Questions for the Record for Dr. Sean George, Chief Executive Officer of Invitae,
From Senator Mazie K. Hirono
July 2, 2019

1. Last year, Judge Alan Lourie and Judge Pauline Newman of the Federal Circuit issued a concurring opinion to the court's denial of en banc rehearing in Berkheimer v. HP Inc., in which they stated that "the law needs clarification by higher authority, perhaps by Congress, to work its way out of what so many in the innovation field consider are § 101 problems."

Do you agree with Judges Lourie and Newman? Does § 101 require a Congressional fix or should we let the courts continue to work things out?

Invitae believes that the state of the patent law and also the country as a whole would benefit from allowing the courts to continue to develop the case law on patent subject matter eligibility. Invitae does not share the view expressed by Judges Lourie and Newman. Invitae does not believe that the state of the law regarding assessment of Section 101 patent eligibility is particularly troubled. Many aspects of patent law (claim construction, analysis of infringement by equivalents, written description requirements, etc.), require the courts to apply established patent law principles on a case-by-case basis. That is the current state of the law for Section 101 patent subject matter eligibility. Invitae believes that most objections to the current state of the law rest in a desire for substantive changes in the law (i.e., the proponents want a different outcome with respect to certain categories of patent applications) as opposed to any significant confusion over the application of the recent Supreme Court precedent.

While Invitae maintains that the current statute and its interpretation should not be changed, if Congress were to consider modifications to the law, Invitae believes that the proper course would be to codify the existing Supreme Court precedent which excludes from patent eligibility abstract ideas, natural phenomena, and natural laws. To the extent that there is genuine concern about how these principles apply in a specific case, Congress could enact procedural steps for evaluating Section 101 patent eligibility in the course of patent prosecution before the USPTO or early in the adjudication of patent validity in a US District Court, which could streamline these determinations and reduce the costs and uncertainty of litigation for all concerned. It is worth noting that even apparent "critics" of the state of Section 101 law such as Judges Lourie and Newman do not appear to disagree with the proposition that these categories should be excluded from patentable subject matter. By contrast, the proposed draft legislation would retain none of these exclusions because it would abrogate this line of case law and not replace it with a codification of the existing exclusions from patentable subject matter of patent claims directed to abstract ideas, natural phenomena, and/or natural laws and recreate the need for the courts to adjudicate on these matters

a. The Federal Circuit rejected a "technological arts test" in its en banc Bilski opinion. It explained that "the terms 'technological arts' and 'technology' are both ambiguous and ever-changing." The draft legislation includes the requirement that an invention be in a "field of technology."

b. Do you consider this a clear, understood term? If so, what does it mean for an invention to be in a "field of technology"?

Invitae does not consider the term "field of technology" to be a clear, understood term that would provide a predictable boundary for the division between that which would and would not be eligible for patenting. It would be expected to lead to a substantial amount of litigation and serve as a vehicle for addressing some of the goals raised in the line of cases that the authors of the draft legislative propose to abrogate by statute. In general, innovation in the United States has been well-served by the application of general patent principles across all areas of technology. The principle legislative exception to this rule, the "Semiconductor Chip Protection Act of 1984," which was enacted to address an asserted gap in the application of intellectual property law to a specific technology, has been universally ignored. Invitae counsels against repeating this error. The "field of technology" test would be a poor substitute for the existing case law establishing criteria for patentable subject matter.

2. The European Union, China, and many other countries include some sort of "technology" requirement in their patent eligibility statutes. What can we learn from their experiences?

Invitae does not believe that these requirements in other jurisdictions are good models for addressing the policy challenges of the current Supreme Court case law on patentable subject matter. First, quite apart from issues of patent eligible subject matter, both the Chinese and European patent systems are generally more restrictive than the USPTO in terms of the scope of patent coverage that can be obtained from a given patent application. This different context can make it difficult to extract from the use of a technology requirement a lesson relevant to the US patent system. Second, the issue under consideration in the draft legislation is whether and how to address the policy questions associated with the Supreme Court's holdings that patent claims directed to natural laws, natural phenomena, and abstract ideas should not be patentable. It is quite possible to present such claims in association with some conventional technology (e.g. exploitation of an abstract idea using a computer) and doing so does not, under current law, render such claims patentable. Invitae believes that there are sound policy reasons for preserving these categories of excluded subject matter and a "technology requirement" is inadequate to differentiate between claims that should and should not be excluded from patenting.

As an example, consider gene patents. Assume that new patents on human genetic sequences determined and published would not be patentable to the extent that the human genome has already been published. However, a short sequence constituting a portion of a human gene having a freshly observed mutation could very well be patented under the legislative proposal because it would be new. A "technology requirement" might distinguish between the sequence as it exists in the cell and a short fragment of DNA used as a laboratory tool, such as a primer or a probe. A patent directed to primers or probes having such a sequence constituting a fragment of a gene with a specific mutation might satisfy the "technology requirement," but it would amount to a patent blocking the use of conventional laboratory techniques that have been in use for decades to detect and study such a mutation. If there is a policy goal to exclude gene patents from the revised patent law, patents that preempt the conventional exploration or

manipulation of newly discovered gene variants should also be excluded. Concepts such as a technology requirement as the prerequisite for patent eligibility are inadequate to the task.

a. Is a claim that describes a method for hedging against the financial risk of price fluctuations—like the one at issue in the Bilski case—in a "field of technology"? What if the claim requires performing the method on a computer?

This question helps illustrate how amorphous a term such as "field of technology" could be in the context of defining a prerequisite for patentability. A credible case for either outcome can be made for each of these questions and, consequently, one can expect that one's answer will be determined by one's policy preferences for the outcome. Thus, Invitae believes that it is not fruitful to frame the issue in terms of a new amorphous term such as "field of technology" instead of addressing as directly as possible the policy questions concerning the kinds of subject matter that is suitable for patent.

b. What changes to the draft, if any, do you recommend to make the "field of technology" requirement more clear?

Invitae does not see particular value in the "field of technology" requirement in the proposed language for Section 100 in the draft legislative proposal. Invitae would forego this approach and instead articulate explicitly and clearly what are excluded categories of patentable subject matter directed to abstract ideas, natural phenomena, and natural laws.

3. Sen. Tillis and Sen. Coons have made clear that genes as they exist in the human body would not be patent eligible under their proposal.

Are there other things that Congress should make clear are not patent eligible? There are already statutes that prevent patents on tax strategies and human organisms. Are there other categories that should be excluded?

Invitae believes that the current ineligibility of abstract ideas, natural laws, and natural phenomena is actually sound policy and if statutory changes are going to be made, then these exceptions should be reflected in any statute addressing patent-eligible subject matter. The below example of the category of patent claims directed to correlations such as those between genetic sequence status and disease risk have been found to be patent ineligible under current case law because they are abstract (simply determining genetic status and associating it with a diagnostic outcome) as well as natural laws (the observed correlation between biomarker and outcome).

Human genetic sequences and individual variations in those sequences, along with the messenger RNA they express and the proteins they encode (which we collectively refer to as "biomarkers") constitute information that defines us as human beings and as individuals. That information, along with its meaning for diagnosing and treating a specific individual, should not be patentable. Examples of the meanings of this information are the observed correlations between having certain variants of standard genes and increased risk of certain diseases or conditions such as hereditary risk of breast cancer. We are in the early stages of understanding the significance of many of these naturally occurring associations between biomarkers and

health, and the patent system should not stand in the way of researchers and individuals' ability to learn, understand and use information inherent to their own bodies.

The promise of personalized medicine requires that a doctor and her patient have access to all of the biomarker information to diagnose and treat the patient based on a thorough understanding of the molecular biology underlying the patient's disease. Over the last decade, we have made tremendous progress toward that goal. The reintroduction of patent rules that allow private monopolies covering individual biomarkers will inhibit that progress and inevitably degrade the quality of care while increasing the cost of health care.

Invitae appreciates that Sens. Tillis and Coons have expressed their intention that genes as they exist in the human body not be patentable. However, this is not the sole issue related to patentable subject matter concerning human genes or their interpretation for human medical purposes. First, it is a fallacy to draw a distinction between genes as they exist in the human body and genes isolated, because scientifically, this distinction does not exist. In his expert witness testimony to AMP v. Myriad, our Chief Medical Officer, Dr. Robert Nussbaum, explained that when isolating a DNA segment of interest, neither extracting total cellular DNA away from non-DNA substances nor separating a particular DNA segment away from the rest of DNA produces a substance that is "structurally distinct from any substance found in the human body." Instead, an isolated DNA segment essentially embodies genetic information, whether that segment is enclosed within a chromosome in the cell or is isolated as a gene segment and is not significantly different in any fundamental way from the same segment of DNA in the cellular DNA from which it was derived. Further, any differences between isolated DNA and DNA in chromatin are actually "epigenetic" changes (note, they are not "genetic"), which means they are superimposed upon genes and not part of a gene itself. Additionally, while technology can be used to break the covalent phosphodiester bonds between the nucleotides in a DNA strand in a laboratory setting, this same process occurs naturally and continuously in certain cells within the body and hence, does not result in novel DNA. The Supreme Court decision in AMP v. Myriad affirmed this as well rendering all naturally occurring genetic sequences, including those isolated from the human body, as not being eligible for patent protection.

Additionally, it is important to understand that genes are fundamentally expressions of information via a code. This is why we speak of our cellular machinery "reading" a gene in order to produce a copy of a protein encoded by the gene. As individuals, we differ from each other genetically, even regarding our propensity to develop a specific disease, because there is variation in the specific sequences of our genes. As a famous example, certain variations in a person's sequence of their BRCA1 gene are statistically associated with a vastly greater lifetime risk of contracting breast cancer. Myriad Genetics (and some of its licensors) had patented not just the BRCA1 gene sequence, but also the association of many different specific observations of naturally occurring mutations and their correlation with greatly elevated disease risk. Some of the Myriad patent claims simply covered the determination of a patient's status with respect to certain high-risk mutations in the BRCA1 or BRCA2 genes. The presence or absence of any mutations in your germline genetic sequences is an inherent fact about your body and it can be highly relevant to your health. Myriad had monopolized through patenting the ability for patients

to learn their own health information in the context of their own genetic data (unless they purchased a $4,000 test from Myriad.)

The case law that the draft legislative proposal would abrogate did not just outlaw patenting human genes as they exist in the body, but also blocked the privatization of knowledge about the clinical significance of a patient's specific genetic data (e.g. the presence or absence of known mutations). This sort of a patent, which rests upon the observation of a correlation between certain genetic characteristics and certain disease risks or patient outcomes, would once again be patentable. While the Human Genome Project may be complete, the determination of the meaning of the sequence of the human genome and the significance for one's health of any observed variations is very much still in its early days. Thus, in order to preserve the ability for individuals to be counseled by clinical practitioners on the significance of their specific genetic data, any new statute codifying the scope of patentable subject matter should exclude not just genes but all patents directed to the information they represent. Thus patent claims directed to correlations between genetic sequence data, and other observable biomarkers, and any clinical status, diagnosis or treatment recommendation should also be ineligible for patenting.

As mentioned above, the genetic discoveries directed to correlations between genetic mutations and patient health can reliably be expected to continue as more and more patients have their genetic material sequenced and then analyzed as part of large datasets looking for such correlations. We do not need the patent incentive to drive the collection of this knowledge. Rather the proliferation of new patents on knowledge about the significance of genetic sequence data would result in thickets of patents held by many different parties such that no one would have the freedom to operate necessary to counsel patients about their own genetic information and its relevance to their health. Additionally, this would have implications to achieving the goals of federally funded research programs including the All of Us Study, the Million Veterans Program, NCI Match trial, and the ClinVar Project.

4. I have heard complaints that courts do not consistently enforce Section 112 with respect to claims for inventions in the high tech space.

a. Are these valid complaints?

Inconsistency in the application of the law is an unfortunate consequence of a highly decentralized court system. Appellate courts certainly bring some corrective action to these problems.

b. Do the proposed changes to Section 112 adequately address those complaints and limit the scope of claims to what was actually invented?

No, the proposed changes to Section 112 do not adequately address the consequences of a highly decentralized court system. It is not clear that the proposed changes to Section 112 in the draft legislative proposal would improve consistency. Rather it would result in a change in the law that would require litigation for the proper application of the new law and standards to become consistent.

c. Are you concerned that the proposed changes will make it too easy for competitors to design around patent claims that use functional language?

Invitae is concerned that the proposed changes will enable patenting of abstract ideas, natural phenomena, and/or natural laws, potentially creating patent thickets that prohibit innovation in the field of diagnostics and restrict patient access to their genetic information.

5. There is an intense debate going on right now about what to do about the high cost of prescription drugs. One concern is that pharmaceutical companies are gaming the patent system by extending their patent terms through additional patents on minor changes to their drugs. My understanding is that the doctrine of obviousness-type double patenting is designed to prevent this very thing.

The Federal Circuit has explained that obviousness-type double patenting "is grounded in the text of the Patent Act" and specifically cited Section 101 for support.

Would the proposed changes to Section 101 and the additional provision abrogating cases establishing judicial exceptions to Section 101 do away with the doctrine of obviousness-type double patenting? If so, should the doctrine of obvious-type double patenting be codified?

If a new statute restating Section 101 and abrogating some of the case law interpreting it were passed, there is a genuine risk that the existing law on obviousness-type double patenting could be changed if the statute remains silent on this point. While Invitae does not see the need for the proposed changes to the statute, Invitae does agree that it likely would be worth codifying this doctrine if Congress also opts to codify the requirements for patent-eligible subject matter.

6. In its *Oil States* decision, the Supreme Court explicitly avoided answering the question of whether a patent is property for purposes of the Due Process Clause or the Takings Clause.

What are the Due Process and Takings implications of changing Section 101 and applying it retroactively to already-issued patents?

Invitae does not currently have a position on whether a patent is property for purposes of the Due Process Clause or the Takings Clause.

If the draft legislative proposal were enacted and it applied retroactively, it is likely that many patents and patent applications that had previously been held invalid could be revived. This scenario raises the question of whether a later accused infringer of such a revived patent could assert a property interest in its prior freedom to operate that would be lost as a consequence of the change in the law. Such a scenario is distinct from the initial grant of a patent in that the accused infringer may have relied upon the prior, full adjudication of the unpatentability of the revived patent claims.

If Congress sought to codify the existing patent subject matter jurisprudence, then there would be less of an argument for a taking.