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FibroGen v Akebia: Arnold LJ back in the Patents Court

Brian Cordery (Bristows) · Wednesday, April 29th, 2020

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On 20 April 2020, Arnold LJ (sitting as a High Court Judge) gave judgment in the case between FibroGen Inc and Astellas Pharma Inc (together the "**Claimants**"), and Akebia Therapeutics Inc and Otsuka Pharmaceutical Company Limited (together the "**Defendants**") which concerned six patents owned by FibroGen and exclusively licensed to Astellas (the "**Patents**"). In a comprehensive 640 paragraph judgment, Arnold LJ considered a plethora of different patent issues from obviousness to insufficiency to infringement by equivalence and threatened indirect infringement of medical use claims. Arnold LJ ultimately found all the Patents to be invalid (although some of claims would have been infringed, if they had been valid). The judgment also provides some helpful guidance on the instruction of experts and the need for primers in patent cases.

Background

The Patents (which were split into two families, the "**Family A Patents**" and "**Family B Patents**") all concerned the use of inhibitors of an enzyme called hypoxia inducible factor-prolyl hydroxylase ("**HIF-PH**") for treating various types of anaemia and related conditions. In September 2019, Astellas had obtained an MA in Japan for the first oral HIF-PH inhibitor, roxadustat, and intended to launch the product in the UK (and elsewhere). The case began when Akebia and Otsuka sought to 'clear the way' for their HIF-PH inhibitor, vadadustat (which is currently in Phase III clinical trials). Astellas subsequently brought a cross-claim for threatened infringement.

Instructing experts & the preparation of primers

Before turning to the more technical aspects of the judgment, it is worth noting that Arnold LJ has provided some general guidance with regards to the instruction of experts for the purposes of UK proceedings and the necessity for a primer.

Referring back to his judgment in *MedImmune v Novartis* in which he introduced the concept of 'sequential unmasking', Arnold LJ made the following comments:

• The lawyers instructing an expert should ensure that the expert discloses all their own previous relevant publications and, where appropriate, explains them in their

report. Similarly, an expert should exhibit their CV to their report.
• While it is desirable to instruct experts in sequence (i.e. first asking about the CGK, then showing them the prior art, before finally revealing the patent) to try and minimise hindsight where possible, there is no rule or principle that requires experts to be instructed in this way. Indeed, there are often real practical problems in doing so (e.g. if new prior art is introduced after the expert has read the patent).

Lamenting the absence of a primer in this "**case of considerable complexity**", Arnold LJ considered that the preparation of a technical primer should be regarded as mandatory in cases with a technical difficulty of 4 and 5 unless there are good reasons to the contrary.

Obviousness

As regards the Family A Patents, a number of the claims were alleged to be obvious over a cited prior art publication ("**Epstein**"). The question of obviousness turned on whether the skilled person, starting from Epstein and conducting a routine search for additional HIF-PH inhibitors to treat or prevent anaemia associated with chronic kidney disease, would arrive at a particular compound claimed in the Family A Patents ("**Compound C**"). Arnold LJ ultimately concluded that the evidence did not establish that Compound C would be found by this route. This obvious attack therefore failed.

As regards Family B, a number of claims were alleged to be obviousness over the international application for the Family A Patents ("**WO 997**"). Here, it was common ground that the question of obviousness turned on whether it would be obvious to use the compounds disclosed in WO 997 for the purposes claimed in the Family B Patents. Arnold LJ ultimately considered that it was.

Insufficiency

Akebia and Otsuka raised two distinct insufficiency attacks against the Patents – excessive claim breadth and ambiguity (or uncertainty, as it is now to be known).

With regards to excessive claim breadth, the Defendants' allegation against the Family A Patents was based on the fact that the relevant claims encompassed a "*staggeringly large*" number of compounds by reference to a general formula (Formula I). After an extensive review of the relevant case law, the Arnold LJ considered:

(i) whether the disclosure of the patent made it plausible that the invention will work across the scope of the claim; and
(ii) whether the evidence established that, in fact, the invention cannot be performed across the scope of the claims without undue burden.

As to question (i), it was accepted that the invention was made plausible with respect to the compounds exemplified in the specification. However, Arnold LJ did not consider the claims plausible across their whole scope (i.e. for all compounds described by Formula I). The Claimants' argument that the inclusion of a functional limitation in a claim limited the claim to only those compounds that actually work was rejected by Arnold LJ. In the present case, the patent was implicitly promising that substantially *all* the compounds which satisfy the structural definitions in the claims

would have the claimed therapeutic efficacy. As this was not supported by the specification, the claims in issue were therefore insufficient for lack of plausibility (the claims were also obvious on *AgrEvo* grounds for the same reason).

As to question (ii), Arnold LJ concluded that the invention could not be performed across the scope of the claims in issue without undue burden because a "*substantial research project*" was required to identify any more than a tiny fraction of the claimed compounds which met the criteria for efficacy, aside from those specifically identified in the specification.

With regards to the allegation of uncertainty, Arnold LJ applied the recent Court of Appeal judgment in *Anan Kasei v Neo*. In that case, the Court of Appeal held that, if there is a large territory where the claim is uncertain, an allegation of insufficiency cannot be overcome simply because there is something within the claim that is clear (e.g. Compound C). The claims at issue contained the expression "*structural mimetic of 2-oxoglutarate*". After considering evidence, Arnold LJ agreed that the skilled team would not know what this constituted and, in particular, what test to apply to distinguish between a compound which is and a compound which is not a "*structural mimetic of 2-oxoglutarate*". Although Compound C was clearly such a compound, this could not solve the problem (applying Anan). As a result, these claims were held invalid for uncertainty.

As regards the Family B Patents, applying the same approach, Arnold LJ found all but one claim to be insufficient on the basis of excessive claim breadth and found all claims to be insufficient on the basis of uncertainty.

Infringement by equivalence

It was common ground that a claim in the Family A Patents limited to Compound C was not infringed by the Defendants' HIF-PH inhibitor (vadadustat) on a normal interpretation of the claim, as the structures of the two compounds differed. However, it was alleged that vadadustat infringed by virtue of the doctrine of equivalents. Applying the reformed *Improver* questions, Arnold LJ held that there was no infringement. *Vadadustat* had a "quite different" structure to Compound C and it had not been shown that the molecule achieved substantially the same result (treating renal anaemia by inhibiting HIF-PH) in substantially the same way. Furthermore, it was clear that the patentee intended that strict compliance with the normal meaning of "*Compound C*" was an essential requirement of the claim.

Indirect infringement of medical use claims

It was common ground that, if and when the product was authorised, Akebia and Otsuka intended to market vadadustat in the UK. However, Akebia and Otsuka argued that the indications for which an MA would be sought would not infringe the Family B Patents (which were limited by medical use). FibroGen and Astellas nonetheless alleged that there was threatened indirect infringement due to the fact that it would be obvious to a reasonable person that vadadustat would be suitable for the infringing use. In addressing this issue, Arnold LJ considered the current state of the clinical evidence and whether it was foreseeable that clinicians will prescribe vadadustat off-

label for the uses claimed in the Family B Patents. The clinical evidence did not suggest that it was likely that vadadustat would be used off-label in an infringing way and if clinical practices were to change, this would take several years. Arnold LJ therefore found that there was no threat by the Defendants to infringe the Family B Patents.

This judgment represents another tour de force on patent law and practice in the UK from one of its most remarkable Judges. As noted above, the decision is littered with points of interest and, given that it has been rendered by a Lord Justice of Appeal, albeit one sitting at first instance, it will carry significant weight. Patent practitioners in the UK, many of whom will now have tidy gardens and spotless fridges following this extensive period of working from home, would do well to read the judgment but are reminded not to attempt to print it out on their home printers unless they are well stocked with paper and ink cartridges.

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