

Alternative Pricing Models for Remdesivir and Other Potential Treatments for COVID-19

Public Comments



July 13, 2020

BY ELECTRONIC DELIVERY

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Re: Alternative Pricing Models for Remdesivir and Other Potential Treatments for COVID-19

Dear Dr. Pearson:

We are writing regarding the Institute for Clinical and Economic Review's (ICER's) "Alternative Pricing Models for Remdesivir and Other Potential Treatments for COVID-19," released on May 1, 2020. In this document, ICER developed a preliminary cost effectiveness analysis for remdesivir, which demonstrated a potential clinical benefit in the treatment of COVID-19. ICER also developed as part of this report a never before discussed or validated "cost recovery" model for pricing this therapy. ICER subsequently published an update to its initial assessment on June 23, 2020, which incorporated some updated data and developments since the first report. On July 2, 2020, ICER published a white paper describing several potential pricing models – including the cost recovery approach.

The introduction and application of a new, untested and unvalidated cost recovery model, without public notice and comment, is of significant concern. Continued use or expansion of this model in ICER's work warrants further public discussion and input. Conceptually, this model fails to appreciate the cumulative value of innovation and the clinical and scientific reality that existing compounds can have therapeutic benefits for newly emerging diseases and conditions such as COVID-19. At a minimum, a debate about how society may appropriately value a treatment for this, and the next pandemic, is crucial – especially when no other treatment options exist.

BIO and its members have long advocated for open and transparent value assessment. While we have strongly disagreed with the way ICER incorporates stakeholder feedback, the choices and assumptions it makes in building its framework, and its dismissal of critical elements of value, we have been somewhat heartened that ICER has attempted to create a process that could provide the opportunity for more open discussion and transparency. It has also established timelines and processes (including a stand-alone engagement document) so that developers whose products are or might be the subject of an ICER review are aware of how the process will unfold. These timelines and procedures are necessary (but not sufficient in and of themselves) to ensuring value assessments are conducted in a fair, unbiased, and open manner.

Inexplicably, however, ICER now seeks to circumvent nearly every step of its own established processes to develop and publish a model for assessing the potential value of COVID-19 therapies. Public comment was not invited on the need for such a model, nor was the developer contacted about the report's publication or solicited for their input on data or

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methods. Moreover, it appears that key details were not publicly released, denying stakeholders and interested parties the ability to replicate the model's outputs. The followup report was similarly released without public notice and with no formal structure for ICER to respond or incorporate any feedback received. This lack of transparency is unacceptable.

Our longstanding concerns with ICER's methodology are also amplified by the unprecedented public health emergency of the COVID-19 pandemic. In our comments on the updates to ICER's value framework last year, we noted the pitfalls of conducting premature value assessment, and recommended ICER not conduct assessments before it has a full understanding of a therapy's potential benefits and risks. Model development for a product whose clinical benefits are still being studied and on which available data has not been validated or peer reviewed only creates unnecessary uncertainty and does not support sound policymaking. There is also a high level of uncertainty around the underlying disease, progression, transmission, and outcomes of COVID-19. Furthermore, though ICER acknowledges the limitation in not using a societal perspective, in the context of an unprecedented global pandemic, significant loss of life, pain, suffering, and economic impact, it is imperative that ICER at least attempt a modified societal perspective. Absent this perspective, ICER sends misleading signals about the value of COVID-19 therapies at a time when biopharmaceutical developers, government around the world, and the public are desperately searching for solutions.

We have serious concerns with the integrity of ICER's work if key steps necessary to demonstrate a transparent value assessment process are not routinely followed, particularly in the face of a global pandemic. Now more than ever, society needs thoughtful, coherent analysis built on a discussion of and agreement on those elements of value that we would consider vital for any potential COVID-19 therapy to address – not a rushed, cursory review. In the time following publication of the first report, many commenters offered feedback that could have aided ICER in initially developing a more robust model representing a wider range of inputs – if only it had solicited comment in advance.¹ That ICER's June 23 update included refinements based on inputs from both the developer and other stakeholders evidences the benefit of robust stakeholder engagement in developing an accurate representation of a therapy's value.

The release of these reports also calls into question the rationale for engagement with ICER on future updates to its value framework. Why would stakeholders participate in an engagement process (and why would one even be developed in the first place) if ICER will simply disregard it when it suits its interests?

¹ See for example: Deverka, Bright, Garrison, and Nussbaum, "Measuring Value: COVID-19 Forces a Reassessment," May 20, 2020. Innovation and Value Initiative. Available at:

https://www.thevalueinitiative.org/measuring-value-covid-19-forces-a-reassessment/; Dubois, "It's Time To Talk About COVID-19 Prices," May 20, 2020. *Health Affairs*. Available at:

https://www.healthaffairs.org/do/10.1377/hblog20200518.302353/full/; Kamal-Bahl, Willke, Puckett, and Doshi, "The Case for Using Novel Value Elements When Assessing COVID-19 Vaccines And Therapeutics," June 23, 2020. Health Affairs. Available at: https://www.healthaffairs.org/do/10.1377/hblog20200616.451000/full/

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We urge ICER to follow through on its stated commitment to an open and transparent process for the development of value assessments for all future products.

Sincerely,

/s/

Crystal Kuntz Vice President Healthcare Policy and Research



Martin D. Marciniak, PhD Vice President US Medical Affairs, Customer Engagement, Value Evidence and Outcomes GlaxoSmithKline

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July 14, 2020

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Re: Alternative Pricing Models for Remdesivir and Other Potential Treatments for COVID-19 – updated version (06/24/2020)

Dear Dr. Pearson,

GlaxoSmithKline (GSK) has reviewed ICER's updated versions of COVID-19 pricing models (06/24/2020) for remdesivir including the "Adaptations to the ICER methods for evaluation of therapies for COVID-19." While there have been some promising developments, GSK would like to take the opportunity to provide some further feedback. As the pandemic continues to move across the globe and the US, GSK continues to respond and contribute to the fight against COVID-19. GSK is harnessing science, technology and our portfolio to support development of medicines and vaccines for the prevention and treatment of COVID-19. GSK also donated \$10 million to the COVID-19 Solidarity Response Fund, created by the UN Foundation and World Health Organization (WHO) to support WHO and partners to prevent, detect and manage the pandemic, particularly where the needs are the greatest. GSK's main concerns with the updated approach relate to continued use of the cost recovery model and methods with cost-effectiveness analysis and are discussed below.

Cost recovery model.

ICER continues to provide analysis and pricing based on the cost recovery approach. While the model has been updated to include R&D costs from a public announcement by Gilead, there remains much uncertainty with respect to this approach. The costs of production are based on exports from India¹,² and Bangladesh³. This may not accurately reflect US operating costs especially at a time when global trade, is being heavily

¹ Hill et al. Minimum Costs to Manufacture New Treatments for COVID-19. Journal of Virus Eradication. Online April 2020. http://viruseradication.com/journal-details/Minimum_costs_to_manufacture_new_treatments_for_COVID-19/ Accessed July 2, 2020)

² House, DW. Remdesivir OK'd in India at \$39-52 per dose. June 21, 2020. Seeking Alpha. https://seekingalpha.com/news/3584771-remdesivirokd-in-india-39minus-52-per-dose (Accessed July 2, 2020)

³ Siddiqui, Z. Exclusive: Bangladesh's Beximco to begin producing COVID-19 drug remdesivir – COO. Reuters. https://www.reuters.com/article/us-health-coronavirus-bangladesh-remdesi/exclusive-bangladeshs-beximco-to-begin-producing-covid-19drug-remdesivir-coo-idUSKBN22H1DD (Accessed July 2, 2020)



impacted by COVID-19. At this time, there is a huge amount of strain on global manufacturing and this creates great uncertainty with such a costing approach.

Previous research⁴ has shown it takes on average \$2.6 billion to bring a new drug to the market with a high percentage of trial failures⁵ therefore cost recovery on a per treatment basis is not an appropriate pricing model. Additionally, the pharmaceutical industry is highly dependent on a profit margin in order to support the development of all future medicines. Therefore, the type of approach undertaken here to price COVID-19 treatments could not only have short term impacts on company revenue but also have longer term consequences on the development of future medicines. The level of risk (both in duration and potential numbers of patients to treat) and opportunity cost need to be reflected within rewarding innovation in order to stimulate maximum investment at a time when society most needs and values breakthrough treatments and therapies otherwise companies may choose to continue with pre COVID-19 programs.

GSK asks ICER to remove this approach from their COVID-19 assessments and to concentrate instead on value assessment and on rewarding innovation in medicine at this very critical time.

Methodology of cost-effectiveness analysis

1. The base case threshold remains at \$50k/ QALY.

GSK notes ICER continues to emphasize the price related to the **\$50k/QALY threshold**. ICER reasons⁶ this as due to the "scale of patients likely to require treatment and in the light of the shared goal of making treatments available rapidly and equitably." Therefore, the potential value of remdesivir has been decreased in order to accommodate a perceived high impact on overall budgets which is not consistent with previous ICER methodology or other HTA around the globe such as NICE, CADTH and PBAC. In fact, it is not clear how the budget impact has been factored into the threshold ICER cites within the base case.

This threshold remains notably below the \$100k-\$150k / QALY threshold announced in the VAF 2020 and continues to send a signal to those developing medicines that the reward for developing / launching a treatment for COVID-19 will be valued less. Such pricing levels rely heavily on altruism at a time when the economy is moving into a recession⁷. Timelines within existing R&D portfolios, for potential future medications, have been heavily impacted during this pandemic as early stage lab work is put on hold with

⁴ Tufts University. **Tufts Center for the Study of Drug Development**. Cost to Develop and Win Marketing Approval for a New Drug Is \$2.6 Billion.

https://static1.squarespace.com/static/5a9eb0c8e2ccd1158288d8dc/t/5ac66adc758d46b001a996d6/1522952924498/pr-coststudy.pdf (Accessed July 2, 2020)

⁵ Wong, C et al. Estimation of clinical trial success. Biostatistics, Vol 20 (2). April 2019. 273-286.

⁶ ICER. Adaptations to the ICER methods for evaluation of therapies for COVID-19. <u>file:///C:/Users/ct407382/OneDrive%20-%20GSK/Documents/ICER/remdesivir/Adaptations-to-the-ICER-methods-for-evaluation-related-to-treatments-for-COVID-19.pdf</u> (Accessed July 14, 2020)

⁷ The National Bureau of Economic Research. Determination of the February 2020 Peak in US Economic Activity <u>https://www.nber.org/cycles/june2020.html</u> (Accessed July 2, 2020)



"stay at home" orders in place. New trials are delayed and existing studies are paused as biopharma tries to operate with more limited resources and extenuating factors such as access to patients and CRO partners⁸. Given, there is a high degree of uncertainty associated with COVID-19 with respect to the duration of this pandemic as well as number of people likely to benefit from such treatments, drug developers will be more likely to develop treatments if the reward to do so appropriately accounts for the level of risk undertaken.

Hence, a lowering of the value for COVID-19 treatments could in fact have the opposite consequences of what was originally intended by ICER; rather than making treatments available more rapidly, we could see fewer treatments coming through in the COVID-19 space as developers of medicines concentrate their efforts on longer term goals where longer term values are more certain.

GSK asks that ICER considers increasing the health benefit price benchmark (previously called valuebased price benchmark) in order to allow an assessment of the effectiveness of COVID-19 treatments within previously agreed fair value price ranges.

2. Inclusion of future unrelated healthcare costs

Within the cost-effectiveness analysis, future unrelated healthcare costs have been included in the model. Where remdesivir extends life, there is a healthcare cost associated with each subsequent year of life which essentially accrues a healthcare cost penalty to those patients who survive. This is not in line with the methods employed by HTA authorities such as NICE. NICE guidelines for technology assessment⁹ advise that "Costs related to the condition of interest and incurred in additional years of life gained as a result of treatment should be included in the reference case analysis. Costs that are considered to be unrelated to the condition or technology of interest should be excluded." Although the US panel on cost-effectiveness does recommend the inclusion of future unrelated medical costs¹⁰, this would appear to differentially impact the elderly population who within a cost-effectiveness framework are then naturally forced to incur QALYS at a higher price. This is exemplified in the current model as the age of death is now higher (72 years) and has the effect of a large decrease in the cost-effective price because the mortality benefit is seen in an older population i.e. less QALYs are gained and at a higher cost per QALY. The unrelated healthcare costs accrued are \$20,071 per year for those aged 65-84 years of age and \$38,900 per year for those aged 85+ years. Given an age-based utility of 0.736 is applied to the 85+ years age group, each year saved is above the current threshold applied of \$50k/QALY (i.e. an intervention cannot be considered cost-effective in this age group). The economic model overall is highly sensitive to the inclusion of future healthcare costs and ICER should consider removing this from the calculations. This is especially important given patients within the model are not accruing "benefits" such as return to work, caring for children, ill relatives etc. due to the narrow focus of the model.

⁸ Forbes. "Strategic Planning in Biotech During a Pandemic Crisis. March 26, 2020.

https://www.google.com/amp/s/www.forbes.com/sites/brucebooth/2020/03/26/strategic-planning-in-biotech-during-a-pandemiccrisis/amp/ (Accessed July 2, 2020)

⁹ National Institute for Health Care and Clinical Excellence (NICE).: Guide to the methods of technology appraisal (2013). <u>http://nice.org.uk/process/pmg9</u> (Accessed July 14, 2020)

¹⁰ Sanders, G.D., Neumann, P.J., Basu, A., et al.: Recommendations for conduct, methodological practices, and reporting of costeffectiveness analyses second panel on cost-effectiveness in health and medicine. JAMA **316**(10), 1093–1103 (2016)



GSK recommends that ICER remove the inclusion of future unrelated healthcare costs from the base case of the economic model.

3. Adjustment for shorter hospital duration

ICER has now implemented a scenario analysis to allow for reduced hospital costs for patients on remdesivir who spend a shorter duration of time in hospital. This is based on the findings of the ACTT-1 trial¹¹ which shows a shorter time to recovery in the remdesivir group compared to placebo, 11 days v 15 days (rate ratio for recovery 1.32 (1.12, 1.55) p<0.001). This is a vital addition to the model as shorter hospital durations are likely to have a huge impact on resources both from a payer perspective and societal/ healthcare provider perspective as more resources are available to treat patients as hospital beds are available sooner. Hence, hospitals will have an increased capacity to treat both COVID-19 patients and those requiring treatments for other conditions which is critical in a pandemic as we have witnessed hospitals across the country reaching capacity to treat patients and additionally delaying elective procedures for other patients.

However, this shorter time to recovery and associated decrease in hospital stay duration, has been included as a scenario analysis only as ICER states "per diem payment is a rarity in the US healthcare context." However, according to stats published by American Hospital Association, only 25% of community hospitals across the US participate in bundled payments model¹². Additionally, if payments are made as bundled payments, the hospital still realizes cost and resource savings from a broader healthcare perspective. The model is highly sensitive to this scenario with the cost-effective price moving to \$11,710.

GSK recommends that the cost offsets for shorter hospital duration should form part of the base case given the substantial impact this has not only for payers but also for patients and healthcare providers.

4. Inclusion of newly published data

In addition to the above, new data¹³ comparing COVID-19 patients receiving remdesivir (in the SIMPLE-SEVRERE trial) has been compared to a real-world retrospective cohort of patients with similar baseline characteristics and shows day 14 mortality is improved for those on remdesivir compared to those who are not (7.6% v 12.5%, adjusted odds ratio 0.38 (0.22, 0.68) p=0.001). The current ICER model uses the adjusted mortality hazard ratio of 0.74. Therefore, these latest findings suggest a greater benefit in mortality from that which was previously identified. Given the cost-effectiveness modelling was undertaken on early trial data, the models should be updated to reflect the latest data. This is in line with the VAF 2020 in which ICER outlined a commitment to explore how real-world observational evidence can contribute to a more comprehensive and accurate view of risks, benefits and costs associated with an intervention.

¹¹ Biegel JH, Tomashek KM, Dodd LE. "Remdesivir for the Treatment of Covid-19 – Preliminary Report." NEJM, Online May 22nd, 2020.

¹² American Hospital Association. https://www.aha.org/bundled-payment

¹³ Gilead. "Gilead Presents Additional Data on Investigational Antiviral Remdesivir for the Treatment of COVID-19." <u>https://www.gilead.com/news-and-press/press-room/press-releases/2020/7/gilead-presents-additional-data-on-investigational-antiviral-remdesivir-for-the-treatment-of-covid-19</u> (accessed July 13, 2020)



GSK would ask that potentially impactful new data is incorporated into the models as it becomes available.

As the pandemic continues to evolve across the globe and have a shocking impact with the loss of lives, impact on quality of life and devastating effect on the economy, it is critical we stimulate innovation within both the prevention and treatment of COVID-19. GSK also understands the need to make such treatments accessible. However, the current framework being employed by ICER could be viewed as a hurdle to creating the optimum environment for medical advance at a critical time. It is therefore paramount that we have the correct, fair, robust and transparent framework in place to bring life changing medications to fruition and to our patients.

Please feel free to contact us should you wish to discuss these recommendations in further detail.

Sincerely,

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Martin D. Marciniak, PhD Vice President US Medical Affairs, Customer Engagement, Value Evidence and Outcomes

<u>Amgen Comments: ICER COVID-19 Alternative Pricing Models</u> <u>for Remdesivir and Other Potential COVID-19 Treatments</u>

Summary Overview

Amgen appreciates the opportunity to comment on *ICER's Preliminary Report on Alternative Pricing Models for Remdesivir and Other Potential Treatments for COVID-19* posted on May 1, 2020 and its first model update posted on June 24, 2020.

COVID-19 has created an unprecedented burden on individuals and society. This public health crisis amplifies the importance of healthcare and treatment innovation, with an economic impact that approaches levels not seen since the Great Depression. The principles of how value is assessed do not change in a pandemic, and the value of innovation is likely even higher in a pandemic. Also, it is important to recognize that pandemic drugs have limited affordability risks because their lifespan is typically only 1-2 years until a vaccine and viable measures are available to contain and/or eventually eradicate a disease. At the same time, there is a value/access trade-off that needs to be managed differently in a pandemic. Never before has the biopharmaceutical industry come together more rapidly and collaboratively to find solutions, to proactively address potential access concerns. What enables industry to rapidly respond in a pandemic crisis situation with little-to-no cost options is the existence of a robust and resilient healthcare ecosystem that rewards and incentivizes innovation. As the value/access trade-off continues to be addressed, value should not be conflated with affordability and measures taken should protect the balance needed to preserve a healthy innovation ecosystem. Amgen is invested in collaborating with healthcare providers, payers and patient advocacy organizations for the rapid acceleration of new treatments for SARS-CoV-2, accompanied by scientifically robust assessment and patient access to these treatments.

We acknowledge ICER's interest in shaping the COVID-19 pricing dialogue and our comments aim to help inform a more balanced, science-based approach reflected in ICER's revised model and report(s) as follows:

- **Cost Recovery:** In this crisis situation where industry is proactively offering measures to enable access at minimum cost, a cost recovery approach does more harm than good: rather than informing the value/access trade-off, this confuses it by marginalizing the value of innovation and potentially disincentivize future innovation. We encourage ICER to retract the remdesivir cost recovery model and revise the cost-effectiveness model adhering to good value assessment principles, enabling a fair assessment of value, separate from affordability.
- **Cost-Effectiveness:** ICER has an opportunity to further revise its cost-effectiveness model for remdesivir with appropriate methodology, increased reporting and model analysis transparency, and inclusion of more robust data inputs that have substantial impact on results. Our recommendations are intended to help produce an overall balanced approach.

Our recommendations are detailed below. The Amgen team is available to further discuss our comments with ICER and University of Colorado, with the aim of enabling a more informative and credible assessment.

Background and Context

COVID-19 has created an unprecedented burden on individuals and society. Since January 2020, SARS-CoV-2 (novel coronavirus) has been responsible for over 7 million cases and nearly half a million deaths globally.¹ Approximately 15% of positive COVID-19 patients (depending on study and testing) are hospitalized, 25% of those hospitalized end up in the intensive care unit (ICU), and 80-100% of ICU patients will need ventilation.^{2,3,3} Although ventilation is potentially life-saving, it is correlated with massive organ failure, responsible for more COVID-19 deaths and disability than respiratory failure itself.^{4,5,6} Additionally, the long-term effects of COVID-19 are still being researched but preliminary data suggests an estimated 20-30% long-term long damage or pulmonary fibrosis in those who are hospitalized.⁷ Hospitalization is also costly. The average hospital stay of 6-12 days costs \$12,000-\$34,000 per patient, while an ICU stay extends the stay on average by 4 days costing a total of \$40,0000-\$90,000 per patient.^{8,9}

This public health crisis amplifies the importance of healthcare and treatment innovation. More than ever before, the criticality of vaccines and treatments are central to solving the current crisis in which billions of people are suffering around the globe. Innovation and the rewards associated with this must be balanced with the extreme pressure that communities currently face in affording treatments. This is not to say that value should be conflated with affordability: these are two very different challenges. Undeniably, treatments and vaccines have incalculable value, however, this must be recognized separately from society's ability to fund new treatments, in light of this pandemic's profound financial and health-related burden.

The economic impact of the virus according to the IMF, approaches levels not seen since the Great Depression.^{10,11,12,13} The U.S. government has approved a two trillion dollar stimulus bill with an estimated incremental cost per QALY ranging from \$300,000 to \$2.5 million,¹⁴ however, the economic impact of COVID-19 will completely eclipse this. With over 40 million people in the US applying for unemployment, Morgan Stanley forecasts a 38% drop in economic growth in the 2nd quarter alone, resulting in a loss of \$8.2 trillion or \$25k per person.¹⁵ At minimum, GDP impact will likely be 5% per month for the duration of the crisis representing more than \$12 trillion over the next year.¹⁶ People sheltering in place have been looking in great anticipation towards a vaccine or treatment to help alleviate this crisis, and while value is defined differently by individual, there is general consensus that a new vaccine or treatment would have incalculable value.

Amgen's Comments

The principles of how value is assessed do not change in a pandemic. It is an irrefutable tenet that the value of a life does not change during a pandemic. Equally, the need to protect those who are vulnerable also remains constant.¹⁷ In keeping with this, value frameworks and health technology assessment methodologies and processes must be robust enough to weather pandemics and other changes, maintaining their validity even under this pressure. At the same time, this must be balanced with the flexibility to address challenges in data collection characterized by the acceleration of trials and regulatory approval at earlier stages in the trial process.

The value of innovation is likely even higher in a pandemic. While the method to determine value does not change, the totality, scale and speed of COVID-19 means that the reach and impact of any treatment in saving lives is hard to match. Despite this, given the sheer number of individuals in need, treatments can be both accessible and affordable. This is typically seen in payer negotiations with manufacturers, whereby increased volume decreases prices, with the most notable example be seen in the "Grand Bargain" from the Omnibus Budget Reconciliation Act of 1990.¹⁸

Pandemic drugs have limited affordability risks because their lifespan is typically only 1-2 years until a vaccine and viable measures are available to contain and/or eventually eradicate the disease. ¹⁹ As of June 9th 2020, there are 161 vaccines in development, with many lead candidates starting Phase 1 or Phase 2 testing. ^{20,21} It is highly likely that a successful vaccine will become available, making it increasingly possible to hopefully eradicate SARS-CoV-2. This means that the lifetime sales of COVID-19 treatments take on an irregular pattern deviating from traditional drugs for chronic disease. This is characterized by intense demand in the first few years trickling to negligible demand, likely after 5 years as vaccines and herd immunity take hold.²²

There is a value/access trade-off that needs to be managed differently in a pandemic. While value assessment does not change during a pandemic, the sheer scope and magnitude of those impacted necessitates that access and affordability must adjust to accommodate this. COVID-19 arguably effects every single global industry, every economy, every provider, individual and patient. For this reason, it is important that access to treatments adhere to WHO-defined care that is physically accessible, financially affordable and inclusive in its ability to motivate patients to receive treatment, absent of social, cultural, sex, ethnic, age or religious disincentives.²³ In essence, even during a pandemic, it is essential that patients are able to afford and physically access COVID-19 treatment, but also feel motivated to seek care regardless of current health status or the presence of pre-existing conditions.

The biopharmaceutical industry has come together to find rapid solutions, proactively addressing potential access concerns. Representing the urgency and immediacy of this effort, in a period of less than 5 months, there has been a revolution in unique treatments from zero to over 247 unique treatments²⁴ and nine vaccine candidates currently tested in 660 clinical trials as shown in Table 1.^{25,26} Equal to this challenge, Amgen are working with policy makers and advocacy organizations, exploring novel solutions to continuity of care. Amgen are collaborating with biotechnology companies, academic institutions, the Administration and other government research entities to identify effective treatments for COVID-19 as quickly as possible, including The National Institutes of Health (NIH) and the Foundation for the NIH's (FNIH) Accelerating COVID-19 Therapeutic Interventions and Vaccines (ACTIV) partnership.²⁷ We are also actively investigating Otezla[®] (apremilast), as a potential immunomodulatory treatment in adult patients with COVID-19; and partnering with Adaptive Biotechnologies for the identification of tens of thousands of naturally occurring antibodies from survivors of COVID-19 to select those that neutralize SARS-CoV-2.

COVID-19 Response	Small Snapshot of Participating Companies
Developing Potential New Treatments and Vaccines - ૻૣ	 Moderna made headlines earlier in May when it became the first company to publish promising phase 1 data. A total of 8 vaccine candidates are in clinical trials, led by pharmaceutical companies and health institutes in the U.S., China, and Germany. Over 200 drugs have begun pre-clinical or clinical testing.
Repurposing Existing Treatment	 Gilead Sciences has led the way in repurposing of remdesivir for COVID-19, recently upping its donation to the federal government equaling 1.5 million individual doses. Other companies working to repurpose treatments include Amgen (Otezla[®]), Novartis (hydroxychloroquine), AstraZeneca (Calquence[®], Farxiga[®]), Genentech (Actemra[®]), and many others.
Partnerships	 Biopharmaceutical companies are working with one another and with national agencies to advance development of vaccines and therapies. U.S. pharmaceutical company Pfizer and BioNTech SE of Germany are just one partnership working on a vaccine.
Monetary & In-Kind Support	 In addition to medical and supply donations, pharmaceutical companies have given millions in financial support for various causes. AbbVie is donating \$35 million to partners including Feeding America, Direct Relief, and International Medical Corps. Collectively among charitable funds, well over \$100M has been donated.
Supply Chain Integrity	 To ensure the COVID pandemic does not impact other essential medicines, companies are bolstering their supply chain. AstraZeneca, Boehringer Ingelheim, Daiichi Sankyo, Eli Lilly and many other producers of life saving drugs are all working to prevent shortages

Table 1: Pharmaceutical Industry Response to COVID-19

What enables industry to rapidly respond in a pandemic crisis situation with little-to-no cost options is the existence of a robust and resilient healthcare ecosystem that rewards and incentivizes innovation. While the value / access trade-off is managed, value should not be conflated with affordability and the measures taken should not offset the balance needed to preserve a healthy innovation ecosystem. The current healthcare ecosystem supports and encourages innovation necessary to enable the industry to react nimbly and address crisis situations. This means value should not be undermined even in a pandemic, and measures put in place to address the <u>value-access</u> trade-off in pandemic crisis situations <u>do not</u> apply to non-pandemic situations. The current ecosystem/drug approval system relies on key innovative companies receiving patents for their treatments in order to recoup their capital costs once given

approval however, rushed assessments put future innovation at risk, possibly hamstringing an ecosystem such that it cannot effectively respond to the next pandemic or health crisis.^{28,29}

Amgen Recommendations for ICER's Value Assessment of COVID-19 Treatments

There is a distinction between the value and access trade-off that needs to be managed thoughtfully in a pandemic, without confusing the concept of value with cost/affordability. The notion of a lower threshold proposed in ICER's cost-effectiveness model for COVID-19 sacrifices value for affordability, stating the use of *"lower thresholds to accommodate both the uncertainty and to maintain affordability for immediate broad use. That is why in this case we are emphasizing the threshold price at \$50,000 per incremental quality-adjusted life year (and equal value of a life-year gained). "³⁰ Traditionally ICER bases its evaluation on a flexible range of cost-effectiveness thresholds between \$50K to \$150K per QALY gained, and this range is already designed to address uncertainty and the preferences reflected in the complex system of budget holders that characterizes the U.S.³¹ Even in pandemics, thresholds should consistently address value and the incremental cost of providing greater health and allocative efficiency: lower thresholds suggest that there is less money available in the healthcare system to address this impact. Contrary to this, payers are doing better financially than before the pandemic, marked by a reduction in healthcare spending in the first three months of the year of 18% compared to past years.³²*

While our comments to ICER remain consistent as in the past regarding methodology, we also believe this initial step incorrectly interprets and addresses the pandemic situation regarding value. We encourage ICER to retract the remdesivir cost recovery model and revise the cost-effectiveness model adhering to good value assessment principles, enabling a fair assessment of value, separate from affordability. In this crisis situation where industry is proactively offering measures to enable access at minimum cost, a cost recovery approach does more harm than good – rather than informing the value/access trade-off - it confuses it by marginalizing the value of innovation, potentially disincentivizing future innovation.

• The methodology proposing cost-recovery is completely inappropriate and the wrong way to assess value during a pandemic (even more so than in a non-pandemic environment). Industry is already offering measures to respond at minimum cost to address immediate access issues where feasible; this does not warrant direction. ICER's choice of applying a cost recovery model to remdesivir - a significant and unexpected departure from the 2020 Value Framework - has dangerous implications, devaluing innovation. Underpinning this are the data sources that ICER uses. ICER bases its cost recovery analysis on the work of Hill *et al.*, which reports that remdesivir pricing is a quarter of that of saline (\$0.93/day for remdesivir vs. a saline IV infusion at \$4.00 per day).³³ How can saline – a sterile combination of salt and water – be more expensive than a treatment that can reduce hospitalization by 3-4 days? Instead of recognizing the unique circumstances of the pandemic with regard to access, pricing, and the benefits of an innovative ecosystem, ICER's approach "doubles-down" on their flawed methodology by focusing more on affordability and cost (again) instead of actual value, hence confusing these elements.

ICER in this analysis has an opportunity to more fully account for the vast impact of COVID-19 on society and the remarkable potential that treatments or vaccines offer in potentially alleviating this crisis. With the intent of anchoring the debate on COVID-19 pricing, ICER recognizes the preliminary nature of its models, which do not reflect stakeholder input and fall short of many of the core principles that ICER itself has committed to, including transparency, stakeholder input and patient engagement. ICER states that it is: *"aware that a very effective treatment for COVID-19 may alter how society contemplates the risk/reward tradeoffs of relaxing social distancing measures, which in turn could spur an economic recovery."* ³⁴ ICER has an opportunity to revise their analysis with appropriate methodology, more robust data inputs and a more balanced approach yielding a more informative and credible assessment:

- ICER can more appropriately reflect the healthcare system perspective by being more inclusive of all healthcare costs in its analysis of COVID-19 treatments. The analysis currently fails to account for the substantial impact of healthcare job losses and decreased revenue. Additionally there has been the direct cost brought on by the need to be COVID-ready: hospitals have spent \$660 million investing in the preparation for COVID-19 and Congress has set aside \$100 billion to support hospital response to the pandemic. ^{35,36} Additionally, non-surgical procedures have been placed on hold and areas important to health such as cancer screening have fallen to a fraction of their level before the pandemic, which will lead to higher costs as cancers are captured later and more lives lost as patients wait until it is too late to seek care unrelated to the virus.^{37,38,39} Further, while spending is 18% lower on COVID-19 for payers, many hospitals could find themselves struggling to stay viable and so ICER should also consider the long-term impact of narrower networks on overall healthcare costs. Equally, it is now widely acknowledged that the virus has had a significant effect on the behavioral health of healthcare workers and so ICER should include the QALYs for all healthcare workers directly and indirectly affected by the virus.
- ICER should capture the substantial potential impact of a pandemic treatment on society in keeping with their 2020 Value Framework. As highlighted by a recent article by Cohen, Neumann and Ollendorf of Tufts,⁴⁰ ICER's recently released Value Framework recommends the inclusion of societal benefits when they are substantial: *these societal benefits are substantial*. For example, remdesivir has an opportunity to impact the economy by reducing hospital resource utilization and help in the re-opening of the nation's economy. Yet, ICER bases its price of treatment on numbers that disregard broader societal consequences. There is no place that more deservedly justifies the incorporation of lost productivity that new treatments can allay. This analysis must be inclusive of the needs of those impacted, including substantial devastation not only to those who have lost their lives but their livelihoods. Moreover, there are significant costs that are just being quantified now, which include substantial outlays resulting from changes to workplace processes.
- ICER should reflect outcomes specific to underserved and vulnerable populations, such as those who are immunocompromised, suffer from chronic conditions; and address racial disparities: the analysis currently does not address these. While many say that COVID-19 is the ultimate leveler, this has not proven to be true empirically as the virus disproportionately affects people of color, the elderly and those who already have chronic

health conditions.⁴¹ Importantly, the virus has a significant impact diminishing health and social equity and this value should be specifically captured in ICER's analysis.

Lastly, ICER should prioritize having an open engaging dialogue over a desire for speed and relevance to anchor a debate with publicly released information that does not take into account core principles that ICER itself has committed to, such as transparency, public input, and patient perspective. As ICER evolves its model, we encourage it to create a collaborative platform with stakeholder input, utilizing appropriate methods for 'value assessment' and separately identify mechanisms that payers consider to address potential affordability concerns. Unlike other ICER assessments and pricing evaluations, ICER did not notify stakeholders prior to this report's release, it has not opened a comment period on the revised methodology or report and it is unclear how ICER will proceed going forward. ICER should release the model and equally, render the methodology, data sources, model inputs and evaluation more transparent and invite comments from impacted stakeholders.

Amgen Recommendations Specific to ICER's Cost-Effectiveness Approach

Update analyses and reporting related to elements that have a substantial impact on results

We agree with ICER on the need for further updates of the analyses related to elements that have a substantial impact on the estimates of cost-effectiveness, including:

- differences between remdesivir and standard of care related to the proportion of patients in each highest hospitalization level of care, and
- the impact of health care resource use and cost from shorter duration of hospital stay driven by shorter time to recovery. The cost-offsets resulting from shorter hospital stays is accounted for only in sensitivity analysis. These cost-offsets should be part of the base case analysis, or at the very least presented alongside the other scenarios included in Table 2 of the updated report. The shorter time to discharge results in a resource and cost saving per patient and will increase capacity in the health care sector overall to treat more COVID-19 patients.

Additionally, the "Scenario analysis assuming no mortality benefit" should be replaced with a short-term scenario analysis including mortality benefits to be aligned with the base case inclusion of mortality benefits.

Increase reporting and model analysis transparency

Several clarifying questions related to data inputs, assumptions and analyses with a potential significant impact on results would benefit from a more robust and transparent reporting and sharing of the model source code including: 1) details on the model update of average age for those who died to be higher than those who recover. In particular, a more detailed description of how the average age of patients at death is derived from the sources referenced and details on how a higher average age for surviving patients with remdesivir affects long-term estimates of patient life-years, QALYs and costs; 2) implementation of the age and gender-specific mortality for the long-term model predictions (i.e. detail if separate health states were specified for males and females, versus a combined health state, as indicated in the model diagram in the appendix of the updated report); 3) clarity of included health care cost categories and inflation adjustment sources;

4) implementation of the data and approach used for the evLYG analyses (the results in Appendix Table 3 indicates that the average US population utility used is much lower than the stated 0.851);5) implementation of remdesivir discontinuation in the model analyses.

Conclusion

Amgen is invested in collaborating with healthcare providers, payers and patient advocacy organizations for the rapid acceleration of new treatments for SARS-CoV-2, accompanied by scientifically robust assessment and patient access to these treatments. Any analysis that ICER performs, whether during a pandemic or outside it, should remain true to the Value Framework that ICER has developed. We encourage ICER to consistently apply the processes that it has developed through its Value Framework including consultation on new methodologies and approaches even during a pandemic. Importantly, times of emergency and crisis like the one we all find ourselves in, necessitates a more collaborative and rigorous approach to evaluation, not a departure from validated, consultative, scientifically robust and inclusive processes.

References

² Guan W, Ni Z, Hu, Y, Liang W, Ou C, He J, et al. Clinical Characteristics of Coronavirus Disease 2019 in China. NEJM. 2020 Feb; Online Only. Link

³ ICNARC: Intensive care National Audit & Research Centre. ICNARC report on Covid-19 in critical care. Available From: <u>Link</u>

⁴ Bhatraju PK, Ghassemieh BJ, Nichols M, Kim R, Jerome KR, Nalla AK, et al. Covid-19 in Critically III patients in the Seattle Region- Case Series. NEJM. 2020 Mar. <u>Link</u>

⁵ Grasselli G, Zangrillo A, Zanella A, et al. Baseline Characteristics and Outcomes of 1591 Patients infected with SARS-CoV-2 Admitted to ICUs of the Lombardy Region, Italy. JAMA. 2020 Apr. <u>Link</u>

⁶ Liang W, Guan W, Chen R, Wang W, Li J, Xu K, et al. Cancer Patients in Sars-Cov-2 Infection: a nationwide analysis in China. Lancet Oncology. 2020 Feb; 21 (3): P335-337. <u>Link</u>

⁷ Reed J, Hutchinson S. Coronavirus: Warning thousands could be left with lung damage. BBC News. 23 June 2020. <u>Link</u>

⁸ Rae M, Claxton G, Kurani N, McDermott D, Cox C. Peterson-KFF: Health System Tracker. Potential costs of Covid-19 treatment for people with employer coverage. Health Spending Briefs. Available From: <u>Link</u>

⁹ Fair Health. The Projected Economic Impact of the Covid-19 Pandemic on the US healthcare system. Link

¹⁰ Chan SP. Coronavirus: 'World faces worst recession since Great Depression'. BBC. 14 April, 2020. Link

¹¹ Thompson D. It's the Pandemic, Stupid. The shutdowns aren't what's driving the worst unemployment crisis since the Great Depression. The Atlantic. May 8, 2020. <u>Link</u>

¹² Zumbrun J. Coronavirus Slump Is Worst Since Great Depression. Will It Be as Painful? WSJ. May 10, 2020. Link.

¹³ Reinicke C. 'Painfully evident' damage: Deutsche Bank now thinks the US economy will shrink by nearly 40% in the 2nd quarter following coronavirus lockdowns. Business Insider [Internet]. 2020 May 11 [cited 2020 Jun 08]. Link ¹⁴ Broek-Altenburg EV, Atherly A. Economic Cost of Flattening the Curve. The Incidental Economist. Link

¹⁵ Winegarden W. ICER'S Cost Model is not only wrong It's also Dangerous. Forbes. Available From: Link

¹⁶ Makridis C, Harley J. The Cost of COVID-19: A Rough Estimate of the 2020 US GDP Impact. COVID-19 Crisis

Response, Policy Briefs. Mercatus Center, George Mason University. April 6, 2020. Link.

¹⁷ Lorgelley and Adler state: "*the middle of a pandemic is not the best time to debate the value of life.*" In Lorgelly PK, Adler A. Impact of a Global Pandemic on Health Technology Assessment. Applied Health Economics and Health Policy. 2020 May 7:1-5. p. 341.

¹⁸ Omnibus Budget Reconciliation Act of 1990. Link

¹⁹ Abdelnour A, Babbitz T, Moss S. Pricing in a pandemic: Navigating the Covid-19 crisis. Mckinsey & Company. 01 May 2020 [date cited 09 Jun 2020]. Link

²⁰ Covid-19 Treatment and Vaccine Tracker. Milken Institute. Accessed on 09 June 2020. Available From: Link

²¹ Covid-19 Update: May 26 Edition. The Incidental Economist-The health services research blog. 26 May 2020 [cited on 09 June 2020]. Link

²² Curley C. A covid-19 Vaccine by January? Here's why it's possible but not likely. Health News [Internet]. 20 May 2020 [cited on 08 June 2020]. Link

²³ Evans DB, Hsu J, Boerma T. Universal health coverage and universal access. Bulletin of the World Health Organization 2013;91:546-546A. Link

²⁴ PhRMA. Treatments in development by phase as of May 1, 2020. Note – some medicines may be in two different phases at the same time.

²⁵ Analysis of publicly available databases such as cilnicaltrials.gov, AdisInsights and the World Health Organization's International Clinical Trials Registry Platform (WHO ICTRP) as of May 1, 2020.

²⁶ ABPI. What are pharmaceutical companies doing to tackle COVID-19? 2020. Link Accessed June, 9 2020.

²⁷ The ACTIV partnership aims to develop a collaborative framework for prioritizing vaccine and drug candidates, streamlining clinical trials, coordinating regulatory processes, and/or leveraging assets among all partners to rapidly respond to the COVID-19 and future pandemics.

²⁸ ICER Presents alternative pricing models for Remdesivir as a treatment for Covid-19. ICER [Internet]. 1 May 2020 [date cited: 08 Jun 2020]. Link

²⁹ Winegarden W. Icer's Cost Model is Not only wrong it's also dangerous. Forbes. 11 May 2020. [date cited: 07 Jun 2020]. Link

¹ John Hopkins Coronavirus Resource Center. Link.

³⁶ Kaiser Family Foundation. Estimated Cost of Treating the Uninsured Hospitalized with Covid-19. Link.

³⁷ Epic: screenings for cervix, colon and breast are down by 86% to 94% compared to the average volume in the last

3 years. Delayed Cancer Screenings. Epic Health Research Network. 2020 May 04. [cited 2020 May 19]: Link

³⁸ Robbins R. Routine Cancer screenings have plummeted during the pandemic, medical records data show. Health. 2020 May 04. [cited 2020 May 19]: Link

³⁹ Albelson R. Hospitals Struggle to restart lucrative elective care after coronavirus shutdowns. NYTimes. 2020 May 09 [cited 2020 May 20]: Link

⁴⁰ Joshua T. Cohen JT, Neumann PJ, Ollendorf DA. Valuing And Pricing Remdesivir: Should Drug Makers Get Paid For Helping Us Get Back To Work? Health Affairs. May 20, 2020. Link

⁴¹ Millett GA, Jones AT, Benkeser D, Baral S, Mercer L, Beyrer C, *et al.* Assessing Differential impacts of Covid-19 on black communities. Annals of Epidemiology. 2020 May; Online: <u>Link</u>

³⁰ ICER Presents alternative pricing models for Remdesivir as a treatment for Covid-19. ICER [Internet]. 1 May 2020 [date cited: 08 Jun 2020]. Link

³¹ Sussman M. Pandemic Pricing: The risks and rewards of fast-tracking value-based drug evaluations. Pharmacy Times [Internet]. 2020 May 26 [Cited 2020 Jun 08]. Link

³² Coombs B. Plunge in health-care spending a big reason US economy sank in first quarter. CNBC. April 29, 2020. Link

³³ Hill A, Wang J, Levi J, Heath K, Fortunak J. Minimum costs to manufacture new treatments for Covid-19. J.Virus Eradication. 2020 Apr; Online. Link

³⁴ ICER Presents alternative pricing models for Remdesivir as a treatment for Covid-19. ICER [Internet]. 1 May 2020 [date cited: 08 Jun 2020]. Link

³⁵ Rose J. U.S. Field Hospitals Stand down, Most without treating any Covid-19 Patients. NPR. 2020 May 07 [cited 2020 May 20]: Link



August 26, 2020

Steven D. Pearson, MD, MSc Institute for Clinical and Economic Review (ICER) One State Street, Suite 1050 Boston, MA 02109

Dear Dr. Pearson:

Genentech, a member of the Roche Group, is writing in response to ICER's recent COVID-19 related activities, including the reports on alternative pricing models for remdesivir and the recent colloquium series on pricing in a pandemic.¹⁻⁵ We are disappointed that ICER's approach to assessing value in the age of COVID-19 does not more fully align with its guiding principles to develop collaborative, transparent, and evidence-based evaluations, and we are concerned that ICER's actions and approach will not support the innovation and collaboration needed to get the world through the COVID-19 pandemic.⁶ Genentech has collaborated with ICER on more than a dozen assessments and provided recommendations on draft value frameworks and the unsupported price increase report. Given our own current clinical research into COVID-19 treatments and our efforts to ensure access for patients on our medicines during this pandemic, we are committed to supporting an objective and evidence-based discussion of treatment and vaccine value. We share our perspectives with the hope that ICER will adopt them in its efforts to improve its value assessment of potential treatments for COVID-19.

Innovation and collaboration are the tenants that will get the world through COVID-19. In only a few short months, innovation and collaboration have fueled the research and development (R&D) of COVID-19 therapies, vaccines, diagnostic tests, epidemiologic surveillance methods, contact-tracing techniques, and countless other forms of response to the pandemic.⁷⁻¹⁰ We see various industries both innovating and collaborating in ways we would have never thought possible, and with unprecedented speed and urgency. Bio-pharmaceutical, diagnostics and "tech" companies are working closely with academic, governmental, patient, professional, and healthcare delivery organizations on the solutions to this crisis. And yet, in many respects, ICER seems to stand alone. Even with the discourse we have seen within the access, health policy, and health economics circles, ICER seems to be misaligned and subject to criticism.¹¹⁻¹⁴ As one of several independent, health technology assessment organizations in the United States (US), ICER has a responsibility to ensure that its evaluations are rigorous, objective, transparent, and incorporate broad stakeholder engagement to further the discussion on the value of treatments for COVID-19, and we strongly encourage ICER to reconsider its approach.

We urge ICER to anchor to the guiding principles from its Value Assessment Framework as it reviews COVID-19 treatments, and we hope our recommendations contribute to a comprehensive value

assessment that is based on a foundation of rigorous science and methods.⁶ Our input specifically focuses on two categories to enhance the credibility and validity of ICER's current approach:

- 1. **Process Recommendations:** Update ICER's adaptations to its methods for evaluation of therapies for COVID-19 to implement an <u>abbreviated or rapid review framework</u> that includes <u>transparency into monitored therapies</u>, a general protocol, and <u>clear opportunities for stakeholder</u> <u>engagement</u>.
- 2. Methodological Recommendations: Incorporate additional perspectives, broader elements of value, and the impact of post-ventilation morbidity and mortality to <u>comprehensively assess the value that a treatment for COVID-19 could provide</u>.

Process Recommendations

Implement an abbreviated or rapid review framework that includes transparency into monitored therapies, a general protocol, and clear opportunities for stakeholder engagement.

ICER should be transparent with the list of monitored therapies to facilitate timely and comprehensive assessments of treatments for COVID-19. This transparency will allow stakeholders to be better prepared for a potential assessment, which will support efficient engagement and exchange of data with ICER when an assessment begins. Developing assessments of COVID-19 treatments in a vacuum without transparency and robust stakeholder engagement deviates from ICER's guiding principle of civil discourse and increases the risk of spreading incorrect, biased or misleading information into the press and the public domain.⁶

ICER should develop a general protocol for how it will evaluate vaccines and treatments. By clearly outlining a general protocol for COVID-19 assessments, ICER can increase transparency into its methodology, better engage with stakeholders, and support broad collection of the most appropriate data to inform decision making. This approach would align with how ICER shares a scoping document, research protocol, and model analysis plan for a standard review.⁶ To facilitate timely developments of reports, this information could be clearly summarized in a single general protocol that:

- 1. Outlines planned methods for modeling. The proposed methods and data sources could be subject to change based on emerging evidence and could differ for treatments and vaccines. However, an outline of the analysis plan would increase transparency to adhere to published best practices for model development and would also help to ensure that ICER is able to gather consistent and relevant feedback from stakeholders.¹⁵
- 2. Defines the key inputs required in ICER's assessment of value. In the second ICER colloquium on pricing in a pandemic, Dr. Campbell described key inputs that were crucial to assessing the value of COVID-19 therapies.⁴ We encourage ICER to proactively share similar information to champion the collection of data that will be needed to inform future evidence

synthesis work, real world evidence studies, and health economic models. ICER can also use this section of a protocol to detail other data from broader stakeholder groups that could be considered when interpreting assessment results and informing discussion of contextual considerations. This could include patient survey data on COVID-19 impact, hospital data on current use of emerging therapies, or contemporary hospital or payer cost information.

3. Describes the level of hierarchy of evidence ICER will consider in the model. Given the uncertainty in the expected timing between the availability of peer-reviewed evidence and final trial data and regulatory action, ICER could clearly provide a rationale for the inclusion of different types of grey literature (e.g. press releases, preliminary trial results, regulatory decision announcements, manufacturer data on file) to be consistent with its current policy on the inclusion of non-peer reviewed sources.¹⁶

ICER should clearly define stages of the review process including a plan for virtual engagement with broader stakeholders. Adopting a clear stepwise process would allow ICER to anchor to its standard framework while maintaining a flexible timeline to address the needs of stakeholders in the current environment.^{6,17} Only through open discussion throughout the review process, can ICER be better equipped to help advance the methods around assessing COVID-19 treatment value. For example, had ICER outlined a process to engage broader stakeholders prior to publishing the initial report, many of the methodological recommendations detailed below could have been collected and integrated into updated assessments. ICER can align to its guiding principles and ensure a collaborative, transparent, and evidence-based review by:

- 1. Maintaining an open-input period. An open input period for a particular treatment could be based on a rolling timeline or initiated when specific pre-established criteria have been met.
- 2. Denoting initial reports as draft analyses. Given the rapidly evolving treatment landscape, clearly indicating reports based on grey literature or without stakeholder feedback as draft analyses will reduce the risk of misinforming public discussion or policy decisions.
- **3.** Establishing criteria that would lead to a revised or updated report. Although ICER may not be able to provide a timeline for update, being transparent about the types of evidence that will trigger an update will better inform stakeholders about the data needs to further evidence generation.
- 4. Planning for virtual engagements of broader stakeholders. The patient perspective and discussion on the elements of value not captured in the cost-effectiveness analysis (e.g. other contextual considerations) is critical in interpreting how quantifiable, and non-quantifiable, downstream impacts of new treatments should be considered when making policy and pricing decisions.

Incorporate additional perspectives, broader elements of value, and the impact of postventilation morbidity and mortality to comprehensively assess the value that a treatment for COVID-19 could provide

Recognizing that the cost recovery model is a highly conservative scenario, ICER should include a societal co-base case to present the potential range of impact from treatments in a pandemic. A cost-recovery model does not accurately reflect the R&D efforts required to bring a therapy to market and may disincentivize future innovation.¹⁴ We appreciate ICER's efforts to better incorporate R&D costs related to evaluating a treatment for COVID-19 in the updated remdesivir analysis.² However, ICER's methodology does not account for the risk of R&D failure nor opportunity costs. With the rapid innovation to address the public health emergency, many manufacturers are incurring costs for clinical research and increasing manufacturing capacity to ensure the availability of treatments despite uncertainties in the clinical benefit and the risk of trial failure.¹⁸⁻²¹ Moreover, a cost recovery approach continues to provide a floor estimate of price for an intervention. As noted during the first ICER colloquium on pricing in a pandemic, there is a lack of validated methods for modeling cost recovery, estimation is hindered by limited transparency for key estimates, and use of a cost recovery approach to set pricing may lead to negative downstream impacts on funding essential second and third generation COVID-19 treatments and vaccines.^{3,11-14}

We urge ICER to add the societal perspective as a co-base-case and to acknowledge additional dimensions of value in its assessments of COVID-19 treatments. Failure to account for societal and other broader impacts of COVID-19 treatments and vaccines will undervalue treatments and will present a biased estimation of potential downstream economic and health impacts.²² Use of the societal perspective is recommended as a co-base case by the Second Panel on Cost-Effectiveness in Health and Medicine (Second Panel) and is continually supported by ongoing expert dialogue on COVID-19 treatment value.^{11-13,23} Recent debate on COVID-19 treatment pricing highlights the need to consider the broader impact of treatment, with the lack of treatments and vaccines for COVID-19 effectively halting normal US life. As of August 11, 2020, the United States (US) leads the world in the number of confirmed cases and deaths.²⁴ Beyond the health care sector, the COVID-19 pandemic is estimated to result in almost \$8 trillion in economic losses over the next decade.²⁵ Schools continue to debate whether they will open in the fall, and nearly half of adults report that their mental health has been negatively affected due to worry and stress over the virus.^{26,27} We recognize that data on the productivity impact of individual COVID-19 treatments may not be available from clinical trials or from available real world evidence studies. However, ICER can still develop initial estimates of the societal impact through use of patient survey data from patient advocacy groups, estimate the market and non-market productivity losses from patients who die from COVID-19, and/or use proxy information from similar respiratory conditions to inform initial model parameters.^{22,28}

Furthermore, ICER could leverage the growing literature base to discuss the broader expected impact of COVID-19 treatments qualitatively.²⁹ The health economics and outcomes research (HEOR) and academic community have made impressive strides in developing methods to estimate additional value elements under a cost-effectiveness framework.³⁰ While some methods may not be easily applied in the short time frame to develop an assessment, ICER should address additional impacts in the "other benefits or disadvantages" and "contextual considerations" section to ensure that end users of ICER's assessments have balanced information, ranging from cost recovery to standard cost-effectiveness methods to more novel considerations of treatment value (e.g. value of hope, insurance value, fear of contagion). Finally, we suggest that ICER also seek to consider how treatments impact health equity and underlying health disparities given the undeniable observed impact of COVID-19 on disadvantaged populations.^{6,31-33}

ICER's analysis should incorporate the impact of post-ventilation morbidity and mortality to better reflect the long-term burden of COVID-19. Employing a narrow definition of COVID-19 health effects based predominantly on outcomes during an acute stay fails to capture the impact of treatments on important downstream costs and health effects that are relevant to understanding treatment value. Data on the long-term burden of COVID-19 is only just emerging, but existing research suggests that morbidity and mortality impacts will extend far past acute hospital stays.^{34,35} During the second colloquium on pricing in a pandemic Steve Miller (Cigna) reinforced this point, noting that Cigna is seeing tremendous downstream morbidity in patients with COVID-19 tracked in their plan.⁴ As recommended by the Second Panel, a wide range of costs or cost savings-present and future-should be considered in economic evaluations, so long as they result directly from the interventions of interest.²³ Severe COVID-19 has been associated with acute respiratory distress syndrome (ARDS) requiring ventilator support, and existing research has demonstrated that patients discharged after ventilation have worse outcomes and higher costs. Recent data suggests that COVID-19 associated ARDS has similar respiratory system mechanics to historical ARDS, though uncertainty remains about the duration of ventilation and real world long-term impacts.^{36,37} By failing to include the morbidity and mortality of patients with COVID-19 who were on ventilation, ICER risks underestimating the value that a treatment provides and is not accurately reflecting the disease burden experienced by patients. Looking ahead, ICER should continue to monitor emerging data on long-term consequences of COVID-19, and should followed a pre-planned protocol on what should trigger an update to model inputs or a revised report.

Given that hospitals (providers) will be the purchasers of inpatient COVID-19 treatments in most instances, ICER should present a provider perspective or present the per-diem scenario as another base-case. ICER's base-case scenario for remdesivir mixes payer and hospital provider costs to produce base-case findings that do not match current US reimbursement practices and may skew public understanding of report findings. The majority of health systems in the US leverage bundled payments for inpatient care.³⁸ Therefore, in the case of COVID-19, hospital providers are the purchasers who will most commonly face the cost of funding of COVID-19 treatments. Currently, the ICER health system base-case mixes perspectives, effectively double counting the cost of COVID-19 treatments by assuming

an incremental cost for the treatment on top of a conventional bundled inpatient reimbursement.³⁹ This approach is particularly problematic given that press headlines and public discourse focus on summary statements around base-case conclusions. We recommend that ICER follow documented best practices for defining costs for the US payer perspective and remove the incremental cost for inpatient COVID-19 treatments for the health system base-case.²³ ICER's updated "hospital per-diem" scenario is a welcome addition to the assessment of remdesivir as it allows for providers and payers who operate under this type of reimbursement to see the important interplay between investing in a treatment and the impacts of that treatment on resource use and costs given potential changes in care setting (e.g. intensive care unit [ICU], non-ICU) and length of stay.² We recommend that ICER include this analysis as another base-case to more accurately reflect real world practice and better assess the value of hospital interventions

Conclusion

During these unprecedented times, collaboration and discussion among stakeholders across the health care sector is critical to developing and enabling access to solutions that address the needs of patients and society. ICER plays a vital role in providing evidence to inform the broad, multi-stakeholder conversations on the pricing and policy that will not only impact emerging treatments today but will also shape future innovation for COVID-19 and other possible pandemics. To support non-biased and evidence-based critical debate, we urge ICER to adhere to its long-standing principles of a fair and transparent assessment, robust engagement with a range of health care stakeholders, and an unwavering adherence to methodological best practices.

We look forward to working with ICER and other stakeholders to determine system-wide solutions that can lower costs for patients while also sustaining innovation and ensuring patient access. Working together, we have the best chance of quick and lasting success in alleviating this life-changing pandemic.

Sincerely,

Jan Elias Hangen

Jan Elias Hansen, Ph.D. Vice President, Evidence for Access Medical Unit U.S. Medical Affairs, Genentech, Inc.

References:

- Institute for Clinical and Economic Review. Alternative Pricing Models for Remdesivir and Other Potential Treatments for COVID-19: Preliminary Assessment. 2020; <u>https://icerreview.org/topic/covid-19/</u>. Accessed August 12, 2020.
- Institute for Clinical and Economic Review. Alternative Pricing Models for Remdesivir and Other Potential Treatments for COVID-19: Updated Assessment. 2020; <u>https://icerreview.org/topic/covid-19/</u>. Accessed August 12, 2020.
- 3. Institute for Clinical and Economic Review. Pricing in a Pandemic. Session One: Cost-Recovery Pricing. 2020; <u>https://icer-review.org/blog/pricing-in-a-pandemic-webinar-session-one-cost-recovery-pricing/</u>. Accessed July 24, 2020.
- 4. Institute for Clinical and Economic Review. Pricing in a Pandemic. Session Two: Cost-Effectiveness and Value-Based Pricing. 2020; <u>https://icer-review.org/blog/pricing-in-a-pandemic-session-two/</u>. Accessed July 31, 2020.
- 5. Institute for Clinical and Economic Review. Pricing in a Pandemic. Session Three: Monetary Prizes, Compulsory Licensing, Advanced Market Commitments 2020; <u>https://icer-review.org/blog/icer-colloquium-series-pricing-in-a-pandemic/</u>. Accessed August 7, 2020.
- 6. Institute for Clinical and Economic Review. 2020-2023 Value Assessment Framework. 2020; https://icer-review.org/meeting/2020-value-assessment-framework/. Accessed August 12, 2020.
- 7. U.S. Food and Drug Administration. Coronavirus (COVID-19) Update: FDA Collaborations Promote Rigorous Analyses of Real-World Data to Inform Pandemic Response. 2020; <u>https://www.fda.gov/news-events/press-announcements/coronavirus-covid-19-update-fda-collaborations-promote-rigorous-analyses-real-world-data-inform</u>. Accessed August 12, 2020.
- 8. PhRMA. The Latest on the Biopharmaceutical Industry's Efforts to Beat Coronavirus. 2020; <u>https://phrma.org/coronavirus</u>. Accessed August 12, 2020.
- America's Health Insurance Plans. Health Insurance Providers Respond to Coronavirus (COVID-19). 2020; <u>https://www.ahip.org/health-insurance-providers-respond-to-coronavirus-covid-19/</u>. Accessed August 12, 2020.
- 10. National Health Council. COVID-19 Awareness. 2020; <u>https://nationalhealthcouncil.org/issue/covid-19/</u>. Accessed August 12, 2020.
- 11. Cohen JT, Neumann PJ, Ollendorf DA. Valuing And Pricing Remdesivir: Should Drug Makers Get Paid For Helping Us Get Back To Work? 2020; https://www.healthaffairs.org/do/10.1377/hblog20200518.966027/full/. Accessed July 21, 2020.
- 12. Dubois RW. It's Time To Talk About COVID-19 Prices. 2020; https://www.healthaffairs.org/do/10.1377/hblog20200518.302353/full/. Accessed July 21, 2020.
- Kamal-Bahl S, Willkek R, Puckett JT, Doshi JA. The Case For Using Novel Value Elements When Assessing COVID-19 Vaccines And Therapeutics. 2020; https://www.healthaffairs.org/do/10.1377/hblog20200616.451000/full/. Accessed July 21, 2020.
- 14. Garthwaite C. Beware of Underpriced Drugs for COVID-19 Treatments. Washington Post. May 18, 2020.
- 15. Eddy DM, Hollingworth W, Caro JJ, Tsevat J, McDonald KM, Wong JB. Model transparency and validation: a report of the ISPOR-SMDM Modeling Good Research Practices Task Force-7. Medical decision making : an international journal of the Society for Medical Decision Making. Sep-Oct 2012;32(5):733-743.
- Institute for Clinical and Economic Review. Policy on Inclusion of Grey Literature in Evidence Reviews. <u>https://icer-review.org/methodology/icers-methods/icer-value-assessment-framework-</u> 2/grey-literature-policy/. Accessed August 12, 2020.

- Institute for Clinical and Economic Review. Adaptations to the ICER methods for evaluation of therapies for COVID-19. 2020; <u>https://icer-review.org/wp-content/uploads/2020/06/Adaptations-</u> <u>to-the-ICER-methods-for-evaluation-related-to-treatments-for-COVID-19.pdf</u>. Accessed August 12, 2020.
- Genentech Inc [Press Release]. Genentech Provides an Update on the Phase III COVACTA Trial of Actemra in Hospitalized Patients With Severe COVID-19 Associated Pneumonia. 2020; <u>https://www.gene.com/media/press-releases/14867/2020-07-28/genentech-provides-an-update-onthe-phas</u>. Accessed August 17, 2020.
- Sanofi [Press Release]. Sanofi and Regeneron provide update on Kevzara® (sarilumab) Phase 3 U.S. trial in COVID-19 patients. 2020; <u>https://www.sanofi.com/en/media-room/press-</u> releases/2020/2020-07-02-22-30-00. Accessed August 17, 2020.
- 20. National Institutes of Health. NIH halts clinical trial of hydroxychloroquine. 2020; <u>https://www.nih.gov/news-events/news-releases/nih-halts-clinical-trial-hydroxychloroquine</u>. Accessed August 17, 2020.
- 21. Moscicki R. The biopharmaceutical industry's unique role in responding to COVID-19. 2020; <u>https://catalyst.phrma.org/rd-focus-the-biopharmaceutical-industrys-unique-role-in-responding-to-covid-19</u>. Accessed August 17, 2020.
- 22. Kim DD, Neumann PJ. Analyzing the Cost Effectiveness of Policy Responses for COVID-19: The Importance of Capturing Social Consequences. Medical decision making : an international journal of the Society for Medical Decision Making. Apr 2020;40(3):251-253.
- 23. Sanders GD, Neumann PJ, Basu A, et al. Recommendations for Conduct, Methodological Practices, and Reporting of Cost-effectiveness Analyses: Second Panel on Cost-Effectiveness in Health and Medicine. Jama. Sep 13 2016;316(10):1093-1103. <u>https://pubmed.ncbi.nlm.nih.gov/27623463/</u>
- 24. Johns Hopkins University. Mortality Analyses. 2020; <u>https://coronavirus.jhu.edu/data/mortality</u>. Accessed August 12, 2020.
- Congressional Budget Office. Comparison of CBO's May 2020 Interim Projections of Gross Domestic Product and Its January 2020 Baseline Projections. 2020; <u>https://www.cbo.gov/publication/56376</u>. Accessed July 21, 2020.
- 26. Kaiser Family Foundation. The Implications of COVID-19 for Mental Health and Substance Use. 2020; <u>https://www.kff.org/coronavirus-covid-19/issue-brief/the-implications-of-covid-19-for-mental-health-and-substance-use/</u>. Accessed August 12, 2020.
- 27. Kaiser Family Foundation. How Many Teachers Are at Risk of Serious Illness If Infected with Coronavirus? 2020; <u>https://www.kff.org/coronavirus-covid-19/issue-brief/how-many-teachers-are-at-risk-of-serious-illness-if-infected-with-coronavirus/</u>. Accessed August 12, 2020.
- 28. Padula WV, Malaviya S, Reid NM, Tierce J, Alexander GC. Economic Value of Treatment and Vaccine to Address the COVID-19 Pandemic: A U.S. Cost-Effectiveness and Budget Impact Analysis. SSRN. 2020.
- 29. Shafrin J, Lang K, Maclean R. COVID-19 Pandemic Vindicates the ISPOR Value Flower. J Clin Pathways. 2020;6(5):53-56.
- Lakdawalla DN, Doshi JA, Garrison LP, Jr., Phelps CE, Basu A, Danzon PM. Defining Elements of Value in Health Care-A Health Economics Approach: An ISPOR Special Task Force Report [3]. Value in health : the journal of the International Society for Pharmacoeconomics and Outcomes Research. Feb 2018;21(2):131-139. <u>https://pubmed.ncbi.nlm.nih.gov/29477390/</u>
- 31. Shafrin J, Venkatachalam M. Creating Incentives To Narrow The Gap In Health Outcomes: Expanding Value Assessment To Incorporate Health Inequality. 2020;

https://www.healthaffairs.org/do/10.1377/hblog20200708.876257/full/. Accessed August 12, 2020.

- Asaria M, Griffin S, Cookson R, Whyte S, Tappenden P. Distributional cost-effectiveness analysis of health care programmes--a methodological case study of the UK Bowel Cancer Screening Programme. Health economics. Jun 2015;24(6):742-754. <u>https://pubmed.ncbi.nlm.nih.gov/24798212/</u>
- Gilead Sciences Inc [Press Release]. Gilead Presents Additional Data on Investigational Antiviral Remdesivir for the Treatment of COVID-19. 2020; <u>https://www.gilead.com/news-and-press/pressroom/press-releases/2020/7/gilead-presents-additional-data-on-investigational-antiviralremdesivir-for-the-treatment-of-covid-19</u>. Accessed August 12, 2020.
- 34. Hornig M, Tuller D. Why Do Some Recover From COVID-19 Quickly, While Others Seem Likely To Face Long-Term Disability? 2020; https://www.healthaffairs.org/do/10.1377/hblog20200603.471204/full/.
- 35. Herridge MS, Tansey CM, Matté A, et al. Functional disability 5 years after acute respiratory distress syndrome. The New England journal of medicine. Apr 7 2011;364(14):1293-1304. https://pubmed.ncbi.nlm.nih.gov/21470008/
- 36. Fan E, Beitler JR, Brochard L, et al. COVID-19-associated acute respiratory distress syndrome: is a different approach to management warranted? The Lancet Respiratory Medicine. July 6 2020. <u>https://doi.org/10.1016/S2213-2600(20)30304-0</u>
- Almeshari MA, Alobaidi NY, Al Asmri M, et al. Mechanical ventilation utilization in COVID-19: A systematic review and meta-analysis. medRxiv. 2020. <u>https://doi.org/10.1101/2020.06.04.20122069</u>
- 38. Kaiser Family Foundation. Comparing Private Payer and Medicare Payment Rates for Select Inpatient Hospital Services. 2020; <u>https://www.kff.org/medicare/issue-brief/comparing-private-payer-and-medicare-payment-rates-for-select-inpatient-hospital-services/</u>. Accessed August 12, 2020.
- Kim DD, Silver MC, Kunst N, Cohen JT, Ollendorf DA, Neumann PJ. Perspective and Costing in Cost-Effectiveness Analysis, 1974–2018. PharmacoEconomics. July 22 2020. <u>https://doi.org/10.1007/s40273-020-00942-2</u>