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Datasheet for the decision of 28 January 2021

Case Number: T 2260/19 - 3.3.01

Application Number: 12783818.3

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Language of the proceedings: EN

Title of invention:
COMPOUND COMPRISING A MAO TARGETING/ SEEKER MOIETY FOR TREATING HUMAN GLIOMAS

Applicants:
The Methodist Hospital Research Institute
Baskin, David, S.
Sharpe, Martyn, Alun

Relevant legal provisions:
EPC Art. 123(2), 84, 111(1)

Keyword:
Amendments - added subject-matter (no)
Claims - clarity after amendment (yes)
Appeal decision - remittal to the department of first instance (yes)

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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
Fax +49 (0)89 2399-4465

Case Number: T 2260/19 - 3.3.01

D E C I S I O N
of Technical Board of Appeal 3.3.01
of 28 January 2021

Appellant: (Applicant 1)	The Methodist Hospital Research Institute 6565 Fannin, MS D200 Houston, TX 77030 (US)
Appellant: (Applicant 2)	Baskin, David, S. 1656 North Boulevard Houston, TX 77006 (US)
Appellant: (Applicant 3)	Sharpe, Martyn, Alun 1908 Marshall Street Apt. 2 Houston, TX 77098 (US)
Representative:	Forresters IP LLP Skygarden Erika-Mann-Straße 11 80636 München (DE)
Decision under appeal:	**Decision of the Examining Division of the European Patent Office posted on 25 February 2019 refusing European patent application No. 12783818.3 pursuant to Article 97(2) EPC.**

Composition of the Board:

Chairman	A. Lindner
Members:	R. Hauss
	P. de Heij

Summary of Facts and Submissions

I. The decision under appeal is the examining division's decision, announced on 23 January 2019 and posted on 25 February 2019, refusing European patent application No. 12 783 818.3.

II. The decision is based on an amended main request and auxiliary requests 1 and 2 (all filed by letter of 21 January 2019).

Claims 1 to 3 of the main request read as follows:

> "**1.** A compound for treating cancer comprising
>
> a first targeting/seeker moiety comprising 1-methyl-1,2,3,6-tetrahydropyridine or 1-cyclopropyl-1,2,3,6-tetrahydropyridine,
>
> a first therapeutic moiety
>
> wherein the first targeting/seeker moiety is operably linked to the first therapeutic moiety via at least a first linker moiety.
>
> **2.** The compound of claim 1, wherein the first linker moiety is a carbamate, or is a compound selected from the group consisting of 2-methylpropanamide, cyclohexane, and a salt thereof.
>
> **3.** The compound of claim 1, wherein the first therapeutic moiety is selected from the group consisting of a DNA acylating agent, a DNA damaging agent, a nitrogen mustard, a sulfur mustard, a platin tetranitrate, vinblastine, docetaxel, etoposide, irinotecan, camptothecin, APE SN38, and carmustine."

III. According to the decision under appeal:

(a) Claim 2 of the main request contained added subject-matter in so far as it specified that the linker moiety was a carbamate (Article 123(2) EPC).

(b) Claims 1 and 3 of the main request lacked clarity (Article 84 EPC) due to the use of functional definitions ("linker moiety", "therapeutic moiety", "DNA acylating agent" and "DNA damaging agent").

(c) Certain terms employed in the claims of auxiliary requests 1 and 2 lacked clarity (Article 84 EPC).

IV. The applicants (appellants) filed an appeal against this decision.

V. In the course of the appeal proceedings, the appellants replaced all claim requests previously on file with a single set of amended claims, filed with their submission of 7 January 2021. These amended claims read as follows:

"**1.** A compound for use in treating glioma comprising

a first targeting/seeker moiety selectd from the group consisting of 1-methyl-1,2,3,6-tetrahydropyridine or 1-cyclopropyl-1,2,3,6-tetrahydropyridine,

a first therapeutic moiety

wherein the first targeting/seeker moiety is operably linked to the first therapeutic moiety via at least a first linker moiety;

or wherein the compound is 2-R_3-N-R_2-N-R_1-2-(1-X-1,2,3,6-tetrahydropyridin-4-yl) acetamide, 4-phenyl-1-X-1,2,3,6-tetrahydropyridine, 4-cyclohexyl-1-X-1,2,3,6-tetrahydropyridine,

wherein R_1, R_2 and R_3 are each halogen, hydroxyl, oxo, cyano, nitro, amino, alkylamino, dialkylamino,

alkyl, alkoxy, alkylthio, haloalkyl,aryl, arylalkyl, heteroaryl, heteroarylalkyl, heterocycle, heterocyclealkyl, $-NR_aR_b$, $-NR_aC(=O)R_b$, $-NR_aC(=O)NR_aNR_b$, $-NR_aC(=O)OR_b$, $-NR_aSO_2R_b$, $-C(=O)R_a$, $-C(=O)OR_a$, $-C(=O)NR_aR_b$, $-C(=O)NR_aR_b$, $-OR_a$, $-SR_a$, $-SOR_a$, $-S(=O)_2R_a$, $-OS(=O)_2R_a$, $-S(=O)_2ORa$, substituted alkyl, substituted aryl, substituted arylalkyl, substituted heterocycle, or substituted heterocyclealkyl;

wherein R_a and R_b are the same or different and, are, independently, hydrogen, alkyl, haloalkyl, substituted alkyl, aryl, substituted aryl, arylalkyl, substituted arylalkyl, heterocycle, substituted heterocycle, heterocyclealkyl or substituted heterocyclealkyl,

and further wherein **X** is a chemotherapeutic moiety selected from the group consisting of a nitrogen mustard, a sulfur mustard, a platin tetranitrate, *cis*-platin, or salt thereof.

2 The compound for the use of claim 1, wherein the first linker moiety is a compound selected from the group consisting of 2-methylpropanamide, cyclohexane, and a salt thereof.

3. The compound for the use of claim 1, wherein the first therapeutic moiety is selected from the group consisting of a DNA damaging agent, a nitrogen mustard, a sulfur mustard, a platin tetranitrate, vinblastine, docetaxel, etoposide, camptothecin, and carmustine.

4. The compound for the use of any one of the preceding claims, wherein the compound is admixed with one or more pharmaceutically-acceptable carriers, diluents, excipients, or any combination thereof and with one or more other antineoplastic agents, one or more other cytotoxic agents, one or more cytostatic agents, one or more chemotherapeutic agents, including

a compound selected from the group consisting of irinotecan, camptothecin, temozolomide, SN 38, vinblastine, docetaxel, etoposide, carmustine, a sulfan, a platin tetranitrate, a cis-platin, a topoisomerase inhibitor, a chemotherapeutic, and any combination thereof

5. The compound for the use of any one of the preceding claims, wherein the compound is admixed with one or more pharmaceutically-acceptable carriers, diluents, excipients, or any combination thereof.

6. The compound for the use of any one of the preceding claims for use in treating human glioma, Glioblastoma Multiforme (GBM), recurrent Glioblastoma Multiforme (rGBM), astrocytoma, ependymoma, oligodendroglioma, brainstem glioma, mixed glioma, or any combination thereof, including a tumor that is diagnosed or identified as an advanced-stage or an advanced-grade type of cancer, a radiation-resistant glioma, or a tumor that comprises one or more glioma stem cells."

VI. The appellants argued as follows:

(a) The amended claims no longer defined the linker moiety as being a carbamate and their subject-matter did not extend beyond the content of the claims and description as filed.

(b) The person skilled in the art would seek to interpret the claims in a technically meaningful way. Contrary to the examining division's view, the skilled person would be able to distinguish the therapeutic moiety from the linker moiety in a given compound. The term "DNA acylating agent" had been deleted from claim 3. The term "DNA damaging agent", retained in the current claims, was a well-known term in the art.

VII. The appellants requested that the decision under appeal be set aside and that the case be remitted to the examining division for further prosecution on the basis of the amended set of claims filed with the submission of 7 January 2021.

Reasons for the Decision

1. The appeal is admissible.

2. Amendments (Article 123(2) EPC)

2.1 The current claims (see point V. above) address the examining division's objection of added subject-matter (see point III.(a) above) as they no longer define the linker moiety as being a carbamate.

2.2 The board sees no reason to object to these claims under Article 123(2) EPC.

2.3 The basis for the claims cannot be derived solely from the claims as filed. Since the claims as filed all refer back to "any preceding claim" the claim dependencies do not directly and unambiguously result in particular claim combinations. However, the required basis in the application as filed may be found in the following passages:

claim 1: claim 8 as filed and page 5, lines 24 to 27; page 1, lines 10-13; page 6, lines 1-2; page 9, lines 12-30

claim 2: page 8, lines 14-15 and claim 11

claim 3: page 5, lines 29-33

claims 4 and 5: page 10, lines 4 to 16

claim 6: page 12, lines 9 to 15

3. Clarity (Article 84 EPC)

3.1 Starting from the finding that the enzyme MAO-B (monoamine oxidase B) is up-regulated on the surface of glioblastomal mitochondria compared with mitochondria of healthy cells, the application relates to the development of tetrahydropyridine "targeting moieties". As MAO-B-specific substrates, these targeting moieties permit the selective delivery of chemotherapeutic anticancer agents ("therapeutic moieties") to gliomal mitochondria. For this purpose, the targeting moiety is linked to the drug by a "linker moiety".

3.2 The current claims are restricted to a medical use (compound for use in treating glioma) in the claim format provided for in Article 54(5) EPC.

3.3 Independent claim 1 relates to several alternative definitions of the tripartite compound described in the application.

(a) While the first alternative (see the first part of the claim up to "first linker moiety") only defines the targeting/seeker moiety, the therapeutic moiety is defined implicitly by the therapeutic indication of claim 1 since it must be a drug which is useful in treating glioma.

The board is furthermore convinced that the person skilled in the art is capable of identifying, in a given molecule, (1) the therapeutic moiety (a drug useful in treating glioma) and (2) any linker moiety linking the therapeutic moiety to the tetrahydropyridine targeting moiety. Thus the skilled person can determine if a compound is within the scope of claim 1. In this context, the argument that the linker moiety might

alternatively be regarded as part of the therapeutic moiety appears to be artificial.

(b) The other three alternatives (see the second part of claim 1 starting from "or wherein the compound is...") give an explicit definition of each molecule, including the chemotherapeutic moiety X.

Hence, the board considers that the definition provided in claim 1 clearly defines the subject-matter for which protection is sought and thus meets the requirements of Article 84.

3.4 Dependent claim 3 specifies that the therapeutic moiety may be a DNA-damaging agent. While generic, this term does not lack clarity. It is known that the concept of aiming at DNA as a target for anticancer compounds resulted in the development of numerous anticancer drugs. As a consequence, DNA-damaging agents are widely used in cancer chemotherapy and the term is well-established in the art.

4. Remittal (Article 111(1) EPC)

4.1 The decision under appeal exclusively concerns objections under Articles 123(2) and 84 EPC raised against the claims of the requests considered by the examining division.

4.2 As the appellants' amended claim request meets the requirements of Articles 123(2) and 84 EPC, the board finds it appropriate to remit the case to the examining division, in accordance with the appellants' request. The limited scope of the examination of the claims by the examining division constitutes a special reason according to Article 11 RPBA.

Order

For these reasons it is decided that:

1. The decision under appeal is set aside.

2. The case is remitted to the examining division for further prosecution.

The Registrar: The Chairman:

M. Schalow A. Lindner

Decision electronically authenticated