An Open Letter from Merdad Parsey, MD, PhD, Chief Medical Officer, Gilead Sciences

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In less than one year, the world has moved from a sense of desperation to understand an unknown disease spreading all too quickly and taking lives, to one of hope that we now have enough knowledge and a growing set of tools to help fight COVID-19. With today's FDA approval, and regulatory approvals or temporary authorizations in approximately 50 additional countries around the world, Veklury® (remdesivir) is one of the tools available today. It is the first antiviral treatment proven to help patients hospitalized with COVID-19 recover more quickly – a significant benefit for patients and their families, for healthcare providers and hospitals, and for society at large. As a physician focused on critical care medicine, I saw firsthand the isolation and anxiety of hospitalized patients fighting illness while separated from loved ones and know very well that for them, every day matters.

Rapid Mobilization While Navigating Unknowns

The development pathway for Veklury as a COVID-19 treatment has been extraordinary. The first patient with COVID-19 received Veklury in January of this year through emergency use protocols, at a time when very little was known about the disease. The case report, published in the *New England Journal of Medicine* that same month, began the rigorous journey of establishing Veklury's efficacy and safety profile as a COVID-19 treatment in multiple global, randomized, controlled clinical trials – even as scientists were still learning about the course of the disease itself. Though this journey had many unknowns, our path was guided by decades of experience in antiviral research and development and an unwavering focus on the best interests of patients. Supporting this atypical development pathway was the commitment of clinical trial investigators, patients and their families, and regulatory authorities – all working with the shared goal of rapidly advancing the science to help patients in need.

In parallel with the clinical trials of Veklury, we worked to rapidly expand drug supply, knowing that if proven effective, there would be significant patient need for Veklury. By increasing our internal manufacturing capacity, expanding our external manufacturing network and refining processes to shorten the production timeline, we will have enough Veklury supply to treat all clinically appropriate patients globally next week.

Conclusive Evidence from Rigorous Clinical Trials

Nine months later, results from the randomized, controlled trials of Veklury involving thousands of patients have been published in peer-reviewed journals, conclusively demonstrating the clinical benefits of treatment with Veklury. In clinical research, the gold standard for demonstrating the efficacy and safety of a drug is the randomized, double-blind, placebo-controlled trial. This type of study reduces the potential for bias and provides the highest quality scientific evidence. The National Institute of Allergy and Infectious Diseases' ACTT-1 trial of Veklury in hospitalized adult patients with moderate to severe COVID-19 is one such trial. We know from the ACTT-1 trial that Veklury leads to a five-day faster recovery in hospitalized patients overall, and a seven-day faster recovery in people who required oxygen support at baseline.[i] We also know that Veklury reduces the likelihood of patients requiring new or more intensive oxygen support.[i] And, we have seen evidence that Veklury may reduce the likelihood of death, with a numerical trend toward reduced mortality in the overall ACTT-1 population[i] and, in a post-hoc analysis, a reduction in mortality in patients on low-flow oxygen at baseline.[ii] There was no difference in mortality in other subgroups.[ii] The ACTT-1 study sets a high bar for clinical evidence that must be considered as new data emerge.

Based on the ACTT-1 trial results and the data from two Gilead-sponsored global, randomized, open-label Phase 3 trials, the FDA approved Veklury for adults and adolescents (at least 12 years of age and weighing at least 40 kg) for the treatment of COVID-19 requiring hospitalization. Veklury is contraindicated in patients who are hypersensitive to remdesivir or any of its components; please see below for additional important safety information.

As we have worked to understand COVID-19 – and to rapidly advance Veklury – we have remained sharply focused on ensuring that we are gathering the right scientific data to understand how it works. Last week, interim results from the World Health Organization's Solidarity trial were released and seem to suggest different conclusions than the ACTT-1 study. It is important to remember that when the Solidarity trial initiated in March of this year, there were few opportunities for patients to access investigational COVID-19 treatments, particularly in parts of the world that typically do not participate in global studies. The Solidarity trial design prioritized access to Veklury and other investigational treatments in these parts of the world over the ability to draw definitive conclusions, due to the variability in the implementation of the study, standard of care controls and patient populations across trial sites.

From a drug development perspective, one of the most challenging aspects of the COVID-19 pandemic has been designing trials in real-time, balancing the need to generate conclusive evidence with the very real and immediate needs of patients, the scientific community's incomplete understanding of the disease itself and the challenges of often overburdened healthcare systems. While the Solidarity trial provided information about Veklury in real-world settings in the early days of the pandemic, it does not negate other study results – particularly from a trial designed with the strictest of scientific standards, as is the case with ACTT-1.

Ongoing Research Aimed at Improving Outcomes

We have definitively demonstrated that Veklury can help patients with COVID-19, and we are studying ways to help improve outcomes for more patients. Data on trials combining Veklury with anti-inflammatory medicines have begun to read out, and we expect more results by year-end. Based on the strength of evidence from the ACTT-1 trial, Veklury is now the antiviral backbone of combination therapy approaches being assessed in the National Institutes of Health's clinical trials of COVID-19. Beyond combination trials, we continue to study Veklury in specific populations, including pediatric patients, and in the outpatient setting, and we anticipate sharing data from these trials in the first half of next year. In addition, we continue to study different methods of delivering Veklury, including in alternative care settings outside of hospitals and with an investigational inhaled solution of Veklury being studied in patients with earlier stages of disease.

At Gilead, our clear and steadfast focus has always been to follow science to understand whether, where and at what stage Veklury can benefit patients. With that aim, we have adhered to the rigorous scientific process of conducting randomized, controlled clinical trials stringently designed to generate conclusive evidence on how Veklury could help patients with COVID-19. There is more work to be done to understand the full potential of Veklury, in different settings and as part of combination therapy approaches, to improve outcomes for more patients. We are approaching this work with the same level of urgency that has driven our actions to date. Ultimately, what's at stake is public health and patient lives, and this responsibility is what drives us forward every day. We continue this work with deep gratitude for the many investigators and patients involved in the clinical trials of Veklury, whose participation is fundamental to driving advances with the potential to help patients with COVID-19 around the world.

U.S. Indication for Veklury® (remdesivir)

Veklury is indicated 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.

U.S. Important Safety Information for Veklury® (remdesivir)

Contraindication

- Veklury is contraindicated in patients with a history of clinically significant hypersensitivity reactions to Veklury or any of its components.

Warnings and precautions

- Hypersensitivity, including infusion-related and anaphylactic reactions: Hypersensitivity, including infusion-related and anaphylactic reactions, has been observed during and following administration of Veklury. Monitor patients under close medical supervision for hypersensitivity reactions during and following administration of Veklury. Symptoms may include hypotension, hypertension, tachycardia, bradycardia, hypoxia, fever, dyspnea, wheezing, angioedema, rash, nausea, diaphoresis, and shivering. Slower infusion rates (maximum infusion time ≤120 minutes) can potentially prevent these reactions. If a severe infusion-related hypersensitivity reaction occurs, immediately discontinue Veklury and initiate appropriate treatment (see Contraindications).
- Increased risk of transaminase elevations: Transaminase elevations have been observed in healthy volunteers and in patients with COVID-19 who received Veklury; these elevations have also been reported as a clinical feature of COVID-19. Perform hepatic laboratory testing in all patients (see Dosage and administration). Consider discontinuing Veklury if ALT levels increase to >10x ULN. Discontinue Veklury if ALT elevation is accompanied by signs or symptoms of liver inflammation.
- Risk of reduced antiviral activity when coadministered with chloroquine or hydroxychloroquine: Coadministration of Veklury with chloroquine phosphate or hydroxychloroquine sulfate is not recommended due to antagonism observed in cell culture, which may lead to a decrease in antiviral activity of Veklury.

Adverse reactions

- The most common adverse reaction (≥5% all grades) was nausea.
- The most common lab abnormalities (≥5% all grades) were increases in ALT and AST.

Drug interactions

- Drug interaction trials of Veklury and other concomitant medications have not been conducted in humans.

Dosage and administration

- Dosage: For adults and pediatric patients ≥12 years old and weighing ≥40 kg: 200 mg on Day 1, followed by once-daily maintenance doses of 100 mg from Day 2 administered only via intravenous infusion over 30 to 120 minutes.
- Treatment duration: For patients not requiring invasive mechanical ventilation and/or extracorporeal membrane oxygenation (ECMO): 5 days; may be extended up to 5 additional days (10 days total) if clinical improvement is not observed. For patients requiring invasive mechanical ventilation and/or ECMO: 10 days.
- Testing prior to and during treatment: Perform eGFR, hepatic laboratory, and prothrombin time testing prior to initiating Veklury and during use as clinically appropriate.
- Renal impairment: Veklury is not recommended in individuals with eGFR <30 mL/min.
- Dose preparation and administration: See full Prescribing Information.

Pregnancy and lactation

- Pregnancy: There are insufficient human data on the use of Veklury during pregnancy. Pregnant women hospitalized with COVID-19 are at risk for serious morbidity and mortality. Veklury should be used during pregnancy only if the potential benefit justifies the potential risk for the mother and the fetus.

- Lactation: It is not known whether Veklury can pass into breast milk. Breastfeeding individuals with COVID-19 should follow practices according to clinical guidelines to avoid exposing the infant to COVID-19.

Please see full Prescribing Information for Veklury, available at Gilead.com.

Forward-Looking Statement

This letter includes forward-looking statements within the meaning of the Private Securities Litigation Reform Act of 1995 that are subject to risks, uncertainties and other factors, including the risk that remdesivir may not be successfully commercialized or that Gilead may be unable to effectively manage the global supply and distribution of remdesivir. There is also the possibility of unfavorable results from ongoing and additional clinical trials involving remdesivir and the possibility that Gilead and other parties may be unable to initiate and complete one or more of such trials in the currently anticipated timelines or at all. These risks, uncertainties and other factors could cause actual results to differ materially from those referred to in the forward-looking statements. The reader is cautioned not to rely on these forward-looking statements. These and other risks are described in detail in Gilead's Quarterly Report on Form 10-Q for the quarter ended June 30, 2020, as filed with the U.S. Securities and Exchange Commission. All forward-looking statements are based on information currently available to Gilead, and Gilead assumes no obligation to update any such forward-looking statements.

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[i] Beigel JH, et al. Remdesivir for the Treatment of Covid-19 — Final Report. *N Engl J Med.* Published online on October 8, 2020. doi: 10.1056/NEJMoa2007764.

[ii] Gilead press release and data on file.