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Case Number: T 0250/24 - 3.3.04

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Language of the proceedings: EN

Title of invention:
MND promoter chimeric antigen receptors

Patent Proprietor:
2seventy bio, Inc.

Opponent:
Boult Wade Tennant LLP

Headword:
MND promoter/2SEVENTY BIO

Relevant legal provisions:
EPC Art. 100(c)

Keyword:
Grounds for opposition - subject-matter extends beyond content of earlier application (yes)

Decisions cited:
G 0002/98, G 0002/10, T 1362/15, T 0895/18, T 0350/20

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Boards of Appeal

Chambres de recours

Boards of Appeal of the
European Patent Office
Richard-Reitzner-Allee 8
85540 Haar
GERMANY
Tel. +49 (0)89 2399-0

Case Number: T 0250/24 - 3.3.04

D E C I S I O N
of Technical Board of Appeal 3.3.04
of 9 April 2025

Appellant: (Opponent)	Boult Wade Tennant LLP Salisbury Square House 8, Salisbury Square London EC4Y 8AP (GB)
Representative:	Boult Wade Tennant LLP Salisbury Square House 8 Salisbury Square London EC4Y 8AP (GB)
Respondent: (Patent Proprietor)	2seventy bio, Inc. 60 Binney Street Cambridge, MA 02142 (US)
Representative:	Forresters IP LLP Skygarden Erika-Mann-Straße 11 80636 München (DE)
Decision under appeal:	**Decision of the Opposition Division of the European Patent Office posted on 23 January 2024 rejecting the opposition filed against European patent No. 3689899 pursuant to Article 101(2) EPC**

Composition of the Board:

Chairwoman	M. Blasi
Members:	O. Lechner
	A. Chakravarty

Summary of Facts and Submissions

I. The opponent (appellant) filed an appeal against the opposition division's decision to reject the opposition against European patent No. 3 689 899.

II. The patent was granted on European patent application number 19 218 258.2 (application as filed), which is a divisional application of European patent application number 15 782 739.5. The latter had been filed as an international application under the PCT published as WO 2015/164759 (earlier application as filed).

III. In its decision, the opposition division decided that none of the grounds for opposition under Article 100(a), (b) and (c) EPC prejudiced the maintenance of the patent as granted.

IV. With its statement of grounds of appeal, the appellant maintained objections under Article 100(a) EPC in combination with Articles 54 and 56 EPC, Article 100(b) and (c) EPC. It also filed new document D18.

V. The patent proprietor (respondent) replied to the statement of grounds of appeal and resubmitted the sets of claims of auxiliary requests 1 to 9, which were first filed on 22 September 2023, during opposition proceedings and also filed sets of claims of new auxiliary requests 10 to 19.

VI. The board summoned the parties to oral proceedings as requested.

VII. The appellant submitted a further letter.

VIII. The board issued its communication pursuant to Article 15(1) RPBA setting out its preliminary opinion on several issues.

IX. The respondent replied to the communication pursuant to Article 15(1) RPBA.

X. Oral proceedings before the board took place on 9 April 2025.

During these oral proceedings, the respondent submitted copies of the following documents: T 1362/15, WO 2006/020211, and the set of claims of auxiliary request 2, underlying T 1362/15.

In the course of the oral proceedings, the respondent withdrew all auxiliary requests and also the request for remittal of the case to the opposition division.

At the end of the oral proceedings, the Chairwoman announced the board's decision.

XI. Claim 1 of the patent in suit reads:

"1. A lentiviral vector comprising a polynucleotide comprising a myeloproliferative sarcoma virus enhancer, negative control region deleted, dl587rev primer-binding site substituted (MND) promoter operably linked to a nucleic acid encoding a chimeric antigen receptor (CAR), wherein the CAR comprises:

(a) an scFv that binds B cell maturation antigen (BCMA);

(b) a CD8α hinge region;

(c) a CD8α transmembrane domain;

(d) a CD137 co-stimulatory signaling domain; and

(e) a CD3ζ primary signaling domain."

XII. The appellant's arguments, relevant to the decision, are summarised as follows:

(a) *Amendments - Article 100(c) EPC - claim 1*

Claim 1 as granted introduced added subject-matter by combining features (a), (c), and (d) in a manner not directly and unambiguously disclosed in the application as filed or the earlier application as filed.
Specifically, feature (a), an scFv that binds BCMA, required a selection from a long list of antigens (claim 2(a) of the earlier application as filed) and was not disclosed in individualised form; the scFv format was only disclosed in general terms (e.g. page 20, lines 14 to 30), and BCMA was merely one of many listed targets.
Feature (c), a CD8α transmembrane (TM) domain, was only disclosed as "derived from CD8α" (claim 7 of the earlier application as filed), which was not equivalent to "a CD8α TM domain" as claimed.
Feature (d), a CD137 co-stimulatory domain, required a further selection from a list of eight options provided e.g. in claim 2(c) of the earlier application as filed, and CD137 was not singled out as being preferred.

Due to their multiple dependencies, claims 1, 2, 7, 12 to 14, 20 and 24 of the earlier application as filed in combination with page 20, lines 14 to 30 could not provide a direct and unambiguous disclosure of the subject-matter of claim 1.
In the context of assessing whether the subject-matter of a claim resulting by combining subject-matter of claims with multiple dependencies should be treated differently from that formed by combining claims with "US-style" single dependencies (i.e., where each

dependent claim refers back individually to the independent claim), reference was *inter alia* made to the Case Law of the Boards of Appeal, 10th ed., 2022, II.E.1.6.4, and especially T 1362/15, which addressed the situation of "US-style" dependencies and T 350/20, which dealt with claims having multiple dependencies.

Examples 1 and 8 of the earlier application as filed also failed to provide a direct and unambiguous disclosure of the claimed combination of features. Example 1, which related to anti-CD19 and anti-kappa light chain (kLC) CARs, not BCMA, and Example 8, which referred to anti-BCMA CAR T cells, lacked any structural detail of the CAR and referred to Example 1 for manufacturing methods, not vector structure. Even if Examples 8 and 1 were read together, the subject-matter of claim 1 lacked many of the details provided for the lentiviral vectors described in these examples and, thus amounted to an impermissible intermediate generalisation of the lentiviral vectors disclosed in Examples 8 and 1 and the more broadly defined vectors in the remaining parts of the earlier application as filed.

XIII. The respondent's arguments, relevant to the decision, are summarised as follows:

(a) *Amendments - Article 100(c) EPC - claim 1*

The preamble of claim 1 found basis in claim 1 (polynucleotide comprising an MND promoter linked to a CAR), claim 20 (viral vector), and claim 24 (lentiviral vector) of the earlier application as filed.

Feature (a) found basis in claim 2 (anti-BCMA CAR); page 20, line 14 of the earlier application as filed

identified an scFv as a preferred embodiment of a CAR's antigen binding domain and also identified BCMA as target. Further basis could be found on page 27, lines 28 and 29. An anti-BCMA CAR was also the subject of Example 8 (page 103) of the earlier application as filed which also explained that "[a]*nti-BCMA expressing CAR T cells were manufactured as described in Example 1, supra*.". Thus, the construct used in Example 8 was identical to the one shown in Figure 1A, except that the anti-CD19 scFv was replaced by an anti-BCMA scFv.

Feature (b) found basis in claims 13 and 14 of the earlier application as filed.

Feature (c) was based on claim 7 of the earlier application as filed, which stated that the TM domain is "derived from CD8α". The absence of the term "derived from" from feature (c) in claim 1 did not add subject-matter, as the skilled person would understand that any TM domain "derived from" CD8α necessarily included at least the CD8α TM domain, as defined on page 25, lines 5 to 6. Consequently, claim 7 of the earlier application as filed, when read in light of this definition, provided a direct and unambiguous disclosure for a CD8α TM domain according to claim 1.

Feature (d) was disclosed in claim 12 of the earlier application as filed, which specified CD137 as a co-stimulatory domain.

Feature (e) found basis in claim 2 of the earlier application as filed.

The combination of features was directly and unambiguously derivable from claims 1, 2, 7, 12 to 14,

20 and 24 of the earlier application as filed in combination with page 20, lines 14 to 30. Importantly, the dependent claims were not only dependent on independent claim 1 but also dependent on multiple claims, i.e. claim 7 on claim 1 to 6; claim 12 on claims 1 to 8; and claim 14 on claim 13 which depended on claim 1 to 12. Only a single selection to specify BCMA as target antigen had to be made.
In that context reference was *inter alia* made to G 2/10 and the Case Law of the Boards of Appeal, 10th ed., 2022, II.E.1.6.4 and especially T 1362/15 and T 895/18.

Likewise, Example 8 on page 103 of the earlier application as filed clearly pointed to anti-BCMA CAR T cells, which were manufactured using the same vector architecture as in Example 1. The only difference between the polynucleotides of Example 1 and Example 8 was the target antigen, i.e. CD19 *versus* BCMA, respectively. Likewise, Tables 3 and 4 showed the components that made up the polynucleotide sequence of an anti-CD19 and anti-kLC CAR, respectively.

XIV. The parties' requests relevant to the decision were as follows.

(a) The appellant requested that the decision under appeal be set aside and that the patent be revoked.

(b) The respondent requested that the appeal be dismissed, implying that the opposition be rejected and patent be maintained as granted.

Reasons for the Decision

Patent as granted - sole request

Amendments - Article 100(c) EPC

1. It was undisputed that the earlier application as filed (published as WO 2015/164759) and the application as filed are identical (with the exception that the claims of the former appear in the description of the latter under the heading "*The invention can be further defined with reference to the following embodiments or clauses:*").

   As the application as filed was filed without claims, the assessment of whether the subject-matter claimed in the patent comprises added subject-matter is identical in relation to the application as filed and in relation to the earlier application as filed. In the following, the reference is made to the earlier application as filed, more specifically, to publication WO 2015/164759.

Claim 1 - combination of features

2. The opposition division held that Article 100(c) EPC did not prejudice the maintenance of the patent as granted. This was contested by the appellant on appeal.

3. The board considers that at least the following features need to be selected from multiple lists to arrive at the subject-matter of claim 1, thereby creating a specific combination of features that is not directly and unambiguously derivable from the earlier application as filed.

3.1 Feature "(a) an scFv that binds B cell maturation antigen (BCMA)"

BCMA must be selected as the scFv target from the list of antigens provided in claim 2 of the earlier application as filed. Also the earlier application as filed only discloses BCMA in lists of target antigens, such as on page 2, last paragraph; page 12, last paragraph; page 15, paragraph 1; page 20, lines 20 to 30; page 27, line 19 to page 31, line 21, without a pointer to BCMA being the preferred target molecule.

Moreover, the examples cannot provide a specific pointer to BCMA as a target antigen, because they disclose three different alternative target antigens: CD19 (Examples 1, 5), kLC (Examples 1, 3, 4, 6, 7), and BCMA (Example 8).
Thus, BCMA needs to be selected from a list of alternative antigens.

Page 20, lines 14 and 15 of the earlier application as filed provides a pointer towards the scFv format as being preferred.

3.2 Feature "(b) a CD8α hinge region"

Claim 14 of the earlier application as filed discloses the presence of the hinge region of CD8α. However, by virtue of its dependence on claim 13, and thus claims 1 to 12, this specific embodiment requires selection from a range of options resulting from the various dependencies.

3.3 Feature "(d) a CD137 co-stimulatory signaling domain"

The one or more co-stimulatory signalling domain need(s) to be selected from the three alternatives disclosed in claims 10 to 12 (or claim 9) of the earlier application as filed.

4. The board considers that, contrary to the respondent's argument, the claimed combination cannot be directly and unambiguously derived from claims 1, 2, 7, 12 to 14, 20, 24 and page 20, lines 14 to 30 of the earlier application as filed. Due to the multiple options provided in these claims and page 20, lines 14 to 30 and the multiple dependencies of claims 7, 12 to 14, 20 and 24, the claimed subject-matter with its particular combination of features cannot be directly and unambiguously derived from these passages in the earlier application as filed.

4.1 In that context, the parties referred to decisions T 350/20, T 895/18, and T 1362/15. In the board's view these decisions reaffirm the general principles established by opinion G 2/98 and decision G 2/10, i.e. that for assessing whether the claimed subject-matter extends beyond the content of the earlier application as filed, the claimed subject-matter must be directly and unambiguously disclosed in the (whole of) the earlier application as filed, as read by the skilled person at the relevant date using common general knowledge.

4.1.1 In decision T 350/20 (Reasons 2.5 to 2.7), the responsible board held that even where multiple dependencies exist, the presence of numerous optional features may result in a "forest" of possibilities, from which a specific combination may not be directly

and unambiguously derivable. The mere fact that each individual feature is disclosed in the application as filed, and that the claimed combination may fall within the universe of possible embodiments, is not sufficient under Article 123(2) EPC to reach the conclusion that there is a direct and unambiguous disclosure of subject-matter derived from a combination of separately disclosed features, a clear pointer to that specific combination is required.

4.1.2 In decisions T 895/18 (Reasons 3.1.3) and T 1362/15 (Reasons 3.7.1), the respective boards emphasised that the presence of "US-style" claim dependencies, where dependent claims refer only to the independent claim, does not, by itself, justify assuming that all combinations of features are disclosed. Instead, under Article 123(2) EPC, each claimed combination must be individually assessed to determine whether it is directly and unambiguously derivable from the application as filed. Both decisions underscore that neither claim structure nor the presence of broad embodiments suffices to support intermediate generalisations unless the specific combination of features can be directly and unambiguously inferred from the disclosure of the application as filed.

5. The respondent also argued that in the present case, Examples 1 and 8 provided a pointer to subject-matter having the combination of features as claimed.

6. The board notes that Example 8 discloses that "[a]*nti-BCMA expressing CAR T cells were manufactured as described in Example 1, supra.*" Example 1, in Tables 3 and 4, gives the identity, Genbank reference, source name and citation for the various nucleotide segments

of the pMND-CD19 CAR and anti-kappa light chain (kLC) CAR, respectively.
Figures 1A and B show the structure of a pMND-CD19 CAR construct (A) and a pMND-kLC CAR construct (B) and Figures 2 and 3 show the vector maps for pMND-CD19 CAR and pMND-kLC-CAR, respectively.

The person skilled in the art would understand the disclosure in Examples 8 and 1 such that in order to produce the anti-BCMA CAR lentiviral vector, the instructions of Example 1 was followed, with the anti-CD19 scFv/anti-kLC-scFv being replaced by an anti-BCMA scFv.

However, claim 1 does not relate to lentiviral vectors having all features of the lentiviral vector constructs disclosed in Table 3 or 4 of Example 1 (apart from the specificity for BCMA) and thus, Examples 8 and 1 cannot provide a basis for the subject-matter of claim 1. This is considered to represent an intermediate generalisation falling between the lentivirus vector disclosed in Example 8 (in combination with Example 1) and the lentiviral vectors described elsewhere in the description or the claims of the earlier application as filed, but which is not disclosed therein.

7. In summary, to arrive at the subject-matter of claim 1 at least three selections from lists in the earlier application as filed are necessary, (a) BCMA as target antigen (see point 3.1 above), (b) the CD8 hinge region (see point 3.2 above), and (d) the CD137 co-stimulatory domain (see point 3.3 above).
However, the earlier application as filed does not contain a pointer to this specific combination of features. In the absence of such a pointer, the skilled person would not directly and unambiguously derive the

claimed subject-matter from the disclosure of the earlier application as filed. Moreover, the omission of additional features present in the specific lentiviral vector constructs disclosed in the examples results in subject-matter which is an undisclosed intermediate generalisation between a general and a specific disclosure in the earlier application as filed. Consequently, the subject-matter of claim 1 extends beyond the content of the earlier application as filed and, by the same token, of the application as filed.

8. Thus, the ground for opposition under Article 100(c) EPC prejudices the maintenance of the patent as granted.

9. As maintenance of the patent as granted is the respondent's sole request, no further claim request is to be considered.

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:

I. Aperribay M. Blasi

Decision electronically authenticated