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"Listening Session on Joint USPTO-FDA Collaboration Initiatives"

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I. Introduction

My name is Corey Salsberg, and I am Vice President, Global Head of IP Affairs for Novartis. On behalf of our company, thank you for the opportunity to participate in today's listening session, and to share our perspectives on the proposed initiatives for collaboration between FDA and PTO.

II. Background

Novartis is a science-based healthcare company whose purpose is to reimagine medicine to improve and extend people's lives. Our products, which include innovative chemical and biologic medicines, cell and gene therapies, radiopharmaceuticals, and high quality generics and biosimilars through our Sandoz division, reach hundreds of millions of patients each year, treating diseases that range from cancer, to heart failure, to multiple sclerosis, to immunological and rare genetic disorders, to malaria and many more. Across these therapeutic areas, our treatments aim to address significant unmet patient needs and to tackle some of society's most challenging healthcare issues through cutting-edge science and technology that pushes the boundaries of modern medicine. Some of our recent breakthroughs include the approval in 2017 of the world's first chimeric antigen receptor T-Cell (CAR-T) therapy, Kymriah®, a personalized one-time treatment for certain forms of leukemia and lymphoma that uses a patient's own T-cells to fight cancer;[i] the approval in 2019 of Zolgensma®, the world's first gene therapy to treat children with spinal muscular atrophy (SMA), a leading genetic cause of infant mortality;[ii] the approval in 2021 of Leqvio®,[iii] a revolutionary approach to lowering LDL cholesterol through a small interfering RNA (siRNA) therapy; and the approvals in 2018 and 2022 of two of the world's first Peptide Receptor Radionuclide Therapies (PRRTs), Lutathera®[iv] and Pluvicto,™[v] which precisely deliver radiation to treat neuroendocrine tumors and certain types of prostate cancer.

As these examples demonstrate, these are revolutionary times for science, medicine and biopharmaceutical innovation, and transformational ones for patients, who have better access to effective treatments today, and more reason to hope for cures, than in any prior time in history. Between 2015 and 2021, Novartis alone had 26 novel molecules approved, and 23 FDA breakthrough therapy designations. Industrywide, the number of novel drug approvals continues to increase over time, with the last five years witnessing some of the highest annual figures in history.[vi]

These successes are due in no small part to the robust US innovation ecosystem, with its world-leading patent system and inspired policies under laws like the Bayh-Dole Act that encourage and enable deep private-sector investments in complex, risky fields of R&D like ours, as well as collaboration between the public, private and academic sectors to convert basic science into lifesaving medicines and therapies. On account of these laws and policies, we invest over $9 billion annually in R&D—which in 2021 amounted to 18.5% of our global net sales—a figure which places us among the top 20 R&D investors in any industry.[vii] This same robust ecosystem is why we have made the United States home to the global headquarters of our Novartis Institutes for BioMedical Research (NIBR), what we call our "innovation engine," and why our newest technologies like cell and gene therapies, were developed and continue to be manufactured here, providing many thousands of jobs to Americans in cutting-edge fields that also serve the interests of patients and the public good.

Speaking of patient interests, our approach to intellectual property (IP), including patents, derives from our broader efforts to develop breakthrough treatments that improve health outcomes and extend people's lives. Our research follows where disease burdens, potential patient benefits, and the latest science take us. Our patents reflect solutions to the complex scientific challenges that must be overcome, and the many technological problems that must be solved, on the long and difficult road to a single safe and effective medicine. That road takes 10 to 15 years on average, and is only successful around 12% of the time, even once clinical trials begin.[viii] Patents and other IP rights are what makes the journey possible, enabling the discovery and development of transformative medical innovations, facilitating their delivery to the patients who need them, and allowing us to contribute substantially to the Constitution's vision of promoting scientific and technological progress.

III. Statement

With that background, I would like to focus my remarks today on what we consider to be one of the most important topics on the list of interagency collaboration initiatives, the FDA's stated concerns over allegations that innovative medicines companies misuse the patent system in the form of alleged "patent thickets, "evergreening" and "product hopping" (Topic1(h)). We view this topic as among the most important, because the "solutions" that some have proposed to address these alleged problems, such as limiting the ability to secure patents in various ways on legitimate inventions with real-world patient impact that advance the field of medicine, would be devastating to our work and to the future of biopharmaceutical innovation.

To be clear, as a company that reached 766 million patients in 2021 with our innovative, as well as generic and biosimilar medicines, we strongly share your agencies' goal of "ensuring that our innovation system strikes the appropriate balance" between "encouraging meaningful innovation in drug development while supporting a competitive marketplace that can promote greater access to medicines for American families."[ix] We are concerned, however, that the pursuit of this legitimate goal has been unduly influenced, and risks being undermined, by misleading statements and false narratives about the patent system and our industry's use of it that have dominated media headlines and permeated political debates over the last several years.

More specifically, common allegations of "misuses" of the system, including many of the concerns raised in the FDA's September 10, 2021 letter, appear to be rooted in either fundamental misunderstandings of how the patent system and biopharmaceutical innovation work, or ideologies and goals that are inconsistent with United States patent law and the innovation policies that have stood behind it since its enshrinement in the Constitution. In some cases, these allegations have also been accompanied by alleged "data" on numbers of patents and years of market exclusivity that are grossly inaccurate, but have gone largely unchecked, and have harmfully made their way into official policy discussions.

To help keep your work in this area on-mission and consistent with the patent laws and policies that have helped give rise to nearly every medicine available today, we would like to suggest that two core objectives be included in any interagency work on this topic. First, your agencies should ensure that you are carefully distinguishing between *actual* misuses of the patent system, and legitimate uses that critics of the system simply call "misuse" in an effort to substitute their

own preferences for how they want the patent system to work. Second, efforts should be made to ensure that any facts, data and evidence considered or incorporated into your work are accurate, reliable, and relevant.

A.

On the first objective, far too often, critics of the patent system allege "misuse" simply by employing inflammatory labels like "thicketing" and "evergreening," without any effort to define these terms or to reach any consensus on what they mean. We implore your agencies to view any sources who use these bare, unhelpful labels with extreme skepticism, and to instead adopt the thoughtful mandate set forth in the Administration's Executive Order that initiated this interagency dialogue. That mandate asks your agencies to work together to ensure that "the patent system, while incentivizing innovation, does not also unjustifiably delay generic drug and biosimilar competition beyond that reasonably contemplated by applicable law."[x] This mandate encompasses two important principles. One, there is nothing remarkable or wrong about seeking, obtaining, or enforcing patents on pharmaceutical inventions in ways that comply with our nation's patent law. Two, there is nothing remarkable or wrong about the appropriate use of those patents to protect the innovations they cover, which may postpone entry of generic drugs and biosimilars during the patent term. The patent system was consciously designed to allow just that, providing exclusivity to inventors for as long as a valid and enforceable patent lasts, which of course is what creates the economic incentive that makes the system work. It is only when delays are unjustified that they should raise any potential concerns.

These principles provide important context for many of the allegations that critics and media have lodged against our industry in recent years. In the vast majority of cases, activities vilified as "misuse" through conclusory terms like "evergreening" and "thicketing" are not only lawful, they are critical to innovation and represent exactly the types of uses that the patent system was designed to incentivize. Examples that have become ubiquitous include allegations that it is "misuse" to obtain more than one patent on a product, "misuse" to obtain patents on aspects of a medicine other than its active compound or substance, and "misuse" to obtain patents on improved versions or aspects of a medicine after it is launched. These assertions have never been the law, and had they been, most of the medicines we rely on today would likely never have been developed.

The claim that it is "misuse" to obtain multiple patents per product fundamentally misunderstands patent law and the innovation process. Patents are not issued for commercial products. They are issued for *inventions*, which the law has defined to include processes (such as manufacturing methods), manufactures, engines, machines, devices, and "any improvement" thereof since 1790,[xi] and "compositions of matter" since 1793.[xii] It is commonplace in our technologically advanced society today for commercial products in almost every field to be comprised of many different constituent inventions. Smartphones, by some counts, include over 250,000 patented (or once patented) inventions.[xiii] Even a golf ball may contain as many as 70 separate inventions.[xiv] With an average 10-15 year timeline to develop a single medicine, and an average 12% success rate even once clinical trials begin, it should not come as a surprise that a technology as complex and as difficult to develop as a medicine also typically gives rise to many

different inventions on or for that medicine by the time it is launched. Those inventions may include novel chemical forms, formulations, indications, dosage forms, routes of administration, and dosage regimens, as well as consistent and efficient manufacturing methods. All are a direct result of the biopharmaceutical innovation process, and reflect the many challenges we have to overcome, and the problems we have to solve, to develop a compound into a safe, effective, and scalable medicine that can reach the patients who need it around the world. The diversity of inventions that make up a medicine, and their legitimacy, are of course also recognized in the Hatch-Waxman Act, which requires the listing of patents not just on a medicine's "active ingredient," but also, for example, on its "formulation or composition" and its "method of us[e]."[xv]

The related assertion that inventions in a medicine beyond its active compound are not deserving of patent protection, or are inherently of lesser importance, is also wrong. As already noted, our patent system was designed from the outset to encourage a broad array of technological forms, including manufacturing processes, technological methods, and all types of compositions of matter.[xvi] The very first patent issued in the United States, signed by George Washington in 1790, was not for a novel ingredient or other physical item, but for a *method of manufacturing* potash.[xvii] In our field, too, some of the most important breakthroughs in biopharmaceutical and medical history have been processes, such as polymerase chain reaction (PCR), or medicines patented only as uses, formulations or derivatives, such as Prontosil, the first synthetic antibiotic and the subject of the 1939 Nobel Prize for Medicine.

As a practical matter, the ability to secure patents "beyond the compound" is also critical for incentivizing innovation in our field because of the harsh realities of the types of R&D that we do, and the complex nature of the science at the heart of our treatments. Compound patents are typically filed early in the R&D process. With a 20-year patent term measured from filing, and our average 10-15 year development timeline, the few years of exclusivity that remain on a compound patent by the time a medicine is launched are seldom enough on their own to create the level of incentives needed to sustainably finance our work.[xviii] As a separate point, the emerging technologies that are defining the future of medicine, such as personalized cell and gene therapies, gene editing, and RNA-based medicine, are increasingly based on innovative processes and methods, and a variety of other inventions beyond traditional compounds, that need broad incentives to nurture their growth. In short, these practices are not "thicketing," but instead reflect the realities of pharmaceutical science, and appropriate uses of the patent system that enable the development of medicines, while contributing new knowledge and technologies to the field and broader society.

Last, the frequent claim that inventions made after a medicine is launched are somehow trivial and undeserving of patent protection again ignores our laws, the nature of science, and patients' interests in gaining access to the best medicines possible. As previously noted, patents have been available for "improvements" to prior inventions since the very first Patent Act of 1790. That inspired policy reflects the understanding that all scientific progress builds on what comes before, and that innovation is a *process* that does not end with the introduction of a first-generation product. After we launch a new medicine, we continue to look for ways to make it

safer, more effective, more convenient, or otherwise more beneficial for patients. And because today's medicines often work on targets and pathways common to other diseases, we consistently seek to discover new ways to further develop them for other indications. As one famous example, the first medicine approved to treat HIV, azidothymidine (AZT), was a failed cancer treatment candidate from the 1960s, whose antiretroviral attributes and utility to treat HIV were only discovered and developed decades after the compound had been abandoned. Some more recent examples from our own company include

- Our Alzheimer's medicine, Exelon®, originally an oral drug, which we reformulated to administer through a transdermal patch, resulting in improved patient compliance and elimination of a gastric side effect.

- Our cardiovascular drug, Entresto®, which is comprised of an innovative combination of a previously-approved ingredient with one that was never before approved, and is now a standard of care for heart failure; and

- Our novel breast cancer drug Piqray®, which was later further approved as Vijoice® after we further developed it as the first treatment to address the root cause of rare disease PROS.

Each of these examples, and many similar ones in our portfolios and those of our peers, required substantial additional investment in R&D after the original medicine was launched. Without the ability to obtain patents on these post-launch inventions, most of them, and the benefits they bring to existing and new patient populations, would not exist. This is not "evergreening" but again is an appropriate use of the patent system to advance and enable further pharmaceutical innovation.

B.

For the reasons I've discussed, it is highly unfortunate that conclusory terms like "evergreening" and "thicketing" have been allowed to be used interchangeably for what is, in most cases, not only legal, but scientifically appropriate and necessary activity that reflects the complexity, length, and diversity of solutions to the problems we need to solve to develop safe and effective medicines.

As I mentioned, in addition to the proliferation of these unhelpful terms, narratives alleging widespread misuse of the system have also been plagued by inaccurate representations about the numbers of patents on most medicines, and false assertions about what those numbers (even if they were accurate) mean. It would be one thing if the patents on most medicines indeed delayed generic competition for the multiple decades that critics and the media commonly allege. But study after study that has looked at the *actual* time that most new medicines spend on the market before losing exclusivity to generics have concluded that the average is *well* below the 20 years that the US and global patent systems have adopted as their basic patent term, and right in line with the minimum 14 years that our patent-term extension (PTE) system aims to provide.[xix] An August 2021 analysis, for example, found that the average period of market exclusivity for FDA-

approved new-molecular entity based drugs from 1995 to 2019 was between 12.2 and 14.6 years,[xx] and a 2017 study of drugs from the period 1996-2015 put the figure at 13.5 years.[xxi]

Despite these objective, easily measurable, fact-based figures, some of the most commonly cited sources continue to claim that "patent thickets" are unfairly and systemically delaying generic entry well beyond 20 years. These allegations, however, are invariably based either on inaccurate data, or misleading calculations that add up consecutive terms on separate patents without regard for whether those patents have any real-world impact on generic entry.

Concerns of exactly this nature have been expressed by a growing number of academics who study this issue, as well as at least one US Senator.[xxii] Unfortunately, those concerns also match our experience. As one example, an October 2017 report published by the Initiative for Medicines, Access & Knowledge (I-MAK) claims that our groundbreaking cancer medicine, Gleevec®, had a "patent duration of 35 years," suggesting that generic competition would only be possible in 2029,[xxiii] when in fact competitors began launching generic versions in early 2016, almost two years before the report was even published. The actual time that Gleevec® spent on the US market without generic competition was less than 15 years.[xxiv] The same report claims that Gleevec® was covered by "a total of 73 patents,"[xxv] when the real number of issued US patents on Gleevec® was *five*, with another one to four *possibly* covering some of the ways of making it, but only if those methods were (optionally) used. At least in our case, I-MAK appears to have reached its inflated figures by including 44 *abandoned* patent applications that never issued as patents, as well as a variety of patents that don't cover our drug.

Examples like this show why, in our view, it is imperative that your agencies treat sources and data that have rightly been questioned with a high degree of skepticism, and work to ensure that your efforts and conclusions instead proceed on an accurate, reliable, and relevant evidence-base.

IV. Conclusion

We hope that our comments and examples provide you with a better understanding of how we use patents of many different types to drive and enable our pursuit of breakthrough treatments that improve and extend lives. I thank you again for the opportunity to speak today, and look forward to your questions and future dialogue.

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[i] US Food & Drug Administration, FDA approval brings first gene therapy to the United States, August 30, 2017.
[ii] US Food & Drug Administration, FDA approves innovative gene therapy to treat pediatric patients with spinal muscular atrophy, a rare disease and leading genetic cause of infant mortality, May 24, 2019,
[iii] US Food & Drug Administration, FDA approves add-on therapy to lower cholesterol among certain high-risk adults, Dec. 22, 2021.
[iv] US Food & Drug Administration, FDA approves new treatment for certain digestive tract cancer, Jan. 26, 2018.
[v] US Food & Drug Administration, FDA approves Pluvicto for metastatic castration-resistant prostate cancer, March 23, 2022.
[vi] https://www.nature.com/articles/d41573-022-00001-9
[vii] *See* 2021 EU Industrial R&D Investment Scoreboard.
[viii] DiMasi JA, Grabowski HG, Hansen RW. Innovation in the pharmaceutical industry: New estimates of R&D costs. J Health Econ. 2016;47:20-33.
[ix] Federal Register, Vol. 87, No. 214, November 7, 2022, 67020.

[x] Executive Order on Promoting Competition in the American Economy, Sec. 5(p)(vi), July 9, 2021 (emphasis added).
[xi] Patent Act of 1790. Note that the period term for processes was "arts."
[xii] Patent Act of 1793.
[xiii] *See* New York Times, *Apple-Samsung Patent Battle Shifts to Trial*, July 29, 2012 ("Because a smartphone combines many communications and computing technologies, as many as 250,000 patents may touch the device.")
[xiv] Popular Science, Building a Better Golf Ball, Nov. 24, 2008.
[xv] Food. Drug & Cosmetic Act, Section 505(b)(1)(A)(viii).
[xvi] *See, e.g., Diamond v. Chakrabarty*, 447 U.S. 303, 315 (1980) ("The subject matter provisions of the patent law have been cast in broad terms to fulfill the constitutional and statutory goal of promoting 'the Progress of Science and the useful Arts' with all that means for the social and economic benefits envisioned by Jefferson.")
[xvii] *See* USPTO, Milestones in US Patenting
[xviii] Patent Term Extensions (PTEs) and Patent Term Adjustments (PTAs) may help to bridge the frequent disconnect between a patent's normal term and the time it takes to achieve FDA approval and have patents issued, but these are not always sufficient on their own, and these too have now fallen under attack.
[xix] *See* 35 U.S. § 156(c).
[xx] See Grabowski, et. al., Continuing trends in U.S. brand-name and generic drug competition, August 2021.
[xxi]IQVIA, Lifetime Trends in Biopharmaceutical Innovation, Jan. 2017.
[xxii] *See, e.g.* Mossoff, A., *Unreliable Data Have Infected the Policy Debates Over Drug Patents*, January 2021; George Mason University Center for Intellectual Property x Innovation Policy, *UC Hastings' Evergreen Drug Patent Search Database: A Look Behind the Statistics Reveals Problems with this Approach to Identifying and Quantifying So-Called "Evergreening"* March 4, 2021; Lietzan, Erika and Acri née Lybecker, Kristina M.L., *Solutions Still Searching for a Problem: A Call for Relevant Data to Support 'Evergreening' Allegations* (September 26, 2022). Fordham Intellectual Property, Media & Entertainment Law Journal, Vol. 33, University of Missouri School of Law Legal Studies Research Paper Forthcoming, Available at SSRN: https://ssrn.com/abstract=4230310; Letter from Senator Thom Tillis to FDA and PTO, January 31, 2022.
[xxiii] *Id.*
[xxiv] Gleevec was originally approved in May 2001, and the first generics launched in February 2016. *See* 21-335 Gleevec Approval (fda.gov) and Sun Pharma launches Imatinib Mesylate in USA.
[xxv] I-MAK, *America's Overspend,* October 25, 2017 at 7.