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Datasheet for the decision of 23 July 2007

Case Number: W 0013/07 - 3.3.04

Application Number: PCT/EP 2006/007661

Publication Number: WO 2007/014772

IPC: A61K 39/395

Language of the proceedings: EN

Title of invention:
Direct and indirect effector cell protease receptor-1 (EPR-1) inhibitors as antiplatelet agents.

Applicant:
Thrombotargets Europe, S.L.

Headword:
EPR-1 effectors/THROMBOTARGETS

Relevant legal provisions:
EPC Art. 17(3)(a)
PCT R. 13.1, 13.2

Keyword:
"Unity of invention (yes)"
"Refund of additional search fees (yes)"
"Refund of protest fee (yes)"

Decisions cited:
G 0001/89

Catchword:
-

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Case Number: W 0013/07 - 3.3.04

International Application No. PCT/EP 2006/007661

D E C I S I O N
of the Technical Board of Appeal
of 23 July 2007

Appellant: Thrombotargets Europe, S.L.
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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 15 November 2006.**

Composition of the Board:

Chair: U. Kinkeldey
Members: B. Claes
T. Bokor

Summary of Facts and Submissions

I. International patent application No. PCT/EP 2006/007661 having the title "Direct and indirect effector cell protease receptor-1 (EPR-1) inhibitors as antiplatelet agents" was filed with 38 claims.

Independent claims 1, 30 and 34 read:

"1. Use of an effector cell protease receptor-1 (EPR-1) effector for the manufacture of an antiplatelet pharmaceutical composition."

"30. A method for forming a non-thrombogenic coating in the surface of a medical device for surgical operations which comprises contacting the surface of said medical device with an effector cell protease receptor-1 (EPR-1) inhibitor or antagonist."

"34. A method for treating a condition associated with platelet activation and/or platelet aggregation, or a thrombus or embolus mediated disease, which comprises administering to a subject in need of said treatment a therapeutically effective amount of an effector cell protease receptor-1 (EPR-1) inhibitor or antagonist."

Claims 2 to 29 were directly or indirectly dependent on claim 1, claims 31 to 33 were directly or indirectly dependent on claim 30, whereas claims 35 to 38 were directly or indirectly dependent on claim 34.

Dependent claims 3 and 4 read:

"3. Use according to claim 1, wherein said EPR-1 effector is selected from a direct EPR-1 effector and an indirect EPR-1 indirect effector."

"4. Use according to claim 3, wherein said indirect EPR-1 effector is selected from an effector of an EPR-1 ligand and an effector of a stimulator of an EPR-1 ligand."

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 two additional search fees, i.e. a sum of 3.230 Euros, in accordance with Article 17(3)(a) PCT and Rule 40.1 PCT.

III. The invitation to pay additional search fees identified and defined the following (groups of) inventions:

1. claims: 1, 2, 6-26, 29, 34-38 complete and claim 3 partially;

   Use of an effector cell protease receptor-1 (EPR-1) effector for the manufacture of an antiplatelet pharmaceutical composition.

2. Claims: 4, 5, 27, 28 complete and claim 3 partially;

   Use of an indirect EPR-1 effector for the manufacture of an antiplatelet pharmaceutical composition.

3. Claims: 30 to 33;

A method of forming a non-thrombogenic coating on the surface of a medical device for surgical operations using an EPR-1 inhibitor or antagonist.

The reasons for finding lack of unity of invention were that "[t]*he problem underlying the present application is the provision of an effector cell protease receptor-1 (EPR—1)* [sic] *for the manufacture of an antiplatelet pharmaceutical composition.*

The inventions identified above are different solutions to this problem, their general common concept being the provision of EPR—1 effectors acting on EPR—1, where EPR—1 effectors act directly on EPR—1 or act indirectly on EPR—1 for use as pharmaceutical compositions (inventions I and II) and for medical devices (invention III).

The document of Bouchard et al., 1997 (JBC, 272(14): 9244—9251) discloses a direct EPR—1 effector, i.e. an EPR—1 inhibitor or antagonist which is an antibody that exhibits a specific binding activity for EPR—1 (see abstract, page 9248, right—hand column, paragraph 1 to page 9294, right—hand column, last paragraph, fig.5, page 9250, right—hand column, paragraph 2, table 1). This antibody, named B6, is a monoclonal antibody that exhibits a specific binding activity for EPR—1: the antibody compites [sic] *with a platelet bound factor Va/factor Xa complex and its binding is inhibited by this complex to a 50% suggesting that the antibody and the complex share a common EPR—1 epitope. The antibody*

inhibits prothrombinase catalyzed thrombin generation on activated platelets.

In view of this prior art, the above common concept is not novel anymore and thus, the problem underlying the present application can be redefined as the provision of further EPR–1 effectors for the manufacture of an antiplatelet pharmaceutical composition.

Since the general common concept is not novel, the requirement of Rule 13.1 PCT is not fulfilled, and hence, there is lack of unity. Neither the description, nor the claims revealed any further features that could be considered special in the sense of Rule 13.2 PCT. In consequence the group of inventions 1–3 are not so linked as to form a single general inventive concept as required by Art. 17(3) and Rule 13.1 PCT."

IV. The applicant paid two additional search fees under protest according to Rule 40.2(c) PCT for the searches of the further inventions and expressed its protest to the ISA's finding that the application lacked unity of invention. The applicant essentially argued that Bouchard *et al.* the did not disclose an EPR-1 effector for use as an antiplatelet agent, i.e. an agent capable of directly or indirectly blocking platelet activation and/or platelet aggregation. The general common concept of the application was therefore novel. Accordingly, the application complied with the requirement of unity of invention.

V. The protest was reviewed in accordance with Rule 40.2(e) PCT by a review panel of the ISA within the meaning of Rules 105(3) EPC and 68.3(c) PCT. The review panel

confirmed the ISA's opinion regarding lack of unity, held that the invitation to pay the additional 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 document D1 (Bouchard *et al.*) *"discloses an antibody which specifically binds EPR-1 and inhibits EPR-1 binding to factor Va/factor Xa complex on the platelet surface. Therefore, said antibody is an EPR-1 effector, namely a direct EPR-1 effector, and which is used as an antiplatelet agent as defined by the applicant, i.e. "...an agent capable of directly or indirectly block platelet activation and/or platelet aggregation." (see page 1, item 2 of the letter of reply). Even if the antibody is not used in purified form but as an ascites fluid, based on the teachings of Dl, the skilled person would recognize without the exercise of an inventive skill that the antibody disclosed in Dl can be used as an antiplatelet agent, and thus the common concept is not novel and not inventive. Therefore, Rule 13.1 PCT is not fulfilled."*

VI. The applicant paid the protest fee.

Reasons for the Decision

1. According to Rule 13.1 PCT, the international patent application shall relate to one invention only or to a group of inventions so linked as to form a single inventive concept. If the ISA considers that the claims lack unity of invention, it is empowered, under

Article 17(3)(a) PCT, to invite the applicant to pay additional fees. Having regard to decision G 1/89 of the Enlarged Board of Appeal (OJ EPO 1991, 155), the ISA is empowered to raise a non-unity objection "*a posteriori*", i.e. after having taken the prior art into closer consideration (see also PCT Search Guidelines, Chapter VII, 9).

2. According to Rule 13.2 PCT, the requirement of unity of invention shall be fulfilled only when there is a technical relationship among those inventions involving one or more of the same or corresponding special technical features. The expression "special technical features" shall mean those technical features that define a contribution which each of the claimed inventions, considered as a whole, makes over the prior art.

3. The question to be decided by the board in the present protest procedure is therefore whether or not the subject-matter of those inventions defined by the ISA and for which additional search fees have been paid by the applicant, i.e. inventions 2 and 3 as listed by the ISA (see section III above), is part of a general concept which is common to the subject-matter of the invention identified as first mentioned in the claims, i.e. in the present case invention 1.

4. It can be taken from the description of the application that haemostasis involves two different processes, i.e. *primary haemostasis*, characterised by the occurrence of vasoconstriction at the vascular lesion site and platelet aggregate formation; and *secondary haemostasis*, in which the fibrin cloth is formed due to the action

of the different coagulation cascade proteolytic proteins. Platelet aggregate formation plays a key role in haemostasis in capillaries, being particularly relevant in mucocutaneous haemorrhaging; in contrast, fibrin cloth formation is much more important in large vessel haemostasis, being more relevant in internal haemorrhaging (page 1, lines 12 to 22).

5. In accordance with the description the invention underlying the application relates to the treatment of platelet activation and/or platelet aggregation mediated diseases with EPR-1 effectors and to the use of such effectors in the manufacture of an antiplatelet pharmaceutical composition which can be used for the prevention and/or treatment of a condition associated with platelet aggregation (see page 10, lines 26 to 29 and page 12, line 2 to 5).

6. Invention 1, as defined in independent claim 1, is directed to the use of an EPR-1 effector for the manufacture of an antiplatelet pharmaceutical composition. Invention 2, as defined in the second alternative of dependent claim 3, specifies an indirect EPR-1 effector for the same use as the effector of invention 1. Invention 3, as defined in independent claim 30, is directed to a method of forming a non-thrombogenic coating on the surface of a medical device for surgical operations using an EPR-1 inhibitor or antagonist.

7. The board considers that all three defined inventions concern *a priori* a common concept, i.e. the provision of an EPR-1 effector, being a direct or indirect effector, for use as an antiplatelet agent effecting

platelet activation and/or aggregation. These agents can be used for the treatment of conditions associated with **primary hemostasis**, i.e. before the fibrin cloth is formed and even before platelet aggregation takes place.

8. An *a posteriori* non-unity could arise if this concept had already been part of the prior art. In the invitation to pay additional fees, the ISA has argued that the application lacked unity of invention, because the common concept, which was seen in "the provision of EPR-1 effectors acting on EPR-1" was considered not novel in view of Bouchard *et al.* (1997, J. Biol. Chem., Vol. 272, No. 14, pp. 9244-9251, D1) which disclosed a "direct" EPR-1 effector, i.e. a monoclonal antibody that exhibited a specific binding activity for EPR-1.

9. Document D1 discloses an EPR-1 effector which is an antibody, i.e. monoclonal antibody B6 with a specific binding activity for EPR-1. The antibody is reported to inhibit prothrombinase catalysed thrombin generation on activated platelets and it is disclosed that both EPR-1 and membrane bound factor Va are required to mediate factor FXa binding to the activated platelet to form a functional prothrombinase complex. The document therefore refers to the B6 antibody as an EPR-1 effector which is an inhibitor of the formation of the fibrin cloth during the **secondary haemostasis** and thus involving the assembly of a functional prothrombinase complex at the site of platelet aggregation. Accordingly, D1 does not disclose the common concept as defined by the board above, i.e. the provision of an EPR-1 effector for use as an antiplatelet agent effecting platelet activation and/or aggregation.

Consequently, contrary to the finding of the ISA there is a common concept to which all three defined inventions relate and which is novel.

9.1 Unity of invention can furthermore be at stake if the claimed subject-matter does not involve an inventive step because this equally may take away an *a priori* present common concept. According to decision G 1/89 (*supra*), restraint should however be exercised in the assessment of novelty and inventive step and in borderline cases it should be refrained from considering an application as not complying with the requirement of unity of invention on the ground of lack of novelty or inventive step.

In the present case, the assessment of an inventive step of the claimed subject-matter over document D1 (as partially conducted by the review panel; see section V above) would involve complex considerations, which, in order to give the applicant fair treatment, would require to provide the applicant with the right to be heard. The present case is therefore not a case in which an assessment of inventive step should be made in the context of unity of invention.

10. In view of the above considerations therefore and having regard to Rule 13.2 PCT, the board considers that there is a technical relationship among the claimed subject-matter of inventions 1, 2 and 3 as defined by the ISA involving at least one of the same "special technical features".

11. Consequently, the application is considered to comply with the requirement of unity of invention under Rule 13.1 PCT.

Order

For these reasons it is decided that:

1. The two additional search fees are reimbursed.

2. The protest fee is reimbursed.

The Registrar: The Chair:

P. Cremona U. Kinkeldey