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Datasheet for the decision of 7 February 2013

Case Number: T 1036/09 - 3.3.08

Application Number: 95941352.7

Publication Number: 787207

IPC: C12Q 1/68

Language of the proceedings: EN

Title of invention:
New method for identifying and evauluating biologically active molecules

Patent Proprietor:
ARIAD PHARMACEUTICALS, INC.

Opponent:
SANOFI

Headword:
Active dimeric non-peptidic agents/ARIAD

Relevant legal provisions:
EPC Art. 56
RPBA Art. 12(4)

Keyword:
"Admissibility of new documents (no)"
"Main and sole Request (granted claims) - problem not solved over the whole claimed scope, reformulation of the technical problem; inventive step (no)"

Decisions cited:
G 0001/03, T 0363/00, T 0870/02, T 0946/02, T 0898/05, T 0087/08, T 0018/09

Catchword:
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Case Number: T 1036/09 - 3.3.08

D E C I S I O N
of the Technical Board of Appeal 3.3.08
of 7 February 2013

Appellant: (Patent Proprietor)
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Decision under appeal:
Decision of the Opposition Division of the European Patent Office dated 9 February 2009 revoking European patent No. 787207 pursuant to Article 101(3)(b) EPC.

Composition of the Board:

Chairman: M. Wieser
Members: P. Julià
D. S. Rogers

Summary of Facts and Submissions

I. European patent 0 787 207 was opposed on the grounds of Articles 100(a) and (b) EPC. The opposition division considered that the sole request before it (claims as granted) did not fulfil the requirements of Article 56 EPC and, accordingly, revoked the patent.

II. The patentee (appellant) lodged an appeal against this decision and filed, with the statement setting out its Grounds of Appeal, three new documents D26 to D28. The appellant requested that the decision under appeal be set aside and the patent be maintained as granted.

III. The opponent (respondent) replied to the appellant's Grounds of Appeal and requested that documents D26 to D28 not be admitted into the appeal proceedings and that the appeal be dismissed.

IV. A communication pursuant to Article 15(1) of the Rules of Procedure of the Boards of Appeal (RPBA) was sent by the board as an annex to the summons to oral proceedings. The parties were informed of the preliminary, non-binding opinion of the board on the relevant issues of the case, in particular those concerning Article 56 EPC. The board commented on the relevance of the post-published document D25 (cited as expert opinion) and, in view thereof, concluded that there was no reason to deviate from the decision under appeal which led to the revocation of the patent. According to the board's preliminary opinion, documents D26 to D28 should not be admitted into the appeal proceedings.

V. No further substantive submissions were filed by any of the parties and both parties informed the board of their intention not to attend the oral proceedings.

VI. Oral proceedings took place on 7 February 2013 in the absence of the parties. At the end of the proceedings, the Chairman announced the decision of the board.

VII. Appellant's sole request, the claims as granted, contained 7 claims. Claim 1 read as follows:

"1. A method for producing a non-peptidic agent capable of activating a cellular signal transduction pathway mediated by a polypeptide selected from a growth factor, cytokine and hormone, the method comprising:

(a) identifying a first non-peptide compound capable of selectively binding to an endogenous receptor for said polypeptide;
(b) identifying a second non-peptide compound capable of selectively binding to an endogenous receptor for said polypeptide; and
(c) covalently linking the first and second non-peptide compounds to each other to form a non-peptidic agent which is capable of selectively binding to more than one of the receptor molecules."

Claims 2 to 7 referred to preferred embodiments of the method of claim 1.

VIII. The documents cited in the present decision are:

D1: WO-A1-94/18317 (publication date: 18 August 1994);

D2: D.M. Spencer et al., Science, 12 November 1993, Vol. 262, pages 1019 to 1024;

D23: S-S. Tlan et al., Science, 10 July 1998, Vol. 281, pages 257 to 259;

D24: S.A. Qureshi et al., Proc. Natl. Acad. Sci. USA, 12 October 1999, Vol. 96, No. 21, pages 12156 to 12161;

D25: P.J. Connolly et al., Bioorganic & Medicinal Chemistry Letters, 2000, Vol. 10, pages 1995 to 1999;

D26: WO 2007/080325 (publication date: 19 July 2007);

D27: M.L. Doyle et al., J. Biol. Chem., 14 March 2003, Vol. 278, No. 11, pages 9426 to 9434;

D28: P.A. Clemons, Curr. Opinion in Chem. Biol., 1999, Vol. 3, pages 112 to 115.

IX. The arguments of the appellant, so far as relevant to this decision, are summarized as follows:

Article 56 EPC

The technical problem underlying the patent was the provision of a method for producing a non-peptidic agent capable of activating a cellular signal transduction pathway mediated by a polypeptide. Document D25, disclosing experiments in which erythropoietin- (EPO) binding compounds were covalently linked, did not report any positive result in a

subsequent cell proliferation assay. However, claim 1 was explicitly limited to a method in which an active agent was effectively obtained. Thus, the claim excluded methods producing compounds, such as those of document D25, which were obviously not capable of activating a cellular signal transduction pathway. This way of interpreting a method claim was in accordance with the established case law of the Boards of Appeal.

The patent informed a skilled person how to perform the claimed method and disclosed functional assays that allowed to assess an agent's capability to active signal transduction (cf. *inter alia*, paragraphs [0017]-[0018] and [0025]-[0027] of the patent-in-suit). The disclosure of document D25 contained numerous flaws and technical inadequacies in its experimental design. Its disclosure was not sufficient to raise serious doubts that the method of claim 1 could not be carried out as claimed. A first possible reason for the negative results reported in document D25 was the lack of linker optimisation. The linkers employed in this document were only used because they were commercially available. No routine optimization was carried out to explore the effects of distance and linker hydrophobicity. Step (c) of the method of claim 1 was actually not performed in document D25. On the other hand, the patent-in-suit contained abundant disclosure on linkers, which were in any event well-known in the art and could easily be optimised at the priority date.

Since the linkers used in document D25 were hydrophobic, their stickiness could have rendered them unsuitable for the cellular assays because it could have prevented them from accessing the EPO-receptor on the cell

surface due to non-specific hydrophobic interactions. No controls were carried out to check whether these compounds were capable of binding to the EPO-receptor in a cellular context.

There were further possible reasons for the negative results in the cellular assay of document D25 which depended on the experimental setup. Indeed, all information on how the cell proliferation assay was actually carried out was withheld in document D25. No experimental conditions were disclosed in this document, such as, for instance, the concentrations at which the compounds were assayed, the controls used for excluding possible toxic effects of the compounds, etc.

The isolated and unclear results of document D25 were inconsistent with the evidence on file which confirmed that the patent-in-suit provided a technical solution to the problem underlying it and indeed led to active compounds. Document D24 directly contradicted the results shown in document D25 since a non-peptidyl agent which activated EPO-receptor signalling was obtained following the method of claim 1. Other documents on file showed similar results with several other receptors, such as document D26 for non-peptidic FGF receptor agonists or documents D23 and D27, *inter alia*, for non-peptidic CSF receptor agonists.

X. The arguments of the respondent, so far as relevant to this decision, are summarized as follows:

Article 56 EPC

The critical question was whether the method of claim 1, defined by steps (a),(b) and (c), allowed a skilled person to obtain active compounds, thereby solving the technical problem formulated in the patent. The mere indication in claim 1 of the result desired to be achieved did not limit the claimed method to one obtaining this result. The production of inactive compounds was not excluded as this would have required an additional selection step that was not present in claim 1. The fact that inactive compounds were obtained by following the steps of claim 1, as shown in document D25, demonstrated that the technical problem was not solved over the whole breadth of the claims. The cited case law did not support appellant's argumentation.

The method in document D25 comprised step (c) of claim 1. The compounds used for obtaining the exemplified dimeric non-peptide compounds were first selected for a strong EPO-receptor antagonist activity and then covalently linked by using different linkers. These dimeric compounds were assayed for EPO-receptor affinity and a functional test was carried out with the two best dimeric compounds. However, none of them was functional in a cellular proliferation assay. No evidence was on file showing that these negative results were due to the nature of the linker. The information given in paragraphs [0020] to [0023] of the patent-in-suit for the selection of a linker was vague and of a general character. There was no indication in the patent of a method suitable for allowing a skilled person to select and optimize the linker. The method disclosed in document D25 contained the same steps as

claim 1. In case of failure, the patent did not suggest the modification, change or optimization of the linker and also did not teach how to carry out such an optimization for achieving the desired result. Appellant's arguments were based on assumptions only and there was no evidence to support them.

Likewise, none of the other documents on file disclosed a method for obtaining active dimeric non-peptide compounds as they were concerned with either monomeric (documents D23, D27) or octameric (document D24) non-peptide compounds. The late-filed documents D26 and D28 showed that the actual invention was performed later in time, with information not available at the priority date of the patent and as a result of a long research program.

XI. The appellant (patentee) requested in writing that the decision under appeal be set aside and that the patent be maintained as granted.

XII. The respondent (opponent) requested in writing that the appeal be dismissed.

Reasons for the Decision

Article 56 EPC

1. The decision under appeal is concerned with the issue of inventive step only. It is mainly based on the post-published document D25 (cited as expert technical opinion) which led the opposition division to decide that the technical problem as defined by the appellant,

was not solved over the entire scope of the claim. The submissions of the parties in the appeal proceedings are exclusively directed to this issue.

2. Claim 1 is directed to a method for the production of "*a non-peptidic agent capable of activating a cellular signal transduction pathway mediated by a polypeptide selected from a growth factor, cytokine and hormone*" (cf. Section VII *supra*). Indeed, this is identical to the technical problem as identified by the opposition division (cf. page 4, point 1.3.a of the decision under appeal).

3. According to decision G 1/03 (OJ EPO, 2004, page 413, point 2.5.2 of the Reasons) "*... (i)f an effect is expressed in a claim, there is lack of sufficient disclosure. Otherwise, i.e. if the effect is not expressed in a claim but is part of the problem to be solved, there is a problem of inventive step ...*". In the present case, claim 1 contains such an effect, which is the result desired to be achieved, and thus, in line with the criteria set out in the decision G 1/03 (*supra*), the issue raised in the decision under appeal is, in principle, an issue under Article 83 EPC.

4. However, the relationship between Articles 56, 83 and 57 EPC is acknowledged in the case law (cf. *inter alia*, T 18/09 of 21 October 2009, points 16 and 18 of the Reasons and T 898/05 of 7 July 2006, point 6 of the Reasons). In view of the prosecution of the present case in the first instance proceedings, in particular, the reasons given in the decision under appeal for the revocation of the patent-in-suit, and the parties' submissions in appeal proceedings (cf. point 1 *supra*),

the board considers it more appropriate in the present case to consider the above identified critical issue of the present appeal proceedings under the requirements of Article 100(a) EPC/Article 56 EPC.

5. In order to achieve the desired result, the method of claim 1 comprises the three specific steps (a), (b) and (c) (cf. Section VII *supra*). These steps, explicitly mentioned in the claim, are thus the solution proposed by the patent-in-suit to solve the above identified technical problem. In the board's view, a skilled person must therefore achieve the desired result when carrying out these three specific steps.

5.1 Claim 1 requires the claimed method to produce non-peptide agents with a specific function. There is nothing in claim 1 to suggest that products with this function cannot be achieved by following the three steps indicated in the claim. This is not argued by the respondents or by the opposition division in the decision under appeal.

5.2 The argument put forward by the respondent, which was followed by the opposition division, relies on the post-published document D25 which discloses a method comprising steps (a), (b) and (c) of claim 1. In particular, non-peptide compounds are screened (tested/identified) in an immobilized EPO receptor (EBP) binding assay (cf. page 1995, right-column, page 1996, Tables 1, 2, page 1997, Table 3) and dimeric analogues are prepared "*in which two moderately potent EPO competitors were connected by a hydrocarbon or polyether linking group*" (cf. page 1997, left-hand column, first full paragraph). However, "*despite EPO*

receptor binding affinity ... the best dimeric analogues ... did not promote proliferation in the FDC-P1 cell assay" (cf. paragraph bridging pages 1997 and 1998).

5.3 The board does not share appellant's opinion that document D25 was not relevant because the method disclosed therein did not effectively produce active non-peptide dimeric agents and did not, therefore, fall within the scope of claim 1 (cf. Section IX *supra*). Indeed, the method, defined and characterized by specific technical steps which are identical to those of claim 1, is appropriate for the intended purpose, which is identical to that of claim 1. But, for whatever reason (linker, activity assay, conditions of this assay, etc.), it leads to failure. According to the established case law of the Boards of Appeal, occasional failure may well be encountered but it must be overcome without undue burden or the exercise of inventive skill (cf. "Case Law of the Boards of Appeal of the EPO", 6th edition 2010, II.A.4.2, page 236 and, *inter alia*, T 363/00 of 30 March 2004, point 2 of the Reasons and T 946/02 of 14 June 2006, points 6, 8 and 12 of the Reasons; all in the context of Article 83 EPC).

5.4 The appellant pointed out to several possible deficiencies and technical problems in the disclosure of document D25 which allegedly could be the reason for the failure to obtain active non-peptide agents, such as the optimization of (activity) assay conditions, the flexibility and/or hydrophobicity of the linker, etc. (cf. Section IX *supra*). However, the actual wording of claim 1 does not require that the claimed method is

limited to specific linkers, binding conditions, cell proliferation assay etc., and the board does not consider the general information in the description of the patent to be sufficient for a skilled person to overcome occasional failure without undue burden or the exercise of inventive skill. Indeed, the same standard is to be applied for both the disclosure of the patent-in-suit and that of the prior art document (cf. *inter alia*, decision T 870/02 of 16 September 2004, point 6 of the Reasons).

5.5 Moreover, if specific technical features, elements and/or steps turn out to be essential for the achievement of a desired result, here the production of a non-peptidic agent capable of activating a cellular signal transduction pathway mediated by a polypeptide, the absence of these features, elements and/or steps in a claim, even if mentioned in the description of the patent-in-suit, is an indication that the identified technical problem cannot be solved over the entire scope of the claim.

5.6 In this respect it is noted that the appellant contemplates the presence of an additional (implicit) screening step to identify active non-peptide agents in the method of claim 1, however, this step is not actually present in the claim. The board regards this additional screening step to be essential for the claimed method to achieve the desired result and to thereby solve the technical problem defined by the appellant. No evidence substantiating the possibility of successfully implementing the claimed method without a final screening step has been put forward.

5.7 The above considerations lead the board to conclude that the technical problem identified by the appellant and accepted by the opposition division is not solved over the entire scope of the claims.

6. In support of its arguments, the appellant further referred in its Grounds of Appeal to documents D23 and D24, which were already on file, and to documents D26 to D28 newly filed with these Grounds of Appeal (cf. Section II *supra*).

6.1 In its communication pursuant to Article 15(1) RPBA, the board already noted that no reasons were given to justify the introduction of documents D26 to D28 at such late stage of the proceedings and why they could not have been filed at an earlier stage (Article 12(4) RPBA). As stated in Section V *supra*, the appellant has not provided further submissions in this regard.

6.2 The board also noted in its communication that document D26, a patent application from the respondent, claimed a priority date of 2006, which is eleven years after the priority date claimed by the patent-in-suit. Thus, document D26 is not useful as evidence of the prior art and the common general knowledge of the skilled person at the priority date. Documents D27 and D28 were cited by the appellant for substantiating the relevance of the disclosure of document D23. However, in view of the monomeric structure of the agents disclosed in document D23 and of the nature of the method used to obtain them, neither document D23 itself, nor any document pointing to its relevance for the present case, are considered to be of importance for the present appeal proceedings and for the board to arrive at a decision. Likewise,

the disclosure in document D24, referring to octamers having a very specific structure and using a particular linker, is not relevant for the present case.

6.3 Thus, in view of the above considerations, the board, exercising its discretion under Article 12(4) RPBA, decides not to admit documents D26 to D28 into the appeal proceedings.

Reformulation of the technical problem

7. According to the established case law of the Boards of Appeal, when applying the "problem-solution approach" for assessing inventive step, in case the technical problem is considered not to be solved, it is necessary then to reformulate the technical problem in a less ambitious way (cf. "Case Law", *supra*, I.D.4.4, page 172 and, *inter alia*, T 87/08 of 11 February 2010, see Headnote and point 6.3 of the Reasons).

8. In its communication pursuant to Article 15(1) RPBA, the board explicitly noted that the opposition division in the decision under appeal failed to reformulate the technical problem. Also none of the parties to this appeal proceeding, not even after being prompted thereto by the board in its communication pursuant to Article 15(1) RPBA, has made any attempt to reformulate the technical problem. In fact no substantive submissions were filed in reply to the communication of the board (cf. Section V *supra*).

9. In the light of this specific situation, documents D1 or D2 are considered as equally representing the closest prior art, as also decided by the opposition

division on page 5, point 1.3(b) of the decision under appeal. Considering the disclosures of these documents, the board sees the actual technical problem underlying the patent-in-suit in the provision of a method for producing a non-peptidic agent of whatever activity. The solution to such a trivial technical problem is certainly obvious and does not require any inventive activity. Appellant's sole request therefore lacks an inventive step and does not meet the requirements of Article 56 EPC.

Order

For these reasons it is decided that:

The appeal is dismissed.

The Registrar: The Chairman:

A. Wolinski M. Wieser