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**Datasheet for the decision
of 18 December 2014**

Case Number: T 0821/09 - 3.3.08
Application Number: 00976188.3
Publication Number: 1230375
IPC: C12N15/63
Language of the proceedings: EN

Title of invention:
Inhibiting gene expression with dsRNA

Patent Proprietor:
Cancer Research Technology Limited

Opponents:
Sanofi-Aventis Deutschland GmbH
Quark Biotech, Inc.
Sirna Therapeutics
Nucleonics, Inc.
Silence Therapeutics AG
Glaxo Group Limited

Headword:
Medical use of dsRNA/CANCER RESEARCH TECHNOLOGY

Relevant legal provisions:
EPC Art. 54(2), 54(3), 83, 84, 111, 123(2), 123(3)
RPBA Art. 12(4), 13

Keyword:
"New main request and first auxiliary request - not admitted
Second auxiliary request - admitted
Compliance with Articles 123(2)(3), 84 and 83 - (yes)
Novelty - (yes)
Remittal - (yes)"

Decisions cited:

T 0524/01

Catchword:



**Beschwerdekammern
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Case Number: T 0821/09 - 3.3.08

**D E C I S I O N
of Technical Board of Appeal 3.3.08
of 18 December 2014**

Appellant: Cancer Research Technology Limited
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Decision under appeal: Decision of the Opposition Division of the
European Patent Office posted on 30 January 2009
revoking European patent No. 1230375 pursuant to
Article 101(3) (b) EPC.

Composition of the Board:

Chairman M. Wieser
Members: M. R. Vega Laso
J. Geschwind

Summary of Facts and Submissions

- I. European patent No. 1 230 375 with the title "Inhibiting gene expression with dsRNA" was granted on European patent application No. 00976188.3, which was filed on 17 November 2000 as international application PCT/GB00/04404 claiming the priority of a previous application in Great Britain (19 November 1999). The application was published as WO 01/36646 (in the following "the application as filed"). The patent was granted with 35 claims.

- II. Six oppositions to the grant of the patent were filed based on the grounds for opposition under Article 100(a) in conjunction with Articles 52(4), 53(a), 54(1), 54(3) and 56; Article 100(b) and (c) EPC. The opposition by opponent 06 was deemed not filed, and opponent 02 withdrew its opposition by letter dated 13 May 2008

- III. By a decision of an opposition division of the European Patent Office under Article 101(3)(b) EPC posted on 30 January 2009, the patent was revoked. In the decision, the opposition division held that none of the requests then on file (main request and first to seventh auxiliary request) met the requirements of the EPC.

As regards the sixth auxiliary request then on file, the opposition division found that the amendments introduced into the claims did not offend against Article 123(2)(3) EPC (see section 10.1.1 of the decision under appeal), the amended claims met the requirements of Article 84 EPC and the claimed invention was sufficiently disclosed in the patent (Article 100(b) EPC) (see sections 10.1.2 and 10.2 of

the decision under appeal). Moreover, it was found that the content of documents (2), (5) and (8) (see section XIII below), which constituted prior art under Article 54(3)(4) EPC 1973, did not anticipate the claimed subject-matter because none of these documents described the inhibition of gene expression either in embryonic stem cells or oocytes (see section 10.4 of the decision under appeal). However, the opposition division considered that, among the various documents constituting prior art under Article 54(1)(2) EPC 1973 cited by the opponents, documents (11) and (12) (see section XIII below) prejudiced the novelty of the subject-matter of claim 6 and claims 1 to 6 and 18, respectively (see section 10.5 of the decision under appeal).

- IV. By letter dated 19 February 2009, opponent 04 withdrew as a party to the proceedings.
- V. The patent proprietor (appellant) lodged an appeal against the decision of the opposition division. Together with its statement of grounds of appeal, the appellant submitted additional documentary evidence and two sets of amended claims as new main and first auxiliary request, respectively, and re-filed the set of claims according to the sixth auxiliary request underlying the decision under appeal as its second auxiliary request in appeal proceedings. As a subsidiary request, the appellant requested oral proceedings.
- VI. Opponents 01, 03 and 05 replied to the statement of grounds of appeal.

- VII. By letters dated 3 June 2013 and 11 March 2014, opponents 01 and 03 withdrew their respective oppositions.
- VIII. The remaining parties were summoned to oral proceedings. In a communication under Article 15(1) of the Rules of Procedure of the Boards of Appeal (RPBA) attached to the summons, the board made some observations on procedural and substantive issues, in particular issues under Articles 123(2), 84, 83, 54 and 56 EPC. With regard to the new requests and evidence filed in appeal proceedings, the board drew attention to Article 12(4) RPBA.
- IX. By letter dated 13 November 2014, opponent 05 withdrew its opposition.
- X. In reply to the board's communication, the appellant submitted additional arguments and further evidence.
- XI. During the oral proceedings, which were held on 18 December 2014, the appellant submitted a set of amended claims that replaced the claims of the previous second auxiliary request.
- XII. Claim 1 of the **second auxiliary request** now reads:
- "1. The use of an RNA in the manufacture of a medicament for inhibiting the expression of a target gene in a mammalian cell, wherein the target gene causes or is likely to cause disease and wherein the mammalian cell is an embryonic stem cell of a non-human pre-implantation embryo, the RNA comprising a double stranded structure having a nucleotide sequence, which nucleotide sequence is 100% identical to at least a part of said target gene in said mammalian cell which

double stranded structure is at least 25 bases long, and which nucleotide sequence is derived from an endogenous template, and wherein the RNA comprises two separate complementary RNA strands."

Dependent claims 2 to 4 specify further features of the use according to claim 1.

XIII. The following documents are referred to in the present decision:

- (2): WO 00/44895, published on 3 August 2000;
- (5): WO 00/63364, published on 26 October 2000;
- (8): WO 00/44914, published on 3 August 2000;
- (11): WO 99/32619, published on 1 July 1999;
- (12): WO 99/49029, published on 30 September 1999;
- (79): R. W. Wagner and L. Sun, 19 February 1998, Nature, Vol. 391, pages 744 and 745.

XIV. The submissions made by the appellant concerning issues relevant to this decision, were essentially as follows:

*Main request and first auxiliary request -
Article 12(4) RPBA*

The sets of claims according to the main request and the first auxiliary request presented with the statement setting out the grounds of appeal should be admitted into the proceedings. According to Article 12(4) RPBA, everything presented by the parties in accordance with Article 12(1) RPBA - which referred,

inter alia, to the grounds of appeal - shall be taken into account by the board to the extent it relates to the case under appeal and meets the requirements of Article 12(2) RPBA. The intention behind the opening statement in Article 12(4) RPBA to the effect that admissibility was a matter of discretion of the board, was to strike a balance between the right to be heard and procedural economy.

Even though Article 13 RPBA was not applicable in the present case, the criteria specified in this article should be applied by the boards when exercising the discretion conferred by Article 12(4) RPBA. With regard to those criteria, it should be noted that by filing the new request (i) complexity had not been increased given that the claimed subject-matter was defined in terms of features which had been assessed by the opposition division, (ii) the state of proceedings when the claim sets were filed had been early, namely together with the grounds of appeal, and (iii) in terms of procedural economy, the number of requests had been brought down from eight to three.

The new requests did not represent an attempt to prosecute subject-matter which, at least in very similar form, had not already been assessed by the opposition division. In the decision under appeal, eight sets of claims - a main request and seven auxiliary requests - were discussed. In contrast, in appeal proceedings the requests had been limited to three claim sets, one of which was identical to one of the sets of claims assessed by the opposition division. The new sets of claims (main request and first auxiliary request) were directed to subject-matter which was (i) narrower than that defined by the main request as assessed by the opposition division, and

furthermore (ii) defined only in terms of features which had also been already presented in claims which have been decided upon by the opposition division.

In the case law of the boards of appeal it had been held inadmissible to bring an entirely fresh case or raise entirely new issues. However, there was - albeit limited - scope for amendment of the claims. Compared to the claims assessed by the opposition division, the new main request and first auxiliary request did not give rise to new issues, nor was an entirely fresh case being built.

The new requests had been filed as a reaction to the adverse findings on Article 123(2) EPC in the decision under appeal. Claim 1 of the new requests had been amended to specify, *inter alia*, that "... *the nucleotide sequence of which double stranded structure is at least 90%, 95% or 100% identical ...*". A basis for the sequence identity values was found in claim 13 of the application as originally filed. Support for the language "*the nucleotide sequence of which double stranded structure*" could be found in the passage on page 7, lines 14 to 15, and the immediately following passage on page 8, first full paragraph. The second passage specified more concretely, namely in terms of numerical values, what was intended by the generic term "*substantially identical*" as used in the first passage.

Second auxiliary request

Articles 123(2) (3), 84 and 83 EPC

The opposition division correctly acknowledged compliance with Articles 123(2) (3), 84 and 83 EPC. The same applied to the present second auxiliary request.

Novelty

Article 54(3)(4) EPC 1973

In the decision under appeal, the opposition division had correctly acknowledged that the medical use of dsRNA in embryonic stem cells was not described in documents (2), (5) and (8).

Article 54(2) EPC

Document (11)

Document (11) was not novelty-destroying for the subject-matter of present claims 1 to 4. Not only was the medical use in embryonic stem cells not enabled by the content of this document, but also a particular length of the double stranded structure - as specified in claim 1 - was not derivable from document (11).

Document (12)

There was no disclosure whatsoever of dsRNA in document (12) and its overall teaching was obscure. Thus, this document did not make available, directly and with certainty, the subject-matter of the present claims.

- XV. The appellant (patent proprietor) requested that the decision under appeal be set aside and the patent be maintained on the basis of the claims of the main request or the first auxiliary request, both filed together with the statement setting out the grounds of appeal, or that the case be remitted to the opposition division for further prosecution on the basis of the

claims 1 to 4 of the second auxiliary request filed during the oral proceedings.

Reasons for the Decision

Main request and first auxiliary request - Article 12(4) RPBA

1. Together with the statement of grounds of appeal, the appellant filed two sets of amended claims as new main request and first auxiliary request. The appellant has not indicated any circumstances that may have prevented it from filing these new sets of claims in opposition proceedings. The objections that the appellant tries to overcome with the amended claims had been raised by the opponents already in their notice of opposition. The board observes that, in opposition proceedings, amended claims were filed in reply to the oppositions, and that during the oral proceedings before the opposition division the patent proprietor (present appellant) was given ample opportunity to react to the adverse findings by introducing further amendments to the claims. Under these circumstances, the admission of the new requests into the appeal proceedings is at the board's discretion (Article 12(4) RPBA).

2. Even though individual features introduced into, *inter alia*, claim 1 of the new sets of claims may have been included in one or more of the sets of claims underlying the decision under appeal, the board is now confronted with claims directed to subject-matter characterised by a specific combination of features which the opposition division did not consider, and on which it did not express an opinion as to its patentability.

3. More importantly, the amendments introduced into the claims of the new main request and first auxiliary request do not, *prima facie*, remedy deficiencies discussed in the decision under appeal in respect of amendments to the claims underlying the requests then on file, but give rise to new issues under Article 123(2) EPC and, possibly, also Article 84 EPC. In particular, serious doubts arise about the basis in the application as filed for the feature "[the] *double-stranded structure is **at least** 90%, 95% or 100% identical to at least a part of the target gene*" (emphasis added by the board) included in claims 1, 7, 9 and 18 of the main request, and claims 1, 6 and 15 of the first auxiliary request.

4. Claim 13 of the application as filed, on which the appellant relied as basis for the amendment, reads "... *the nucleotide sequence has 90%, 95% or 100% identity with at least a part of the target gene*" and does not specify ranges, but only specific degrees of identity. A sequence identity "*greater than 90% or 95%*" is disclosed in the passage on page 8, lines 20 to 23 of the application as filed. However, it is clearly apparent from this passage that these percentages apply to the sequence identity "... *between **the inhibitory RNA** and the part of the target gene*" (see page 8, lines 20 and 21; emphasis added by the board), rather than between the double-stranded structure and the target gene, as specified in claim 1. In fact, the relevant passage reads "... ***dsRNA** having [...] greater than 90% or 95% sequence identity may be used in the present invention*" (emphasis added by the board). As stated in the decision under appeal (see paragraph bridging pages 8 and 9), the terms "inhibitory RNA", "dsRNA" and "RNA" are used in the application as filed as equivalents to designate "... *the entire RNA*

*molecule, which molecule comprises a double stranded structure". This interpretation, which is endorsed by the board, is based on, *inter alia*, the passage on page 7, lines 14 to 15 to which the appellant referred ("The dsRNA comprises a double stranded structure, the sequence of which is "substantially identical" to at least a part of the target gene"). Hence, *prima facie*, neither claim 13 nor the passage on page 8, lines 20 to 23 of the application as filed can be regarded as an appropriate basis for the introduced amendment.*

5. Contrary to the appellant's view, the criteria applied by the board for refusing to admit the main request and the first auxiliary request in the present case do not differ from those outlined in decision T 524/01 of 21 October 2005 (see section 38 of the Reasons). The time of filing, the reasons why a request has been filed late and its *prima facie* allowability, in particular as regards the requirements of Articles 123 and 84 EPC, are mentioned in decision T 524/01 as relevant criteria for taking late-filed requests into consideration.
6. Applying these criteria, the board decides not to admit into the proceedings the new main request and first auxiliary request filed together with the statement of grounds of appeal.

Second auxiliary request

Admission into the proceedings - Article 13 RPBA

7. Claims 1 to 4 of the second auxiliary request filed during the oral proceedings before the board correspond essentially to claims 1 to 3 and 5 of the sixth auxiliary request underlying the decision under appeal,

except that the wording "... or expression vector encoding such an RNA" has been omitted, and the wording "... 100% identical to at least a part of a target gene in a mammalian cell ..." has been replaced by "... 100% identical to at least a part of **said** target gene in **said** mammalian cell ..." (emphasis added by the board). Even though these amendments have been introduced at a very late stage of the appeal proceedings, they do not give rise to new issues and could reasonably be expected to be dealt with by the board without adjournment of the oral proceedings. Moreover, the amendments introduced to the claims are necessary and appropriate to meet the ground for opposition of Article 100(a) in conjunction with Article 54 EPC, and the amended claims are *prima facie* allowable under Articles 123(2) (3), 84 and 83 EPC. Hence, the board decides to exercise its discretion by admitting the amended claims according to the second auxiliary request into the appeal proceedings.

Articles 123(2) (3), 84 and 83 EPC

8. Claim 17 of the application as filed is directed to the use of an RNA in the production of an agent for inhibiting the expression of a target gene in a mammalian cell, the RNA comprising a double stranded structure having a nucleotide sequence which is substantially identical to at least a part of the target gene and which is derived from an endogenous template. Claim 18 of the application as filed, which depends on claim 17, refers to the features specified in any one of method claims 2 to 15.
9. The additional features in present claim 1 that the nucleotide sequence of the double stranded structure has 100% identity with at least part of the target

gene, and that the RNA comprises two separate complementary RNA strands are derivable from, respectively, claim 13 and claim 11 of the application as filed, to which claim 18 refers. It is apparent from both claim 14 and the passage starting on page 9, line 21 of the application as filed, in which the medical use of the RNA is disclosed, that the target gene to be inhibited causes or is likely to cause disease. As indicated by the opposition division in the decision under appeal, inhibition of gene expression in embryonic stem cells from pre-implantation embryos is disclosed in the passage on page 20, lines 21 to 25 of the application as filed, and an RNA having a double stranded structure (duplex region) having at least 25 bases is described on page 9, lines 1 to 3. The board is thus satisfied that Article 123(2) EPC is complied with.

10. Present claim 1, which is derived from claim 9 as granted, includes additional limiting features, *inter alia*, that the double stranded structure has a length of at least 25 bases and a nucleotide sequence which is 100% identical to at least a part of the target gene, and that the RNA comprises two separate complementary RNA strands. Dependent claims 2 to 4 specify further limiting features. Thus, the amendments do not contravene Article 123(3) EPC.

11. As regards Article 84 EPC, the opposition division stated in the decision under appeal that there was no doubt that the percentage of identity indicated in the claim referred to the entire sequence of the double stranded structure. The board shares this view. Moreover, having regard to the wording "*said*" included in the present claim 1, it is clear that the target gene and the mammalian cell mentioned in connection

with the percentage of identity are the same as mentioned in the preamble of the claim and in further characterising features. The requirements of Article 84 EPC are thus met.

12. In the decision under appeal, the opposition division found that the invention as claimed according to the sixth auxiliary request then on file was sufficiently disclosed within the meaning of Article 100(b) EPC. This finding has not been contested in appeal proceedings. The board is satisfied that the same applies with regard to the disclosure requirement of Article 83 EPC for the present second auxiliary request.

Novelty

Article 54(3) (4) EPC 1973

13. The findings in the decision under appeal concerning the novelty of the claimed subject-matter of the sixth auxiliary request then on file with regard to documents (2), (5) and (8) (see section 10.4 of the decision under appeal) apply also to the present claims. None of these documents describes the use of an RNA as defined in present claims 1 to 4 for inhibiting the expression of a target gene in an embryonic stem cell.

Article 54(2) EPC

Document (11)

14. The opposition division found that the subject-matter of claims 1 to 5 of the sixth auxiliary request then on file was novel over document (11) because this document

did not enable the medical use of inhibitory dsRNA in embryonic stem cells. The same applies, *mutatis mutandis*, to claims 1 to 4 of the present second auxiliary request. As stated in the decision under appeal, embryonic stem cells are mentioned in document (11) only in connection with the generation of transgenic organisms, but not in the context of a therapeutic use. Thus, novelty over document (11) is acknowledged.

Document (12)

15. In the decision under appeal, the opposition division held that document (12) anticipated the subject-matter of, *inter alia*, claim 1 of the sixth auxiliary request then on file, because the content of this document enabled "... the medical use of **expression vectors** encoding dsRNAs which induce target gene expression inhibition in embryonic stem cells ..." (see page 41, lines 15 to 17 of the decision under appeal; emphasis added by the board).
16. This finding does not apply to present claim 1 which no longer encompasses the medical use of an expression vector encoding an RNA. Thus, claim 1 - and dependent claims 2 to 4 - are novel over document (12).

Admission of document (79) into the proceedings

17. Document (79) was filed together with the statement of grounds of appeal as evidence for the perception in the art at the priority date that gene silencing by dsRNA would not occur in mammals. The content of this document appears to be relevant to the assessment of inventive step. Therefore, document (79) is admitted into the proceedings.

Remittal for further prosecution

18. In the decision under appeal, inventive step (Article 56 EPC) was not assessed for the medical use of a dsRNA for inhibiting the expression of a target gene in a non-human embryonic stem cell. Thus, the board, exercising the discretion conferred by Article 111(1) EPC, decides to remit the case to the opposition 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 opposition division for further prosecution on the basis of the claims 1 to 4 according to the second auxiliary request filed during the oral proceedings.

The Registrar:

The Chairman:



A. Wolinski

M. Wieser

Decision electronically authenticated