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Datasheet for the decision of 20 August 2013

Case Number: T 2466/09 - 3.3.01

Application Number: 00983997.8

Publication Number: 1246839

IPC: C07K 11/00, C07K 5/10, A61K 38/15

Language of the proceedings: EN

Title of invention:
Depsipeptide and congeners thereof for use as immunosuppressants

Patent Proprietor:
Cyclacel Pharmaceuticals, Inc.

Headword:
Depsipeptide as immunosuppressant/ CYCLACEL

Relevant legal provisions:
EPC Art. 123(2), 111(1)
RPBA Art. 13(1)

Keyword:
"Main request: added matter (yes)"
"Auxiliary request 1: admissibility (no)"
"Auxiliary request 2: remittal"

Decisions cited:
-

Catchword:
-

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Case Number: T 2466/09 - 3.3.01

D E C I S I O N
of the Technical Board of Appeal 3.3.01
of 20 August 2013

Appellant: (Patent Proprietor)
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Decision under appeal: **Decision of the Opposition Division of the European Patent Office posted 22 October 2009 revoking European patent No. 1246839 pursuant to Article 101(3)(b) EPC.**

Composition of the Board:

Chairman: A. Lindner
Members: L. Seymour
C.-P. Brandt

Summary of Facts and Submissions

I. European patent No. 1 246 839, filed as application number 00 983 997.8, based on the international application published as WO 01/42282, was granted on the basis seventy-nine claims, forty-one of which were independent. Claims 52 and 74 to 76 as granted read as follows:

"52. Use of FR901228 for the manufacture of a medicament for inducing anergy or apoptosis in activated T-cells while maintaining overall T-cell counts.

...

74. Use of FR901228 for the manufacture of a medicament for treating a condition in an animal, the treatment of which is affected or facilitated by reduction of lymphocyte proliferation and/or activation.

75. Use of FR901228 for the manufacture of a medicament for preventing or treating inflammatory diseases.

76. Use of FR901228 for the manufacture of a medicament for treating a hyperproliferative skin disease."

II. An opposition was filed and revocation of the patent in its entirety requested pursuant to Articles 100(b) and 100(a) EPC (lack of novelty and inventive step).

III. The appeal lies from the decision of the opposition division, based on a single request filed with letter of 1 November 2005, revoking the patent under Article 101(3)(b) EPC, for contravention of Article 123(2),(3) EPC.

IV. The appellant (patentee) lodged an appeal against this decision. With the statement of grounds of appeal, the appellant filed a main request and five auxiliary requests.

V. Following the reply of the then respondent of 29 July 2010, the appellant filed, with letter of 5 November 2010, a further set of requests, consisting of a main request and five auxiliary requests, to replace those previously on file.

VI. A communication by the board, dated 23 May 2013, was sent as annex to the summons for oral proceedings. Attention was drawn to a number of formal matters that gave rise to concern.

VII. With letter of 27 June 2013, the then respondent (opponent) withdrew its opposition.

VIII. With letter of 17 July 2013, the appellant filed a main request and two auxiliary requests to replace those previously on file.

The main request consists of four claims (cf. above point I for claims 52 and 74 to 76 as granted):

Claim 1 differs from claim 52 as granted only in the deletion of the option "anergy".

The following marked-up version of claim 2 (emphasis and deletions added by the board) highlights the amendments to claim 74 as granted:

"2. Use of FR901228 for the manufacture of a medicament for treating a condition in an animal, the treatment of which is affected or facilitated by reduction of **T-**lymphocyte ~~proliferation and/or~~ activation **and inhibition of immune function; and wherein the condition is selected from an inflammatory disease or an hyperproliferative skin disease.**"

Claim 3 is identical to claim 75 as granted.

Claim 4 differs from claim 76 as granted in the addition of the following feature highlighted in bold (emphasis added):

"4. Use of FR901228 for the manufacture of a medicament for treating a hyperproliferative skin disease **by inducing apoptosis in activated T-cells.**"

Claims 1 to 4 of auxiliary request 1 are identical to claims 52 and 74 to 76 as granted (cf. above point I), respectively, apart from the deletion of "anergy or" in claim 52 (now claim 1) and "proliferation and/or" in claim 74 (now claim 2).

Auxiliary request 2 consists of two claims which are identical to claims 1 and 3 of both the main request and auxiliary request 1.

IX. Oral proceedings were held before the board on 20 August 2013.

X. The appellant's arguments, insofar as they are relevant to the present decision, may be summarised as follows:

As regards the basis in the application as originally filed for subject-matter of claim 2 of the main request (Article 123(2) EPC), the appellant submitted that FR901228 was individualised as the preferred compound throughout the application as originally filed.

In addition, the appellant pointed, in particular, to page 19, lines 22 to 25, as disclosing that a compound of structure (I) was provided to treat a condition, "the treatment of which is affected or facilitated by reduction of lymphocyte proliferation and/or activation". This closely reflected the language used in the first part of claim 2.

The amendment of "lymphocyte" to "T-lymphocyte" in claim 2 could, for example, be derived from the reference on page 19, line 24, to the "downregulation of CD25 and/or CD154", which were known to be typical markers of activated T-cells (see e.g. page 21, line 35). Moreover, it was derivable from the application as originally filed as a whole, such as the passage on page 22, lines 7 to 9, that T-lymphocyte activation was a crucial feature of the methods disclosed. Similarly, there was repeated reference to reduction of IL-2 secretion (page 5, lines 21, 22; page 20, lines 12 to 15), the production of which was a key hallmark of T-cell activation (page 22, lines 14, 15).

Concerning the second part of claim 2, the appellant referred to page 19 of the application as originally filed. On page 19, lines 28 to 30, "inhibition of immune function" was specifically disclosed, in combination with conditions such as inflammation or

"any of a number of indications such as those herein described, that are immunologically induced" (page 19, lines 29, 30). Such conditions clearly included "inflammatory diseases" and "hyperproliferative skin diseases" as disclosed on page 19, line 12.

With respect to the subject-matter of claim 4 of the main request, the appellant submitted that this also complied with Article 123(2) EPC. Examples of "hyperproliferative skin disease", such as psoriasis, were disclosed throughout the application as originally filed in the context of immune-related diseases (e.g. page 18, line 20; page 23, line 27; page 24, lines 6). Moreover, the emphasis throughout the application as originally filed was on the use of FR901228 as an immunosuppressant. In this context, the role of FR901228 in "inducing apoptosis in activated T-cells" was also disclosed (e.g. page 20, lines 19 to 22). The skilled person would thus clearly recognise the functional relationship between the combination of features recited in claim 4.

Turning to the issue of admissibility of auxiliary request 1, the appellant argued that the amendments in claims 2 and 4 had been introduced in response to objections raised under Article 123(2) EPC by the then respondent in its letter of 29 July 2010 and by the board in its communication of 23 May 2013, and clearly overcame those objections. Moreover, the amendments were of low complexity, since the wording of claims 2 and 4 of auxiliary request 1 corresponded to claims as granted. In addition, the appellant argued, with reference to the criteria appearing in Article 13(1) of the Rules of Procedure of the Boards of Appeal (RPBA,

see Supplement to OJ EPO 1/2013, 38 to 49), that the complexity of the requests had been significantly reduced with respect to those previously on file, owing to the reduction in the number of independent claims, and that overall procedural economy had been furthered as a result.

XI. The appellant (patent proprietor) requested that the decision under appeal be set aside and that the case be remitted to the first instance for further prosecution on the basis of the main request, or alternatively on the basis of auxiliary requests 1 or 2, all filed with letter dated 17 July 2013.

XII. At the end of the oral proceedings, the decision of the board was announced.

Reasons for the Decision

1. The appeal is admissible.

2. *Main request - Admissibility*

The main request, filed with letter of 17 July 2013, is identical to auxiliary request 5 filed with letter of 5 November 2010. This request is considered to be admissible, since the amendments can be considered to have been introduced by the appellant in reaction to arguments presented by the then respondent with letter of 29 July 2010 (cf. explanation of appellant provided in letter of 17 July 2013, point 2.1.1).

3. *Main request - Article 123(2) EPC*

3.1 The main request consists of four independent claims drafted as second (further) medical use claims in the Swiss-type form, and relating to the use of a single compound, namely, FR901228.

As detailed in above point VIII, claims 1 and 3 of the main request correspond to claims 52 and 75 as granted, and are therefore not open to objection under Article 123(2) EPC.

In contrast, a number of amendments to the definition of the conditions to be treated have been introduced into claims 2 and 4 of the main request with respect to claims 74 and 76 as granted (cf. above point VIII). The question that therefore has to be decided here is whether a direct and unambiguous basis can be found in the application as originally filed for the combination of features now claimed in these claims.

3.2 In this context it is noted that the known depsipeptide FR901228, which is the drug recited in both claims 2 and 4, is the only compound specifically named throughout the application as originally filed, and is clearly to be viewed as being preferred (cf. e.g. page 7, line 12 to page 9, line 1).

3.3 Concerning the conditions to be treated as defined in claims 2 and 4, it is noted that "hyperproliferative skin disease" appears in both these claims.

In the application as originally filed, the compounds of the invention are generally disclosed as having

immunosuppressant activity, for example, on page 1, lines 4 to 8. An extensive list of more specific medical uses is provided on page 18, lines 9 to 31. This is followed by a further list on page 19, lines 11 to 21, the first lines of which read as follows (emphasis added):

"**Further uses** may include the treatment and/or prophylaxis of: inflammatory and **hyperproliferative skin diseases** and cutaneous manifestations of immunologically mediated illnesses...".

The board wishes to emphasise that this is the only disclosure of the term "hyperproliferative skin disease(s)" in the application as originally filed.

3.4 Claim 2, in addition to defining "hyperproliferative skin disease" as one of the conditions to be treated, includes the further functional definition that the condition is one "the treatment of which is affected or facilitated by reduction of T-lymphocyte activation and inhibition of immune function".

The corresponding paragraph on page 19, lines 22 to 31, of the application as originally filed reads as follows (emphasis added by the board):

"In one embodiment, a method of **treating a condition in an animal, the treatment of which is affected or facilitated by reduction of lymphocyte** proliferation and/or **activation** (*e.g.*, downregulation of CD25 and/or CD154) comprising the administration of an effective amount of a compound of structure (I) is provided. The method of treating a condition in an animal, the

treatment of which is facilitated by inhibition of lymphocyte proliferation and/or inhibition of activation markers (*e.g.*, CD25 and CD154), **and inhibition of immune function**, **wherein the condition** may be autoimmunity, inflammation, graft/tissue rejection, or **includes** any of a number of indications such as **those herein described**, that are immunologically induced or exacerbated is provided."

This paragraph was referred to by the appellant as providing the basis for the combination of features in claim 2. However, as can be seen from the passages highlighted above in bold, in order to arrive at the subject-matter of claim 2, it is necessary to select and modify elements from the first sentence of this paragraph (i.e. choice of "activation" over "proliferation", and replacement of "lymphocyte" by "T-lymphocyte"), combine these with certain elements of the second sentence appearing in a different context, and further select a specific use from the list in the previous paragraph (i.e. "hyperproliferative skin disease"). This amounts to an unallowable combination of features to create an embodiment, which is not unambiguously disclosed in the application as originally filed.

3.5 In claim 4, the treatment of the condition "hyperproliferative skin disease" is defined as being achieved "by inducing apoptosis in activated T-cells".

The appellant argued that the basis for the expression "inducing apoptosis in activated T-cells" was to be found in various passages of the application as originally filed. However, the board notes that the

context in which it appears is more specific than that disclosed in claim 4. For example, the sentence referred to by the appellant on page 20, lines 19 to 22, reads as follows (emphasis added):

"Further, treatment of previously **activated** CD4 and CD8 **T-cells** with compounds of the class of FR901228, ..., inhibits their growth and **induces apoptosis** within a short time, while leaving resting T-cells apparently unaffected."

Moreover, this sentence is embedded within an extensive discussion detailing the numerous mechanisms of action of FR901228 that may be playing a role in its immunosuppressant activity (see page 20, line 9 to page 22, line 9).

Therefore, in order to arrive at the subject-matter claimed in claim 4, the appellant has selected and generalised a single aspect of this complex pathway and combined it with a specific disease appearing in a list in a different context elsewhere in the application as originally filed.

3.6 The argument of the appellant that the skilled person would clearly recognise the functional relationship between the combination of features recited in claims 2 and 4 is not considered to be convincing.

As detailed above, the immune response is described in the application as originally filed as being highly complex, with multiple points at which FR901228 may be intervening. It cannot therefore be accepted that the skilled person would directly and unambiguously extract

from the application as originally filed as a whole the information that a particular mechanistic aspect was to be viewed as being determinant in defining a subclass of a specific disease disclosed elsewhere in the specification.

In particular, it is to be noted that claims 2 and 4 define the condition "hyperproliferative skin disease" with further reference to different functional features, as distinct embodiments in independent claims. In the absence of any specific pointers to these combinations, it is not considered to be allowable under Article 123(2) EPC to take the application as originally filed as a reservoir from which any number of distinct therapeutic uses may be created.

3.7 Hence, the subject-matter of claims 2 and 4 according to the main request contravenes the requirements of Article 123(2) EPC.

4. *Auxiliary request 1 - Admissibility*

4.1 In auxiliary request 1, independent claim 2 of the main request has been amended so as to relate to one of the alternatives of independent claim 74 as granted, and claim 4 of the main request has been amended to be identical to claim 76 as granted (cf. above points I and VIII). This request was filed by the appellant around one month prior to oral proceedings before the board. It constitutes a change to the appellant's case at a very late stage of the proceedings, and its admissibility is therefore to be assessed in view of Article 13 RPBA. According to Article 13(1) RPBA, the board's discretion in this respect shall be exercised

in view of *inter alia* the complexity of the new subject-matter submitted, the current state of the proceedings and the need for procedural economy.

In the present case, the then opponent sought revocation of the patent in suit pursuant to Articles 100(b) and 100(a) EPC (lack of novelty and inventive step). With its response of 1 November 2005, the patentee filed a single request in which additional features had been introduced into claims 74 and 76 as granted; these claims were renumbered as claims 67 and 69, respectively. This request formed the basis for the decision under appeal (cf. above point III).

With the statement of grounds of appeal, as its main request, the appellant re-filed the request that it had defended before the opposition division; in addition, five auxiliary requests were filed, in which claims corresponding to claims 67 and 69 were either present or had been deleted.

In the main request and five auxiliary requests that followed with letter of 5 November 2010, claims corresponding to said claims 67 and 69 were again either present or further modified.

Therefore, up to this point in the opposition and appeal proceedings, despite having taken advantage of numerous opportunities to amend its claims, the appellant chose not to defend claims corresponding to claims 74 and 76 as granted, but rather regarded amendment or deletion of these claims to be the appropriate course of action to overcome the objections raised.

In view of this background, a return at a very late stage in appeal proceedings to independent claims as granted, which had not been defended in the opposition or appeal proceedings thus far, can only be seen as an attempt to start the proceedings anew with respect to these claims. The admission of auxiliary request 1 would therefore run counter to the principle of procedural economy.

4.2 The appellant's arguments justifying the late filing of auxiliary request 1 are not considered to be convincing for the following reasons:

The filing of this request with letter of 17 July 2013 cannot be justified as being a direct response to the then respondent's letter of 29 July 2010, since the appellant had already reacted thereto by filing a main request and five auxiliary requests with letter of 5 November 2010. Moreover, as outlined above, the subject-matter of the newly filed claims in question diverged from that of the corresponding claims previously submitted. Their filing cannot therefore be seen as a timely or appropriate reaction to said letter of the then respondent.

The appellant further argued that this request had been filed in reaction to the board's communication of 23 May 2013. However, in point 5.1 of said communication, which related to the issue of Article 123(2) EPC, the board based its analysis on the objections raised by the then respondent in it letter of 29 July 2010. Therefore, since the corresponding arguments had long been known to the appellant, the

communication of the board cannot be taken as a justification for submitting said request at such a late stage in the proceedings.

Finally, the argument with respect to the low complexity of the wording of claims 2 and 4 is not considered to be persuasive. As explained above, admitting these claims would have meant a return to the point of departure of the proceedings. Moreover, if the board were to accept the appellant's argument relating to the significant reduction in the number of independent claims, this would be tantamount to condoning the filing of requests containing an excessive number of independent claims, which could later be deleted in order to boost the chances of admittance. This could hardly be seen as being in the interest of an efficient conduct of proceedings.

4.3 Consequently, the board decided to exercise its discretion under Article 13(1) RPBA not to admit auxiliary request 1 into the appeal proceedings.

5. *Auxiliary request 2 - Remittal*

The claims of this request correspond to claims that have been maintained throughout the opposition and appeal proceedings. They were not objected to under Article 123 EPC, which was the ground for revocation in the decision under appeal (see above point III). Although the opposition division did indicate its opinion on certain additional objections in a section entitled "Further Observations", this did not form part of the decision under appeal.

Consequently, the opposition division has not yet taken a decision on the claims of auxiliary request 2 with respect to the grounds of opposition raised pursuant to Articles 100(b) and 100(a) EPC (see above point II).

Under these circumstances, the board finds it appropriate to exercise its discretion under Article 111(1) EPC to remit the case to the first instance for further prosecution, as requested by the appellant (see above point XI).

Order

For these reasons it is decided that:

1. The decision under appeal is set aside.

2. The case is remitted to the first instance for further prosecution on the basis of the second auxiliary request, filed with letter dated 17 July 2013.

The Registrar: The Chairman:

M. Schalow A. Lindner