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NOVARTIS

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Novartis Comments in Response to USPTO's "Patent Eligibility Jurisprudence Study Request for Information" (86 Fed. Reg. 36257–36260 (July 9, 2021))

As one of the companies that testified on "The State of Patent Eligibility in America" before the Senate Committee on the Judiciary's Intellectual Property Subcommittee in 2019,[1] Novartis is pleased to contribute the following comments to the USPTO's ("Office's") study on the same subject, and to share our updated perspectives on this important issue of innovation policy.

I. Introduction and General Comments

Novartis is a global healthcare company whose purpose is to reimagine medicine to improve and extend people's lives. Our products, which include innovative medicines, cell and gene therapies, radiopharmaceuticals, and, through our Sandoz division, high-quality generics and biosimilars, reach almost 800 million patients around the world annually, treating diseases that span the field of medicine from oncology, cardiology, immunology, and neuroscience, to rare genetic disorders, infectious diseases, and many more. As a research-driven organization with a deep commitment to patients, we are especially proud of our record of developing and delivering treatments that push the boundaries of science and medicine and transform patient care. In the last 6 years alone, our innovative treatments have earned *twenty* FDA breakthrough therapy designations, and we have secured over 100 major new approvals for our medicines, including 24 that comprise new molecular entities (NMEs). These include treatments at the cutting-edge of modern medicine, such as the world's first chimeric antigen receptor T-cell (CAR-T) therapy (Kymriah®), the world's first gene replacement therapy for spinal muscular atrophy (Zolgensma®), and the first FDA-approved Peptide Receptor Radionuclide Therapy (Lutathera®). We also have one of the industry's most competitive pipelines, with over 160 projects in clinical development, ninety percent of which are anticipated to be first-in-class or first in a specific medical indication.

[1] *See* Testimony of Corey Salsberg, Vice President and Global Head Intellectual Property Affairs for Novartis, June 11, 2019, https://www.judiciary.senate.gov/imo/media/doc/Salsberg%20Testimony.pdf; https://www.judiciary.senate.gov/imo/media/doc/Salsberg%20Responses%20to%20Questions%20for%20the%20Record.pdf.

While science and our patient focus drive achievements like these, the patent system creates the practical conditions that make them possible. Every year, we invest over USD 9 billion in innovative research and development (R&D), making us one of the world's top R&D investors in any field or industry. This level of sustained investment is necessary to navigate the complexities, uncertainties, and risks inherent in the work that we do. In a field where less than 12% of medicines succeed even once clinical trials begin, the ability to patent promising inventions and discoveries—each of which reflects a solution to a problem that must be solved, or an obstacle that must be overcome along the 10–15-year road to one approval—is essential to enabling our work and purpose. In an average year, we file some 500 patent applications in the United States, and have had over 2,600 US patents granted since 2010—figures which reflect the expansive range of inventive contributions that we make to science and medicine in the course of our work, and which underscore what it takes to support an innovative R&D program of the scope and scale needed to tackle some of society's most pressing healthcare challenges.

With patents playing such a central role in what we do, and R&D timelines that require investment and development decisions to be made years, and sometimes decades, in advance of commercialization, clarity and long-term predictability are attributes that we consider essential to any functioning patent system. This is particularly true for patent eligibility standards like Section 101—the gateway to the US patent system—because the rules and boundaries that it sets directly impact our decisions as to where, within a vast field of important unmet medical needs and scientific possibilities, we can sustainably direct our R&D investments. That is why, from the early stages of *Mayo* over a decade ago, to the Senate IP Subcommittee hearings in 2019, we have been an active voice on this issue, providing the Office, the Courts, and Congress with our real-world perspectives on how an unclear doctrine, and the shrinking scope of patent eligibility that it has produced, have impacted our business, and have begun to undermine the confidence we need to invest in risky fields of innovative R&D that will not fully mature for many years to come.

As we testified in 2019, many of those fields—precision medicine, cell & gene therapies, certain types of biologics, and digital health—appear to lie directly in the expansion path of a body of case law that, at that time, had already foreclosed the possibility of patents for the entire field of medical diagnostics, cloned organisms, certain modified proteins, biomarkers, and DNA primers, to name but a few. Since that time, the state of patent eligibility has only gotten worse. The Federal Circuit has continued to expand the scope of what constitutes an ineligible "law of nature," "natural phenomenon," and "abstract idea," finding even garage door openers[2] and drive shaft manufacturing methods[3] ineligible, among many others, in a series of often inconsistent decisions that have further blurred the lines between what is eligible and what is not. Even decisions aimed at restoring some clarity to the law, by reformulating

[2] *Chamberlain Group Inc. v Techtronic Industr. Co.,* 935 F.3d 1341 (Fed. Cir. 2019).

[3] *Am. Axle & Mfg., Inc. v. Neapco Holdings ("Am. Axle II")*, 966 F.3d 1347, 1348 (Fed. Cir. 2020).

the *Mayo* test, recharacterizing how it should be applied, or reaching different outcomes than previous decisions on similar claims, have largely had the opposite effect, often exacerbated by dissenting views that render any precedential value illusory. As Judge Newman aptly summarized in one of the Circuit's most recent Section 101 decisions, "[t]he court's rulings on patent eligibility have become so diverse and unpredictable as to have a serious effect on the innovation incentive in all fields of technology."[4] That observation matches experience, particularly in fields like precision medicine, where the difference between eligible and ineligible subject matter now apparently *sometimes* (though not always) comes down not to the actual substance of the claimed invention, but to whether a court will ultimately construe it as a "diagnostic," a "method of treatment," or a "method of preparation."[5]

The potential consequences of this state-of-affairs were already troubling in 2019, but are especially so in these extraordinary times. The ongoing pandemic illustrates just how critical diagnostics, innovative gene-based technologies (e.g. mRNA vaccines), and software-based tools have become for global health and economic stability, in addition to their longer-term promise of curing some of humanity's most devastating diseases, and solving many of the world's healthcare challenges, through applications like precision medicine, cell and gene therapy, nuclear medicine, and gene editing. As a pioneer in many of these fields—and as a partner in an increasingly interdependent global innovation ecosystem, where important technologies from outside contribute to our work—we need clear and predictable patent eligibility standards that encourage the high levels of investment needed to take these fields to their next level, and that will continue to hold up through future waves of technological change. The United States must keep pace in this regard if it is to maintain its distinction as the venue-of-choice for the technological revolutions that will define our future.

Below, we are pleased to provide more specific comments and examples in response to the questions posed, which we hope will assist the Office in further understanding and documenting how the current state of eligibility law is impacting innovators in our field.

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[4] *Am. Axle II,* 966 F.3d at 1357 (Newman, J., dissenting in denial of rehearing en banc); *see also Am. Axle & Mfg., Inc. v. Neapco Holdings ("Am. Axle III"),* 977 F.3d 1379, 1382 (Fed. Cir. 2020) (Moore, J., concurring in denial of stay of mandate) (The Court is "at a loss as to how to uniformly apply §101," and is "slowly creating a panel-dependent body of law."); *Interval Licensing LLC v. AOL, Inc.,* 896 F.3d 1335, 1348 (Fed. Cir. 2018) (Plager, J., concurring-in-part, dissenting-in-part) (Section 101 jurisprudence is an "incoherent body of doctrine" that "renders it near impossible to know with any certainty whether [an] invention is or is not patent eligible."); *Athena v. Mayo*, 915 F.3d 743 (Fed Cir., 2019) (Newman, J., dissenting) ("This court's decisions on the patent-ineligibility of diagnostic methods are not consistent, and my colleagues today enlarge the inconsistencies....")

[5] *Illumina v. Ariosa,* 952 F.3d 1367 (Fed. Cir. 2020).

II. Comments in Response to Selected Questions

The current state of patent eligibility law has negatively impacted our business, the broader innovation ecosystem, and the United States' status as an innovation leader in a variety of ways. Given substantial overlap in the Study questions, we address them collectively here, organized by subject.

A. The current state of patent eligibility jurisprudence has negatively impacted our business in a variety of ways and, if left uncorrected, stands to undermine investment in important technological fields that will shape the future of medicine [Questions 1, 2, 3, 9].

1. Denial of patents and loss of claim scope

As the *Mayo* framework has become increasingly unclear through the case law, we have been denied patent claims through Section 101 rejections on a range of technologies of potential benefit to patients that plainly fit the statutory categories of eligible subject matter, and that should have granted under any sensible approach to eligibility. As described in our 2019 testimony, these have included:

1) patent claims to a new digital microscope for use in ophthalmic surgery that included a physical "primary lens" coupled with "an image sensor," that were rejected under Section 101 as an "abstract idea;"[6]

2) patent claims to a "system comprising a laser device" "applied to" a human "tissue region" in surgery, coupled with a "control computer" to calculate tissue gas levels, which were also rejected as an "abstract idea;"[7] and

3) patent claims to a novel "pharmaceutical composition" to treat osteoarthritis, made up of a modified protein that does not exist in nature, which was found to be an ineligible "product of nature," despite the fact that the sequence was different from that of any natural protein, and that the desired medical effect was present only in our modified product.[8]

As an additional recent example, we have also received Section 101 rejections of claims to diagnostic "method[s] for predicting therapeutic responsiveness" of a patient to a novel medicine (a particular "α7-nAChR agonist treatment" identified in the claims), for the stated practical medical purpose of "treatment of a cognitive impairment, psychotic and/or neurodegenerative disorder."[9] These claims were rejected again for the same reasons when amended to cover "method[s] of selecting an individual suffering from" these same medical conditions "for treatment with" the same

[6] US Patent Application No. 15/118070, Non-Final Office Action, dated August 9, 2018.

[7] U.S. Patent Application No.14/420501, Final Office Action, dated December 18, 2019.

[8] U.S. Patent Application No.14/859126, Final Office Action, dated December 8, 2017.

[9] U.S. Patent Application No.15/788942, Final Office Action, dated September 29, 2021.

specific α7-nAChR agonist.[10] While these claims include *steps* that identify and employ certain biomarkers, they are clearly directed to a specific *practical application* of those biomarkers—to identify patients in the real world that are likely to medically benefit from treatment of their diseases with a specific new medicine—not to the mere existence of those biomarkers in the body, or to any "law of nature" or "abstract idea." Yet, like the previous examples, under the current *Mayo* framework, these claims were deemed to be ineligible for patenting.

In some of these cases, we received final rejections and were not able to have a patent granted.[11] In others, we were forced to amend the claims in ways that relinquished significant and appropriate claim scope, not because that scope existed in the prior art or covered subject matter that we did not invent, but simply as a result of vague eligibility laws that have been taken well beyond their original intent.

Losing patents and claim scope can have significant impact on innovation. While we rarely make investment decisions solely on the basis of a single patent, the accumulated loss of patents in a field or project over time significantly undermines our ability to continue to devote substantial resources to that field or project. At a minimum, such losses—particularly if they involve a patent that proves important for the protection of a commercial form of an invention—represent one more risk in a field where the scientific, technological, regulatory and market odds are already stacked significantly against us.

2. Impact on precision medicine and methods of treatment

The *Mayo* framework's lack of clarity, and the ever-growing body of inconsistent cases, has also created enduring unpredictability for innovators, particularly in important areas like precision (or "personalized") medicine. Precision medicine, which both improves patient outcomes and helps to ensure that medicines are being used in a cost-effective manner, relies upon the use of innovative diagnostic methods to identify patients with specific biomarkers (e.g., a particular gene mutation) in order to select the treatment or parameters for treatment best suited to that patient and their particular version or expression of disease. As has been well documented, and lamented, patent eligibility law has already effectively led to "a *per se* rule that diagnostic kits and techniques are ineligible."[12] Certainly, this has and will continue to severely undermine incentives for standalone diagnostics manufacturers to invest in and develop innovative diagnostics useful for this approach to medicine, which negatively impacts pharmaceutical innovators like us that sometimes rely on third party partners to develop

[10] *Id.*

[11] *See, e.g., Ex parte Schumacher et. al.* (U.S. Patent Application No. 14/420501, Appeal No. 2018-003406), April 2, 2019 (S.101 rejections for claims to a "system comprising a laser device" and a "control computer" for measuring gas levels in tissue in surgery upheld on appeal); *see also* Final Office Action, dated December 18, 2019.

[12] See *Athena Diagnostics, Inc. v. Mayo Collaborative Servs.,* 927 F.3d 1333, 1352, 1354 (Fed. Cir. 2019) (Moore, J., dissenting) ("Since *Mayo*, we have held every single diagnostic claim in every case before us ineligible," turning it into "a per se rule that diagnostic kits and techniques are ineligible.")

"companion" diagnostics for our particular therapies. It also undermines our own efforts in this area, since our in-house work developing companion diagnostics often results in inventions that have much broader use. That is a serious issue of innovation policy which should concern all, particularly given how important the broader role of diagnostics has become in fields like public health, as the COVID-19 pandemic has demonstrated.

But a different kind of issue—one of legal clarity and predictability, as well as innovation policy—surrounds the patenting of "methods of *treatment*" in the context of precision medicine, and possibly beyond. Given that the Supreme Court in *Mayo* itself made a clear distinction between the ineligible diagnostic claims in that case, and claims to methods of treatment, which it said are eligible subject matter,[13] it was long assumed that such methods were safely outside the reach of Section 101 scrutiny. In *Vanda v. Westward*, however, the Federal Circuit unsettled that assumption when a divided panel could not unanimously agree that claims expressly directed to "a method for treating a patient" were patent-eligible.[14] In that case, then-Chief Judge Prost dissented, seeing no meaningful difference between the method-of-treatment claims and the claims found ineligible in *Mayo.*

This uncertainty and unpredictability—within a broader eligibility framework that now-Chief Judge Moore has already aptly called a "panel-dependent body of law"[15]—severely complicates patent counseling and efforts to provide reliable legal advice to our business as to whether particular inventions in this area will be found patent-eligible. And it is not merely a theoretical concern. As we testified in 2019, we have in several cases been unable to secure patent claims specifically directed to "methods of treatment" in the precision medicine context. As one example, we sought claims directed to a "method of selectively treating a subject having breast cancer, a tumor of the head and neck, kidney cancer, or pancreatic cancer" that involved steps of first checking to ensure that the patient actually had the specific genetic mutation that the novel drug targeted before proceeding with treatment.[16] These claims were rejected under Section 101, because, according to the examiner, the fact that *some* patients would be found to lack the relevant mutation and thus not be treated with the drug, means that this "method of treatment" is no more than a "law of nature." Rejections like these make little sense, logically or from a policy perspective. If a method-of-treatment is a patent-eligible invention—as the Supreme Court has said it is, and the United States government agrees is "entirely correct"[17]—it is difficult to understand

[13] *Mayo v.Prometheus*, 132 S. Ct. 1289, 1302 (2012) (Unlike the diagnostic claims at issue, patents on a "new way of using an existing drug" are "particular applications" of natural laws that are patent-eligible.)

[14] *Vanda* 887 F.3d 1117.

[15] *Am. Axle III*, 977 F.3d at 1382 (Moore, J., concurring).

[16] U.S. Patent Application No. 14/387653, Final Office Action, dated May 19, 2017.

[17] Brief of the United States as Amicus Curiae in *Hikma Pharmaceuticals USA Inc. v. Vanda Pharmaceuticals Inc.*, Case No. 18-817, Dec. 6, 2019 ("[A]s evidenced by the dissenting opinion

how it ceases to be eligible simply because that treatment is targeted only to those most likely to benefit from it. For public policy reasons—both because this approach to medicine improves patient outcomes and reduces costs—this is precisely the type of invention that should be encouraged, yet the patent laws are having the opposite effect.

For the same reasons of logic and policy, eligible claims in this area of medicine should not be limited to those that begin with the magic words "method of treatment." Properly considering a "claimed invention as a whole," as the Supreme Court has instructed is the correct approach,[18] any method that reflects a practical and specific use of biomarkers to identify patients likely to benefit from a human-made medicine should be patent-eligible. Yet, countless patents of this type have been rejected under rigid application of the *Mayo* test, including ours directed to "method[s] for predicting therapeutic responsiveness" described earlier in these comments, which specifically related to "treatment of a cognitive impairment, psychotic and/or neurodegenerative disorder" with a particular "α7-nAChR agonist treatment." [19]

While the Federal Circuit seems to be trying to back away from such rigid distinctions, its latest cases in this area do not restore or provide the needed certainty. In *Illumina*, for example, the Court found claims to what are essentially diagnostic methods, but worded as "methods for preparing" useful DNA fragments, eligible, even after finding extremely similar claims ineligible in previous decisions.[20] But it was another split decision with a dissent. Coupled with earlier cases that have gone the other way, and our own recent experience losing even claims directed to "methods of treatment," the Court's holding—that "this a not a diagnostic case. And it is not a method of treatment case, it is a method of preparation case"—is no comfort.[21]

3. Impact on nascent and emerging technologies shaping the future of medicine

The unpredictability of today's eligibility law also threatens to undermine badly needed investment in the nascent technologies that are defining the future of medicine. These emerging fields—which, again, include cell and gene therapy, nuclear medicine, mRNA vaccines and therapeutics, gene editing, and digital medicine, among others—

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below, it is arguably unclear how the longstanding and entirely correct rule that method-of-treatment claims are patent-eligible can be reconciled with mechanical application of *Mayo*'s two-step framework.")

[18] *Diamond v. Diehr*, 450 U.S. 175 (1981).

[19] U.S. Patent Application No.15/788942, Final Office Action, dated September 29, 2021.

[20] *Illumina v. Ariosa,* 952 F.3d 1367 (Fed. Cir. 2020).

[21] The Office's own efforts to add clarity in this area, including the "*Vanda* memorandum," and its 2019 Revised Eligibility Guidance, have been helpful, as we relayed in previous comments. *See, e.g.* Novartis Comments on 2019 Revised Patent Subject Matter Eligibility Guidance, March 7, 2019 https://www.uspto.gov/sites/default/files/documents/eligibility2019comments_e_novartis_2019mar07.pdf; Novartis Comments on "Well-Understood, Routine, Conventional" Test, August 13, 2018 https://www.uspto.gov/sites/default/files/documents/eligiblity2018comments_e_novartis_13aug2018.pdf. This guidance, however, is of course non-binding, provides little certainty over what the courts may find, and has not prevented outcomes like the ones described in the examples above.

are particularly susceptible to uncertainty in the law, because the science is novel and complex, and there are a vast number of new R&D directions to explore. The possibilities for these technologies are almost limitless, yet early successes of certain therapies for certain diseases do not guarantee reproducibility for others. In other words, these are the fields where both promise and risk tend to be highest, where significant failures are therefore expected, and where the large investments necessary to support success need constitutional incentives like patents the most.

Regrettably, the current eligibility framework calls into question whether the patent system is fit to support these emerging fields. As discussed, under current law, the possibility of patent protection has already been denied to a range of gene and protein-based technologies, the entire field of diagnostics, cloned organisms, other "nature-based" technologies, and computer-implemented inventions, which does not bode well for new fields that are based on applying biological principles and processes to replace, manipulate and modify genes; mimic antibodies and other proteins; manipulate viruses, cell biology and cellular structures; harness and redirect the body's immune system; or those that rely on software and digital tools to realize their potential.

As a pioneer in many of these fields, we are particularly concerned about where Section 101 jurisprudence seems to be heading. While these cutting-edge technologies have fortunately not yet been foreclosed from patent-eligibility, the undeniable trend in the case law has been a dramatic expansion of what constitutes a "law of nature" and a "natural phenomenon," coupled with a steady raising of the bar as to how much modification or application is "enough" to distinguish an eligible invention from the natural elements on which it (and, really, all technology) is based. This is an inevitable consequence of a legal standard that, with a "well understood, routine or conventional" test as its arbiter, is preordained to become harder to satisfy with each advance of the state-of-the-art. Having already lost claims to medically useful inventions created by modifying natural products, we are deeply concerned that, if not corrected, the case law will continue to advance in this direction, and the dogma of what constitutes "natural laws" and "products of nature" will continue to swallow critical inventive components of these nascent fields, if not the entire technologies themselves.

The consequences of further uncertainty, and even partial "ineligibility creep" into these areas, would be grave. As the FDA said when it approved our chimeric antigen receptor T-cell (CAR-T) therapy Kymriah® in 2017, the milestone marked only the beginning of "a new frontier in medical innovation" that "hold[s] out the potential to transform medicine and create an inflection point in our ability to treat and even cure many intractable illnesses."[22] Similar observations were made with the approval of our gene therapy Zolgensma®, with FDA calling it "another milestone in the transformational power of gene and cell therapies" that "provides hope for the

[22] US Food & Drug Administration, *FDA approval brings first gene therapy to the United States,* August 30, 2017, https://www.fda.gov/news-events/press-announcements/fda-approval-brings-first-gene-therapy-united-states.

future."[23] Since that time, we and several other companies have indeed developed CAR-T for other forms of cancer, and the technologies used in Zolgensma® are being tested as potential treatments for genetic forms of ALS (a.k.a. Lou Gehrig's disease) and Rett syndrome, and even as a potential vector for a novel COVID-19 vaccine.[24] Many other technologies with similar roots in "nature," including gene editing, radioligand therapy—which uses modified peptides, antibodies and other ligands to precisely target cancer cells with radioisotopes derived from elements like lutetium—and of course, mRNA-based medicine, the impact of which has been on full display during the pandemic, are also only in their very early stages, and promise a future full of incredible possibilities.

At the same time, AI and other cutting-edge software-driven tools are helping us reinvent the way we work, conduct our R&D, and deliver our treatments to patients. Already, we have used these technologies to help make drug discovery and R&D more efficient, to bring "virtual" clinical trials into the home, and to work with healthcare providers and patients to better diagnose, manage, and live with their diseases. We are, again, only in the very early stages of this "digital medicine" revolution, where in addition to applications like these, digital tools will help us realize the full potential of the vast amounts of scientific, health and medical data that hold the keys to solving many of the world's healthcare challenges.

With such possibilities on the horizon, now is the time to strengthen the system of incentives that has made most of the early successes possible. But eligibility law in America instead seems to be narrowing the gateway to the patent system, casting doubt on whether it will still be there to enable and support the next generation of treatments and potential cures.

4. Impact on patent enforcement and litigation

The current state of eligibility law has also negatively impacted patent enforcement and litigation, creating additional burdens on patent owners and the courts, and in some cases, exacerbating the state of the law itself. Section 101-based invalidity defenses have now become common in patent disputes, including pharmaceutical cases. The very fact that litigants have been emboldened—in some cases successfully—to raise Section 101 challenges to patents claiming subject matter like garage door openers,[25] cardiac monitoring devices,[26] drive shaft manufacturing

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[23] 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, https://www.fda.gov/news-events/press-announcements/fda-approves-innovative-gene-therapy-treat-pediatric-patients-spinal-muscular-atrophy-rare-disease.

[24] *AAVCOVID Vaccine Program from Mass. Eye and Ear and Mass General Enters Manufacturing Agreement with Gene Therapy Leader AveXis, a Novartis Company,* May 28, 2020 https://masseyeandear.org/news/press-releases/2020/05/aavcovid-vaccine-program-enters-manufacturing-agreement-with-avexis.

[25] *Chamberlain,* 935 F.3d 1341.

[26] *CardioNet, LLC v. InfoBionic, Inc.*, 955 F.3d 1358 (Fed. Cir. 2020)

methods,[27] and methods of treatment[28] underscores just how far the law has strayed from its original and sensible purpose of preventing patents on universal constants and elements of the natural world.[29] Whenever policy doctrine crosses the line into litigation strategy, lawmakers should be concerned, as they rightly were a decade ago when the America Invents Act eliminated the "best mode" as a litigation defense for similar reasons.[30]

The addition of Section 101 defenses to a growing number of cases across an expanding array of technological fields raises litigation costs and burdens, and consumes court time and resources, particularly where such defenses entirely lack merit, which is still the case more often than not. Of course, this trend is also how the law itself has expanded over time, in our field converting *Mayo* from a case about "the particular claims before us"[31] into "a *per se* rule that diagnostic kits and techniques are ineligible,"[32] and *Myriad* from a case that "merely h[e]ld that genes and the information they encode are not patent eligible" into a formula for taking out DNA primers and vectors, biomarkers, modified proteins, cloned organisms, and more.

B. The US has not kept pace with other competitive jurisdictions in ensuring that its eligibility laws promote the newest technologies, which threatens its future innovation leadership and weakens its reliability as a place to invest in the next generation of therapies [Questions 4, 5, 6, 10, 11, 12]

As the scope of eligibility in the United States has narrowed and become increasingly unclear for biotechnology, diagnostics, and other important fields, other countries have maintained or strengthened their eligibility and overall patent regimes to ensure robust incentives in these areas. Genes, DNA segments, and other biological materials and substances, in particular, are patent-eligible in Europe, Japan, China, and Korea, among other places, at least so long as these inventions are isolated from nature. In Europe, for example, the Biotechnology Directive makes explicit that "Biological material which is isolated from its natural environment or produced by means of a

[27] *Am. Axle II*, 966 F.3d 1347.

[28] *Vanda*, 887 F.3d 1117.

[29] As the Supreme Court has explained, the "laws of nature," "natural phenomena" and "abstract idea" exceptions were created to prevent patents on subject matter like "a new mineral discovered in the earth," "a new plant found in the wild," "$E=mc^2$,"and "the law of gravity." *Diamond v. Chakrabarty*, 447 U.S. 303, 309 (1980).

[30] *See, e.g.,* Congressional Record Volume 157, Number 91, Pence Extension, E1174-E1175 (June 22, 2011) ("Best mode . . . has become a vehicle for lawsuit abuse" and "imposes extraordinary and unnecessary costs on inventors."); *see also* Congressional Research Service, *Patent Reform in the 112th Congress: Innovation Issues* (June 30, 2011), quoting Advisory Commission on Patent Reform, *A Report to the Secretary of Commerce* (August 1992), 101 ("The disturbing rise in the number of best mode challenges over the past 20 years may serve as an indicator that the best mode defense is being used primarily as a procedural tactic. A party currently can assert failure to satisfy the best mode requirement without any significant burden.").

[31] *Mayo*, 132 S. Ct. at 1294.

[32] *Athena,* 927 F.3d at 1354 (Moore, J., dissenting).

technical process may be the subject of an invention *even if it previously occurred in nature*," a rule which includes "an element isolated from the human body or otherwise produced by means of a technical process, *including the sequence or partial sequence of a gene . . . even if the structure of that element is identical to that of a natural element*."[33] Courts in Europe have likewise upheld isolated DNA claims, even where the claims do not directly specify that the genes were "isolated" or "obtained by a technical process,"[34] as well as diagnostic claims that were virtually identical to those rejected by United States courts.[35] Notably, patent-eligibility for these technologies in these other competitive biopharmaceutical innovation economies has not led to the negative impacts on research, scientific progress, innovation, or access that those who oppose Section 101 reforms portend. To the contrary, each of these markets has only grown in their competitiveness with the United States as a contributor to scientific research and as a producer of innovation.

Like many patent owners, in fields where eligibility has been narrowed here in recent years, we now regularly face different outcomes on the same patent claims in these other jurisdictions versus the United States. For instance, in the recent example described above of the claims to a diagnostic "method for predicting therapeutic responsiveness" of a patient to our novel α7-nAChR agonist treatment, the exact claims rejected in the United States have so far been granted in other countries, including Australia, Japan, New Zealand, and Taiwan.

While the inability to secure particular patents for particular inventions is never alone a basis to determine where to conduct our R&D, where to invest in building innovation infrastructure and manufacturing, or where to prioritize launches of our latest medicines, the certainty and strength of any country's patent laws are critically important factors for each of these decisions, especially for some of the nascent technologies discussed throughout these comments. Biotechnology, and more recently, cell and gene therapy, mRNA, and gene editing, for example, largely emerged in the United States in the first place because of a unique innovation ecosystem supported by a strong IP system and smart IP policies like those at the heart of the Bayh-Dole Act, that encourage both private investment in R&D, and private sector collaboration with research universities and research institutions. This ecosystem is one of the primary reasons why we invested USD 2.9 billion—a third of our global R&D spend—in the United States last year alone, and why our global R&D headquarters (the Novartis Institutes for BioMedical Research (NIBR)), a major part of our global drug development operations, and some of our most cutting-edge sites, like our first manufacturing facility for Kymriah®, and our manufacturing sites for

[33] Biotechnology Directive Article 3(1), 5(2) (emphasis added).

[34] *Receptor Tyrosine Kinase*, X ZR 141/13 (Bundesgerichtshof 2016).

[35] *Illumina Inc v Premaitha Health Plc,* EWHC 2930 [2017] at 189 (upholding claims to methods of detecting fetal DNA in maternal blood—the same rejected in *Ariosa Diagnostics, Inc. v. Sequenom, Inc.*, 788 F.3d 1371 (Fed. Cir. 2015)—because "the claims are not directed to information about the natural world, but rather to a practical process, namely a 'detection method' which uses information about the natural world.")

Zolgensma,® are all located in the United States. Collectively, our operations at these and other US sites employ around 16,000 people—over a third of which are physicians, scientists, and other R&D professionals—and in 2020 contributed over USD 25 billion to the US economy.

This continued level of activity and investment only make sense in an environment where we can be confident that the local ecosystem will continue to support the invention and development of the latest technologies and approaches to treatment—whether they come from our own laboratories, as many do, or through development partnerships with academia and other innovative companies—and that it will continue to offer world-leading protections of our investments in both R&D and state-of-the-art manufacturing. As uncertainty grows around the Section 101 gateway, and as more fields of technology fall to the expanding range of exceptions, the case for maintaining such a heavy US focus may weaken, particularly as other countries maintain or move to strengthen their IP regimes in the fields that are defining the future.[36]

C. The current state of patent eligibility law does not serve the public interest, because it undermines incentives to continue to innovate in fields that improve health outcomes and help lower costs [Question 13].

We approach the patent system across our business and across the world as a means to enable and advance meaningful innovation for the benefit of patients and broader society.[37] We are also committed to ensuring that our treatments and therapies reach as many people as possible. As a company with one of the industry's most innovative pipelines, as well as one of the world's leading positions in generics and biosimilars, we know from experience that overly restrictive patent-eligibility criteria, like those now in place under the *Mayo* framework, do nothing to improve access to medicine or to lower healthcare costs. In fact, given the types of innovations that current Section 101 jurisprudence has already impaired, and those that its expanding trajectory threatens, failure to address the current eligibility crisis is likely to have just the opposite effect.

Diagnostics, for example, enable early detection and diagnosis of a growing number of diseases, including cancer, and genetic and infectious diseases (as the current pandemic aptly illustrates), allowing for earlier interventions and treatments,

[36] China, for example, has steadily strengthened its patent laws in the biopharmaceutical sector over the last few years (albeit with many remaining shortcomings), and just weeks ago released an "Outline of Building a Powerful Intellectual Property Nation (2021-2035)" that specifically includes plans to strengthen and "speed up legislation on intellectual property rights in new industries such as big data, artificial intelligence and genetic technology." *See* http://www.news.cn/politics/zywj/2021-09/22/c_1127889618.htm.

[37] For more information about our patient-centric approach to IP, including our role as a founding member and signatory of the IP Principles for Advancing Cures and Therapies (IP PACT), see https://www.novartis.com/esg/access/patents-and-licensing; http://www.interpat.org/ip-principles-for-advancing-cures-and-therapies/.

which in turn can avoid the need for hospitalization, and reduce the chances of premature death. As discussed above, diagnostics also play a central role in precision medicine, helping to ensure that the right patient gets the right treatment for the right disease, and that the wrong medicine does not go to waste. These diverse uses of diagnostics all help to lower healthcare costs, and, from a health economics perspective, help people return to and lead more productive lives that contribute more to society and the overall economy.

In emerging technological fields, one-time treatments like our SMA gene therapy Zolgensma®, and CAR-Ts like Kymriah®, have the potential to cure once fatal diseases early and efficiently, without the need for a lifetime of more conventional and ultimately more expensive therapies and supportive hospital care. Meanwhile, cutting-edge digital and AI-driven tools hold the promise to make drug discovery and clinical trials more efficient, in addition to further increasing diagnostic accuracy and making medicine more accessible.

In all of these fields, the availability of patents for inventions meeting the patentability criteria not only creates incentives to invest in their creation and development, but increases competition by encouraging multiple innovators to enter these fields with different innovative approaches. Of course, as patents expire, they also pave the way for lower cost generic versions, that further lower costs and increase access.

While it is a cliché, the maxim that "the most expensive drug is the one that is never invented" is particularly apt in the context of the eligibility discussion. Far from raising pricing or access concerns, the broad scope of patent-eligible subject matter contemplated by the Constitution and by Congress under statute since this country's founding[38] is an important part of a thoughtful solution.

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Novartis appreciates the opportunity to continue sharing our perspectives on this important issue. We hope that the above comments prove useful, and look forward to continuing dialogue on these and other matters of patent policy.

Respectfully submitted,

/s/ Corey Salsberg

Corey Salsberg
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[38] *See Chakrabarty*, 447 at 315 ("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.")