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D E C I S I O N
of 10 August 2005

Case Number: W 0002/05 - 3.3.4
Application Number: PCT/DK 03/00901
Publication Number: WO 04/56865
IPC: G01N 33/566, C07K 7/00,
A61K 38/00, C07K 14/71
Language of the proceedings: EN

Title of invention:

Method of modulation of interaction between receptor and
ligand

Applicant:

ENKAM PHARMACEUTICALS A/S

Opponent:

-

Headword:

Method of modulation/ENKAM

Relevant legal provisions:

EPC Art. 154
PCT Art. 16, 17(3)(a)
PCT R. 13.1, 13.2, 40.1, 40.2(c), 40.2(e)
PCT Guidelines, Chapter 10

Keyword:

"Invitation to pay additional fees sufficiently reasoned
(yes)"
"Lack of unity a posteriori (yes)"

Decisions cited:

W 0003/93

Catchword:

-



Case Number: W 0002/05 - 3.3.4

International Application No. PCT/DK 03/00901

D E C I S I O N
of the Technical Board of Appeal 3.3.4
of 10 August 2005

Applicant: ENKAM PHARMACEUTICALS A/S
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Representative: HOIBERG A/S
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Subject of this decision: Protest according to Rule 40.2(c) of the Patent Cooperation Treaty made by the applicants against the invitation (payment of additional fees) of the European Patent Office (International Searching Authority) dated 1 July 2004.

Composition of the Board:

Chair: U. Kinkeldey
Members: G. Alt
B. Günzel

Summary of Facts and Submissions

- I. International patent application No. PCT/DK 03/00901 having the title "Method of modulation of interaction between receptor and ligand" was filed with fifty-four claims.

Claim 1 read:

"1. A method of modulating the interaction between at least two different proteins, wherein one of the at least two different proteins is represented by a functional cell-surface receptor, or a fragment, or a variant thereof, and another of the at least two different proteins is represented by a polypeptide having a binding site to said receptor, wherein at least a part of said binding site comprises at least one of the sequences set forth in SEQ ID NOS: 1-146, or fragments, or variants, or homologues of said sequences, or fragments or variants of said homologues, comprising

i) providing a compound capable of interacting with the receptor and/or poly-peptide thereby interfering with said receptor and said polypeptide interaction,

ii) presenting the compound of step (i) to the at least two different proteins."

The application contained twelve further independent claims.

- II. The European Patent Office (EPO), acting in its capacity as International Searching Authority (ISA) under Article 16 PCT and 154 EPC, informed the

applicant that the application did not comply with the requirement of unity of invention (Rule 13.1 PCT) and invited the applicant to pay fees for 145 additional inventions, i.e. a sum of 137.025 Euros in accordance with Article 17(3)(a) PCT and Rule 40.1 PCT.

In the invitation the ISA identified document D1 = WO 97/38708 as the closest prior art document. It then stated that the technical feature common to inventions 1 to 146 was a method for finding compounds which modulated the interaction between the receptor FGFR and another polypeptide and that document D1 disclosed such a method, because it referred to the interaction between FGFR and FGF-2 and its use for searching modulators.

The ISA then defined 146 inventions in the international application. They were characterized as follows:

"Invention I (claims 1-44 and 48-54, all partly)

The special technical features which make a contribution over this prior art (Rule 13.2 PCT) are the following: a method for modulating the interaction of FGFR receptor and a second polypeptide comprising the binding site comprising SEQ ID NO:1 and for finding compounds which modulate the interaction of an FGFR and this second polypeptide by using a polypeptide comprising SEQ ID NO:1.

Invention I relates to the problem of providing a method for modulating the interaction between the receptor FDFR and a polypeptide comprising SEQ ID NO:1

and finding compounds which are capable of interacting with FGFR and a protein comprising the binding site to FGFR which binding site is SEQ ID NO 1 (FGFR binding motif of NCAM FN III, 2). This problem is solved by using a polypeptide having a binding site for FGFR comprising SEQ ID NO 1.

Inventions 2-146: subject-matter essentially as defined above for invention 1, but limited to the respective SEQ ID NOs: 2-146, whereby invention 2 relates to SEQ ID NO: 2, invention 3 to SEQ ID NO:3 etc and invention 146 relates to SEQ ID NO: 146.

As both problems and solutions are technically so different, no single general concept can be formulated based on the technical features of the inventions. Consequently, the requirements of Rule 13.1 PCT are not met."

- III. The applicant paid one additional search fee for a search of invention 9 under protest (Rule 40.2(c) PCT).
- IV. The protest was reviewed in accordance with Rule 40.2(e) PCT by a review panel of the ISA. It held that the invitation to pay the additional search fees was justified and invited the applicant to pay a protest fee for further examination of the protest in accordance with Rule 40.2(c) PCT. The review panel stated *inter alia* that from the formula no significant structural element could readily be ascertained and thus no technical feature be determined. Further it stated that an additional search had been carried out for invention 9 (SEQ ID NO: 9 = TIMGLKPETRYAVR).

V. The applicant paid the protest fee and answered to the review panel's communication.

VI. The applicant's arguments set out in the letter of protest and the response to the review panel's communication can be summarized as follows:

(i) The invitation was legally ineffective for lack of sufficient reasoning. The only substantiation in the invitation was that no common concept linking together the independent claims could be found. This was not straightforward for the inventions 1 to 146.

(ii) The 146 sequences of the application had a common feature linking them together. They all contained a structural motif with the following underlying amino acid sequence:

L1-A-L2-B-L3-C-L4-D-L5 wherein at least one of A, B, C, D is selected from a basic amino acid residue, glutamine or asparagine,
at least one of A, B, C, D is selected from a hydrophobic amino acid residue,
at least one of A, B, C, D is selected from an acidic amino acid residue, glutamine or asparagine,
at least one of A, B, C, D is glycine or alanine, and
L1, L2, L3, L4 and L5 may be selected from a chemical bond or an amino acid sequence having n amino acid residues, wherein n is an integer of from 0 to 5, or represent fragments, variants or homologues of a sequence containing said structural motif.

The proteins identified in the international application and comprising this motif represented low affinity ligands of FGFR.

The known (document D1) low-affinity binding site on FGF-2 spanned residues 106 to 115 of this protein. This sequence, however, did not contain the motif of the low-affinity binding site of the application. Consequently, the binding of the compounds of the application to FGFR occurred at a position which was different from the known site. Therefore, the unifying structural feature of sequences 1 to 146 was novel over the prior art.

(iii) Moreover the applicant noted that the ISA performed an erroneous additional search because, in view of the International Search Report, invention 2 instead of invention 9 had been searched.

VII. Requests

The applicant requested

- reimbursement of the protest fee and the additional search fee
- an additional search for invention 9 of claims 1 to 54

Reasons for the Decision

1. The protest is admissible.
2. The applicant's protest is based on two lines of arguments: a) The invitation to pay additional fees is not sufficiently substantiated. b) The ISA's finding of the lack of a common concept is not justified.
3. *Lack of substantiation*

Rule 40.1 PCT stipulates that the invitation under Article 17(3)(a) PCT to pay additional fees must specify the reasons why the international application is not considered to comply with the requirement of unity of invention.

- 3.1 The applicant submits in the letter accompanying the protest that "the only substantiation in the invitation is that no common concept linking together the independent claims can be found. The applicant cannot see that this is straightforward for the inventions 1-146."

The board is not convinced that this is so for the following reasons:

- 3.2 The ISA's statement on page 1 of the extra sheet to form PCT/ISA/206 that "the application has been considered to contain 146 inventions which are not linked such that they form a single general inventive concept", is followed by detailed observations setting out, on the one hand, the ISA's finding of a posteriori non-unity and, on the other, the nature of the special

technical features (see section II above). The reasoning ends with an explanation as to why the special technical features are not the same or corresponding or, in other words, why a single general inventive concept is lacking: "As both problems and solutions are technically so different, no single general concept can be formulated based on the technical features of the inventions. Consequently, the requirements of Rule 13.1 PCT are not met." Thus, the applicant's argument that "the only substantiation in the invitation is that no common concept linking together the independent claims can be found" does not hold good.

3.3 The purpose of the provision under Rule 40.1 PCT is to enable the applicant (and the board in case of a protest) to examine whether the invitation is justified. This requires that the invitation must be drafted in a form that it is suited to fulfil this purpose, i.e. the reasoning must be comprehensible.

3.4 The ISA's invitation has irregularities. For example, the reasoning as to why the special technical features are not linked, is not structured according to the "classical" form of the problem-solution-approach - definition of the closest prior art - definition of the problem - definition of the special technical features which provide a solution to the problem, but the special technical features are recited before the problem has been formulated. Nevertheless, even though not in the proper order, all the elements of the problem-solution-approach are there and identifiable. Furthermore, there are linguistic inconsistencies, for example, at one place the term "special technical

features" is used, whereas, when it comes to the conclusion why the special technical features are not linked, the term "solution" ("As both problems the solutions are technically different...") is used. This may cause confusion because the term "solution" had not been mentioned before in the reasoning.

Nevertheless, the board is convinced that the addressee of the ISA's invitation would have no difficulty in understanding the reasoning because it is a person who can be expected to be familiar with the legal and technical terms of the PCT search procedure.

Hence, the ISA has fulfilled its obligation to substantiate its findings of non-unity.

4. *The ISA's findings*

4.1 In his letter accompanying the protest the applicant submits that all sequences of the application are linked by a structural motif (see section VI above) representing the structural element of a low-affinity binding site for fibroblast growth factor receptor (FGFR). It is argued that the sequence of a known low-affinity binding site of FGFR does not encompass the motif of the sequences of the application. Consequently, this motif is a structural feature that has not been disclosed before and has therefore to be regarded as a special technical feature linking the subject-matter of the claims.

4.2 The PCT Guidelines state in Chapter 10.01 that the determination if the inventions in an international application are so linked as to form a single general

inventive concept is "made on the contents of the claims as interpreted in the light of the description and drawings (if any)".

Thus, according to these Guidelines, the evaluation of the issue of unity of invention on the basis of what is derivable from the disclosure of the application is a correct approach justifying an invitation to pay additional fees if unity of invention cannot be acknowledged on the basis of such evaluation.

Said approach derives from the very nature of the invitation procedure under Rule 40 PCT. The ISA's evaluation of the question of unity of invention is not a final and binding opinion on the matter, but is only relevant for determining the amount of additional fees to be paid by the applicant for a full search. The international search procedure is governed by a tight time schedule. The invitation to pay additional fees preserves the applicant's potential interest in having the entire subject-matter of his application searched, but at the same time it aims and must aim at determining quickly the extent of the search to be made by the ISA. No discussion with the applicant by exchange of arguments is possible, and therefore not foreseen. Hence, the disclosure in the application is the only basis for the ISA for assessing whether or not the subject matter contained in the application is so linked as to form a single general inventive concept within the meaning of Rule 13.1 PCT.

- 4.3 In the present case, the sequence motif referred to by the applicant is not explicitly mentioned in the international application documents. Nor can it be

taken implicitly from them because it provides for so many sequence variables that it is prima facie not recognizable as a motif by the reader of the application. Hence, this motif constitutes a feature that was not available to the ISA at the time when the invitation was drafted and could therefore not have been relied on when evaluating the subject-matter for the purposes of unity. Thus, the applicant's argument based on the unifying nature of this motif fails.

- 4.4 The letter of protest does not contain any other arguments as to why the ISA's findings as to lack of unity are not correct. In view of this and of decision W 3/93 (OJ EPO 1994, 931) which states in point 4 that the board cannot investigate ex officio whether an objection of lack of unity would have been justified for reasons other than those given in the invitation, the board concludes that the protest is not justified.

5. *Additional search*

Under Article 154(3) EPC the boards of appeal rule on protests against additional fees charged by the ISA under Article 17(3)(a) PCT. Under Rule 40.2(c) PCT they examine the protest and, to the extent that they find it justified, order the total or partial reimbursement of the fees.

It follows from these provisions that the board is not competent to deal with the applicant's request for an additional search for invention 9 (corresponding to SEQ ID No. 9).

Order

For these reasons it is decided that:

The protest according to Rule 40.2(c) PCT is dismissed.

Registrar:

Chair:

P. Cremona

U. Kinkeldey