TRENDS-in-MEDICINE

BULLETIN:

SANOFI AND REGENERON PHARMACEUTICALS FIGHT TO SAVE PRALUENT

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by Lynne Peterson

In a very unusual step, a Sanofi lawyer and other officials held a teleconference with reporters to discuss the litigation going on with Amgen over Praluent (alirocumab), a PCSK9 inhibitor that it is marketing with Regeneron Pharmaceuticals. Remember, Amgen won an injunction that would have forced Praluent off the market leaving Amgen's Repatha (evolocumab) the only approved PCSK9 inhibitor on the market. Then, recently an appeals court panel stayed the injunction, giving Sanofi time to appeal the lower court ruling. This may be the first teleconference by pharmaceutical company attorneys with reporters over patent litigation, so it was very unusual.

John Conway, vice president, global head of Sanofi's Intellectual Property Department, said, unsurprisingly, that Sanofi is "very pleased with the stay of the injunction…It was the right decision. And, of course, it really means that we are able to keep our very important drug Praluent on the market because in all of this we were very concerned about the injunction taking away access…to patients who need it…The court decision really shows that they took a deliberate measure of our position…It is our long-standing position that the Amgen patents are invalid."

Chan Lee, North American general counsel for Sanofi, cited three specific areas relating to the case:

1. **The "unprecedented nature of the district court ruling."** Lee said, "From my perspective, this [Praluent] is the first innovator biopharmaceutical product that would have been withdrawn solely for patent reasons…I've seen references to human growth hormone [HGH] and pegylated EPO products as products blocked for patent reasons in the past, but they are not good analogies for this case. In my view, those were follow-on biologics before the biosimilar pathway was established. Unlike HGH and EPO, alirocumab is a completely different molecule than evolocumab and has established safety and efficacy through its own rigorous trials."

2. **Why Sanofi "firmly believes" the Amgen patent is not valid.** Lee said, "Certainly, from a pure patent perspective, we believe that the patent in question lacks written description and lacks enablement. From a policy perspective, we believe this patent is overly broad and would stifle innovation."

   He cited the example of statins as a good analogy, "If Merck were able to get a broad genus patent that covered all statins when it first discovered this space, then I think society would have ended with Mevacor [lovastatin] and Zocor [simvastatin] as statins, and we would not have a benefit from the advances and innovation of Lipitor [Pfizer, atorvastatin] and Crestor [AstraZeneca, rosuvastatin]. So, very much like statins, even after the FDA approvals, we continue to learn about PCSK9 inhibitors."

3. **The differences in the two PCSK9 inhibitors and the "continuing emerging science" of these PCSK9 inhibitors even after their FDA approval.** Lee said, "The two molecules [alirocumab and evolocumab] are entirely different. They have different product profiles, different dosing regimens. The two molecules have different approaches on LDL management: Praluent's approach is to manage LDL to goal; Repatha, at a high level, its approach is to manage LDL to a maximum lowering effect."

Lee continued, "I would note that from a patient perspective, the termination of bococizumab, a PCSK9 by Pfizer that was in a Phase III trial…Going back to the statin example, to demonstrate the fact that not all statins are alike, not all PCSK9s are alike…Baycol [Bayer, cerivastatin] was withdrawn due to kidney failure…Thus, the importance of different treatment options for physicians and patients in the PCSK9 space."

In response to a clarifying question, he added, "They have very different product profiles…They bind to different sites and have vastly different sequences…Amgen recently announced their outcomes trial [results], and we look forward to the outcomes trial data from our own study…As we analyze these data, I think we will have a better understanding of the product profiles of these two PCSK9 inhibitors."

What is the next step for Sanofi and Regeneron? Stephanie Donahue, senior director of patent litigation for Sanofi, said Sanofi is very positive about the litigation, and laid out this 6-12 month timeline:

- February 17, 2017 – deadline for opening appeal brief. Sanofi has an expedited appeal, which will "compress" the timeline for filings to the end of March 2017.
- The court will set a date for an oral hearing, which Sanofi expects to be in spring or early summer.
- After the oral hearing, the court will consider and render an opinion. Donahue said, "We expect that decision could come from June to December, but it is up to the court's discretion."

What are the options for court action? Donahue said they are:

- The appeals court reverses the lower court, which means **Sanofi and Regeneron win**. Conway said, "That moots the injunction, and there are no damages either because the patent is invalidated…And we would expect Amgen to appeal to the full court en banc. That is technically available to them." Donahue added, "If it is a complete reversal, then the Amgen patents are invalidated."
- The appeals court affirms the lower court, which means **Sanofi and Regeneron lose**. Donahue said, "The court could make a decision on damages, and as part of that, the court could award Amgen a royalty for past and future sales." Conway added, "If Amgen wins, the appeals court would then decide on the appropriateness of an injunction – whether it should come back into play, or maybe it is not the right remedy, and they could go on to a damages phase." She said there are two options in this case, and Sanofi will do one or both:
  - Sanofi requests a review by the full appeals court en banc.
  - Sanofi appeals to the Supreme Court.
- The appeals court vacates the lower court ruling and remands it for a **new trial in Delaware**. Conway said, "If we did that, and Sanofi loses [the retrial], then Amgen could ask for another injunction. If the remanded trial judge felt that an injunction is not the appropriate remedy, then they could have a proceeding to determine damages against Sanofi and Regeneron and, as part of that, could award Amgen ongoing royalty."

Does the possibility of an injunction still stand? Conway said, "We think it is remote, but it still stands."

Do Sanofi or Regeneron have any pending patent claims against Amgen? Not in the PCSK9 space.

How much of a factor is the unprecedented nature of removing an innovator product? Conway said, "I would remind you that even at the trial court level, the judge found the public interest factor squarely in Sanofi and Regeneron's favor…We think that factor is very important in the analysis of any injunction decision, and we think it will heavily weigh in our favor through these proceedings…because there are differences between our molecule and Amgen's, and removing a lifesaving option is really very hurtful to the public."

Asked if there were every any royalties paid by one statin-maker to another, Lee said, "I can't definitely say there weren't any patent infringement issues…If Merck, as the first innovator, had gotten a broad genus patent that covered all statin molecules, that would have stifled – and I think Amgen patent would stifle – innovation…Amgen did not invent evolocumab…or other PCSK9 inhibitors in the clinic now."

Asked about the uniqueness of this litigation, Conway said, "When you take a look at historical patent battles, there are a couple of cases you can look at in terms of attempts by other companies to control a broad class…[Johnson & Johnson/]Centocor [had a] patent on Remicade [infliximab, a TNF inhibitor for rheumatoid arthritis] and tried to sue Abbott over Humira [adalimumab]…Centocor did not request an injunction in that case…Then, there was a case between AbbVie and J&J over J&J's Stelara [ustekinumab], an anti-IL12. In that situation, AbbVie lost the battle, and there were no damages or injunction…And there was litigation between Merck and Gilead Sciences over HCV [hepatitis C virus] drugs. So, there have been other battles prior to this where companies try to get a commanding position in a new field…[but they have not been successful]."

Asked if this litigation is a damper on drug development, Conway said, "Internally no, but that is a real danger of this type of litigation, where a company like Amgen overly claims a field…If this injunction holds, it would really squelch innovation by other companies."

Asked if Sanofi is negotiating with Amgen, Conway said No.