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Datasheet for the decision of 30 September 2025

Case Number: T 1121/23 - 3.3.08

Application Number: 15813826.3

Publication Number: 3234134

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Language of the proceedings: EN

Title of invention:
TARGETED RNA EDITING

Patent Proprietor:
ProQR Therapeutics II B.V.

Opponents:
STRAWMAN LIMITED
Margaret Dixon Limited

Headword:
Targeted RNA Editing/PROQR THERAPEUTICS II

Relevant legal provisions:
EPC Art. 54, 56, 123(2), 111(1)
RPBA 2020 Art. 11, 12(4)

Keyword:
Main request and Auxiliary request 7, 14 to 18 - novelty (no)
Auxiliary requests 12, 13, 19 to 23 - inventive step (no)
Auxiliary requests 24 to 27 - added subject-matter (yes),
Admission of new evidence (yes)

Decisions cited:
G 0001/24, T 2027/23, T 0731/17

Catchword:

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Beschwerdekammern

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Case Number: T 1121/23 - 3.3.08

D E C I S I O N
of Technical Board of Appeal 3.3.08
of 30 September 2025

Appellant: (Opponent 1)	STRAWMAN LIMITED Orchard Lea Horns Lane Combe Witney, Oxfordshire OX29 8NH (GB)
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Decision under appeal: **Interlocutory decision of the Opposition Division of the European Patent Office posted on 2 June 2023 concerning maintenance of the European Patent No. 3234134 in amended form**

Composition of the Board:

Chairwoman T. Sommerfeld
Members: D. Pilat
A. Bacchin

Summary of Facts and Submissions

I. European patent No. 3 234 134 is based on European patent application No. 15 813 826.3, filed as an international application published as WO 2016/097212.

II. Two oppositions were filed on the grounds set out in Article 100(a) in conjunction with Articles 54 and 56 EPC, and Article 100(b) and (c) EPC. In an interlocutory decision, the opposition division held that the patent in amended form according to auxiliary request 1, filed as auxiliary request 4 on 21 July 2021 and renumbered as auxiliary request 1 at oral proceedings, fulfilled the requirements of the EPC.

III. Opponents 1 and 2 (appellants I and II, respectively) each lodged an appeal against the decision of the opposition division. With their statements of grounds of appeal, appellant I submitted new documents D35 to D44 (renumbered A36 to A45 by the board) and appellant II submitted new document D35 (renumbered A35 by the board).

IV. With its reply to the appeals, the patent proprietor (respondent) requested that the appeal be dismissed and the patent be maintained on the basis of the claims found allowable by the opposition division (main request) and submitted auxiliary requests 1 to 36.

V. With the rejoinder, appellant I submitted further document A46.

VI. The parties were summoned to oral proceedings. The board sent a communication pursuant to Article 15(1) RPBA.

VII. With letter dated 12 September 2025, the respondent withdrew auxiliary requests 28 to 36.

VIII. Oral proceedings took place as scheduled, in the absence of appellant I who had announced, in a letter dated 11 August 2025, that it would not attend oral proceedings. At oral proceedings, the respondent withdrew auxiliary requests 1 to 6 and 8 to 11, so that at the end of oral proceedings the requests pending were the main request and auxiliary requests 7 and 12 to 27.

IX. Claims 1 and 5 of the **main request** read as follows:

"1. An oligonucleotide construct for the site-directed editing of a nucleotide in a target RNA sequence in a eukaryotic cell, said oligonucleotide construct comprising:
(a) a targeting portion, comprising an antisense sequence complementary to part of the target RNA; and
(b) a recruiting portion that is: capable of forming an intramolecular stem loop structure; capable of binding and recruiting an RNA editing enzyme naturally present in said cell; and capable of performing the editing of said nucleotide
wherein one or more of the nucleotides in the oligonucleotide construct comprise a chemical modification."

"5. The oligonucleotide construct according to any one of claims 1 to 4, wherein the nucleotide that is the target for editing is an adenosine."

X. Claim 1 of **auxiliary request 7** is identical to claim 1 of the main request.

Claim 1 of **auxiliary requests 12 and 13** differs from claim 1 of the main request in that the recruiting portion of claim 1(b) is specified to be "not complementary to the target RNA".

Claim 1 of **auxiliary requests 14 to 18** differs from claim 1 of the main request in that in claim 1(b) the following amendment was made: "~~and~~ wherein the RNA editing enzyme is capable of performing the editing of said nucleotide".

Claim 1 of **auxiliary requests 19 to 23** combines the amendments of auxiliary requests 12 and 14.

Claim 5 of **auxiliary requests 24 to 27** is identical to claim 5 of the main request.

XI. The parties' submissions, insofar as they are relevant to the decision, are discussed in the Reasons for the Decision, below.

XII. The documents cited in this decision include the following:

D2 Woolf *et al.*, (1995) Proc. Natl. Acad. Sci. USA, vol.92, pages 8298 to 8302

D19 Macbeth *et al.*, (2004) RNA, vol. 10, pages 1563 to 1571

A35 Structure of the sequence of the end-blocked 34mer of D2 (Woolf)

A36 Folding data for chemically modified 34mer construct of D2 (RNAfold)

A37 Folding data for chemically modified 34mer construct of D2 (RNAStructure)
A38 Folding data for chemically modified 34mer construct of D2 (RNAFold)
A39 Höfler and Carlomagno (2020) Current Opinion in Structural Biology, vol.65, pages 42 to 50
A40 Lorenz R. *et al.* (2011) Algorithms for Molecular Biology, vol.6:26 pages 1 to 14
A41 Tanzer A. *et al.* (2019) Methods, vol.156, pages 32 to 39
A42 Folding data for chemically modified construct of Dll (SEQ ID NO: 51)
A43 WO 2019/043027 Al
A44 Merkle T. *et al.* (2019) Nat. Biotechnol, vol. 37, page 133 to 138

XIII. The parties' requests, in so far as they are relevant to the present decision, are as follows:

Appellant I requested in writing that the decision under appeal be set aside and the patent be revoked. Furthermore, it requested that documents A36 to A44 be admitted into the proceedings.

Appellant II requested that the decision under appeal be set aside and the patent be revoked. Furthermore, it requested that the auxiliary requests filed in appeal not be admitted. It requested that document A35 be admitted and also supported appellant I's request that documents A36 to A44 be admitted.

The respondent (patent proprietor) requested that the appeal be dismissed and the patent be maintained based on the main request (auxiliary request 1 as upheld by the opposition division) or alternatively on the basis of any of auxiliary requests 7 and 12 to 27 filed with

the reply to the appeals. Furthermore, it requested that documents A35 to A46 not be admitted and that if any of the new documents was admitted, that the case be remitted to the opposition division. Besides, it requested that the case be remitted to the opposition division if any aspect of the decision under appeal was reversed.

Reasons for the Decision

Procedural issues

Absence of party at oral proceedings

1. The oral proceedings before the board took place in the absence of appellant I, who had been duly summoned but decided not to attend. Appellant I was thus treated as relying only on its written submissions (Rule 115(2) EPC and Article 15(3) RPBA). The present decision is based on facts and evidence put forward during the written proceedings and on which appellant I has had an opportunity to comment.

Admission of documents A35 to A44 into the appeal proceedings

2. These documents were submitted by appellants I and II with their grounds of appeal (see section III. above). Their admission is thus at the discretion of the board, pursuant to Article 12(4) and (6) RPBA, according to which the board has the discretionary power to hold inadmissible facts, evidence and requests which could have been presented or were not admitted in the first instance proceedings, unless the circumstances of the appeal case justify their admittance.

3. In agreement with the appellants, the board considers that the circumstances of the appeal case justify the admission of documents A35 to A44 because they were filed as a legitimate reaction to a new argument by the patent proprietor and the consequent change of opinion of the opposition division at oral proceedings in relation to what had been their conclusions in the preliminary opinion. In short, in the appealed decision (paragraph bridging pages 28 and 29 and first full paragraph of page 29) the opposition division doubted that the chemically modified construct of document D2 could form a stem loop structure, thereby following an argument which was raised by the respondent for the first time at oral proceedings. In the preliminary opinion (page 22, fifth paragraph from the bottom), the opposition division had concluded that "*[t]he oligomer 34mer is capable of forming an intramolecular stem loop structure (confirmed by the program RNAfold)*" and that therefore document D2 was novelty destroying for claim 1 (penultimate paragraph of page 22). Also at the oral proceedings the opposition division initially maintained this position (minutes, page 2, penultimate paragraph) and in fact it was only with the impugned decision that the appellants became aware that the opposition division followed the new argument instead. Accordingly, the appeal is the appellants' first opportunity to react to the new argument of the respondent and the resulting conclusion of the opposition division.

4. The respondent's arguments as to why documents A35 to A44 should not be admitted into proceedings are not persuasive. The arguments based on the fact that no novelty objection had been raised against claim 11 as granted are not relevant because the feature of said claim is not the one in dispute. With the aim of

overcoming the novelty objection against claim 1 as granted, said feature of granted claim 11 was incorporated into claim 1 of the main request submitted in reply to the oppositions. The respondent did not argue then that the distinguishing feature was that D2's oligomer could not form a stem loop structure as required by the claim, but rather that it did not include chemical modifications as required by claim 11 as granted. However, the opposition division considered in its preliminary opinion (supra) that document D2 also disclosed this feature and that hence claim 1 of the then main request still lacked novelty over the disclosure of document D2 in view of the folding prediction provided in document D3. In these circumstances, even if documents A35 to A44 could have been submitted earlier, there was no reason for the opponents to do so, in the light of the respondent's arguments and the preliminary opinion of the opposition division. As to the respondent's argument that it was on the opponents to provide evidence for their novelty objections, the board notes that the opponents had indeed provided evidence in the form of document D3, and that this evidence was considered convincing by the opposition division and was not challenged by the respondent until oral proceedings. New evidence only became necessary in view of the late arguments of the respondent, and the opposition division's departure from its preliminary opinion, first expressed in its decision.

5. The board did not need to decide on the admittance of documents A45 and A46. In its provisional opinion, contained in the communication under Article 15(1) RPBA, the board indicated that it was not inclined to admit document A45 for lack of relevance (Article 12(4) and (6) RPBA) since it was merely an examination report

on another case, and that admittance of document A46 pursuant to Article 13(1) RPBA would have been discussed if needed at the oral proceedings. No reaction was filed by appellant I on this matter after the board's communication and due to its absence from the oral proceedings no arguments were made relying on these documents.

Admittance of auxiliary requests 7, 12 to 27

6. Appellant II objected to the admittance of all auxiliary requests filed in appeal. In view of the conclusions reached by the board as regards the substance of these requests, the board does not need to provide a reasoning for their admittance into the proceedings.

Request for remittal for further prosecution (Article 111(1) EPC and Article 11 RPBA)

7. The respondent requested to remit the case to the opposition division if any aspect of the decision under appeal was reversed or if the new evidence (documents A35 to A44) was admitted into the appeal proceedings.

8. In accordance with Article 111(1) EPC, the board may either exercise any power within the competence of the department which was responsible for the appealed decision or remit the case to that department for further prosecution. While the decision to remit a case to the department whose decision was appealed lies with the discretion of the board, Article 11 RPBA provides that a board shall not remit a case, unless special reasons present themselves for doing so.

9. The board considers that there are no special reasons justifying remittal of the present case for further prosecution. Although the primary object of the appeal proceedings is to review the decision under appeal in a judicial manner (see Article 12(2) RPBA), there is also no absolute right to have every issue decided at two instances. The new evidence was filed by the appellants in reaction to an argument which was raised by the respondent for the first time at oral proceedings (see point 3. above). Moreover, contrary to the respondent's arguments, it does not constitute a significant departure from the matter at stake in the first instance, rather it pertains to the same issue that was extensively discussed during opposition proceedings, namely novelty over document D2, and merely provides further supporting evidence for what had already been assumed by the opposition division in its preliminary opinion. Hence the present case is essentially distinct from the case underlying decision T 731/17, cited by the respondent in support of their case for remittal, because this latter decision explicitly acknowledged that inventive step had not yet been assessed in detail and that it might also have to be examined if a given document constituted prior art within the meaning of Article 54(2) EPC.

10. In view of these considerations the board decides to exercise its discretion, pursuant to Article 111(1) EPC and Article 11 RPBA, not to remit the case to the opposition division.

Substantive issues

11. At oral proceedings, added-matter of claims 5 and 9 of the main request were first discussed and the board came to the conclusion that both claims contravened the

requirements of Article 123(2) EPC. The respondent then withdrew auxiliary requests 1 to 6 and discussion ensued with auxiliary request 7, the board having come to the conclusion that claim 1 of auxiliary request 7 lacked novelty over document D2. In reaction thereto, the respondent withdrew auxiliary requests 8 to 11, and auxiliary request 12 was then discussed under inventive step and the board arrived at the conclusion that it lacked inventive step. The respondent maintained auxiliary requests 13 to 27 but relied solely on their written submissions for these requests.

12. Since claim 1 of auxiliary request 7 is identical to claim 1 of the main request, in the present decision the two requests will be considered at the same time, and the conclusions reached under added-matter for claim 5 of the main request will be dealt later on, in the context of auxiliary requests 24 to 27.

Main request and auxiliary request 7
Claim interpretation - claim 1

13. Claim 1 is identical for the main request and auxiliary request 7. It is a product claim, directed to an oligonucleotide construct which must be suitable for the site-directed editing of a nucleotide in a target RNA sequence in a eukaryotic cell. The oligonucleotide construct must comprise at least two functionally defined portions: a) a targeting portion and b) a recruiting portion.
The recruiting portion is defined as
1) capable of forming an intramolecular stem loop structure;
2) capable of binding and recruiting an RNA editing enzyme naturally present in said cell; and

3) capable of performing the editing of said nucleotide.

14. Thus, the oligonucleotide construct must have a recruiting portion 1) capable of forming a stem loop regardless of whether or not it binds at the same time to the target molecule. This embodiment is not excluded from claim 1, as is apparent from dependent claim 3. The recruiting portion must be further 2) capable of binding and recruiting an RNA editing enzyme naturally present in the eukaryotic cell. This function must not be achieved by the stem loop structure of the recruiting portion, but may be achieved by any part of the recruiting portion regardless of whether it forms a stem loop structure or not at this time point.

15. Since claim 1 does not specify that the targeting and recruiting portions must not overlap, it cannot be interpreted as including these limitations, i.e. as having a meaning narrower than the wording of the claim as understood by the person skilled in the art (see decision T 2027/23, catchword). While the description and the drawings shall always be consulted to interpret the claims (G 1/24, Catchword), if upon consulting the description for interpreting the claims, the disclosure given in embodiments of the description is narrower and requires additional technical features in the claims, then those features must be included in the claim to take account of this fact (T 2027/23, Reasons 3.5.8).

16. The board hence disagrees with the respondent's argument according to which the targeting and recruiting portions of claim 1 "are separate parts of a whole" based on features set out in embodiments of the invention (paragraphs [0039] and [0042] of the patent). The board notes that even if the "targeting portion" or

"recruiting portion" are disclosed in the description as separate portions of the oligonucleotide construct, i.e. bipartite structure, these functionally defined portions do not require and imply a structural separation. There is no indication in the patent that the claimed portions are separate parts of the claimed oligonucleotide with no overlap, nor can this be implied from Figures 1 to 3 and paragraph [0020] of the patent. On the contrary, the claimed subject-matter refers to any oligonucleotide sequence that targets the oligonucleotide to the target RNA sequence via a targeting portion that is sufficiently complementary and a recruiting portion which is either complementary or non-complementary to at least a part of the target RNA (patent, paragraphs [0020] and [0033]).

17. In the art, the term "stem loop" refers to any complementary "stem" with a loop of oligonucleotides at its end. Stem loop structures are also referred to as hairpins (see patent, paragraph [0011]). One way of determining a stem-loop is to detect a palindromic sequence in a single molecule that can fold back on itself over at least part of its length (patent, paragraph [0032]).

18. As set out in claim 1, the recruiting portion appears to be itself capable of performing editing of a nucleotide in a target RNA sequence, but the patent has not demonstrated how this portion is capable of doing so, i.e. performing editing of a nucleotide in a target RNA sequence in the absence of an RNA editing enzyme. The board therefore agrees with the appellants' interpretation that the recruiting portion of claim 1 is capable of binding and recruiting an RNA editing enzyme naturally present in said cell that is capable

of performing the editing of said nucleotide (in a target RNA sequence).

Novelty – claim 1

19. In agreement with the conclusions of the opposition division, the board considers that document D2 discloses in Figure 2 an oligonucleotide construct (the so-called end-blocked 34mer) for the site-directed editing of a nucleotide in a target RNA sequence in a eukaryotic cell, said oligonucleotide comprising both a targeting portion, comprising an antisense sequence complementary to part of the target RNA, and a recruiting portion that is capable of binding and recruiting an RNA editing enzyme naturally present in said cell, wherein the oligonucleotide construct is chemically modified. That the modified oligonucleotide construct is capable of gene editing is shown in Figure 3A of document D2 and disclosed in the context of a dystrophin gene containing a premature stop codon as the edited gene and dsRAD as the endogenous gene editing enzyme (D2, paragraph bridging pages 8298 and 8299; page 8298, right-hand column, second paragraph), which is recruited by the end-blocked 34mer oligomer (Figure 3A: Figure 1 and the last sentence of its caption). Hence, contrary to the respondent's arguments, the end-blocked 34mer of document D2 comprises a recruiting portion. Although document D2 does not disclose that the targeting and the recruiting portions are separate, the board considers, contrary to the respondent's arguments, that claim 1 does not require this either (see claim interpretation above, points 14. and 16.).

20. It was a matter of dispute whether the recruiting portion of the construct of document D2 was capable of

forming an intramolecular stem loop structure, as required in the claim, or not. The board considers that the evidence on file demonstrates that also this requirement is fulfilled by the construct of document D2. All the *in silico* RNA folding predictions provided for the end-blocked 34mer oligomer (see A36, A37 and A38) demonstrate that this chemically modified oligomer is capable of forming a stem loop as required by claim 1, no matter if they have different stem-loop structures. The stem-loop folding prediction was confirmed by different software tools (RNAfold, RNAStructure, UNAfold using different folding algorithms, constraints and assumptions) and there is no evidence on file to the contrary.

21. The respondent argued that the folding predictions of documents A35 to A38 did not constitute information that was available to the public prior to the priority date. In addition, there was no evidence that exactly the same tools used to provide these predictions were available at the priority date, so that the skilled person could have made the prediction too. Moreover these were mere *in silico* predictions, which depended highly on the parameters used, and it was questionable that a true stem loop would actually be formed in *in vivo* experiments. Finally, these documents only provided predictions, and a prediction even of 95% remained only a probability and was therefore not enough to establish a lack of novelty. The formation of a minimal free energy structure at a frequency of 32% within the ensemble (documents A35 and A36) was insufficient to demonstrate that such a structure would clearly and necessarily form. Further testing was required to establish this beyond doubt.

22. The board disagrees with the respondent's arguments. As stated above, the *in silico* folding predictions A35 and A36 show an intramolecular stem-loop structure. Although the minimum free energy structure, i.e. the thermodynamically most stable secondary structure for an RNA sequence in the ensemble, is only adopted at a frequency of 32,21%, still it is demonstrated that the oligonucleotide is capable of forming an intramolecular stem-loops, even if only transiently. The RNA folding is known to be a dynamic process during which many transient structures can be adopted. The predictions of the structural folding of the RNA in document A37 also demonstrate that adjacent nucleotides of the oligonucleotide of document D2 have a 99% to 95% probability of forming base-pairs, such that this oligonucleotide is also capable of forming an intramolecular stem-loop, even if only transiently (see also A38). Consequently, it is beyond doubt that the end-blocked 34mer of document D2 is capable of forming an intramolecular stem loop structure, which is all that is required by the claim. The use of wet lab techniques to determine which of the predicted RNA folding structure is actually formed is not required, as the sole ability of forming such a stem loop by the recruiting portion of the oligonucleotide is beyond doubt and sufficient.

23. Even though documents A35 to A44 are post-published, they disclose inherent properties of the tested oligonucleotide. The secondary structure of an unmodified and modified oligomer disclosed in document D2 forming a stem loop, as demonstrated in documents D3 and A35, is an intrinsic feature of the product which is made available to the public, as opposed to effects or results that are only revealed when the product is exposed to specific selected conditions that go beyond

the product itself (Case Law of the Board fo Appeal of the EPO, 11th edition 2025, I.C.4.4.). Although the prediction of the secondary structure of the chemically modified 34mer was carried out after the priority date of the present patent, this inherent property of the modified 34mer disclosed in document D2 would inevitably have been present when used. The secondary structure is namely a fixed non-removable characteristic of the end-blocked 34mer oligonucleotide, which is determined by its primary structure (i.e. nucleotide sequence) and requires no external intervention or guidance. Depending on the environmental conditions, such as temperature and ionic concentration, the oligonucleotide spontaneously folds into its thermodynamically most stable secondary structure as predicted in documents A35 to A37 and A38. This oligonucleotide is therefore beyond doubt capable of forming an intramolecular stem loop structure, even if only transiently. The wording of claim 1 does not require that one specific *in silico*-predicted stem-loop structure must form in any environment or under particular conditions. The capability of the oligonucleotide of temporary forming at least one of them is sufficient to fulfil this requirement.

24. Finally, the board cannot share respondent's view referring to the contested decision that an oligonucleotide containing a certain number of G-U pairs, so-called wobble base pairs, would destroy the ability of forming a stem loop. The presence or increased number of G-U wobble base pairs in the recruiting portions of the oligonucleotide is namely mentioned in the patent not to prevent the formation of a stem-loop (paragraphs [0011] and [0012]). Nor were the chemical 2'OMe or the phosphorothioate modifications shown to prevent the formation of a stem

loop in the end-blocked 34mer oligonucleotide of document D2. On the contrary, a GLuR2 oligonucleotide with and without chemical modification are both shown to form a stem loop (see A44, Figure 1b). Since the end-blocked oligonucleotide 34mer includes palindromic sequences "GGAGG" and CCUCC, it must also be capable of forming a stem-loop according to paragraph [0032] (see point 17. above) as already demonstrated in point 20. above.

25. The board thus comes to the conclusion that claim 1 of the main request and of auxiliary request 7 lacks novelty over document D2 (Article 54(2) EPC).

Auxiliary request 12
Inventive step - claim 1

26. Claim 1 of auxiliary request 12 differs from claim 1 of the main request in that it includes the feature that the recruiting portion is not complementary to the target RNA.

27. Starting from document D2 as closest prior art, the subject-matter of claim 1 differs from the disclosure of document D2 in that the end-blocked 34mer oligomer in Figure 3A of document D2 comprises a recruiting portion that is complementary to the target RNA.

28. The experimental data provided in the patent does not allow to attribute any technical effect to this distinguishing feature. Nor does any additional data on file demonstrate any effect.

29. Since no technical effect can be associated with the distinguishing feature identified above, the board cannot share the respondent's view that the technical

problem should be formulated as how to modify the end-blocked 34mer oligomer shown in Figure 3A of document D2 to allow for a more reliable and targeted editing. On the contrary, the board considers that, in agreement with appellant II, the technical problem must be formulated as the provision of an alternative oligonucleotide to the one described in document D2.

30. The skilled person starting from the teaching of document D2, faced with the objective technical problem of providing an alternative oligonucleotide to the one described in document D2, would have turned to document D19 and would have designed an alternative oligonucleotide of document D2 according to the structure of oligonucleotide of document D19, in which the recruiting portion is not complementary to the target RNA. Document D19 shows that in the "R/G hairpin" oligonucleotide, the targeting region and the hADAR2-recruiting hairpin function independently (Figure 2C). The targeting part (R/G 15) binds the target RNA, while the R/G terminal hairpin forms a stem-loop that recruits the gene editing enzyme hADAR2 regardless of the targeting sequence (Figure 6B). Consequently, the targeting region can be freely exchanged, whereas the recruiting hairpin should be retained (D19, page 1568, right-hand column, second paragraph, Figure 7, upper panel). As the technical problem is simply the provision of an alternative oligonucleotide, there is no need for a hint, suggestion or pointer in the prior art to design such a oligonucleotide. Thus, the board considers that starting from document D2, the skilled person, faced with the objective technical problem of providing an alternative oligonucleotide with the same RNA mediated enzymatic editing properties as the one disclosed in

document D2, would have arrived at the claimed subject-matter without inventive step.

31. The respondent essentially argued that oligonucleotides with separate targeting and recruiting moieties were easier and more flexible to design, and that D2 in fact taught away from introducing chemical modifications because the said constructs performed worse (Figure 3 of D2). Moreover D2 only showed targetting of dystrophin and did not teach to extrapolate to other genes. As to the combination with document D19, the respondent argued that the skilled person would not combine the teachings of this document with those of D2, because D19 was a very mechanistic study in contrast to D2 which was related to use in therapy. Moreover D19 did not unambiguously disclose distinct recruiting and targeting portions, so that it could not be concluded that the recruiting portion was not complementary to the target RNA. Nor did it disclose the presence of chemical modifications in the constructs.

32. The board finds the respondent's arguments not convincing. As to the allegation that oligonucleotides with separate targeting and recruiting moieties would be easier and more flexible to design, the board notes that, as discussed above, there is no evidence for an effect of the distinguishing feature, so that such an alleged advantage cannot be taken into account. It is also irrelevant that D2 shows a lower performance for constructs with chemical modifications, because this is not the distinguishing feature to D2 and because the claim is not directed to any production process or use but to a product, and does not require any level of activity for the product. As to the combination of D2 and D19, the board notes that, in view of the

formulation of the technical problem as an alternative, there is no need for a motivation to combine with another document. Finally, in D19 it is undisputed that the construct does recruit a gene editing enzyme through a given part of its sequence, which is therefore the recruiting portion, and that this part of the sequence is not complementary to the target sequence, as discussed above (point 29). Whether D19's constructs have chemical modifications or not is irrelevant, since D2's constructs already comprise this feature.

Auxiliary request 13
Inventive step - claim 1

33. Claim 1 of auxiliary request 13 is identical to claim 1 of auxiliary request 12. Hence claim 1 of auxiliary request 13 also lacks an inventive step (Article 56 EPC).

Auxiliary requests 14 to 18
Novelty - claim 1

34. Claim 1 of auxiliary requests 14 to 18 differs from claim 1 of the main request in that it was further amended to specify that the RNA editing enzyme is capable of editing (see sections IX. and X. for the wording of the claim).

35. The board considers that this amendment, which appears to merely disclose the function of an RNA editing enzyme, cannot confer novelty over the oligonucleotide in document D2. The oligonucleotide disclosed in document D2 uses namely a cellular double-stranded RNA adenosine deaminase (dsRAD). This cellular RNA editing enzyme is capable of performing the editing of said

nucleotide (see D2, Figure 1 and its legend; page 8298, right-hand column, first full paragraph).

36. Hence, claim 1 of auxiliary requests 14 to 18 lacks novelty (Article 54(2) EPC).

Auxiliary requests 19 to 23
Inventive step - claim 1

37. Claim 1 of these requests combines the amendments of auxiliary requests 12 and 14. As discussed above, the feature introduced into claim 1 of auxiliary request 14 is not a distinguishing feature of the oligonucleotide of document D2 and thus cannot contribute for inventive step. Hence, for the same reasons as for auxiliary request 12, claim 1 of auxiliary requests 19 to 23 lack an inventive step (Article 56 EPC).

Auxiliary requests 24 to 27
Article 123(2) EPC - claim 5

38. Claim 5 of these requests is identical to claim 5 of the main request, which was found to contravene the requirements of Article 123(2) EPC for the following reasons.

39. Claim 5 is directed to the oligonucleotide construct of any of claims 1 to 4, "*wherein the nucleotide that is the target for editing is an adenosine*" (for the full wording of the claim, see section IX.).

40. According to the respondent, basis for this claims could be found in the following passages of the application as filed: page 5, line 17; page 6, line 5; page 9 lines 27 to 28; page 16, first paragraph; and page 23, line 2.

41. While page 5, lines 15 to 17 of the application as filed refers to the *"target adenosine"*, it additionally discloses that the targeting portion must also comprise a 2'O-methyl chemical modification, except for the nucleotide opposite the target adenosine and a nucleotide 5' and one 3' adjacent to said nucleotide which should comprise 2'-OH groups. However, claim 5 or any claims from which it depends do not include this structural limitation. For this reason, this passage cannot provide an adequate basis for the subject-matter of claim 5.

42. The first paragraph on page 6 of the application as filed relates to an oligonucleotide comprising a targeting portion and a recruiting portion. The recruiting portion primarily functions to recruit the editing entity, e.g. ADAR, and is not necessarily complementary with the target RNA in the region of *"the adenosine(s) that are the target(s) for editing"*. Although this paragraph refers to target adenosine(s) to be edited in the target RNA, it also refers to an ADAR, albeit as an example, to achieve the editing in the same clause. From this passage it cannot be directly and unambiguously derived that, if the target for editing is one or more adenosine(s), the oligonucleotide comprises also a recruiting portion capable of recruiting an editing entity other than one having adenosine deamination activity or being an adenosine deaminase, and in which one or more of the nucleotide(s) in the oligonucleotide is chemically modified, as required by claim 5.

43. As regards the passages on page 9, line 27 and 28 and the first paragraph on page 16 of the application as filed, although they refer to the *"target*

adenosine(s)", they also relate to a targeting portion which may be chemically modified in its entirety, for example by providing all nucleotide with a 2'O-methylated sugar moieties, except the nucleotide opposite or immediately adjacent to the nucleotide opposite the target adenosine(s). Claim 5 cannot find a basis on these passages, as neither claim 5 nor any claims from which is depends impose such a requirement.

44. Finally, the passage on page 23, lines 2 to 7 of the application as filed is part of the section entitled "The target sequence and the change". It discloses that "*[p]articularly interesting target adenosines for editing using oligonucleotides according to the invention are those that are part of codons that encode amino acid residues with key functions or characteristics,...*". It is specified that the editing reactions are preferably adenosine deamination and cytidine deamination, and that the changes can be brought about on target codons by adenosine deaminase editing (see page 20, line 35 and page 21, lines 18 to 24). Although these passages are identified as preferred embodiments and accordingly are not limiting, there is no direct and unambiguous basis derivable from these passages for an oligonucleotide capable of editing a target adenosine according to claim 5 and comprising one or more chemically modified nucleotide(s), as required by claim 1, wherein the editing is brought about by an RNA editing enzyme that is not restricted to an adenosine deaminase or an adenosine deamination activity.

45. Finally, the subject-matter of claim 5 cannot be derived directly and unambiguously from the examples of the patent application as filed, since they all use a

specific enzyme, ADAR, as the editing enzyme, while claim 5 is not restricted to this enzyme.

46. Hence, claim 5 of auxiliary requests 24 to 27 adds subject-matter, contrary to the requirements of 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 Chairwoman:

C. Rodríguez Rodríguez T. Sommerfeld

Decision electronically authenticated