BL O/003/06

5th January 2006

PATENTS ACT 1977

BETWEEN

Attaca Limited — Claimant

and

Millenium Pharmaceuticals, Inc. — Defendant

PROCEEDINGS

Application under section 72(1) for revocation
of European Patent Number EP 0817792

HEARING OFFICER R. J. Walker

DECISION

Introduction

1 European Patent No. EP 0817792 ("the patent") was filed as an international patent application ("the application") under the Patent Cooperation Treaty on 29th March 1996 and claimed priority from an earlier US Patent Application US 412431, which was filed on 29th March 1995. The application was published on 3rd October 1996 as WO 96/30389 and re-published by the European Patent Office on 14th January 1998. The patent was eventually granted, in the name of Millenium Pharmaceuticals, Inc. ("the defendant"), on 22nd March 2000 with the title "Compositions for the diagnosis, prevention, and treatment of tumor progression".

2 An application under section 72(1)(c) of the Patents Act 1977 ("the Act") for revocation of the patent was filed on 7th July 2004 in the name of Mark Gerard Quigley. The Office raised a number of queries concerning this application for revocation and as a result an amended statement and revised Patents Form 2/77 were filed on 26th July 2004 in the name of Attaca Limited ("the claimant") for revocation of the patent under sections 72(1)(a) and 72(1)(c). The defendant then filed a counter-statement on 19th October 2004, which raised questions about the clarity of the claimant's amended statement. This led the claimant to file a further amended statement on 18th November 2004 seeking revocation under section 72(1)(a) alone on the basis of thirteen documents (AL1 to AL13). This statement was substantially different from both the

original statement and the first amended statement and in a telephone call on 26th November 2004 Mr Mark Quigley for the claimant confirmed that the latest statement was to replace the two earlier statements. The defendant filed a supplementary counter-statement on 14th December 2004 together with supporting documents MPI 53, which gave publication dates for the documents AL1 to AL13. In order to ensure that there was no confusion about the matter to be decided, the Office wrote to both parties on 17th January 2005 to invite comments on the Office's view that the claimant's statement filed on 18th November 2004 superseded the two earlier statements and that the defendant's supplementary counter-statement together with the relief sought in the original counter-statement superseded the remainder of the original counter-statement. The defendant responded by letter, dated 31st January 2005, to state that it had no comments but there was no response from the claimant. The Office wrote to the claimant on 24th February 2005 inviting evidence in support of its statement but once again the claimant did not respond. In view of this the defendant chose not to submit any evidence in reply.

3 In letters dated 14th June 2005 the Office asked both parties whether they would be happy to have a hearing officer consider the application for revocation on the basis of the papers or whether they wanted an oral hearing. The defendant stated that it would be content to have the decision made on the papers and, since there was once again no response forthcoming from the claimant, the matter came to me for a decision on the papers alone.

The patent

4 The patent relates to genes which are differentially expressed in tumor cells and also to compositions for the diagnosis, prevention and treatment of tumor progression. The examples identify a specific gene, referred to as the 030 gene, which is stated to be expressed at a many-fold higher level in non-metastatic tumor cells relative to its expression in metastatic tumor cells. The gene appears in mice (fomy030) and has the cDNA sequence of SEQ ID NO:2 set out in the patent. A human homolog (fohy030) has the cDNA sequence of SEQ ID NO:6 with an alternative spliced form shown in SEQ ID NO:8. The patent also discloses SEQ ID NOs: 7 and 9 which are the deduced polypeptide sequences corresponding to nucleotide sequences SEQ ID NOs: 6 and 8 respectively. The patent states that references to the 030 gene refers to both the murine and human homologs of the gene.

5 The expression pattern of the 030 gene product indicates that it acts to inhibit tumor progression. For example, a reduction in the level of 030 gene expression correlates with an increase in a cell's metastatic potential, i.e. it can induce or predispose a cell to progress to a metastatic state. The patent states that the genes and/or gene products can be used to identify cells exhibiting or predisposed to a disorder involving a tumor progression phenotype, thereby diagnosing individuals having, or at high risk for developing, such disorders. It is also stated that detection of the differential expression of identified genes can be used to devise treatments and preventative intervention

6 The claims of the patent relate to and are based on an isolated nucleic acid comprising:

(a) the nucleotide sequence SEQ ID NO:2 as depicted in Figure 3 of the patent, or

(b) the nucleotide sequence contained within a clone as deposited with the NRRL: pFOMY030 (NRRL accession No. B-21416) that hybridizes to the DNA sequences as shown in SEQ ID NO: 2, 6 or 8 as depicted in Figures 3, 5 and 6 of the patent.

For reasons which will become apparent later in this decision, there is no need to reproduce the claims of the patent here.

Grounds for revocation

7 Revocation is now sought on the grounds that the invention lacks novelty and does not involve an inventive step.

Novelty

8 The claimant contends that documents AL1 – AL13, which were in the public domain prior to the publication of the patent on 14th January 1998, effectively destroy the novelty of the claimed invention since the information they contain, when understood by one skilled in the art, is sufficient to allow anticipation, prediction and reproduction of the claimed invention in all of its aspects and in all of its embodiments. The documents in question are:

AL 1:NCBI Accession AF047714; Mus musculus melastatin mRNA, complete CDs.

AL 2:NCBI Accession AF071787; Homo sapiens melastatin 1 (MLSN1) mRNA, complete CDs.

AL 3:NCBI Accession AA054361; zf54d05.r1 Soares retina N2b4HR Homo sapiens cDNA clone IMAGE:380745 5' similar to contains Alu repetitive element; mRNA sequence.

AL 4:NCBI Accession AA015986; ze32a07.s1 Soares retina N2b4HR Homo sapiens cDNA clone IMAGE:360660 3', mRNA sequence.

AL 5:NCBI Accession AA057431; zf57d10.s1 Soares retina N2b4HR Homo sapiens cDNA clone IMAGE:381043 3' similar to WP:F54D1.5 CE05940; mRNA sequence.

AL 6:NCBI Accession AA047763; zf50g05.s1 Soares retina N2b4HR Homo sapiens cDNA clone IMAGE:380408 3' similar to WP:ZK512.3 CE00409 CED-11 mRNA sequence.

AL 7:(Identical to AL 3).

AL 8:(Identical to AL 5).

AL 9:(Identical to AL 4).

AL 10: NCBI Accession AA054280; zf54d05.s1 Soares retina N2b4HR Homo sapiens cDNA clone IMAGE:380745 3', mRNA sequence.

AL 11: NCBI Accession AA047763; zf50g05.s1 Soares retina N2b4HR Homo sapiens cDNA clone IMAGE:380408 3' similar to WP:ZK512.3 CE00409 CED-11: ;, mRNA sequence.

AL 12: NCBI UniGene information relating to GenBank entry AA047763.1 and Results 1 – 10 of a Google (RTM) search for "EST melastatin".

AL 13: List of 49 ESTs from Human Retina, UniGene Cluster Hs.43265 *Homo sapiens* MLSN1.

9 Documents AL1 to AL11 are National Center for Biotechnology Information (NCBI) Accession documents. NCBI is a division of the National Library of Medicine (NLM) at the National Institutes of Health (NIH) in the United States and creates public databases and disseminates biomedical information. GenBank, the NIH database that is maintained by NCBI, stores all known public DNA sequences and is the database in which the sequences with the above accessions may be found. There is no indication in documents AL1 to AL12 of when they were published. Only document AL13 bears a publication date which is 22nd August 2000.

10 The defendant denies that any of the claims are not new and states in its supplementary counter-statement that the patent was filed on 29th March 1996 and that each claim is entitled to the priority date of 29th March 1995. MPI 53, attached to the defendant's supplementary counter-statement, sets out the publication dates of documents AL1 to AL11 as determined using a revision history facility of the NCBI online database. According to MPI 53:

AL 1 was first seen at NCBI on 16th April 1998;

AL 2 was first seen at NCBI on 22nd June 1998;

AL 3, AL5, AL6, AL7, AL8, AL10 and AL11 were first seen at NCBI on 6th September 1996; and

AL4 and AL9 were first seen at NCBI on 16th July 1996;

The defendant's counter-statement also states that AL12 is a re-statement of the information given in AL11 and is of no earlier date. Thus, in the defendant's view the invention is novel because none of the documents, which are relied on by the claimant, were made available to the public before the priority date of the claimed invention.

Inventive Step

11 The claimant's ground for alleging a lack of inventive step is succinctly stated in its statement in the following terms:

> "There is nothing in the teachings of the invention that suggests a scintilla of inventiveness"

12 The defendant denies that any of the claims are obvious and observes that the claimant's statement is rhetoric and cannot be construed as a reasoned ground.

The law

13 The grounds on which a patent may be revoked are set out in section 72 of the Act. The claimant is seeking revocation under sub-section (1)(a), which reads:

> "*72.-(1) Subject to the following provisions of this Act, the court or the comptroller may on the application of any person by order revoke a patent for an invention on (but only on) any of the following grounds, that is to say -*
>
> *(a) the invention is not a patentable invention;*"

14 What constitutes a patentable invention is defined in section 1 of the Act and for present purposes, in sub-section (1)(a) which requires that the invention is new and in sub-section (1)(b) which requires that the invention involves an inventive step. The criteria for novelty and inventive step are set out in sub-section 2(1) and section 3 of the Act, respectively:

> "*2.-(1) An invention shall be taken to be new if it does not form part of the state of the art*."
>
> "*3. An invention shall be taken to involve an inventive step if it is not obvious to a person skilled in the art, having regard to any matter which forms part of the state of the art by virtue only of section 2(2) above (and disregarding section 2(3) above)*."

Sub-sections 2(2) and 2(3) define the state of the art but here only sub-section 2(2) is relevant for both novelty and inventive step (my emphasis):

> *"(2) The state of the art in the case of an invention shall be taken to comprise all matter (whether a product, a process, information about either, or anything else)* ***which has at any time before the priority date of that invention been made available to the public*** *(whether in the United Kingdom or elsewhere) by written or oral description, by use or in any other way."*

Assessment

<u>Novelty</u>

15 The claimant asserts that the present invention lacks novelty with respect to

AL1 to AL13 because these documents were publicly available before the publication of the patent on 14th January 1998. Whilst it appears that the information in documents AL1, AL2 and AL13 was not published until after 14th January 1998, it seems that AL3 to AL12 (with the possible exception of the Google page which is undated) may have been published prior to this date. However, this is not the correct test for novelty. That the patent was published on 14th January 1998 (and so after the dates when AL3 to AL12 were made available to the public) is of no consequence when assessing the novelty of the invention since section 2 of the Act requires that an invention be judged against the state of the art, which comprises all matter which has at any time **before the priority date** of the invention been made available to the public.

16 According to the information provided by the defendant in MPI 53, the earliest publication date of any of documents AL1 to AL13, that is to say the date at which the sequences were "first seen" at NCBI, is 16th July 1996, nearly sixteen months after the priority date and nearly four months after the filing date of the patent. These publication or "first seen" dates have not been challenged by the claimant and therefore I accept them. In view of this I can only conclude that none of the documents AL1 to AL13 forms part of the state of the art in relation to the claimed invention and so these documents do not destroy the novelty of the invention.

17 Before I leave the matter of novelty I should address what appears to be a further misunderstanding on the part of the claimant. In its amended statement the claimant suggests that to establish whether documents AL1 to AL9 constitute novelty destroying disclosures, it is necessary to examine the history, nature, purpose, function and utility of a consortium known as IMAGE (Integrated Molecular Analysis of Gene Expression). To this end the claimant's amended statement includes a reference to "The Sequence", Kevin Davies, Weidenfield & Nicholson, LONDON 2001 ISBN 0297 64698 2 :

> "At an October 1994 conference in Washington D.C., Michael Morgan, an executive with Britain's Wellcome Trust, hosted a closed meeting of genome leaders to discuss whether to use the EST collection of TIGR (The Institute for Genomic Research).
>
> Collins strongly opposed using TIGR's EST's for such a program and lent his backing to an initiative that had been put forward by the pharmaceutical giant Merck which, like other big pharma companies, had been shut out of the TIGR database.
>
> Alan Wilkinson, Merck's vice president, had conceived the idea of financing a separate program to identify EST's in May 1994. Unlike TIGR's database, all of Merck's sequences (in including EST's of the invention and Patent "792") would be made publicly available without delay and with no strings attached. Merck decided to give Washington University's Bob Waterston and Richard Wilson a grant of $10 million to produce hundreds and thousands of human EST's over the ensuing two years or so. The cDNA clones would be provided by Bento Soares, a Columbia University professor and founding member of a small group of academic researchers who billed themselves as IMAGE (Integrated

> Molecular Analysis of Gene Expression) consortium. Merck's decision was not entirely altruistic, of course: Merck was intent on challenging SmithKline-Beecham's strangle hold on EST rights thanks to its exclusive $125 million deal with Vaseline's company."

The claimant continues by quoting from paragraph 12 of the "*Examination Guidelines for Patent Applications relating to Biotechnological Inventions in the UK Patent Office (November 2003)*:

> "……, an earlier enabling disclosure could destroy the novelty of a later invention even if this earlier disclosure has not actually been "enabled" or reduced to practice'. Actual prior identification of a process or product claimed is not in itself necessary to find a lack of novelty, merely instructions which, if followed would inevitably result in the use of the claimed process or product."

Against this background the claimant concludes that the small, dedicated group of academic researchers of the Integrated Molecular Analysis of Gene Expression consortium and their associated colleagues and, in particular, those appalled by the activities of Haseltine and Venter were fully apprised of innumerable methodologies within molecular and cellular biology and of instructions which, if followed would inevitably lead to the claimed process/product that constitutes the subject matter of the patent. Consequently the patent fails in respect of novelty.

18 If I understand the claimant correctly, it is asserting that the knowledge possessed by the IMAGE consortium researchers in 1994 or thereabouts provides an enabling disclosure of the claimed 030 genes. In supporting this contention the claimant cites the *Examination Guidelines for Patent Applications relating to Biotechnological Inventions in the UK Patent Office*. As is made clear in the introduction to these guidelines, they set out the practice within the UK Patent Office as it relates to patent applications for biotechnological inventions and are meant to supplement guidance given in the Office's Manual of Patent Practice. Thus, like the Manual of Patent Practice, they are guidelines only and are not binding on me. That said, in referring to paragraph 12 from the Guidelines*,* the claimant has not acknowledged the accompanying reference in a footnote to the judgment of Laddie J. in *Evans Medical Ltd's Patent* [1998] RPC 517. In view of the claimant's argument based on the *Examination Guidelines* it is helpful to consider what Laddie J has to say in this judgment on the matter of anticipation by prior disclosure at page 575:

> "It seems to me that the easiest way to analyse *Merrell Dow* is to consider first that part of Lord Hoffmann's speech which deals with anticipation by prior disclosure. The question to be asked is whether the prior art specification "conveyed sufficient information to enable the skilled reader to work the invention" (page 87 line 37). In answering that it must be remembered that
>
> > "Section 2(2) does not purport to confine the state of the art about products to knowledge of their chemical composition. It is the

> *invention* which must be new and which must therefore not be part of the state of the art. It is therefore part of the state of the art if the information which has been disclosed enables the public to know the product under a description sufficient to work the invention" (page 89 line 16).

Lord Hoffmann went on to point out that where the invention is a new product, in most cases knowledge of the product's chemical composition will be necessary to enable the public to work the invention. But that is not always so. Having cited with approval the *EPO BAYER/Diastereomers (Decision T12/81)* [1982] O.J.E.P.O. 296 he said at page 90 line 8:

> "In other words, if the recipe which inevitably produces the substance is part of the state of the art, so is the substance as made by that recipe…" "

and further at page 576:

> "First one must identify what the alleged invention is, that is to say what is covered by the claims in the patent, and then one must decide whether or not that invention, or any part of it, would be made inevitably by following instructions in the prior art."

19 In my opinion the knowledge possessed by those in the IMAGE consortium does not constitute a "recipe" or "instructions" which if followed would lead to a particular product and to the 030 genes in particular. This knowledge is not so specific. Moreover, the claimant has not produced any evidence which establishes that the nucleotide sequences SEQ ID NOs. 2, 6 or 8 would be the inevitable result of applying the molecular and cellular biology techniques commonly used for generating ESTs. Even if it had, it seems to me that a challenge along these lines would be more appropriate in the context of a lack of inventive step rather than a lack of novelty. Thus, I do not accept that the "innumerable methodologies" of the IMAGE consortium researchers provides an enabling disclosure for any aspect of the claimed invention and consequently I find that the patent is not anticipated by these methodologies.

Inventive Step

20 The claimant's ground for alleging the lack of an inventive step is no more than an assertion. The claimant has failed to set out any facts which would allow me to reach a decision on this matter. In particular, the claimant has not established clearly what was the common general knowledge of a person skilled in the relevant field at the priority date of the invention and why it would have been obvious at that time to make the leap from what was known to the subject matter of the invention. I therefore find that there is no basis for the claimant's allegation that the invention lacks an inventive step.

Conclusion

21 I find that the claimant has failed to establish that the claimed invention lacks

novelty. However, I have not come to a view on whether the invention involves an inventive step because the claimant has not provided any reasoned grounds and evidence to support its attack on this ground.

Certificate of contested validity

22 The defendant has requested a certificate of contested validity if I found in its favour. In this decision I have considered the novelty of the claimed invention having regard to the disclosure in certain documents but beyond this I have not considered the validity of the patent. Accordingly I certify that the validity of European Patent No. EP 0817792 was contested on the ground of lack of novelty, having regard to the disclosure in documents AL1 to AL13 identified in this decision, and I have found the patent to be valid.

Costs

23 The defendant has won and is entitled to an award of costs as a contribution to its expenses in defending this application for revocation. I therefore direct the claimant, Attaca Limited, to pay the defendant, Millenium Pharmaceuticals, Inc., the sum of £500 within 7 days of the date of expiry of the appeal period below. Payment will be suspended in the event of an appeal.

Appeal

24 Under the Practice Direction to Part 52 of the Civil Procedure Rules, any appeal must be lodged within 28 days.

R. J. WALKER
Divisional Director acting for the Comptroller