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Sequenom: breadth of '540 patent creates vulnerability to validity challenge despite strength of claims – attorneys

- '540 describes a "pioneering process;" entitled to more breadth
- Aria may be found not to be infringing due to subtle differences in method
- Techniques for amplification and detection alone not patentable
- Injunction to hinge on competition, pricing, and regulatory strategies

Sequenom's (NASDAQ: SQNM) claims for US Patent 6,258,540 ('540) for non-invasive prenatal diagnosis appear strong, though the patent's breadth presents some concern for maintaining validity, patent attorneys said.

Isis Innovation Limited is the named patent holder, with Sequenom the exclusive licensee.

Sequenom is currently engaged in litigation with private diagnostic developers Aria Diagnostics and Natera. Sequenom offers MaterniT21, a laboratory developed test for the non-invasive diagnosis of Trisomy 21 (Down Syndrome), and is currently in pursuit of in-vitro diagnostic clearance. Aria is developing its own non-invasive T21 test, and Natera offers non-invasive prenatal paternity testing.

Verinata Health announced on 23 February that it has commenced an action against Sequenom, seeking a declaratory judgment that its cell-free DNA sequencing analysis techniques used in its prenatal diagnostics do not infringe the '540 patent.

Aria filed suit against Sequenom in December claiming the latter is overly aggressive in its enforcement of the '540 patent, with Aria requesting a declaratory judgment that its test does not infringe the '540 patent. Sequenom then filed against Aria in January with the US District Court for the Southern District of California, alleging Aria infringes the '540 patent, and the infringement has been "intentional, deliberate, and willful."

Natera similarly filed suit against Sequenom in January, claiming it does not infringe the '540 patent and that the patent is invalid. Sequenom subsequently filed suit claiming infringement, and that Natera "knowingly encouraged others" to infringe as it licensed its paternity test to DNA Diagnostics Center, a testing lab.

Aria is comfortable with the IP landscape, said CEO Ken Song. Before launching the company, its founders were aware of the IP landscape and investors would not have jumped in if there were perceived barriers to IP, he said. This was further validated by Aria's recent financing round of USD 53m, raised in only a few weeks time, he said.

A Sequenom spokesperson said the '540 patent is the first patent related to noninvasive prenatal diagnosis using circulating cell free nucleic acids in maternal plasma as the analyte and is platform independent.

Natera did not return a request for comment.

'540 strengths

The patent claims appear strong, said Robert Gould, partner, Duane Morris, who noted the patent "sailed through" the Patent & Trademark Office (PTO) quickly, implying the PTO believed the patent holder had discovered something surprising. The patent claims are very broad, however, because it described a "pioneering process," such that the patent holder is entitled to more breadth than normal, he indicated.

Technically infringement for T21 testing only occurs 10% of the time, as 90% of T21 cases are due to an extra chromosome from the mother - and the patent describes detection of paternally inherited nucleic acid, explained Gerry Norton, partner at Fox Rothschild. However this does not aid Aria nor Natera as "you either are or you aren't" infringing, and there is no such thing as "de minimis infringement," he said.

Anyone dealing with DNA detection from serum is likely to fall under the '540 patent as well as anyone using amplification methods, said one patent attorney.

As the claims are quite broad, the best case for Aria would be if Sequenom's patent is upheld but in such a way that Aria is found to not be infringing, said Brenda Jarrell, practice group leader at Choate Hall & Stewart. She said she expects Aria may argue that it does not infringe because its technology does not directly amplify paternally-inherited DNA in a mother's serum sample, but rather amplifies an artificially generated copy of one strand of that DNA. However, Sequenom can be expected to argue such a distinction makes no difference, with the ultimate product of Aria's process an amplified DNA with the sequence of the paternally-inherited DNA.

'540 validity challenges

Sequenom has a strong defense for proving infringement since the claims of the patent are very broad, but it can also open the door for an invalidity argument by Aria and Natera, said Kirby Drake, a senior associate at Klemchuk Kubasta.

Given the broad claims, George Xixis, partner at Nutter McClennen & Fish, estimated a greater than 50% chance of Aria and Natera prevailing with an invalidity defense, rather than a non-infringement defense. The breadth of the patent in part stems from the fact that the claims are not directed to any specific genetic testing, Xixis noted.

The "lynchpin" of the patent is the claim that DNA is detectable in maternal serum, said Gould. The truth of this statement as of the priority date will be a point of challenge for validity, he said. Aria and Natera can argue the methods described in the patent are not "earth shattering," as they simply describe performing PCR amplification and detection on plasma, he said.

If it is found it was known fetal DNA existed in serum or plasma prior to the patent priority date, the patent does not appear to provide for patentable techniques of amplification or detection other than those well known in the art, said Gregory Hillyer, member, Feldman Gale P.A. The patent could then be subject to challenge for reasons of obviousness, he added.

Indeed, as it was known that fetal cells could be found in the maternal bloodstream from the prior art, though not specifically fetal DNA, as the '540 patent claims, the question for the trial will be whether the two are sufficiently uncoupled for the latter to be patentable, as well as the "paternally inherited nucleic acid" claim limitation, said Norton.

Given how sensitive nucleic acids can be to degradation, it may have been somewhat surprising that sufficient amounts of nucleic acid from the fetus could be detected, suggesting unexpectedly superior results and providing a reasonable chance this patent could hold up in litigation, said Scott Chambers, partner at Patton Boggs.

Aria and Natera will need prior art dated before 1997 that was not referenced in the patent to demonstrate invalidity, said Gould. There may be a problem if Dennis Lo, the inventor of the '540 patent, presented or disclosed this finding in public before submission to the patent office, which could be the case as the research was likely done years in advance, he noted. No such presentations are noted in the prior art references, he added.

Likelihood of permanent injunction?

The burden of demonstrating irreparable harm may not be met even if there is patent infringement, according to Hillyer. While there are several factors to be considered, the most important appears to be whether there is competition between the parties, he said. If Sequenom's product is in direct competition with the other parties, the likelihood of an injunction issuing is much greater, he said.

On 22 February, Sequenom announced it has filed a motion for preliminary injunction against Aria Diagnostics, barring the latter from manufacturing or selling tests for detecting fetal chromosomal aneuploidy, such as Aria's Harmony Prenatal Test, pending resolution of the litigation.

Sequenom has a strong infringement case as both Aria and Natera are working on tests which take serum from a pregnant mother, Gould said, adding the former would be able to get a permanent injunction in the case of clear infringement. However, Sequenom would not be able to get one if the testing is vital to human health, he said. If an injunction is not possible for that reason, then Aria may have to pay a royalty fee, he said. Gould noted a significantly lower cost of testing would be the strongest defense against a permanent injunction; however should the competitor be forced to pay a royalty fee, additional costs would inevitably be added to testing.

Regarding the implications of a permanent injunction against Aria, Sequenom commented it believes it has a diagnostic test and the capacity to better serve the entire market for the foreseeable future and certainly in 2012 and 2013.

As Sequenom alleges Aria's infringement to be "intentional, deliberate, and willful," this is "the phrase that pays" in litigation, Norton said, adding it may just end up all about the money in the end rather than an injunction, as the market is so large.

In their present posture, Aria and Natera may however fall under a safe harbor clause of Hatch-Waxman, which stipulates companies gathering information to submit to the FDA are not infringing IP, noted Chambers. Actionable infringement would only begin at the time at which they try to market a product, he explained, thus the regulatory pathways these two companies pursue will be important.

Sequenom has a market cap of USD 460m.

by Christine Livoti and Anusha Kambhampaty in New York