TAG
Treatment Action Group

Testimony Submitted for the Record
U.S. House Committee on Oversight and Reform

Hearing on "Unsustainable Drug Prices (Part III):
Testimony from AbbVie CEO Richard Gonzalez"

Bryn Gay, HCV Project Director
Annette Gaudino, Policy Strategy Director
Elizabeth Lovinger, Senior Government Relations and Policy Officer
Joelle Dountio Ofimboudem, HCV Project Community Engagement Officer
Suraj Madoori, U.S. and Global Health Policy Director

May 13, 2021

Treatment Action Group (TAG) thanks Chairwoman Maloney, Ranking Member Comer, and members of the House Committee on Oversight and Reform for this opportunity to submit testimony/questions and convening this important hearing investigating anti-competitive practices perpetrated by the company AbbVie, on their products – Humira and Imbruvica.

TAG is an independent, activist and community-based research and policy think tank fighting for better treatment, prevention, a vaccine, and a cure for HIV, tuberculosis (TB), and hepatitis C virus (HCV). We have been leaders in HIV, TB and HCV research and policy advocacy since 1992.

The proceeding testimony and brief details the track record of AbbVie on perpetrating anti-competitive practices that stem from the company's marketing of HCV medications that have kept these cures inaccessible to heavily impacted communities across the globe. This testimony prepared for the Committee, seeks to elucidate the historical context of AbbVie's egregious anti-competitive practices in the marketing and pricing of Humira and Imbruvica as a pattern of behavior that began with the company's HCV portfolio – namely Mavyret. The practices that keep the prices of Humira and Imbruvica inflated are done by strategic design, which we have carefully traced to the company's marketing of its HCV cures. As the brief will detail, these practices include patent abuse, strategic overpricing, and restricting access.

In doing so, the company continues to remain unaccountable for practices that have started as early as 2017 and has now allowed the company to continue a stranglehold on essential medicines that we alarmingly now see with Humira and Imbruvica. AbbVie continues to reap billions in profits, reporting a record-breaking first quarter of 2021, notably hailing this windfall to their immunology portfolio. We urge the Committee to deeply probe the witnesses and representatives from AbbVie to root out these historical practices of anti-competitive behavior and ensure all patients in the U.S. and abroad that stand to have their lives saved by these products, can affordably and equitably access them.

Gaming the System: AbbVie

A brief for the members of the U.S. House Committee on Oversight and Reform
Prepared by Treatment Action Group (TAG)

Background:

Treatment Action Group (TAG) welcomes the House Oversight Committee's investigation into AbbVie's keystone products Humira and Imbruvica, and submits this brief to draw much needed scrutiny to the company's broader history of gaming the U.S. patent system to the detriment of patients worldwide, including in low- and middle-income countries (LMICs) with the highest burdens of diseases which can be treated or cured by their patented medications. TAG has tracked this egregious pattern of anti-competitive practices by AbbVie since 2017, with the FDA approval of their direct-acting antiviral Mavyret (generic name glecaprevir/ pibrentasvir or G/P). Mavyret and generic G/P are highly effective oral cures for chronic hepatitis C virus (HCV) infection, with demonstrated clinical benefits compared with other approved treatments for patients with chronic kidney disease, patients requiring retreatment after failure with another direct acting antiviral, and some pediatric patients.

This pattern of behavior can be summarized as follows:

- evergreening strategies to extend market monopolies beyond the statutory 20-year patent length;
- over-patenting via method of treatment patents in high-income countries;
- refusal to negotiate affordable prices in middle-income countries; and
- complete lack of access in low-income countries due to failure to register the product for generic production despite entering a voluntary licensing agreement with the Medicine Patents Pool.

Patent abuse in high income countries:

Evergreening refers to manipulations of patent criteria and law to extend exclusivity rights beyond the statutory term of 20 years. AbbVie has employed three evergreening strategies: (a) filing of at least one patent application per year from 2014-2019; (b) filing 13 secondary patent applications on **method of treatment** (MOT); and (c) requiring **grant back obligations** in voluntary licensing agreements.

MOT patent applications relate to additional therapeutic uses of Mavyret. These MOT patents indicate AbbVie aims to protect G/P even when used with other direct-acting antivirals (whose patents held by other companies); beyond the FDA approved indication for HCV; for treatment duration; specific doses (such as pediatric formulations); and contraindications.

If we consider the year of international patent filings, between 2011 and 2019 AbbVie filed 24 patent applications regarding glecaprevir, pibrentasvir and the G/P combination, almost two patent applications each year. Most of those patent applications – at least 13 – are related to methods of treatment. For instance, MOT patent WO2017/007934 (Figure 1), filed in 2017, involves the MOT for HCV infection using sofosbuvir in combination with G/P or pibrentasvir alone. However, clinical trials demonstrating the

efficacy were not completed until 2019[1] and 2020.[2] The MOT patent filings fall under the evergreening strategies[3] to extend the monopoly of existing medicines based on the filing of the patents with secondary claims.[4]

Overpricing in middle-income countries, and no access in low-income countries:

AbbVie demanded non-exclusive **grant back obligations** in their voluntary license with the Medicines Patent Pool (MPP), neutering an international, voluntary legal framework intended to expand access to affordable essential medicines for LMICs. Grant back obligations give AbbVie right of first refusal to obtain the sole right to purchase any new G/P formulation in the US and EU, and any patent or know-how required to make the new G/P formulation. "The grant-back clause also requires sublicensees to offer AbbVie an option to a non-exclusive and royalty-free license to commercialise the new G/P formulation outside of the US and EU and outside of the Territory defined by the current license (Article 3.9(b)) (MSF)." Non-exclusive grant back obligations disincentivize generic manufacturers to enter into sublicensee contracts to produce generic or new formulations if there are restrictions put into the terms for the country coverage for commercialization. This is especially true for medicines with little commercial interest due to small patient populations, such as pediatric formulations for children under age 12, or long-acting injectables. This limits generic competition and prolongs market exclusivity.

Restricted access means patients lose:

Under the terms agreed by AbbVie in their license with Medicines Patent Pool, 96 countries can access generic glecaprevir/pibrentasvir; however, 23 countries **–** mostly high burden, upper-, middle-, and low-income countries **–** are excluded, including Brazil, China, Russia, and India, which is licensed as a manufacturing country only. Brand name Mavyret is registered in 8 of the total 83 (9.6%) high-burden HCV countries/regions, including 55 PEPFAR-funded countries. Generic versions of glecaprevir/pibrentasvir are registered in 2 of the total 83 (or 2.4%) countries examined (Argentina and Germany). The lack of registration has led to almost no treatment uptake outside high-income countries. In other words, in the case of G/P for HCV infection, this leaves 5 million patients with difficult to treat HCV subtypes (primarily in Central Africa and Southern Asia), 5.5 million children, and the 5% of all patients who fail their first course of treatment without access to an affordable, effective treatment option.

In the context of the current Administration's willingness to negotiate a WTO TRIPS waiver for COVID-19 vaccines, years of growing frustration on the part of the American people with the failure to act on high prescription drug prices, and the growing awareness among the general public that monopolies are harming American lives and livelihoods, we call on the Committee to exercise your full legal powers to hold AbbVie to account.

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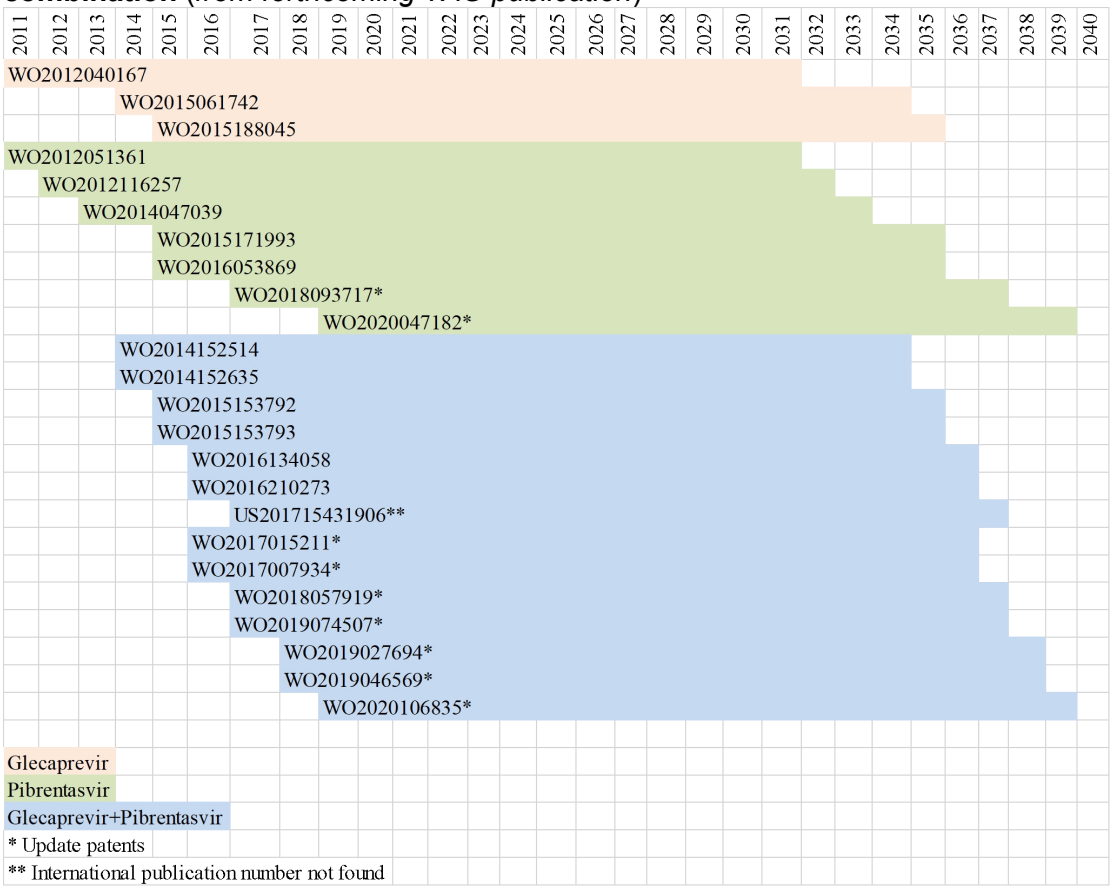
[1] http://dx.doi.org/10.1136/bcr-2019-233098

[2] https://doi.org/10.1016/j.jhep.2021.02.024

[3] Kapczynski A, Park C, Sampat B (2012). Polymorphs and Prodrugs and Salts (Oh My!): An Empirical Analysis of ''Secondary'' Pharmaceutical Patents. PLoS ONE 7(12): e49470. doi:10.1371/journal.pone.00494

[4] This means that they are filed after a primary patent, which is the one related to the active pharmaceutical ingredient (API)[4] and also to the synthetic process of such API. Secondary patents aim to protect pharmaceutical compositions (formulation), methods of treatment, uses (including second medical use), combinations, doses, polymorphs, prodrugs, salts, enantiomers, route of administrations, among others etc. (*from forthcoming TAG publication*).

Figure 1. Timeline* of patent applications related to Glecaprevir, Pibrentasvir, and their combination (*from forthcoming TAG publication*)



Source: the authors. * Estimates based on the international filing date and 20 years of patent term.
Scenario based on existing patents filed in countries and granted.

Figure 1 shows patent filings by year (2011-2019) and with estimated 20-year patent terms. Patent filings precede clinical trial results (below) used to determine safety and efficacy of drug and drug combination. **Filing patents before they are shown to meet patentability criteria -- that proves the innovation is novel, non-obvious, and useful – is an abuse of the U.S. patent system.**

The Patent Cooperation Treaty International Preliminary Report on Patentability for the 6 of the 7 patent/applications related to the combination of glecaprevir and pibrentasvir, identified in the Figure 1 (as the last 7 listed patents), **indicate either lack of inventive step and/or novelty** according to the cited documents used as prior art:

- WO2017/015211: lack of inventive step (claims 1-14)
- WO2017/007934: lack of novelty and inventive step (claims 1-17)
- WO2018/057919: lack of inventive step (claims 1-26)
- WO2019/074507: lack of novelty (claims 1-17; 21-24) and inventive step (claims 1-24)
- WO2019/027694: lack of inventive step (for claims 1-6; 8; 10-13; 15-22)
- WO2019/046569: lack of inventive step (claims 1-20)

- WO2020/106835: suggestive to lack novelty and inventive step (based on International Search Report

Table 1. Comparative pricing data in select high-burden countries[5]

- Other generic pangenotypic direct-acting antivirals (e.g., sofosbuvir/velpatasvir or sofosbuvir/daclatasvir) are widely available for **<US$100/per 12-wk treatment course.**
- **This discrepancy is solely due to lack of scale up and competition in the global generics market for G/P due to AbbVie's failure to register and market their drug.**
- **G/P provides clinical benefits over competitor combinations: a shorter 8 wk treatment course to cure the majority (80%) of patients; a safe, effective pediatric formulation; and proven safe and effective for people with mild/moderate kidney disease and end-stage liver disease.**

Brazil Public tender in Oct 2018	**Registered** Generic G/P R$ 24,081.85 to R$ 34,402.64 (about US$4,371.72 to US$6,244.86/per 12-week treatment course) $9,130 GNI (2019)
India	**Excluded** in the voluntary license (manufacturing-only country) Offered generic G/P about US$2,500/per 12-week treatment course $2,120 GNI (2019)
Russia	**Registered** Generic G/P US$5,000/per 12-week treatment course $11,260 GNI (2019)
US	**Registered** Mavyret (brand) around US$15,000 to US$18,000/per 8-week treatment course in the US $65,850 GNI (2019)

Glecaprevir/Pibrentasvir clinical trial results (from 2017-2020):
This list of clinical trials results relate to seven MOT patents (listed above) filed before results completed; 6 patents found to not meet patentability criteria according to PCT.

[5] 2020. mapCrowd data and input from hepCoalition members.

Safety, Efficacy, and Pharmacokinetic Analysis of Glecaprevir/Pibrentasvir in Pediatric Patients With Genotypes 1-6 Chronic Hepatitis C Virus (HCV) Infection: Part 2 of the DORA Study - (11/13/20)

Real-World Outcomes in Patients With Chronic Hepatitis C Virus Infection and Substance Use Disorders Treated With Glecaprevir/Pibrentasvir for 8 Weeks: A Pooled Analysis of Multinational Postmarketing Observational Studies - (11/13/20)

Integrated Efficacy and Safety Analysis of Genotypes 1-6 Treatment-Naïve, Non-Cirrhotic, and Compensated Cirrhotic Hispanic/Latino Patients Who Received 8 Weeks of Glecaprevir/Pibrentasvir - (11/13/20)

Short-Duration Pan-Genotypic Therapy With Glecaprevir/Pibrentasvir for 6 Weeks Among People With Recent Hepatitis C Viral Infection - Martinello - - Hepatology - Wiley Online Library (https://aasldpubs.onlinelibrary.wiley.com/doi/abs/10.1002/hep.31003)

Glecaprevir/Pibrentasvir clinical trial results (from 2011-2020):
This list of clinical trials results relate to primary + secondary patents during this time.

EASL: MAGELLAN-1, PART 2: GLECAPREVIR/PIBRENTASVIR FOR 12 OR 16 WEEKS IN PATIENTS WITH CHRONIC HCV GENOTYPE 1 OR 4 AND PRIOR DIRECT-ACTING ANTIVIRAL TREATMENT FAILURE - (04/24/17)

EASL: Safety and Efficacy of Glecaprevir/Pibrentasvir in Adults With Chronic Hepati is C Virus Infection Genotype 1-6 as a Function of Chronic Kidney Disease Stage - (04/25/17)

EASL: MAGELLAN-2: SAFETY AND EFFICACY OF GLECAPREVIR/PIBRENTASVIR IN LIVER OR RENAL TRANSPLANT ADULTS WITH CHRONIC HEPATITIS C GENOTYPE 1-6 INFECTION - (04/24/17)

EASL: Safety of Glecaprevir/Pibrentasvir in Adults With Chronic Genotype 1-6 Hepatitis C Virus Infection: An Integrated Analysis - (04/24/17)

EASL: Efficacy and Safety of Glecaprevir/Pibrentasvir in Patients Co-infected With Hepatitis C Virus and Human Immunodeficiency Virus-1: The EXPEDITION-2 Study - (04/20/17)

CROI: GLECAPREVIR AND PIBRENTASVIR INTERACTIONS WITH COMBINATION ANTIRETROVIRAL REGIMENS - (02/20/17)

EASL: Pharmacokinetics and Safety of Glecaprevir/Pibrentasvir in Adults With Chronic Genotype 1-6 Hepatitis C Virus Infection and Compensated Cirrhosis: An Integrated Analysis - (04/21/17)

Glecaprevir and pibrentasvir for 12 weeks for hepatitis C virus genotype 1 infection and prior direct-acting antiviral treatment - (04/13/17)