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Datasheet for the decision of 23 November 2021

Case Number: T 0650/18 - 3.3.04

Application Number: 10014362.7

Publication Number: 2325199

IPC: C07K14/51, A61K38/10, A61K38/17

Language of the proceedings: EN

Title of invention:
Sclerostin binding agents

Patent Proprietor:
Amgen, Inc.

Opponent:
James Poole Limited

Headword:
Sclerostin neutralising antibodies/AMGEN

Relevant legal provisions:
EPC Art. 123(2)

Keyword:
Amendments - added subject-matter (yes)

Decisions cited:
T 2134/10, T 1621/16

Catchword:

Europäisches Patentamt
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Beschwerdekammern

Boards of Appeal

Chambres de recours

Boards of Appeal of the
European Patent Office
Richard-Reitzner-Allee 8
85540 Haar
GERMANY
Tel. +49 (0)89 2399-0
Fax +49 (0)89 2399-4465

Case Number: T 0650/18 - 3.3.04

D E C I S I O N
of Technical Board of Appeal 3.3.04
of 23 November 2021

Appellant: (Opponent)	James Poole Limited One Southampton Row London WC1B 5HA (GB)
Representative:	Carpmaels & Ransford LLP One Southampton Row London WC1B 5HA (GB)
Respondent: (Patent Proprietor)	Amgen, Inc. One Amgen Center Drive Thousand Oaks, CA 91320 (US)
Representative:	J A Kemp LLP 80 Turnmill Street London EC1M 5QU (GB)
Decision under appeal:	**Interlocutory decision of the Opposition Division of the European Patent Office posted on 5 March 2018 concerning maintenance of the European Patent No. 2325199 in amended form.**

Composition of the Board:

Chairwoman	G. Alt
Members:	O. Lechner
	L. Bühler

Summary of Facts and Submissions

I. The appeal of the opponent ("appellant") lies against the opposition division's interlocutory decision to maintain European patent No. 2 325 199 ("the patent") in amended form.

II. The patent is based on European patent application No. 10 014 362.7 ("application"), a divisional application of European patent application No. 06 751 903.3 ("parent application"). The patent is entitled "*Sclerostin binding agents*".

III. The patent had been opposed on the grounds under Article 100(a) in connection with Articles 54 and 56 EPC as well as under Article 100(b) and (c) EPC.

IV. The opposition division decided, *inter alia,* that claim 1 of the main request and auxiliary request 1 complied with the requirements of Article 100(c) in combination with Articles 123(2) EPC (and 76(1) EPC) (see point 4. below for the reasons), whereas claim 12 of the main request did not.

V. With its statement of grounds of appeal, the appellant filed, *inter alia,* arguments why the decision under appeal was wrong to find that claim 1 of auxiliary request 1 complied with the requirements of Article 123(2) EPC.

VI. The patent proprietor ("respondent") replied.

VII. The appellant and the respondent submitted one further submission each. They then each submitted a further submission in reply to the summons for oral proceedings

and then again in reply to the board's communication pursuant to Article 15(1) RPBA.

VIII. In its communication, the board indicated, *inter alia*, that it was inclined to disagree with the reasoning in the decision under appeal that claim 1 of auxiliary request 1 complied with the requirements of Article 123(2) EPC.

IX. Oral proceedings took place as scheduled and, as agreed by both parties, as a mixed-mode hearing (i.e. some persons attending in person, others by video-conference).

At the end of the oral proceedings, the Chair announced the board's decision.

X. Claim 1 of the sole pending claim request ("main request", being identical to auxiliary request 1 dealt with in the decision under appeal), reads as follows:

"1. A monoclonal antibody for use in a method of increasing at least one of bone formation, bone mineral density, bone mineral content, bone mass, bone quality and bone strength in a mammal and thereby treating a condition in which an increase in at least one of bone formation, bone mineral density, bone mineral content, bone mass, bone quality and bone strength is desirable, wherein the monoclonal antibody (a) binds to human sclerostin with a binding affinity of less than or equal to 1 x 10^{-10} M and (b) cross-blocks the binding of antibody Ab-13 or Ab-14 to sclerostin and/or is cross-blocked from binding to sclerostin by antibody Ab-13 or Ab-14, wherein antibody Ab-13 has light chains of SEQ ID NO: 205 and heavy chains of SEQ ID NO: 209 and antibody Ab-14 has light chains of SEQ ID NO: 213

and heavy chains of SEQ ID NO: 217, and wherein the binding affinity is determined by surface plasmon resonance."

XI. The arguments of the appellant relevant for the present decision may be summarised as follows.

Main request

Amendments (Article 123(2) EPC) - claim 1

The definition of the monoclonal antibody in claim 1 was the result of a combination of features requiring multiple selections from different lists. One was the selection of an antibody affinity of $1x10^{-10}$ M from the list of affinities *"of less than or equal to 1 x 10^{-7} M, less than or equal to 1 x 10^{-8} M, less than or equal to 1 x 10^{-9} M, less than or equal to 1 x 10^{-10} M, less than or equal to 1 x 10^{-11} M, or less than or equal to 1 x 10^{-12} M"*.

There was a direct link between a given antibody and its affinity to a given antigen. However, there was no disclosure in the application of monoclonal antibodies defined by a combination of (a) an affinity of "less than or equal to 1 x 10^{-10} M" and (b) the ability to cross-block the binding of Ab-13 or Ab-14 to sclerostin ("forward" cross-blocking) and/or that were cross-blocked from binding to sclerostin by antibody Ab-13 or Ab-14 ("backward" cross-blocking).

If a link between the binding affinity and the reactivity with the particular reference antibody pair were considered to be disclosed in the application for the definition of the monoclonal antibodies, the application as filed pointed to selecting a binding

affinity of 10^{-12} M, and not 10^{-10} M, because the binding affinities reported for Ab-13 and Ab-14 in the application were in the picomolar, i.e. 10^{-12} M, range.

XII. The arguments of the respondent relevant for the present decision may be summarised as follows.

Main request

Amendments (Article 123(2) EPC) - claim 1

The affinity parameter "less than or equal to $1x10^{-10}$ M" was disclosed in a nested series of binding affinities on page 110, lines 29 to 32 of the application:

"*Antibodies according to the invention may have a binding affinity for human sclerostin of less than or equal to 1 x 10^{-7} M, less than or equal to 1 x 10^{-8} M, less than or equal to 1 x 10^{-9} M, less than or equal to 1 x 10^{-10} M, less than or equal to 1 x 10^{-11} M, or less than or equal to 1 x 10^{-12} M.*"

This sentence was worded in general terms and clearly applied to the application as a whole. It would be clear to the skilled person that each of the binding affinities, including the affinity of less than or equal to $1x10^{-10}$ M, may be exhibited by any of the antibodies of the invention. This disclosure applied equally to antibodies that cross-blocked, for example Ab-1, as it did to antibodies that cross-blocked or were cross-blocked by antibodies Ab-13 or Ab-14. Thus, claim 1 had just been shrunk to a smaller group of antibodies.

Decisions T 1621/16 and T 2134/10 supported the view that the claimed combination of features was directly and unambiguously disclosed in the application as filed.

XIII. Requests of the parties relevant to this decision.

The appellant (opponent) requested that the decision under appeal be set aside and that European patent No. 2 325 199 be revoked.

The respondent (patent proprietor) requested that the appeal be dismissed.

Reasons for the Decision

Admissibility of the appeals

1. The appeal complies with the requirements of Articles 106 to 108 and Rule 99 EPC and is admissible.

Main request

2. The description of the divisional application as filed is the same as that of the parent application. The claims of the divisional application as filed are rearranged compared to the claims of the parent application as filed. Hence, the considerations in relation to Article 76(1) and Article 123(2) EPC are the same. In the following, the board deals with the ground for opposition under Article 100(c) in combination with Article 123(2) EPC.

Amendments (Article 123(2) EPC) - claim 1

3. Claim 1 is drafted as a (second) medical "for use" format in accordance with Article 54(5) EPC. The therapeutically used compounds are monoclonal antibodies characterised in that they (a) bind to human sclerostin with a binding affinity of less than or equal to $1x10^{-10}$ M as determined by surface plasmon resonance and (b) cross-block the binding of antibody Ab-13 or Ab-14 - both defined by their respective heavy and light chain sequences - to sclerostin and/or are cross-blocked from binding to sclerostin by antibody Ab-13 or Ab-14.

4. In the decision under appeal, the opposition division decided that the subject-matter of claim 1 of auxiliary request 1 (corresponding to claim 1 of the current main request) did not relate to subject-matter extending beyond the application as filed for the following reasons.

The application disclosed a list of 28 antibodies, including Ab-13 and Ab-14, and a further list with six different binding affinity ranges. The binding affinity range referred to in claim 1 of less than or equal to $1x10^{-10}$ being one of them. Since the extraction of antibodies Ab-13 and Ab-14 from the antibody list was *per se* allowable, the only question to be answered was whether combining the particular antibodies Ab-13 and Ab-14 and the binding affinity range of less than or equal to $1x10^{-10}$ M constituted an allowable selection from two lists.

The opposition division answered this question in the affirmative. The combination of characterising features was not a selection of independent features from two

lists since the binding affinity was an inherent property of an antibody. The selection of one particular binding affinity from the list of binding affinities to specify that inherent property was an allowable limitation and did not result in new technical information. The opposition division saw the circumstances of the current case as being parallel to the circumstances underlying case T 2134/10.

5. For the following reasons, the board is not persuaded by the reasoning in the decision under appeal.

6. As submitted by the appellant - and not contested by the respondent - the binding affinity of a given antibody is (mainly) determined by its heavy and light chain variable regions.

The antibodies according to claim 1 are, however, not defined by specific heavy and light chain variable region sequences but in terms of a functional feature, i.e. by way of their cross-blocking ability: they cross-block the binding of antibody Ab-13 or Ab-14 to sclerostin and/or are cross-blocked from binding to sclerostin by antibody Ab-13 or Ab-14.

Hence, the antibodies according to claim 1 are a structurally undefined and heterologous group of antibodies, i.e. the antibodies encompassed by the group may have any kind of variable region sequences.

7. There is no explicit disclosure in the application that this functionally defined, structurally heterologous group of antibodies displays binding affinities within a specific range. The skilled person, relying on the basis of common general knowledge that binding affinity is linked to an antibody's structure (see point 6.

above), would also not derive this from the disclosure of the application.

8. Therefore, the skilled person would not interpret the disclosure of the list of binding affinity ranges on page 110 in the way the respondent submits, namely that it would be clear to the skilled person, in view of the introductory expression of the paragraph "*Antibodies according to the invention may have a binding affinity of...*", that each of the binding affinities may be exhibited by any of the antibodies of the invention.

9. Assuming that a particular range of binding affinities was linked to the functionally defined, structurally heterologous group of antibodies, the skilled person, would infer, based on common general knowledge, that this could not be each and every range from the list of six affinity ranges provided in the description.

10. Thus, in relation to the reference antibodies referred to in claim 1, i.e. Ab-13 and Ab-14, the affinity ranges in the list are not equivalent. Moreover, since the group of antibodies is not structurally defined, no particular affinity value or range can be considered inherent.

11. Hence, in contrast to the opposition division, the board takes the view that the binding affinity and the cross-blocking ability with reference to antibodies Ab-13 and Ab-14 are independent features disclosed in two different lists.

12. In such circumstances, it is established case law of the boards (see Case Law of the Boards of Appeal, 9th Edition 2019, II.E.2.6) that for the combination of the two features to be allowable, there should be a

disclosure in the application (or it being known from the common general knowledge) pointing to their association, for example, a disclosure in an example.

13. However, in this case, there is no explicit nor implicit disclosure in the application pointing to a combination of a binding affinity of less than or equal to $1x10^{-10}$ M for an antibody capable of cross-competing with Ab-13 and/or Ab-14.

14. In contrast, in the board's view, if guided by the examples as a potential pointer, the skilled person would have chosen a binding affinity similar to the one of the claimed reference antibodies, Ab-13 and Ab-14, i.e. ~$1x10^{-12}$ M (see examples 10 and 11).

15. The respondent referred to decisions T 1621/16 and T 2134/10 to support its position that the combination was allowable.

15.1 With regard to decision T 1621/16 and in particular point 1.7.2 of the Reasons, the respondent submits that the decision confirmed that multiple selections from converging lists were allowable, and so the selection of the range of less than or equal to $1x10^{-10}$ M from the converging list of affinities disclosed on page 110 of the application did not add matter.

However, the board in case T 1621/16 explicitly stated that amendments based on multiple selections from lists of converging alternatives do not necessarily meet the requirements of Article 123(2) EPC. At least two conditions have to be met for such a selection to be allowable. One of them being that the combination should be supported by a pointer in the application as filed (see Reasons, point 1.7.3).

Apart from the fact that in this case only one of the two lists from which the selection is made can be considered converging (namely the list of affinity ranges), the above cited prerequisite that the combination should be supported by a pointer is not met for the reasons explained above in points 13. and 14. Hence, decision T 1621/16 does not help the respondent's case.

15.2 In decision T 2134/10, also relied on in the decision under appeal, the appellant in that case submitted that the subject-matter of claim 1(d), a polynucleotide encoding a polypeptide having an amino acid sequence at least 95% identical to the sequence shown in SEQ ID NO:66, resulted from the combination of items from two lists, it not being possible to derive this combination from the application documents as filed (see Reasons, points 9 and 10).

The board in question reasoned that there is a direct and unambiguous disclosure of amino acid sequences displaying a specified degree of sequence identity with each of those displayed in Table 1 and that the restriction to amino acid sequences having 95% identity with SEQ ID NO:66 is thus the result of a limitation to one specific degree of identity from among all the degrees specified in relation to SEQ ID NO:66. The board considered that a "*specific degree of sequence identity is not a property that, in combination with a particular molecule selected from table 1, could single out a particular molecule or confer properties to the claimed subject-matter not directly and unambiguously derivable from the application as filed*".

However, the circumstances underlying case T 2134/10 and the current case are different.

Firstly, in case T 2134/10, there is a direct nexus disclosed in the application between the sequence IDs and the percentages of sequence identities.

Secondly and perhaps more importantly, qualification of a compound by a particular binding affinity selected from among several binding affinities is different from qualification by a particular sequence identity selected from among several sequence identities. The former qualification may indeed define compounds having properties not directly and unambiguously (explicitly or implicitly) derivable from the application. For example, qualification by a particular binding affinity may result in compounds better suited for medical use than those defined by a different binding affinity.

Hence, decision T 2431/10 does not support the respondent's case either.

16. The board concludes in view of all of the above observations that the application as filed does not directly and unambiguously disclose monoclonal antibodies characterised by the following combination of features: that they (a) bind to human sclerostin with a binding affinity of less than or equal to $1x10^{-10}$ M as determined by surface plasmon resonance and (b) cross-block the binding of antibody Ab-13 or Ab-14 - both defined by their respective heavy and light chain sequences - to sclerostin and/or are cross-blocked from binding to sclerostin by antibody Ab-13 or Ab-14.

17. Consequently, the subject-matter of claim 1 extends beyond the content of the application as filed (Article 123(2) EPC).

Order

For these reasons it is decided that:

1. The decision under appeal is set aside.

2. The patent is revoked.

The Registrar: The Chair:

I. Aperribay G. Alt

Decision electronically authenticated