Prevention (CDC). | GAO-21-272

^aCDC estimated the cost of its intramural remdesivir research associated with all the agreements listed in the table at \$726,000 as of Dec. 31, 2020.

^bAnalog compound is a chemical compound that has a similar structure and similar chemical properties to those of another compound, but differs from it by a single element or group.

DOD Agreements and Funding for Remdesivir Research

DOD identified six agreements and one intramural research project involving remdesivir (table 3). Three agreements and the intramural research project involved the U.S. Army Medical Research Institute of Infectious Diseases (USAMRIID) conducting preclinical research with remdesivir and other Gilead-owned compounds. Two other agreements between the Joint Project Management Office for Medical Countermeasure Systems and Gilead funded the research performed by USAMRIID. USAMRIID is continuing to conduct remdesivir research. The most recent agreement, which took effect in 2020, was between the U.S. Army Medical Materiel Development Activity and Gilead. DOD funding for remdesivir research from 2014 through December 31, 2020, totaled \$39.7 million.

Table 3: DOD Agreements and Funding for Remdesivir Research as of Dec. 31, 2020

Agreement type and research description	Effective dates	DOD funding (in millions \$)	DOD component	DOD partner(s)
Material transfer agreement W81XWH-14-0380 Screening Gilead Sciences' compound library against representative viruses from multiple virus families	9/2014 – 9/2021	—	USAMRIID	Gilead Sciences
Intramural research project CB10291 Characterization of remdesivir efficacy against filoviruses in nonhuman primate disease models	8/2015 – 9/2016	4.7	USAMRIID	N/A

**Appendix II: Federal Agreements and Funding
for Remdesivir Research**

Agreement type and research description	Effective dates	DOD funding (in millions \$)	DOD component	DOD partner(s)
Technology investment agreement W911QY-16-3-0001 A blinded, randomized evaluation of the efficacy of 12-day dose-ranging regimens of remdesivir against Ebola virus in rhesus monkeys	5/2016 – 10/2016	1.2	JPM–MCS	Gilead Sciences
Cooperative research and development agreement W81XWH-16-0297 Generation of further confirmatory data regarding the efficacy and safety of remdesivir in treating nonhuman primates infected with Ebola virus	5/2016 – 5/2021	–	USAMRIID	Gilead Sciences and the Geneva Foundation
“Other transaction” authority agreement for prototype W911QY-16-9-0001 Preclinical development of remdesivir for the treatment of Ebola virus and other filovirus infections	8/2016 – ongoing	33.8 ^a	JPM–MCS	Gilead Sciences
Cooperative research and development agreement W81XWH-16-0472 Five-year research program to complete the preclinical development of remdesivir for treatment of hemorrhagic fever viruses, such as Ebola and Marburg viruses, through various studies	9/2016 – 9/2021	–	USAMRIID	Gilead Sciences and the Geneva Foundation
Cooperative research and development agreement W81XWH-20-0110 Investigational use of remdesivir for the post-exposure treatment of COVID-19 for DOD personnel	3/2020 – 3/2023	–	USAMMDA	Gilead Sciences
Total		39.7		

Legend: COVID-19 = Coronavirus Disease 2019, DOD = Department of Defense, USAMRIID = U.S. Army Research Institute of Infectious Diseases, USAMMDA = U.S. Army Medical Materiel Development Activity, JPM-MCS = Joint Project Management Office for Medical Countermeasure Systems, – = no federal funding provided under the agreement

Source: GAO analysis of DOD documents and funding information. | GAO-21-272

^aUnder the terms of this “other transaction” authority agreement signed in 2016, DOD would provide about \$50 million. According to DOD, the agency obligated \$33.8 million of that amount as of Dec. 31, 2020.

NIH Agreements and Funding for Remdesivir Research

NIH identified multiple agreements and intramural research projects involving remdesivir (table 4). Intramural research was conducted at one of NIH’s federal laboratories, the National Institute of Allergy and Infectious Diseases. NIH-funded university-based research and NIH’s intramural research involving remdesivir is continuing. NIH funding for

**Appendix II: Federal Agreements and Funding
for Remdesivir Research**

remdesivir research from 2014 through December 31, 2020, totaled \$11.9 million.

Table 4: NIH Agreements and Funding for Remdesivir Research as of Dec. 31, 2020

Agreement type and research project title	Effective dates	NIH funding	Recipient of NIH funding
Contracts for preclinical research service			
Preclinical research service contract PC18VB9936 Evaluation of Remdesivir in Hamster Model of Yellow Fever Virus	2018	\$18,000	Utah State University
Preclinical research service contract PC20VB13256 Efficacy of Remdesivir in Hamster Model of Yellow Fever Virus	2019	\$27,000	Utah State University
Preclinical research service contract IV20RDB13570 Evaluation of Remdesivir for In Vitro Antiviral Activity against SARS-CoV-2	2020	\$1,008	Utah State University
Cooperative agreements			
Cooperative agreement U19AI109680 Antiviral Drug Discovery and Development Center – Coronavirus	2014-2020	\$2,500,000	University of Alabama at Birmingham ^a
Cooperative agreement U19AI142759 Antiviral Drug Discovery and Development Center – Coronavirus	2019-2023	\$400,000	University of Alabama at Birmingham ^a
Cooperative agreement UM1AI068632 Pharmacokinetics and Safety of Remdesivir for Treatment of COVID-19 in Pregnant Women in the U.S.	2020	\$942,554	Johns Hopkins University
Grants			
Grant F31AI133952 Coronavirus Antiviral Nucleoside Analogs: Inhibition and Reduced Susceptibility	2017-2019	\$25,140	Vanderbilt University
Grant R01AI132178 Broad-Spectrum Antiviral GS-5734 to Treat MERS-CoV and Related Emerging CoV	2017-2021	\$5,863,765	University of North Carolina at Chapel Hill
Grant R21AI147057 Mechanistic Understanding and Inhibition of Zika NS5 Protein	2020	\$155,000	University of California at Riverside
Grant R00AI123498 Structural Studies of the Corona Virus Life Cycle	2020-2021	\$129,120	University of Wisconsin-Madison
Grant R01AI150246 Small Molecule Screening to Identify Novel SARS-CoV-2 Therapeutics	2021 ^p	\$447,930	University of Pennsylvania

**Appendix II: Federal Agreements and Funding
for Remdesivir Research**

Grant R21AI159246 GS-441524 Is Pharmacodynamically Equivalent to Remdesivir and Pharmacokinetically Superior Drug for the Treatment of COVID-19	2021-2022 ^b	\$442,002	University of Texas
Intramural research^b			
Research project AI001088-08 Disease Modeling of Influenza and Other Emerging Respiratory Viral Pathogens	2016	\$30,417	Laboratory of Virology, NIAID
Research project AI001088-09 Disease Modeling of Influenza and Other Emerging Respiratory Viral Pathogens	2017	\$38,374	Laboratory of Virology, NIAID
Research project AI001088-10 Disease Modeling of Influenza and Other Emerging Respiratory Viral Pathogens	2018	\$162,010	Laboratory of Virology, NIAID
Research project AI001088-11 Disease Modeling of Influenza and Other Emerging Respiratory Viral Pathogens	2019	\$238,496	Laboratory of Virology, NIAID
Research project AI001088-12 Disease Modeling of Influenza and Other Emerging Respiratory Viral Pathogens	2020	\$100,000	Laboratory of Virology, NIAID
Research project AI001259-01 Emerging Respiratory Viruses – Pathogenesis and Countermeasures	2020	\$330,000	Laboratory of Virology, NIAID
Research project EBOV-NHP-033E-9 Evaluation of Zmapp vs. Remdesivir vs. the Combination	2020	\$12,333	NIAID Integrated Research Facility ^c
Total		\$11,863,149	

Legend: COVID-19 = Coronavirus Disease 2019, NIAID = National Institute of Allergy and Infectious Diseases, NIH = National Institutes of Health

Source: GAO analysis of NIH documents and funding information. | GAO-21-272

^aUniversity of Alabama at Birmingham is the lead university in a consortium of research teams from several universities.

^bFunding for the agreement effective in 2021 was obligated before Dec. 31, 2020, according to NIH.

^cNIH identified three material transfer agreements with Gilead Sciences, which enabled NIAID to obtain remdesivir for use in intramural research.

NIH also funded three clinical trials with remdesivir involving human subjects (table 5). In these trials, remdesivir was tested for safety and efficacy against Ebola virus disease and COVID-19. NIH funding for clinical trials involving remdesivir from 2016 through December 31, 2020, totaled \$109.2 million.

**Appendix II: Federal Agreements and Funding
for Remdesivir Research**

Table 5: NIH-funded Clinical Trials Involving Remdesivir as of Dec. 31, 2020

Clinical trial	Effective period	NIH funding (in millions)
Trial NCT 02818582 Partnership for Research on Ebola Virus in Liberia IV (PREVAIL IV)	7/2016 – 11/2017	\$3.2
Trial NCT 03719586 Pamoja Tulinde Maisha (PALM [together save lives])	11/2018 – 8/2020	\$17.4
Trial NCT 04280705 Adaptive COVID-19 Treatment Trial (ACTT)	2/2020 – ongoing	\$88.6
Total		\$109.2

Legend: COVID-19 = Coronavirus Disease 2019, NIH = National Institutes of Health

Source: GAO analysis of NIH documents and funding information. | GAO-21-272

Appendix III: Intellectual Property Provisions in Federal Agency Agreements to Support Remdesivir Research

Beginning in 2013, the Centers for Disease Control and Prevention (CDC), Department of Defense (DOD), and National Institutes of Health (NIH) entered into multiple agreements with Gilead Sciences, Inc. (Gilead) and other entities to support remdesivir research. We analyzed 13 agreements between one of the agencies and Gilead.¹ Our analysis shows that 12 of the 13 agreements included intellectual property provisions recognizing that the agencies could patent inventions that could result from their remdesivir research collaborations with Gilead (table 6). Some of the agreements included government rights to subject inventions, licenses, and data.² Of the 13 agreements, 12 contained provisions recognizing that Gilead retained all rights to its existing intellectual property. Five of the 13 agreements—all five were between DOD and Gilead—listed specific patents and patent applications as Gilead’s intellectual property.

Table 6: Government Intellectual Property Rights in Agreements with Gilead Sciences, 2013-2020

Agreement type	Effective start date	General IP rights	Subject invention rights	License rights	Data rights
CDC					
Material transfer agreement NCEZID-V126727	2/22/2013	X	—	—	—
Material transfer agreement D-389-16	5/24/2016	X	—	—	—
Material transfer agreement D-541-20	9/9/2020	—	—	—	—
DOD					
Material transfer agreement W81XWH-14-0380	9/19/2014	X	—	—	—
Technology investment agreement W911QY-16-3-0001 ^a	5/12/2016	X	X	X	X
Cooperative research and development agreement W81XWH-16-0297 ^a	5/13/2016	X	X	X	X
“Other transaction” authority agreement for prototype W911QY-16-9-0001 ^{a,b,c}	8/17/2016	X	X	X	X

¹There were 11 other agreements between one of the agencies and a university.

²A subject invention is any invention conceived or first actually reduced to practice in the performance of work under a funding agreement. Subject inventions can be made solely or jointly by the parties of an agreement. The government’s rights to subject inventions depend on the type and terms of the agreement.

**Appendix III: Intellectual Property Provisions in
Federal Agency Agreements to Support
Remdesivir Research**

Agreement type	Effective start date	General IP rights	Subject invention rights	License rights	Data rights
Cooperative research and development agreement W81XWH-16-0472 ^{a,b}	9/16/2016	X	X	X	X
Cooperative research and development agreement W81XWH-20-0110 ^a	3/5/2020	X	X	X	X
NIH					
Material transfer agreement 2015-33642	2/19/2016	X	—	—	—
Nonclinical evaluation agreement 2018-00023	3/27/2018	X	X	X	—
Material transfer agreement 2019-0287	5/31/2019	X	—	—	—
Material transfer agreement 2020-0108	2/18/2020	X	—	—	—

Legend: IP = intellectual property, X = provision present in the agreement, — = provision absent in the agreement.

Source: GAO analysis of documents from the Centers for Disease Control and Prevention (CDC), Department of Defense (DOD), and National Institutes of Health (NIH). | GAO-21-272

Notes: General IP rights refer to provisions that recognize an agency's existing IP rights or ability to patent inventions. Subject invention rights refer to provisions that grant the government patent or license rights to inventions made by an agency's scientists, Gilead Sciences' scientists, or both. License rights refer to provisions that grant the government rights to a license to any of Gilead Sciences' existing patents or patentable inventions resulting from the research. Data rights refer to provisions that grant the government rights to technical, scientific, or regulatory data.

^aAgreement between DOD and Gilead Sciences contains a section called "background intellectual property" that lists remdesivir patents and patent applications, which are recognized as the company's intellectual property.

^bAgreement has an amendment that expands the background intellectual property owned by Gilead Sciences.

^cAgreement stipulates that the agreement is not subject to the Bayh-Dole Act requirements.

Appendix IV: Gilead Sciences' Remdesivir Patents

GAO asked Gilead Sciences, Inc. (Gilead), the manufacturer of remdesivir, to provide a list of U.S. remdesivir-related patents and patent applications that was current as of December 31, 2020. Gilead provided information for 16 patents (table 7), including one patent for using remdesivir to treat animals.¹ Gilead listed eight of these patents on its new drug application to the Food and Drug Administration (FDA) for remdesivir under the brand name Veklury for treating COVID-19, which FDA approved on October 22, 2020.²

Table 7: Gilead Sciences' U.S. Remdesivir Patents as of Dec. 31, 2020

Patent number and title	Priority date (issuance date) ^a	Patent type ^b	Patent claims remdesivir's molecular structure ^b	Patent listed in Gilead Sciences' new drug application for Veklury ^c
8,008,264 1'substituted carba-nucleoside analogs for antiviral treatment	4/23/2008 (8/30/2011)	Compound	X	X
8,318,682 1'substituted carba-nucleoside analogs for antiviral treatment	4/23/2008 (11/27/2012)	Compound	X	X
RE46,762 1'substituted carba-nucleoside analogs for antiviral treatment	4/23/2008 (3/27/2018)	Compound	X	X

¹Gilead also provided patent application numbers for eight nonprovisional applications related to remdesivir: 14/926,063; 16/692,966; 16/852,102; 16/863,566; 16/865,209; 16/879,491; 16/881,419; and 17/069,248. The company informed us that it had also submitted several provisional patent applications to the U.S. Patent and Trademark Office (USPTO). An applicant can submit to USPTO a provisional patent application without a formal patent claim to establish an early effective filing date. Applicants have 12 months to file a nonprovisional patent application. All patent applications must be published after the expiration of an 18-month period following the earliest effective filing date or priority date claimed by an application. Following publication, the patent application is no longer confidential. Patents generally expire 20 years after the nonprovisional patent application is filed. For provisional applications, the confidentiality of patent applications, and general patent terms, see 35 U.S.C. §§ 111(b), 122(a)-(b), 154(a), respectively.

²When seeking approval for marketing of a new drug in the United States, the company submits a new drug application to FDA. See 21 U.S.C. § 355 and 21 C.F.R. § 314.50 (2019). The eight patents for Veklury are listed in FDA's publication *Approved Drug Products with Therapeutic Equivalence Evaluations* (commonly known as the Orange Book), which identifies drug products approved on the basis of safety and effectiveness under the Federal Food, Drug, and Cosmetic Act: <https://www.accessdata.fda.gov/scripts/cder/ob/index.cfm>, accessed Nov. 30, 2020.

Appendix IV: Gilead Sciences' Remdesivir Patents

Patent number and title	Priority date (issuance date)^a	Patent type^b	Patent claims remdesivir's molecular structure^b	Patent listed in Gilead Sciences' new drug application for Veklury^c
9,090,642 Methods for the preparation of diastereomerically pure phosphoramidate prodrugs	7/19/2010 (7/28/2015)	Synthetic methods	—	—
9,487,544 Methods for the preparation of diastereomerically pure phosphoramidate prodrugs	7/19/2010 (11/8/2016)	Synthetic methods	—	—
10,065,958 Methods and compounds for treating paramyxoviridae virus infections	7/22/2010 (9/4/2018)	Compound	X	X
10,696,679 Methods and compounds for treating paramyxoviridae virus infections	7/22/2010 (6/30/2020)	Method of use	—	—
9,724,360 Methods for treating filoviridae virus infections	10/29/2014 (8/8/2017)	Compound	X	X
9,949,994 Methods for treating filoviridae virus infections	10/29/2014 (4/24/2018)	Compound	X	X
10,251,898 Methods for treating filoviridae virus infections	10/29/2014 (4/9/2019)	Method of use	—	—
10,695,357 Methods for treating filoviridae virus infections	10/29/2014 (6/30/2020)	Method of use	—	—
10,251,904 Methods for treating arenaviridae and coronaviridae virus infections	9/16/2015 (4/9/2019)	Method of use	—	—
10,695,361 Methods for treating arenaviridae and coronaviridae virus infections	9/16/2015 (6/30/2020)	Method of use	—	X
10,682,368 Methods for feline coronavirus infections	3/14/2017 (6/16/2020)	Method of use	—	—
10,836,787 Crystalline forms of (S)-2-ethylbutyl 2-(((S)-((2R,3S,4R,5R)-5-(4-aminopyrrolo[2,1-f][1,2,4]triazin-7-yl)-5-cyano-3,4-dihydroxytetrahydrofuran-2-yl)methoxy)(phenoxy)phosphoryl)amino)propanoate	5/1/2017 (11/17/2020)	Crystalline forms	—	—
10,675,296 Compositions comprising an RNA polymerase inhibitor and cyclodextrin for treating viral infections	7/11/2017 (6/9/2020)	Formulation	—	X

Source: GAO presentation of information from Gilead Sciences, the U.S. Patent and Trademark Office (USPTO), and Food and Drug Administration (FDA). | GAO-21-272

Notes: This table lists issued U.S. patents that Gilead Sciences identified as related to remdesivir.

Appendix IV: Gilead Sciences' Remdesivir Patents

^aPriority date is the date the initial patent application is filed. Issuance date is the date when USPTO grants the patent and the patent becomes enforceable, which means that the patent owner can prevent others from making, selling, or using the claimed invention. Patents generally expire 20 years after the initial nonprovisional patent application is filed.

^bThe content of this column is based on information provided by Gilead Sciences.

^cThese patents are listed in FDA's publication *Approved Drug Products with Therapeutic Equivalence Evaluations* (commonly known as the Orange Book) for Veklury, Gilead Sciences' brand name for remdesivir. The Orange Book identifies drug products approved on the basis of safety and effectiveness under the Federal Food, Drug, and Cosmetic Act:

<https://www.accessdata.fda.gov/scripts/cder/ob/index.cfm>, accessed Nov. 30, 2020.

Appendix V: GAO Contact and Staff Acknowledgements

GAO Contact

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Staff Acknowledgements

In addition to the contact named above, the following individuals made contributions to this report: Robert J. Marek (Assistant Director), Sada Aksartova (Analyst-in-Charge), Adam J. Brooks, John E. Dicken, Robert Copeland, Eric Charles, Hayden Huang, Rebecca Parkhurst, Patrick Harner, Serena Lo, Louise Fickel, Anika McMillon, and Cheron J. Brooks.

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