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Datasheet for the decision of 26 November 2012

Case Number: T 2323/08 - 3.3.02

Application Number: 01984000.8

Publication Number: 1337274

IPC: A61K 47/48

Language of the proceedings: EN

Title of invention:
Hydroxyapatite-targeting poly(ethylene glycol) and related polymers

Applicant:
Nektar Therapeutics

Headword:
Hydroxyapatite-targeting PEGs/NEKTAR THERAPEUTICS

Relevant legal provisions:
EPC Art. 54, 111

Keyword:
"Main request - novelty (no): disclosure of prior art enabling"
"Auxiliary request I - novelty (yes): claimed subject-matter not specifically disclosed in the prior art"
"Remittal (yes): undecided issues"

Decisions cited:
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Catchword:
-

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Case Number: T 2323/08 - 3.3.02

D E C I S I O N
of the Technical Board of Appeal 3.3.02
of 26 November 2012

Appellant: (Applicant)
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Representative:
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Decision under appeal:
Decision of the Examining Division of the European Patent Office posted 6 June 2008 refusing European patent application No. 01984000.8 pursuant to Article 97(2) EPC.

Composition of the Board:

Chairman: U. Oswald
Members: A. Lindner
D. Prietzel-Funk

Summary of Facts and Submissions

I. European patent application No. 01 984 000.8 was refused by a decision according to the state of the file of the examining division dispatched on 6 June 2008 on the basis of Article 97(2) EPC on the grounds that the main request lacked novelty and inventive step and that the auxiliary request lacked clarity and inventive step.

The examining division came to the conclusion that the subject-matter according to claim 1 of the main request lacked novelty over document (1), as the chemically reactive groups present on TGF-ß constituted chemically reactive groups as defined in said claim 1. Furthermore, in the absence of any evidence proving the contrary, the examining division decided that the disclosure of document (1) was enabling. The subject-matter of claim 31 of the main request was found to lack an inventive step over the teaching of document (1) in combination with document (2). The clarity objection regarding claim 1 of the auxiliary request was based on a contradiction between said claim and its dependent claim 21, as the compound Q-PEG-L-T according to claim 21 was not encompassed by claim 1.

II. The documents cited during the examination and appeal proceedings included the following:

(1) WO 92/20371
(2) J. Fujisaki, et al., J. Pharm. Pharmacol. (1996), 48, 798-800

(21) Nektar Therapeutics AL, Corporation, "Attempted Reproduction of Examples 1 and 2 From WO 92/20371".

III. The applicant (appellant) lodged an appeal against this decision. With the statement of the grounds of appeal, the appellant submitted a new main request and new auxiliary requests I and II.

IV. In the annex to the summons to oral proceedings pursuant to Article 15(1) RPBA, the board gave its preliminary opinion on some of the points to be discussed at the oral proceedings, according to which document (1), the disclosure of which appeared to be enabling, was considered to be pertinent for novelty and inventive step of all requests on file.

V. At the oral proceedings of 26 November 2012, the appellant submitted a new auxiliary request I destined to replace auxiliary request I on file.

VI. The independent claims 1 of the main request, which is identical to the former claim 31, and of the new auxiliary request I read as follows:

(i) main request

"1. A hydroxyapatite-targeting, biologically active polymeric structure comprising a linear or branched water-soluble and non-peptidic polymer backbone having at least two termini, a first terminus being covalently bonded to a hydroxyapatite-targeting moiety and a second terminus covalently bonded to a biologically active agent through a linker, wherein at least one of

the polymer backbone and the linker comprise a hydrolytically or enzymatically degradable linkage."

(ii) auxiliary request I

"1. A hydroxyapatite-targeting, biologically active polymeric structure having the following structure:

D-L'-POLY-L-T

wherein POLY is a water-soluble and non-peptidic polymer, D is a biologically active agent, L and L' are linkers which may be the same or different, and T is a hydroxyapatite-targeting moiety, and wherein at least one of POLY, L, and L' comprise a hydrolytically or enzymatically degradable linkage, and wherein T is a biphosphonate."

VII. Regarding novelty, the appellant essentially argued that the disclosure of document (1) was not enabling in that the use of bis-epoxy PEG for the preparation of TGF-PEG-tetracycline and related conjugates would result in either a tetracycline-PEG-tetracycline product or a large matrix product. In order to prove this assertion, the appellant filed document (21) with the statement setting out the grounds of appeal.

VIII. The appellant requested that the decision under appeal be set aside and that a patent be granted on the basis of the main request submitted with the letter setting out the grounds of appeal, or on the basis of auxiliary request I, submitted during the oral proceedings today, or on the basis of auxiliary request II, also submitted with the letter setting out the grounds of appeal.

Reasons for the decision

1. The appeal is admissible.

2. Main request - novelty

2.1 Document (21) comprises tests in which examples 1 and 2 of document (1) were reworked without, however, arriving at the desired final product. For all experiments bis-epoxy PEG 600 was taken. Example 1 of document (1) does not indicate the molecular weight of the bis-epoxy PEG, in example 2, bis-epoxy PEG 600 and bis-epoxy 1700 are used. In general, PEGs with higher molecular weights are preferred in document (1) (see page 10, lines 29-33, where PEG 3400 is defined as the most preferred embodiment). As a consequence, when the skilled person discovers that example 1 of document (1) cannot be reproduced with bis-epoxy PEG 600, he will repeat the experiment with a bis-epoxy PEG of higher molecular weight as preferred in document (1). Likewise, when he finds out that example 2 cannot be reproduced with bis-epoxy PEG 600, he will redo it with bis-epoxy PEG 1700. As a consequence, the tests according to document (21) are not sufficient for proving that the disclosure of document (1) is non-enabling. Therefore, document(1) is eligible to be taken into concern as appropriate prior art.

2.2 Document (1) discloses a composition comprising a bone growth factor (= biologically active agent) and a targeting molecule having affinity for a tissue of interest, in particular for bone (= hydroxyapatite-targeting moiety). The bone growth factor and the targeting molecule are both chemically conjugated to a

cross-linking agent (see page 6, line 31-35 and page 7, lines 3-4). The targeting molecules having an affinity for bone comprise tetracycline, calcein, biphosphonate, polyaspartic acid, polyglutamic acid, aminophospho-sugars and estrogen (see page 7, lines 3-6). The cross-linking agent is preferably a hydrophilic polymer such as propylene glycol, polyoxyethylene, polyethylene glycol, polytrimethylene glycols, polylactic acid, polyoxyethylene-polyoxypropylene block polymers, starch and heparin (see page 10, lines 11-25), of which polyethylene glycols (PEGs), or derivatives thereof including polymers according to formula R-PEG-R, where R is glycidylether, succinimidyl succinate, or p-nitro-phenylcarbonate, are preferred (see page 15, lines 10-18).

It follows therefrom that document (1) specifically discloses compositions formed by reacting the biologically active agent and the hydroxyapatite-targeting moiety with a cross-linking agent in the form of succinimidyl succinate-PEG-succinimidyl succinate (see page 15, line 13-16). It is noted that the resulting composition comprises ester groups linking the succinate to the PEG which are hydrolytically or enzymatically degradable, which means that said composition is structurally identical to the polymeric structure defined in claim 1 of the main request. As a consequence, the subject-matter of claim 1 of the main request is not novel, the requirements of Article 54 EPC are therefore not met.

3. Auxiliary request I

3.1 Amendments

Claim 1 is based on original claims 31, 33 and 34. As a consequence, the requirements of Article 123(2) EPC are met.

3.2 Novelty

In claim 1 of auxiliary request I, the hydroxyapatite-targeting moiety is limited to a biphosphonate, which means that the skilled person, starting from the disclosure on page 6, lines 31-35 of document (1) has to select both the biphosphonate from the list of hydroxyapatite-targeting moieties and a cross-linking agent such as succinimidyl succinate-PEG-succinimidyl succinate, which then leads to a composition comprising a hydrolytically or enzymatically degradable linkage. The subject-matter of claim 1 of auxiliary request I is novel over document (1), as such a composition is not specifically and unambiguously disclosed therein.

4. Remittal to the department of first instance

Although Article 111(1) EPC does not guarantee an absolute right to have all the issues in the case considered by two instances, it is well recognised that any party should where appropriate be given the opportunity to have two readings of the important elements of the case. Hence, a case is normally referred back if essential questions regarding the patentability of the claimed subject-matter have not yet been examined and decided by the department of

first instance. This applies also to the present case. The board notes that the examining division did not give a reasoned decision about lack of inventive step of original claim 31, let alone of claim 31 in combination with claim 33 and 34, upon which claim 1 of auxiliary request I on file is based (see point 3.1 above). In this regard, the board inspected closely, but without a result the "communications" dated 7 February 2008, 16 October 2006 and 16 February 2007 (the last document being the minutes of the oral proceedings of said day before the examining division), being referred to in the impugned decision. Concerning inventive step of claim 31, the examining division merely stated once that "[the] claims are considered to lack inventive step over D1 in combination with D2" without giving any further explanations (see point 3 of the minutes of the oral proceedings of 16 February 2007). As a consequence, the board concludes that it is appropriate to remit the case to the examining division for further prosecution.

Order

For these reasons it is decided that:

1. The decision under appeal is set aside.

2. The case is remitted to the department of first instance for further prosecution.

The Registrar: The Chairman

N. Maslin U. Oswald