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Datasheet for the decision of 7 April 2022

Case Number: T 2355/18 - 3.3.01

Application Number: 10835979.5

Publication Number: 2510948

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Language of the proceedings: EN

Title of invention:

T CELL ACTIVATION INHIBITOR, PHARMACEUTICAL COMPOSITION CONTAINING SAME, AND SCREENING METHOD FOR T CELL ACTIVATION INHIBITING SUBSTANCE

Patent Proprietor:

Mitsubishi Tanabe Pharma Corporation

Opponent:

AbbVie Inc.

Headword:

RGM inhibiting substances/MITSUBISHI TANABE

Relevant legal provisions:
EPC Art. 100(c), 123(2)

Keyword:
Grounds for opposition - added subject-matter (yes)
Amendments - allowable (no)

Decisions cited:

Catchword:

Europäisches Patentamt
European Patent Office
Office européen des brevets

Beschwerdekammern

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Case Number: T 2355/18 - 3.3.01

D E C I S I O N
of Technical Board of Appeal 3.3.01
of 7 April 2022

Appellant: (Patent Proprietor)	Mitsubishi Tanabe Pharma Corporation 3-2-10, Dosho-machi, Chuo-ku, Osaka-shi Osaka 541-8505 (JP)
Representative:	Hoffmann Eitle Patent- und Rechtsanwälte PartmbB Arabellastraße 30 81925 München (DE)
Appellant: (Opponent)	AbbVie Inc. 1 North Waukegan Road North Chicago, IL 60064 (US)
Representative:	Mewburn Ellis LLP Aurora Building Counterslip Bristol BS1 6BX (GB)
Decision under appeal:	**Interlocutory decision of the Opposition Division of the European Patent Office posted on 5 July 2018 concerning maintenance of the European Patent No. 2510948 in amended form**

Composition of the Board:

Chairman	A. Lindner
Members:	T. Sommerfeld
	R. Romandini

Summary of Facts and Submissions

I. European patent 2510948 is based on application no. 10835979.5, which was filed as an international application and published as WO 2011/071059. The patent is entitled "T cell activation inhibitor, pharmaceutical composition containing same, and screening method for T cell activation inhibiting substance" and was granted with 9 claims.

Claim 1 as granted reads as follows:

"1. A Repulsive Guidance Molecule a (RGMa) inhibiting substance as an active ingredient for use in the prophylaxis or treatment of an autoimmune disease such as cellular autoimmune disease, rheumatism, multiple sclerosis, nervous system autoimmune diseases such as Guillain-Barré syndrome, neuro-Behcet's diseases, malignant anemia, type I diabetes, systemic lupus erythematosus (SLE), inflammatory bowel diseases (IBD), Sjogren's syndrome, atopic dermatitis, Goodpasture's syndrome, Grave' diseases [sic], autoimmune hemolytic anemia, autoimmune thrombocytopenic purpura, glomerulonephritis, myasthenia gravis, Hashimoto's diseases."

II. Opposition was filed against the granted patent, the opponent requesting that the patent be revoked in its entirety on the grounds of lack of novelty and of inventive step (Articles 54(2) and 56 EPC and Article 100(a) EPC), insufficiency of disclosure (Article 100(b) EPC) and added subject-matter (Article 100(c) EPC).

By an interlocutory decision announced at oral proceedings, the opposition division decided that the patent could be maintained in amended form on the basis of auxiliary request 6 filed by letter of 11 April 2018 (Articles 101(3)(a) and 106(2) EPC).

III. The patent proprietor and the opponent both lodged appeals against the decision.

IV. With the statement of grounds of appeal, the appellant-patent proprietor requested that the patent be maintained as granted (main request) or alternatively on the basis of "Auxiliary Request 1, followed by Auxiliary Request 8, followed by new Auxiliary Requests 8B and 8C, Auxiliary Request 5 and 6, new Auxiliary Request 6B, Auxiliary Request 6A, Auxiliary Requests 2 - 4, 7 and 9 - 11, Auxiliary Requests 1A - 5A, 7A - 12A, new Auxiliary Request 15, Auxiliary Request 13A, and Auxiliary Request 14A".

V. With the statement of grounds of appeal, the appellant-opponent requested that the decision be set aside and the patent be revoked in its entirety.

VI. With its reply to the opponent's statement of grounds of appeal, dated 2 April 2019, the appellant-patent proprietor submitted new auxiliary requests AR6C and AR15A.

VII. With its reply to the patent proprietor's statement of grounds of appeal, the appellant-opponent requested that the new claim requests not be admitted.

VIII. With a further letter dated 24 June 2019, the appellant-patent proprietor requested "deliberation only" on the main request and auxiliary requests 8, 6,

6A, 11A, 12A, 14A and 15A, all the other requests being withdrawn from the proceedings. By a letter dated 21 February 2022, sent in reply to the opponent's letter dated 13 December 2019 and the board's communication pursuant to Article 15(1) RPBA, the appellant-patent proprietor re-submitted the pending auxiliary requests with the revised numbering, i.e. as auxiliary requests 1 to 7.

The **main request** consists of the claims as granted.

In **auxiliary request 1** the following amendments have been introduced into claim 1:

"1. A Repulsive Guidance Molecule a (RGMa) inhibiting substance as an active ingredient for use in the prophylaxis or treatment of an autoimmune disease ~~such as~~ selected from the group of cellular autoimmune disease, rheumatism, multiple sclerosis, nervous system autoimmune diseases ~~such as~~ selected from the group of Guillain-Barré syndrome~~,~~ and neuro-Behcet's diseases, malignant anemia, type I diabetes, systemic lupus erythematosus (SLE), inflammatory bowel diseases (IBD), Sjogren's syndrome, atopic dermatitis, Goodpasture's syndrome, Grave' diseases [sic], autoimmune hemolytic anemia, autoimmune thrombocytopenic purpura, glomerulonephritis, myasthenia gravis~~,~~ and Hashimoto's diseases."

Auxiliary request 2 is the set of claims considered allowable by the opposition division. The following amendments have been introduced into claim 1:

"1. A Repulsive Guidance Molecule a (RGMa) inhibiting substance as an active ingredient for use in the prophylaxis or treatment of an autoimmune disease ~~such~~

~~as~~ selected from the group of cellular autoimmune disease, rheumatism, multiple sclerosis, nervous system autoimmune diseases ~~such as~~ selected from the group of Guillain-Barré syndrome~~,~~ and neuro-Behcet's diseases, malignant anemia, type I diabetes, systemic lupus erythematosus (SLE), inflammatory bowel diseases (IBD), Sjogren's syndrome, atopic dermatitis, Goodpasture's syndrome, Grave' diseases [sic], autoimmune hemolytic anemia, autoimmune thrombocytopenic purpura, glomerulonephritis, myasthenia gravis~~,~~ and Hashimoto's diseases, wherein the RGMa inhibiting substance inhibits activation of T cells."

In **auxiliary request 3** claim 1 has been further amended by introducing the features of granted claim 2:

"1. ... (as for AR2)
wherein the RGMa inhibiting substance inhibits activation of T cells, wherein the RGMa inhibiting substance is an anti-RGMa neutralizing antibody."

Auxiliary request 4 contains only one claim, which differs from claim 1 of the main request in that the following amendments have been introduced:

"1. A Repulsive Guidance Molecule a (RGMa) inhibiting substance as an active ingredient for use in the prophylaxis or treatment of ~~an autoimmune disease such as cellular autoimmune disease, rheumatism,~~ multiple sclerosis, ~~nervous system autoimmune diseases such as Guillain-Barré syndrome, neuro-Behcet's diseases, malignant anemia,type I diabetes, systemic lupus erythematosus (SLE), inflammatory bowel diseases (IBD), Sjogren's syndrome, atopic dermatitis, Goodpasture's syndrome, Grave' diseases, autoimmune hemolytic anemia, autoimmune thrombocytopenic purpura,~~

~~glomerulonephritis, myasthenia gravis, Hashimoto's diseases~~ wherein the RGMa inhibiting substance inhibits activation of T cells, and wherein the RGMa inhibiting substance is an anti-RGMa neutralizing antibody."

Auxiliary request 5 differs from auxiliary request 4 in that the claim is restricted to recurrent multiple sclerosis.

Auxiliary request 6 differs from auxiliary request 5 in that the claim has been amended by introduction of the following features:

"1. ... (as AR5)
is an anti-RGMa neutralizing antibody and wherein RGM is expressed in bone marrow-derived dendritic cells (BMDCs) and RGM receptor is expressed on $CD4^+$ T cell and CD11 b^+ macrophage, and wherein Rap1 is activated when RGM binds to RGMa receptor on $CD4^+$ T cell and CD11 b^+ macrophage.

In **auxiliary request 7** the following amendments have been introduced into claim 1 of auxiliary request 3:

"1. ... (as for AR3)
wherein the RGMa inhibiting substance inhibits activation of T cells as compared to the absence of the RGMa inhibiting substance, and wherein said inhibition of activation of T-cells is measured by measuring the levels of IFN-γ, IL-2, and/or IL-17 in the presence of the RGMa inhibiting substance as compared to the absence of the RGMa inhibiting substance, and wherein a reduction of said levels is indicative of an inhibition of the activation of T-cells, and wherein the RGMa inhibiting substance is an anti-RGMa neutralizing antibody."

IX. Oral proceedings before the board took place by videoconference. At the end of the oral proceedings the chairman announced the board's decision.

X. The submissions of the appellant-patent proprietor, in so far as relevant to the present decision, may be summarised as follows:

The application as filed disclosed RGM inhibiting substances in general and specified that there were three RGM subtypes (paragraph [0002]), so at the most there was a shortlist of three possibilities from which to choose. Moreover, there was a clear pointer to RGMa, e.g. in paragraphs [0010], [0013] (which specifically referred to human and rat RGMa) and [0016], while there was no singling-out of the other subtypes. Paragraph [0010] referred to the RGMa receptor: it was irrelevant whether RGMa and RGMb bound to the same receptor or not, and there was no evidence that this was known in the prior art. All the examples concerned RGMa. Paragraph [0032] disclosed the expression pattern of RGMa receptor in specific T cells. Paragraph [0034] disclosed the signal transduction pathways mediated by RGMa. Examples 2 and 3 made use of RGMa neutralizing antibodies.

As to auxiliary request 3, RGMa neutralizing antibodies were used in the examples as the active ingredient in a widely accepted animal model for autoimmune disease, so the claimed subject-matter would be directly and unambiguously derivable from this teaching (e.g. paragraph [0041] in Example 2). The skilled person would immediately understand that the application was about using anti-RGMa neutralizing antibodies for the treatment of autoimmune diseases.

XI. The submissions of the appellant-opponent, in so far as relevant to the present decision, may be summarised as follows:

Claim 1 of the main request added subject-matter because, *inter alia*, there was no basis in the application as filed for an RGMa inhibiting substance in general, let alone in the context of a second medical use claim. Paragraph [0010], referring to the RGMa receptor, did not help further because other RGM molecules could bind to the RGMa receptor as well: in particular, this was the case for RGMb. Apart from the examples, RGMa was only mentioned in the application as filed in paragraphs [0002], [0013] and [0016], and these were either general references (paragraph [0002]) or specific references to given species (paragraphs [0013] and [0016]). The claimed subject-matter was an intermediate generalisation between the general disclosure of RGM inhibiting substances in the description and original claims and the specific disclosure of the examples, which included further features not in the claim. The same applied to auxiliary request 1.

As to auxiliary request 3, the limitation to RGMa neutralizing antibodies was still an intermediate generalisation. Such antibodies were only disclosed in the examples, but these were only specific antibodies such as rabbit polyclonal antibody in Example 2, paragraph [0042]. The same applied to the remaining auxiliary requests 4 to 7.

XII. The appellant-patent proprietor requested that the decision of the opposition division be set aside and that the patent be maintained as granted (main request)

or on the basis of the claims of auxiliary request 1; alternatively, it requested that the opponent's appeal be dismissed (auxiliary request 2), or that the patent be maintained on the basis of any of auxiliary requests 3 to 7, all these auxiliary requests having been filed by letter dated 21 February 2022. It moreover requested that: document D15 not be admitted or, if admitted, that the case be remitted to the department of first instance for further prosecution; that documents D13, D14 and D16 to D20 not be admitted; and that documents newly cited by the opponent, in particular D23, D27 and D28, not be admitted.

XIII. The appellant-opponent requested that the decision be set aside and the patent revoked in its entirety, and that documents D15 and D21 to D30 be admitted. It furthermore requested that auxiliary request 7 not be admitted.

Reasons for the Decision

1. The appeals are admissible.

2. Article 100(c) EPC - main request

2.1 Article 100(c) EPC was relied on by the opponent as a ground for opposition. In particular, the opponent argued that the subject-matter of at least granted claim 1 extended beyond the content of the application as filed.

2.2 Claim 1 of the main request is a purpose-limited product claim, wherein the product (active ingredient)

to be used in therapy is a Repulsive Guidance Molecule a (RGMa) inhibiting substance.

2.3 Throughout the application as filed, reference is made to RGM inhibiting substances but not to RGMa inhibiting substances. It is common ground that RGM and RGMa are not synonymous, RGMa being one of three RGM subtypes, as explained in paragraph [0002] of the application as filed. As a basis for the active ingredient being an RGMa inhibiting substance, the patent proprietor cited paragraphs [0010], [0012] to [0016], [0020], [0024], figures and examples. The patent proprietor moreover argued that, even if a selection had to be made, this was only a selection from a shortlist of three (RGMa, RGMb and RGMc) and that this particular RGM subtype was singled out in the application as filed (e.g. examples) while the other two were not.

2.4 The disclosure in paragraph [0010] specifically concerns an anti-RGM (not RGMa) neutralizing antibody. The same is true for paragraphs [0013], [0014] and [0015], which also refer to an anti-RGM neutralizing antibody without even disclosing medical applications. Paragraph [0012] refers to RGM inhibiting substance (not necessarily RGMa inhibiting substance) and does not teach the medical uses. Paragraph [0016], on the other hand, refers to "Examples of the substance that inhibits expression of RGM", which is more specific than "RGM inhibiting substance" (and not necessarily RGMa inhibiting substance), and again does not disclose the medical uses. Paragraph [0020] refers to a pharmaceutical composition of the invention being "formulated by blending an RGM inhibiting substance as an active ingredient and a pharmaceutically acceptable carrier or an additive as appropriate": again, it does not refer to RGMa specifically and does not disclose

the medical uses. The same is also true of paragraph [0024], directed to screening methods. Examples 2 and 4 disclose the effect of an anti-RGMa neutralizing antibody in a multiple sclerosis mouse model, experimental autoimmune encephalomyelitis "EAE" (Example 2) and in a recurrent multiple sclerosis mouse model (Example 4). Example 3 shows that "the administration of anti-RGMa neutralizing antibody to EAE mouse remarkably attenuates antigen-specific and non-specific T cell activations in EAE mouse" (last sentence of paragraph [0050]).

2.5 The board considers that none of the passages cited above can provide a basis for the subject-matter of claim 1.

2.6 It might have been obvious to the skilled person to conclude that RGMa inhibiting substances could be suitable for the medical uses claimed. However, Article 123(2) EPC, as interpreted in the established case law of the board of appeal, requires that the subject-matter be directly and unambiguously disclosed, and not only made obvious, by the application as filed. This is not so in the present case.

2.7 Contrary to the arguments of the appellant-patent proprietor, it is not a case of selecting RGMa from among a shortlist of three, but rather an intermediate generalisation between the general disclosure of RGM inhibiting substances and the specific disclosure of specific RGMa neutralizing antibodies (Examples). There is no passage in the application as filed teaching that the RGM inhibiting substances are to be chosen from among RGMa, RGMb or RGMc inhibiting substances: instead, paragraph [0002] refers to the three RGM subtypes but without teaching that there are also three

different types of RGM inhibiting substances. Likewise, paragraphs [0010] and [0013] refer to RGMa but not to RGMa inhibiting substances.

2.8 The board also disagrees that there is a clear pointer to RGMa inhibiting substances in general. Instead, there is disclosure of specific RGMa neutralizing antibodies as examples for RGM inhibiting substances. Further references to RGMa in the application as filed are either part of the general disclosure and merely review the background knowledge (paragraphs [0010], [0013] and [0016]), or describe RGMa expression patterns and signal transduction pathways (paragraphs [0032] and [0034]): these passages might provide an incentive to further investigate RGMa inhibiting substances, but do not constitute an individualised disclosure of such substances.

2.9 Claim 1 of the main request is thus considered to add subject-matter. Accordingly, the ground of opposition under Article 100(c) EPC prejudices maintenance of the patent as granted.

3. Auxiliary requests

Admission of auxiliary request 7

3.1 Auxiliary request 7 was filed as auxiliary request 15A with the patent proprietor's reply to the opponent's grounds of appeal, and the opponent objected to its admission. The board decided to exercise its discretion under Article 12(4) RPBA not to exclude auxiliary request 7 from the proceedings. However, in view of the outcome of the appeal, the board does not find it necessary to provide reasons for this part of the decision.

Article 123(2) EPC

3.2 In claim 1 of auxiliary request 1, the active ingredient to be used for therapy is still defined as RGMa inhibiting substance, just as in claim 1 of the main request. Hence, for the same reasons as for the main request, auxiliary request 1 adds subject-matter, contrary to Article 123(2) EPC.

3.3 In claim 1 of auxiliary request 2, the RGMa inhibiting substance is further defined by the functional feature "wherein the RGMa inhibiting substance inhibits activation of T cells". The board considers that this amendment does not overcome the objection discussed above for the main request since the active ingredient is still an RGMa inhibiting substance. Hence auxiliary request 2 is also considered to contravene Article 123(2) EPC.

3.4 Claim 1 of auxiliary request 3 further defines the product to be used in therapy as being an anti-RGMa neutralizing antibody. As a basis for this feature, the patent proprietor referred to the Examples.

The board notes that the application as filed either refers to anti-RGM (not RGMa) neutralizing antibodies in general (see above, sections 2.3 and 2.4) or to specific RGMa neutralizing antibodies which are used in the very specific context of the Examples. There is thus no disclosure in the application as filed of anti-RGMa neutralizing antibodies in general. Hence auxiliary request 3 does not comply with Article 123(2) EPC either.

3.5 The same applies to auxiliary requests 4 to 7, which are all directed to RGMa neutralizing antibodies. Hence auxiliary requests 4 to 7 do not comply with Article 123(2) EPC either.

Order

For these reasons it is decided that:

1. The appealed decision is set aside.

2. The patent is revoked.

The Registrar: The Chairman:

M. Schalow A. Lindner

Decision electronically authenticated