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Datasheet for the decision of 17 December 2021

Case Number: T 1820/18 - 3.3.04

Application Number: 08844924.4

Publication Number: 2209491

IPC: A61K39/395, C07K16/28, A61P35/00

Language of the proceedings: EN

Title of invention:
Molecules and methods for modulating low-density-lipoprotein receptor-related protein 6 (LRP6)

Patent Proprietor:
Novartis AG

Opponents:
Boehringer Ingelheim RCV GmbH & Co KG /
Boehringer Ingelheim International GmbH (Opposition withdrawn)
Merck Patent GmbH

Headword:
LRP6 binding molecules/NOVARTIS

Relevant legal provisions:
EPC Art. 100(c), 123(2)
RPBA 2020 Art. 13(2)

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It can be changed at any time and without notic

Keyword:

Grounds for opposition - added subject-matter (yes)
Amendments - added subject-matter (yes)
Amendment after summons - exceptional circumstances (no) - cogent reasons (no) - taken into account (no)

Decisions cited:

G 0002/10, T 0270/94, T 0656/94, T 0154/95, T 0863/96, T 0620/99, T 0790/03

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Case Number: T 1820/18 - 3.3.04

D E C I S I O N
of Technical Board of Appeal 3.3.04
of 17 December 2021

Appellant: (Patent Proprietor)	Novartis AG Lichtstrasse 35 4056 Basel (CH)
Representative:	Carpmaels & Ransford LLP One Southampton Row London WC1B 5HA (GB)
Respondents: (Joint opponents 1)	Opposition withdrawn on 16 December 2021 Boehringer Ingelheim RCV GmbH & Co KG / Boehringer Ingelheim International GmbH Dr. Boehringer-Gasse 5-11 / Binger Strasse 173 AT-1121 Wien / DE-55216 Ingelheim am Rhein (AT)
Representative:	D Young & Co LLP 120 Holborn London EC1N 2DY (GB)
Respondent: (Opponent 2)	Merck Patent GmbH Frankfurter Strasse 250 64293 Darmstadt (DE)
Decision under appeal:	**Decision of the Opposition Division of the European Patent Office posted on 11 May 2018 revoking European patent No. 2209491 pursuant to Article 101(3)(b) EPC**

Composition of the Board:

Chair	G. Alt
Members:	A. Schmitt
	L. Bühler

Summary of Facts and Submissions

I. The appeal lodged by the patent proprietor (appellant) lies from the opposition division's decision revoking European patent No. 2 209 491 (patent).

Claim 1 of the patent as granted reads as follows:

"1. A low-density-lipoprotein receptor-related protein 6 polypeptide (LRP6) binding molecule comprising an antigen binding portion of a monoclonal antibody that specifically binds to the first propeller of LRP6, wherein the antigen binding portion binds to an epitope within propeller 1 of human LRP6 within or overlapping amino acids 20-326 of
MGAVLRSLLACSFCVLLRAAPLLLYANRRDLRLVDATNGKENATIVVGGLEDA
AAVDFVFSHGLIYWSDVSEEAIKRTEFNKTESVQNVVVSGLLSPDGLACDWLGE
KLYWTDSETNRIEVSNLDGSLRKVLFWQELDQPRAIALDPSSGFMYWTDWGEV
PKIERAGMDGSSRFIIINSEIYWPNGLTLDYEEQKLYWADAKLNFIHKSNLDGTN
RQAVVKGSLPHPFALTLFEDILYWTDWSTHSILACNKYTGEGLREIHSDIFSPMDI
HAFSQQRQPNATNPCGIDNGGCSHLCLMSPVKPFYQCACPTGVKLLENGKTCK
DGATELLLLARRTDLRRISLDTPDFTDIVLQLEDIRHAIAIDYDPVEGYIYWTDDE
VRAIRRSFIDGSGSQFVVTAQIAHPDGIAVDWVARNLYWTDTGTDRIEVTRLNG
TMRKILISEDLEEPRAIVLDPMVGYMYWTDWGEIPKIERAALDGSDRVVLVNTS
LGWPNGLALDYDEGKIYWGDAKTDKIEVMNTDGTGRRVLVEDKIPHIFGFTLL
GDYVYWTDWQRRSIERVHKRSAEREVIIDQLPDLMGLKATNVHRVIGSNPCAE
ENGGCSHLCLYRPQGLRCACPIGFELISDMKTCIVPEAFLLFSRRADIRRISLETNN
NNVAIPLTGVKEASALDFDVTDNRIYWTDISLKTISRAFMNGSALEHVVEFGLD
YPEGMAVDWLGKNLYWADTGTNRIEVSKLDGQHRQVLVWKDLDSPRALALD
PAEGFMYWTEWGGKPKIDRAAMDGSERTTLVPNVGRANGLTIDYAKRRLYWT
DLDTNLIESSNMLGLNREVIADDLPHPFGLTQYQDYIYWTDWSRRSIERANKTS
GQNRTIIQGHLDYVMDILVFHSSRQSGWNECASSNGHCSHLCLAVPVGGFVCGC
PAHYSLNADNRTCSAPTTFLLFSQKSAINRMVIDEQQSPDIILPIHSLRNVRAIDY
DPLDKQLYWIDSRQNMIRKAQEDGSQGFTVVVSSVPSQNLEIQPYDLSIDIYSRY
IYWTCEATNVINVTRLDGRSVGVVLKGEQDRPRAVVVNPEKGYMYFTNLQERS
PKIERAALDGTEREVLFFSGLSKPIALALDSRLGKLFWADSDLRRIESSDLSGANR
IVLEDSNILQPVGLTVFENWLYWIDKQQQMIEKIDMTGREGRTKVQARIAQLSDI
HAVKELNLQEYRQHPCAQDNGGCSHICLVKGDGTTRCSCPMHLVLLQDELSCG
EPPTCSPQQFTCFTGEIDCIPVAWRCDGFTECEDHSDELNCPVCSESQFQCASGQ
CIDGALRCNGDANCQDKSDEKNCEVLCLIDQFRCANGQCIGKHKKCDHNVDCS
DKSDELDCYPTEEPAPQATNTVGSVIGVIVTIFVSGTVYFICQRMLCPRMKGDGE
TMTNDYVVHGPASVPLGYVPHPSSLSGSLPGMSRGKSMISSLSIMGGSSGPPYDR
AHVTGASSSSSSSTKGTYFPAILNPPPSPATERSHYTMEFGYSSNSPSTHRSYSYR
PYSYRHFAPPTTPCSTDVCDSDYAPSRRMTSVATAKGYTSDLNYDSEPVPPPPTP
RSQYLSAEENYESCPPSPYTERSYSHH LYPPPPSPCTDSS;

and wherein the antigen binding portion is capable of antagonizing Wnt1-induced signaling pathway."

II. The patent, entitled "*Molecules and methods for modulating low-density-lipoprotein receptor-related protein 6 (LRP6)*", was granted on European patent application No. 08 844 924.4, which had been filed as an international application under the PCT and was published as WO 2009/056634 (application). The description of this application has 62 pages and contains 239 paragraphs.

Claims 1, 7, 20 and 25 of the application read:

"1. A low-density-lipoprotein receptor-related protein 6 polypeptide (LRP6) binding molecule comprising an antigen binding portion of an antibody that specifically binds to LRP6, wherein the antigen binding portion binds to an epitope of human LRP6 (SEQ ID NO:1) within or overlapping one of the following:
(a) amino acids 20-326 of SEQ ID NO:1;
(b) amino acids 286-324 of SEQ ID NO:1;
(c) amino acids 631-932 of SEQ ID NO:1; or
(d) amino acids 889-929 of SEQ ID NO:1.

7. The LRP6 binding molecule of any of claims 1-5, wherein the antigen binding portion is capable of antagonizing the Wnt signaling pathway.

20. The LRP6 binding molecule of any of the preceding claims, wherein the antigen binding portion is an antigen binding portion of a monoclonal antibody.

25. An antagonizing LRP6 binding molecule of any of the preceding claims, wherein the LRP6 binding molecule inhibits LRP6 binding to one or more of the following

Wnt signaling pathway members: dickkopf 1 (DKK1), DKK2, DKK4, SOST1, SOSD1 (USAG1), sFRP (soluble Fzd-related protein) 1-4, Wise, or Wnt ligands."

III. Two oppositions were filed against the patent in its entirety. The opposition proceedings were based on the grounds of lack of novelty (Article 54 EPC) and lack of inventive step (Article 56 EPC) in Article 100(a) EPC and on the grounds in Article 100(b) and (c) EPC.

IV. In the decision under appeal, the opposition division held that the subject-matter of the claims as granted did not extend beyond the content of the application and was new. However, the patent did not disclose the invention as defined in the claims as granted in a manner sufficiently clear and complete for it to be carried out by a person skilled in the art.

V. With the statement of grounds of appeal, the appellant submitted further sets of claims as auxiliary requests 1 to 3 and arguments in support of its view that the invention as defined in the claims as granted (main request) was sufficiently disclosed in the patent.

Claim 1 of auxiliary request 1 is identical to claim 1 of the patent as granted (see section I. above) except that the phrase "or overlapping" has been deleted.

Claim 1 of auxiliary request 2 is identical to claim 1 of the patent as granted (see section I. above).

Claim 1 of auxiliary request 3 is identical to claim 1 of auxiliary request 1 (see above).

VI. Joint opponents 1 replied to the appellant's statement of grounds of appeal by letter dated 28 January 2019.

They submitted three documents and, *inter alia*, arguments in support of their view that claim 1 as granted comprised subject-matter that extended beyond the content of the application.

VII. Opponent 2 (respondent) neither replied to the appellant's statement of grounds of appeal nor made any substantive submissions during the written proceedings.

VIII. The board summoned the parties to oral proceedings and subsequently issued a communication pursuant to Article 15(1) RPBA, in which it expressed its preliminary opinion that, *inter alia*, claim 1 as granted contained subject-matter that extended beyond the content of the application.

IX. Joint opponents 1 replied to the board's communication and submitted, *inter alia*, further comments in support of their view that claim 1 as granted did not have a basis in the application.

X. On 5 June 2020, the appellant submitted further sets of claims as auxiliary requests 4 to 11 and, *inter alia*, arguments in support of its view that claim 1 as granted and claim 1 of each of the auxiliary requests 1 to 11 had a basis in the application.

Claim 1 of auxiliary request 4 is identical to claim 1 of the patent as granted (see section I.) except that the phrase "antagonizing Wnt1-induced signaling pathway" has been replaced with the phrase "antagonizing Wnt induced signaling pathway by preventing Wnt1 from binding to LRP6".

Claim 1 of auxiliary request 5 is identical to claim 1 of auxiliary request 4 except that the phrase "or overlapping" has been deleted.

Claim 1 of auxiliary request 6 is identical to claim 1 of auxiliary request 4.

Claim 1 of auxiliary request 7 is identical to claim 1 of auxiliary request 5.

Claim 1 of auxiliary request 8 is identical to claim 1 of the patent as granted (see section I.) except that the phrase "antagonizing Wnt1-induced signaling pathway" has been replaced with the phrase "antagonizing Wnt induced signaling pathway by preventing Wnt1, Wnt2, Wnt6, Wnt7a, Wnt7b and Wnt10 from binding to LRP6".

Claim 1 of auxiliary request 9 is identical to claim 1 of auxiliary request 8 except that the phrase "or overlapping" has been deleted.

Claim 1 of auxiliary request 10 is identical to claim 1 of auxiliary request 8.

Claim 1 of auxiliary request 11 is identical to claim 1 of auxiliary request 9.

XI. In reply, joint opponents 1 submitted, *inter alia*, arguments in support of their view that claim 1 as granted and claim 1 of each of auxiliary requests 4 to 11 comprised subject-matter that extended beyond the content of the application.

XII. On 16 December 2021, joint opponents 1 withdrew their opposition.

XIII. The oral proceedings - which had been postponed twice in view of the ongoing Covid-19 pandemic - took place on 17 December 2021. The appellant and opponent 2 (respondent) were represented at the oral proceedings, which were held by videoconference with the agreement of both parties. During the oral proceedings, the board admitted auxiliary requests 8 to 11 into the appeal proceedings. At the end of the oral proceedings, the Chair announced the board's decision.

XIV. The appellant's arguments, where relevant to the decision, are summarised as follows.

Procedural issues

The respondent had not made any submissions during the written part of the appeal proceedings. Therefore, their requests, objections and arguments had been submitted for the first time at the oral proceedings and should not be admitted into the appeal proceedings.

Main request

Amendments (Article 100(c) EPC) - Claim 1

The subject-matter of claim 1 was based on the framework of claims 1, 7 and 20 of the application, amended by two features, specifically a particular antagonism of the Wnt signalling pathway (the Wnt1-induced signalling) and the binding to the first propeller domain of low-density-lipoprotein receptor-related protein 6 polypeptide (LRP6).

The application taught that Wnt ligands could be divided into two classes according to their preferential inhibition by particular LRP6-binding

molecules, namely those that inhibited Wnt3a and those that inhibited Wnt1 (see e.g. paragraphs [34], [38] and [232] of the application). A "Wnt1-specific" antagonist was capable of inhibiting Wnt1, but the inhibition of other members from the same class (Wnt2, Wnt 6, Wnt7A, Wnt7B, Wnt9, Wnt10A and Wnt10B) was not excluded; in fact, the term "Wnt1-specific" was used to group together those Wnt ligands that behaved in the same way. Moreover, it meant only that Wnt1-specific signalling activity was inhibited to a greater extent than Wnt3a-specific signalling activity (see e.g. paragraphs [15] and [236] and Table 2 of the application).

The phrase "*capable of antagonizing Wnt1-induced signaling pathway*" used in granted claim 1 had the same meaning, i.e. that Wnt1-specific signalling activity was antagonised but that antagonising of other Wnt ligands too was not not ruled out. In this context, Wnt1 was not selected from a list of equal alternatives but was highlighted throughout the application as the preferred Wnt ligand, as was evident from the examples and the data in Table 2 of the application.

The antagonism of the Wnt1-specific signalling was achieved by binding to the first propeller domain of LRP1. The basis for the link between the binding to the propeller 1 domain and Wnt1-specificity was disclosed in paragraphs [57] and [235] and further supported by the disclosure in paragraphs [15], [34], [38], [215] and [236] of the application. That the term "Wnt1-specific" was not used in claim 1 did not result in added subject-matter, because it was inherent to the wording of the claim as a property of the antibody binding to the propeller 1 domain of LRP6. The skilled

person was therefore not presented with additional technical information.

Auxiliary requests 1 to 3

Amendments (Article 123(2) EPC) - Claim 1

The appellant did not submit specific arguments as regards the amendments in claim 1 of auxiliary requests 1 to 3.

Auxiliary requests 4 to 7

Admittance (Article 13(2) RPBA 2020)

The amendments to the claims of auxiliary request 4 compared to the claims as granted had been made in response to the board's objection that claim 1 of the main request contained subject-matter that extended beyond the application and were not complicated. There had been no need to submit such amendments during the opposition proceedings since the opposition division's preliminary opinion had been that claim 1 as granted did not contain subject-matter that extended beyond the content of the application.

Furthermore, in their reply to the statement of grounds of appeal, former joint opponents 1 had simply copied their objection into an annex and had not explained why the opposition division's conclusion in this matter had been wrong. This objection had thus not been substantiated.

Therefore, prior to the preliminary opinion of the board, no objection to added subject-matter that the appellant would have needed to answer had been on file.

Auxiliary request 4 had been presented at the first opportunity and should therefore be admitted into the appeal proceedings.

The appellant did not provide specific arguments on admittance of auxiliary requests 5 to 7.

Auxiliary requests 8 to 11

Amendments (Article 123(2) EPC) - Claim 1

The subject-matter of claim 1 of auxiliary request 8 had a basis in claims 1, 7, 20 and 25 and paragraphs [9], [15], [34], [38], [57], [76], [140], [141], [232], [235], [236] and [237] of the application.

Paragraph [9] provided a general disclosure of LRP6-binding molecules of the invention and their ability to interfere with the binding of members of the Wnt pathway. In paragraph [15], it was further disclosed that the LRP6-binding molecules prevented certain Wnt ligands from binding, which, in the final sentence of paragraph [15], were defined as those listed in claim 1 of auxiliary request 8. Moreover, the prevention of Wnt pathway activation disclosed in paragraph [34] was the same as the prevention of Wnt ligand binding.

That antagonising of the Wnt-induced pathway was achieved by preventing the binding of Wnt ligands to LRP6 was also disclosed in paragraphs [38], [57], [76], [140], [141], [232] and [237]. In paragraphs [232] and [237], the term "blocked" would be understood by the skilled person in the sense of prevention of binding. Furthermore, paragraphs [232], [235] and [236] provided pointers to the Wnt1-specific class of Wnt ligands

listed in paragraph [15], which could be blocked by an antibody binding to the propeller 1 domain of LRP6.

The appellant did not submit any specific arguments as regards the amendments in claim 1 of each of auxiliary requests 9 to 11.

XV. The respondent's arguments, where relevant to the decision, are summarised as follows.

Procedural issues

The respondent was a party to the proceedings and therefore had the right to be heard. Since it was relying on the submissions of former joint opponents 1, the requests, objections and arguments presented at the oral proceedings were not late filed but were already part of the appeal proceedings.

Main request

Amendments (Article 100(c) EPC) - Claim 1

The application did not disclose an LRP6-binding molecule that specifically bound to the propeller 1 domain but was merely "capable of antagonizing Wnt-induced signaling pathway", i.e. did not need to be a "Wnt1-specific" antagonist but could also antagonise any of the other Wnt ligands, including Wnt3 and Wnt6. Instead, the molecules that specifically bound to an epitope within the propeller 1 domain of LRP6 disclosed in the application were described as being "Wnt1-specific", which could only be interpreted as antagonists that were specific to the Wnt1 ligand alone, i.e. inhibited only the Wnt1 ligand.

The appellant's definition of the term "Wnt1-specific" as a general antagonist of the Wnt ligands listed in paragraph [232] of the application could not be accepted, because paragraph [232] did not provide an exclusive definition of this term. The application did not contain any indication that the terms "Wnt1-specific" and "Wnt3a-specific" were used in the application as general references to particular classes of ligands. Nor was such a definition commonly used in the prior art.

Furthermore, even if the appellant's definition of the term "Wnt1-specific" were accepted, the subject-matter of claim 1 as granted was not restricted to LRP6-binding molecules able to specifically antagonise Wnt ligands of such a Wnt1 "class", because the LRP6-binding molecule of claim 1 was defined merely as being "capable of antagonizing Wnt1-induced signalling pathway" and therefore did not have any specificity for Wnt1 or members of the Wnt1 "class" but might also inhibit other Wnt molecules that were not members of this class (Wnt3 and Wnt3a).

Besides, the application also lacked the disclosure that antibodies binding to an epitope within the propeller 1 domain of LRP6 were always Wnt1-specific, i.e. that "Wnt1-specificity" was inherent to those antibodies. This was evident from paragraph [34] of the application, which disclosed that an antagonising molecule binding within the first propeller of LRP6 could also inhibit signalling by Wise ligands. Moreover, an inherent property was not relevant in the context of amendments because, by definition, an inherent property was not directly and unambiguously disclosed.

Nor could the Fab molecules described in the examples (paragraphs [231] to paragraph [237] and Table II) support the disclosure of molecules binding to an epitope within the propeller 1 domain of LRP6 and antagonising Wnt1-induced signalling pathway or provide a conclusive definition of the term "Wnt1-specific" because the only Fab fragments described in paragraph [236] as being Wnt1-specific were not present in Table II, and it was therefore not known to which region of LPR6 they bound.

Auxiliary requests 1 to 3

Amendments (Article 123(2) EPC) - Claim 1

Claim 1 of each of auxiliary requests 1, 2 and 3 contained subject-matter that extended beyond the content of the application for the same reasons as claim 1 of the main request.

Auxiliary requests 4 to 7

Admittance (Article 13(2) RPBA 2020)

Since auxiliary request 4 had been submitted with a letter filed subsequent to the statement of grounds of appeal, i.e. neither with the statement of grounds of appeal nor a reply thereto, it was evident from the transitional provisions specified in Article 25(2) RPBA 2020 that not only Article 13 RPBA 2020 but also Article 12(4) to (6) RPBA 2020 applied to this submission.

Claim 1 of auxiliary request 4 comprised the new feature of "preventing Wnt1 from binding to LRP6", which had not been present in any of the claim sets

considered in the proceedings before the opposition division or in the appeal proceedings thus far. It therefore amounted to a change of the case at a late stage of the proceedings that raised new issues under Article 84 EPC and Article 123(2) and (3) EPC and was not in keeping with procedural economy.

Furthermore, since the objection that claim 1 as granted comprised subject-matter going beyond the application had already been raised in the notice of opposition, the appellant should have already submitted auxiliary request 4 during the proceedings before the opposition division. Therefore, in line with Article 12(6) RPBA 2020, these requests should not be admitted into the appeal proceedings.

Moreover, if a request could and should have been submitted during the opposition proceedings, there could be no exceptional circumstances or cogent reasons justifying that it was only submitted under the provisions set out in Article 13(2) RPBA 2020. In any event, the appellant had not provided any justification for the late submission of auxiliary request 4 when filing it. Consequently, auxiliary request 4 should not be admitted into the appeal proceedings.

The same reasoning applied to auxiliary requests 5 to 7, which should therefore not be admitted into the appeal proceedings either.

Auxiliary requests 8 to 11

Amendments (Article 123(2) EPC) - Claim 1

None of the passages of the application which had been cited by the appellant in support of the subject-matter

of claim 1 of auxiliary request 8 disclosed, alone or in combination, an LRP6-binding molecule that bound to the propeller 1 domain of LRP6 and prevented the binding of the particular subgroup of Wnt ligands listed in the claim to LRP6.

Claims 1, 7 and 25 of the application could not provide a basis for the claimed subject-matter, as they did not disclose the prevention of binding of the specific group of Wnt ligands recited in claim 1 of auxiliary request 8 to LRP6.

Paragraph [9] merely referred to an LRP6-binding molecule that "interfered" with the binding of members of the Wnt pathway to LRP6, listed a variety of different Wnt pathway members unrelated to Wnt ligands and did not single out the group of Wnt ligands listed in claim 1 of auxiliary request 8. The same was true for the disclosure in paragraphs [140] and [141]. Paragraph [57] also lacked any disclosure of all Wnt ligands listed in the claim.

Paragraph [15], on the other hand, disclosed a general, non-limiting list of Wnt ligands but not an LRP6-binding antibody that bound to the propeller 1 domain and prevented the binding of the group of these Wnt ligands to LRP6.

Paragraph [34] provided a definition of a Wnt1-specific antagonising LRP6-binding molecule, namely that it could prevent Wnt pathway activation and signalling by any of the recited Wnt ligands, but did not link this disclosure to the binding of this molecule to the propeller 1 domain of LRP6 or the prevention of the binding of these Wnt ligands to LRP6.

Paragraph [38] disclosed an antagonising LRP6-binding molecule defined by a series of features that were not present in claim 1 of auxiliary request 8 and therefore could not provide a basis for the subject-matter of this claim either.

Paragraph [76] of the application also made clear that the interference with the binding of a Wnt pathway member was just one possible way an antagonising LRP6-binding molecule could prevent signal transduction via the Wnt1 signalling pathway and did not provide a basis for the LRP6 antagonising molecules as claimed.

Paragraph [232] disclosed that particular Wnt proteins were "blocked" by Wnt1-specific LRP6 antagonistic antibodies. However, in the context of this paragraph, which reported the results of a Wnt signalling analysis, the term "blocked" was not equivalent to the prevention of binding but only related to inhibiting the Wnt signalling activity. The same was true for the disclosure in paragraphs [235], [236] and [237].

The same objections applied to claim 1 of each of auxiliary requests 9 to 11, which comprised the same feature combination as claim 1 of auxiliary request 8.

XVI. The appellant (patent proprietor) requested that the decision under appeal be set aside and the case be remitted to the opposition division for examination of the ground for opposition of lack of inventive step (Article 56 EPC) based on the main request, or, alternatively, based on the set of claims of one of auxiliary requests 1 to 3, filed with the statement of grounds of appeal, or based on the set of claims of one of auxiliary requests 4 to 11, filed by letter dated 5 June 2020.

XVII. The respondent's (opponent 2's) request, as far as relevant to this decision, was that the appeal be dismissed. It also stated that it was relying on the submissions made by former joint opponents 1.

Reasons for the Decision

1. The appeal complies with Articles 106 to 108 and Rule 99 EPC and is admissible.

Procedural issues

2. In the present appeal proceedings, joint opponents 1 took an active part, whereas opponent 2 (respondent) did not file any requests or submissions in the written proceedings. The day before the scheduled oral proceedings, by letter dated 16 December 2021, joint opponents 1 withdrew their opposition and announced that they would not be attending the oral proceedings (see section XII.). At the oral proceedings, the respondent indicated that it intended to rely on the submissions of former joint opponents 1. The appellant objected to this, arguing that presenting requests and arguments and raising objections for the first time at the oral proceedings was too late and that none of these submission should be admitted.

3. According to Article 99(3) EPC, opponents are parties to the opposition proceedings as well as the proprietor of the patent. It is clear from this provision that several admissible oppositions do not initiate a corresponding number of parallel opposition proceedings, but only a single set (T 270/94, point 2.1 of the Reasons; T 656/94, point 7 of the Reasons;

T 620/99, point 1 of the Reasons). All grounds of opposition raised by the various opponents, as well as the facts, evidence and arguments presented by them, form the legal and factual framework within which the substantive examination of the opposition is to be conducted. None of the parties involved in the opposition proceedings can be prevented from adopting facts, evidence and arguments presented in due time by another party (T 270/94, point 2.1 of the Reasons; T 620/99, point 1 of the Reasons; T 863/96, point 2 of the Reasons; see also T 154/95, point 2 of the Reasons: even documents originating from an opposition that has been declared inadmissible are allowed).

4. The same applies to opposition-appeal proceedings. All parties to the opposition proceedings are necessarily parties to any subsequent appeal proceedings (Article 107 EPC). It is therefore not possible to split the appeal proceedings into different procedures, each dealing separately with the grounds for opposition and the facts, evidence and arguments presented by the individual opponent concerned (T 790/03, point 2.1 of the Reasons). Therefore, each opponent can rely on any grounds, facts, evidence and arguments duly submitted by other opponents (T 620/99, point 1 of the Reasons; T 790/03, point 2.1 of the Reasons). Consequently, the board allowed the respondent to rely on the submissions made by former joint opponents 1 to the extent that these did not give rise to an objection of late filing.

Main request

Claim construction - claim 1

5. Claim 1 as granted relates to a low-density-lipoprotein receptor-related protein 6 polypeptide (LRP6) binding

molecule defined as comprising an antigen-binding portion of a monoclonal antibody that (1) "binds to an epitope within propeller 1 of human LRP6 within or overlapping amino acids 20 to 326" of the sequence recited in claim 1, and (2) is "capable of antagonizing Wnt1-induced signaling pathway" (see section I.). The latter expression is not used as such in the application.

Meaning of the expression "capable of antagonizing Wnt1-induced signaling pathway"

6. The appellant argued that the expression "capable of antagonizing Wnt1-induced signaling pathway" had the same meaning as "capable of antagonizing Wnt1-specific signaling". Furthermore, since the expression "Wnt1-specific" was used in the application to group together a particular class of Wnt ligands (see paragraphs [15], [236] and Table 2), the expression "capable of antagonizing Wnt1-specific signaling" meant that the signalling activity induced by this particular group of Wnt ligands was inhibited to a greater extent by the LRP6-binding molecule than the signalling activity induced by the "Wnt3a-specific" group of Wnt ligands.

7. The board is not persuaded by this construction of the expression, but considers that an LRP6-binding molecule that is defined as being "capable of antagonizing Wnt1-induced signaling pathway" (emphasis added by the board) is a molecule that, while necessarily capable of antagonising the signalling pathway induced by Wnt1, may also be capable of antagonising the signalling pathway induced by any of the other Wnt ligands, including Wnt3a, Wnt3 and Wnt6, without any preference.

8. The board finds support for this interpretation in paragraphs [62] and [231] of the application. Here, LPR6-binding antagonistic Fab fragments are described as "*preferentially*" inhibiting Wnt1-induced Wnt signalling or "*preferentially*" inhibiting Wnt3a-induced Wnt signalling. The term "*preferentially*" is used in these expressions to illustrate that the described Fab fragments inhibit Wnt signalling induced by other Wnt ligands to a lesser extent than Wnt signalling induced by Wnt 1 (or Wnt 3a). If the expression "inhibit Wnt1-induced Wnt signalling" inherently had this meaning, the use of the term "preferentially" would not be required.

Meaning of the expression "capable of antagonizing Wnt1-specific signaling"

9. By contrast, an LRP6-binding molecule defined as antagonising "Wnt1-specific" signalling, is, in line with the common meaning of the term "specific", understood by the person skilled in the art as a molecule that predominantly antagonises the Wnt signalling pathway induced by Wnt1.

10. This interpretation of the term "Wnt1-specific" is supported by paragraphs [15] and [236] of the application, where "Wnt1-specific" is used as an adjective to characterise particular antagonising LRP6-binding molecules ("*Wnt1-specific LRP6 antagonizing binding molecule*") and means, as pointed out by the appellant (see point 6. above), that the antagonism of the LRP6-binding molecule is specific to Wnt1 (or a particular class of Wnt1-related ligands) and excludes other Wnt ligands (which do not belong to this class). The term "Wnt1-specific", however, is not used in the claim.

11. Moreover, neither of paragraphs [15] and [236] contains any disclosure from which it could be derived that "Wnt1-specific" and "Wnt1-induced" have the same meaning.

Meaning of the expression "binds to an epitope within propeller 1 of human LRP6"

12. The appellant furthermore argued that LRP6-binding molecules that bound to an epitope within the propeller 1 domain of LRP6 were always Wnt1-specific and thus it was irrelevant that the term "Wnt1-specific" was not explicitly used in claim 1. However, in paragraph [34] of the application it is disclosed that an antagonising LRP6-binding molecule which binds within the propeller 1 domain of LRP6 could also inhibit signalling by Wise ligands. The board is therefore not persuaded by this argument either.

13. Consequently, the board concludes that the subject-matter of claim 1 comprises molecules that specifically bind to an epitope within the propeller 1 domain of LRP6 and may be capable of antagonising, in addition to the Wnt1-induced signalling pathway, the signalling pathway induced by other Wnt ligands, including Wnt3, Wnt3a and Wnt6, without any particular preference.

Amendments (Article 100(c) EPC) - Claim 1

14. The allowability of an amendment is assessed according to what is known as the "gold" standard as set out in decision G 2/10 of the Enlarged Board of Appeal (OJ EPO 2012, 376, point 4.3 of the Reasons). According to this standard, an amendment can be made only within the limits of what a skilled person would derive

directly and unambiguously, using common general knowledge, from the application as filed.

15. In the case at hand, the board is not persuaded that the application directly and unambiguously discloses a molecule binding to LRP6 which comprises an antigen-binding portion of a monoclonal antibody that is defined by a combination of the two features recited in point 5. above, i.e. that (1) "binds to an epitope within propeller 1 of human LRP6 within or overlapping amino acids 20 to 326" of the sequence recited in claim 1, and (2) is "capable of antagonising Wnt1-induced signaling pathway".

16. The appellant considered that the subject-matter of claim 1 had a basis in claims 1, 7 and 20 and paragraphs [15], [34], [38], [57],[215], [232], [235] and [236] of the application.

17. Claims 1, 7 and 20 of the application relate to an LRP6-binding molecule which comprises an antigen-binding portion of a (monoclonal) antibody that is defined by one of four different options, including that it "binds to an epitope of human LRP6 (SEQ ID NO:1) within or overlapping ... amino acids 20-326 of SEQ ID NO:1", but do not disclose an LRP6-binding molecule "capable of antagonising Wnt1-induced signalling pathway" (see section II. above).

18. Paragraph [15] of the application refers to an LRP6-binding molecule that binds to the propeller 1 domain of LRP6 only in the context of an exemplary list ("*e.g. to human LRP6 propeller 1, propeller 3, or to constituent domains or motifs thereof*") but does not disclose that this molecule is also capable of antagonising the Wnt1-induced signalling pathway.

19. Likewise, paragraph [34] discloses only that "*an antagonizing LRP6-binding molecule (e.g., which binds within the first propeller of LRP6) can inhibit, attenuate, or prevent Wnt pathway activation and signaling by Wise or Wnt ligands*" but not that such a molecule is capable of antagonising the Wnt1-induced signalling pathway.

20. Paragraph [38] does not disclose molecules that bind to the propeller 1 domain of LRP6 and therefore cannot serve as a basis for the claimed molecule either.

21. Paragraph [57] recites that, in one embodiment, "the *antagonizing LRP6 binding molecules are Wnt1 specific, bind to the first propeller of LRP6, and prevent the ligands Wnt1, Wnt6, and/or Wnt7 from interacting with LRP6 and initiating the Wnt pathway*", i.e. it discloses antagonising LRP6-binding molecules defined by features other than those recited in claim 1, including the prevention of the binding to LRP6.

22. In paragraph [215], the use of antagonising LRP6-binding molecules in the diagnosis or treatment of disorders is discussed, but they are only defined by binding "*in a Wnt1-specific fashion, to the first propeller of LRP6*", which is not a disclosure of a molecule that is capable of antagonising the Wnt1-induced signalling pathway as interpreted by the board (see point 13. above).

23. In Example 1 of the application, the identification of antagonistic anti-LRP6 Fabs is described. According to paragraph [231], they "*preferentially inhibit Wnt1- or Wnt3a-induced Wnt signaling*", i.e. these molecules are not merely capable of antagonising the Wnt1-induced signaling pathway but do so preferentially. The same

teaching can be found in paragraph [232], which describes two classes of Wnt signalling pathway proteins "*vis-à-vis the LRP6-binding molecules of the invention*", i.e. vis-à-vis "*Wnt3a-specific*" and "*Wnt1-specific*" LRP6 antagonistic antibodies. These paragraphs do not disclose the LRP6 domain to which these Fabs bind.

24. The domain mapping of LRP6 deletion mutants is then described in Example 3 (paragraph [235]). Here, it is reported that "*Wnt1-specific LRP6 antagonistic antibodies bind to propeller 1*". Again, and in line with the teaching in paragraphs [231] and [232] (see point 23. above), the use of the term "Wnt1-specific" indicates at least a preferential inhibition of Wnt1 over Wnt3a, a feature not present in claim 1. Although paragraph [235] also describes an LRP6 antagonistic antibody that inhibits both Wnt3a and Wn1-induced signaling, it does not disclose the domain of LRP6 to which this antibody binds.

25. Finally, paragraph [236] discloses that "*Fabs capable of binding to propeller 1 or LRP function with Wnt1 specificity" (among them Wnt1-specific Fabs Fab010 and Fab021*)". However, Fab010 and Fab021 are not shown in Table II, and it is therefore not clear how exactly these Fabs affect Wnt signalling in the reporter assay described in Example 1. Therefore, no direct link exists between this sentence and the disclosure in the following sentence that "*Wnt1-, Wnt2-, Wnt6-, Wnt7a-, Wnt7b-, and Wntl0-specific signaling activity can be most effectively inhibited by a Wnt1 specific LRP6 antagonizing binding molecule*". Moreover, even if it were implicitly understood that the antibody described in the second sentence bound to an epitope within the propeller 1 domain of LRP6, the disclosed molecule

would also be required to inhibit Wnt1-, Wnt2-, Wnt6-, Wnt7a-, Wnt7b-, and Wntl0-specific signaling activity, a feature not present in claim 1 as granted.

26. Consequently, the board holds that the application does not directly and unambiguously disclose an LRP6-binding molecule comprising an antigen-binding portion of a monoclonal antibody that specifically binds to the first propeller of LRP6, binds to an epitope within the propeller 1 domain of human LRP6, and is capable of antagonising Wnt1-induced signaling pathway.

27. Claim 1 as granted therefore comprises subject-matter that extends beyond the content of the application as filed (Article 100(c) EPC).

Auxiliary requests 1 to 3

Amendments (Article 123(2) EPC) - Claim 1

28. Claim 1 of auxiliary request 1 is identical to claim 1 of the patent as granted (see section I. above) except that the phrase "or overlapping" has been deleted. Claim 1 of auxiliary request 2 is identical to claim 1 of the patent as granted, and claim 1 of auxiliary request 3 is identical to claim 1 of auxiliary request 1 (see section V. above).

29. Consequently, for the same reasons as for claim 1 of the main request (see points 14. to 27. above), claim 1 of each of auxiliary requests 1, 2 and 3 contains subject-matter that extends beyond the content of the application (Article 123(2) EPC).

Auxiliary requests 4 to 7

Admittance (Article 13(2) RPBA 2020)

30. Auxiliary requests 4 to 7 were submitted after the board had summoned the parties to oral proceedings and had issued a communication setting out its preliminary opinion on, *inter alia*, amendments (see sections VIII. and X.).

31. The admittance of auxiliary requests 4 to 7 into the appeal proceedings is therefore governed by the provisions set out in Article 13(2) RPBA 2020. According to these provisions, as applied to the present situation, auxiliary requests 4 to 7 should not be taken into account unless there were exceptional circumstances, justified with cogent reasons by the appellant.

32. The appellant argued that, prior to the preliminary opinion of the board, no objection to unallowable amendments that it would have needed to answer had been on file. The objections to added subject-matter annexed by former joint opponents 1 to their reply to the appellant's statement of grounds (see annex B.1.2 on pages 24 to 25) were unsubstantiated because they had merely been copied from the notice of opposition into the annex without any reference to the decision under appeal.

33. An objection is substantiated if it indicates facts and arguments that are alleged to support it and the parties to the proceedings and the board understand what the objection is.

34. In the present case, it is first of all evident from the reply filed by former joint opponents 1 to the appellant's statement of grounds of appeal that they maintained their objection to added subject-matter raised in their notice of opposition (see page 21, point 4. of the reply). It is therefore clear that former joint opponents 1 disputed the decision under appeal in this respect.

35. Secondly, from annex B.1.2 on pages 24 to 25 of the reply, it is also evident what the objections were - even without explicitly addressing the reasons in the decision under appeal. In fact, in its communication setting out its preliminary opinion on the appeal (see section VIII.), the board endorsed one of these objections.

36. In view of these considerations, the board is not persuaded by the appellant's argument that former joint opponents 1 failed to substantiate their objection to added subject-matter.

37. Consequently, the board holds that there were no exceptional circumstances which would justify not having filed auxiliary requests 4 to 7 at an earlier point in time. It therefore decided not to admit auxiliary requests 4 to 7 into the appeal proceedings (Article 13(2) RPBA 2020).

Auxiliary requests 8 to 11

Amendments (Article 123(2) EPC) - Claim 1

38. The appellant argued that the subject-matter of claim 1 of auxiliary request 8 had a basis in claims 1, 7, 20 and 25 and paragraphs [9], [15], [34], [38], [57],

[76], [140], [141], [232], [235], [236] and [237] of the application.

39. However, claims 1, 7, 20 and 25 of the application (see section II.) disclose neither the particular group of six specific Wnt ligands recited in claim 1 of auxiliary request 8 (see section X.) nor the prevention of binding of these Wnt ligands to LRP6. The claims as filed thus do not disclose the claimed subject-matter.

40. From the passages of the description cited by the appellant in support of the claimed subject-matter (see point 38. above), only paragraphs [15], [34], [38] and [236] disclose the recited group of six Wnt ligands (Wnt1, Wnt2, Wnt6, Wnt7a, Wnt7b and Wnt10).

41. However, paragraph [15] refers to LRP6-binding molecules which bind to human LRP6 "*so as to prevent certain Wnt ligands from similarly binding. By way of non-limiting example, LRP6-binding molecules which antagonize Wnt signaling pathway prevent Wnt1 or Wnt3a ligands from binding LRP6. For example, Wnt3- and Wnt3a-specific signaling activity can be most effectively inhibited by a Wnt3a-specific LRP6 antagonizing binding molecule. By way of further non-limiting example, Wnt1-, Wnt2-, Wnt6-, Wnt7a-, Wnt7b-, and Wntl0-specific signaling activity can be most effectively inhibited by a Wnt1-specific LRP6 antagonizing binding molecule*."

42. Thus, the last sentence of paragraph [15] only recites, as an example, that the specific signalling activity of the six Wnt ligands can be inhibited by a Wnt1-specific LRP6 antagonising binding molecule but does not directly and unambiguously link this to an LRP6-binding

molecule that prevents the binding of all these six Wnt ligands to LRP6.

43. The same is true for the disclosure in paragraph [34], which discloses, on the one hand, that "[b]*y way of non-limiting example, an antagonizing LRP6 binding molecule can inhibit, attenuate, or prevent Wnt pathway activation and signaling by competing with Wnt signaling pathway members for binding to LRP6*" and, on the other hand, "[b]*y way of further example, a Wnt1 specific antagonizing LRP6 binding molecule can prevent Wnt pathway activation and signaling by any of Wnt1, Wnt2, Wnt6, Wnt7a, Wnt7b and Wntl0*" (emphasis added by the board).

44. Thus, paragraph [34] also refers to the specific group of Wnt ligands only in the context of an LRP6-binding molecule that prevents Wnt pathway activation and signalling. Since the distinct sentences of paragraph [34] relate to separate ("further") and non-limiting examples, the board is not persuaded by the appellant's argument that the prevention of Wnt pathway activation is necessarily linked to the prevention of Wnt ligand binding in this paragraph. Instead, the prevention of Wnt pathway activation by competitive binding is recited in paragraph [34] as an exemplary but not exclusive mechanism.

45. Paragraph [38] discloses "*preventing Wnt pathway activation and signaling by any of*" these six Wnt ligands, and paragraph [236] discloses that "*Wnt1-, Wnt2-, Wnt6-, Wnt7a-, Wnt7b-, and Wnt10-specific signaling activity can be most effectively inhibited by a Wnt1 specific LRP6 antagonizing binding molecule*". Neither of these paragraphs therefore discloses an LRP6-binding molecule that prevents (or inhibits) the

binding of these six Wnt ligands to LRP6 or that the LRP6-binding molecule binds to the propeller 1 domain of LRP6.

46. Paragraphs [9], [57], [76], [140], [141], [232], [235] and [237], cited by the appellant as additional support, do not recite the specific group of six Wnt ligands.

47. Paragraph [9] lists various properties that an LRP6-binding molecule could have, including that it "*can*" (but not "must") "*interfere with LRP6's ability to bind to integral members of the Wnt pathway*". The Wnt pathway members listed in paragraph [9] are the same molecules recited in claim 25 (see section II.), i.e. Wnt ligands are only generally mentioned in a list of various other molecules.

48. The same is true for the disclosure in paragraphs [140] and [141], which both recite potential functional properties of anti-LRP6 antibodies such as "*interfering with LRP6's ability to bind Wnt pathway members (e.g., DKK1 (dickkopf 1), DKK2, DKK4, SOST1, SOSD1 (USAG1), sFRP (soluble Fzd-related protein) 1-4, Wise, or Wnt ligands), and modulating β-catenin phosphorylation and degradation*".

49. That antagonising of the Wnt-induced pathway could be, but is not necessarily, achieved by preventing the binding of Wnt ligands to LRP6 is also evident from paragraph [76], which defines the term "antagonize" as indicating "*the ability to inhibit or arrest, e.g., a signaling pathway such as Wnt*" and explains, "[b]*y way of example*", that "*an antagonizing LRP6 binding molecule of the invention can prevent signal transduction via the Wnt signaling pathway, by e.g.,*

interfering with LRP6's ability to bind Wnt pathway members" (emphasis added by the board).

50. Paragraph [57] describes antagonising LRP6-binding molecules that are "*Wnt1-specific, bind to the first propeller of LRP6, and prevent the ligands Wnt1, Wnt6, and/or Wnt7 from interacting with LRP6 and initiating the Wnt pathway*". Hence, this paragraph discloses a specific group of Wnt ligands that is different to the six Wnt ligands recited in claim 1 of auxiliary request 8 and therefore cannot be taken as a basis for the claimed subject-matter.

51. Paragraph [237] discloses that "*Wnt1 specific antagonistic IgGs inhibit Wnt1 signaling by blocking the physical interaction between Wnt1 and LRP6*". This paragraph therefore does not mention the specific group of Wnt ligands recited in claim 1 either and therefore does not relate to the subject-matter recited in claim 1.

52. Furthermore, the board does not agree with the appellant's assertion that the term "blocked" as used in paragraph [232] would be understood by the skilled person in the sense of "prevention of binding". The reason is that in Example 1, to which paragraph [232] belongs (paragraphs [231] to [233] and Table II), only the inhibition of Wnt signalling by anti-LRP6 Fabs is assessed but not the prevention of a binding event. Therefore, the skilled person would understand the term "blocked" in paragraph [232] as relating to the inhibition of Wnt signalling.

53. The appellant also argued that paragraphs [232], [235] and [236] provided pointers to the Wnt1-specific class of Wnt ligands listed in paragraph [15] which could be

blocked by an antibody binding to the propeller 1 domain of LRP6.

54. However, since Figure 4, to which paragraph [235] refers, is missing from the application documents, and the Fab fragments described in Table II and paragraphs [235] and [236] are not identical, it is not clear whether the "*Wnt1-specific LRP6 antagonistic antibodies*" that, according to paragraph [235], bind to the propeller 1 domain, are the same that block particular Wnt-specific signalling as described in paragraph [232] and Table II of the application. In fact, according to Table II, the only two Fabs described in paragraphs [235] and [236] as "Wnt1-specific" (Fab010 and Fab021) were not analysed for their ability to inhibit Wnt signalling induced by the six Wnt ligands recited in the claim.

Consequently, these paragraphs do not directly and unambiguously disclose LRP6-binding molecules which bind to the propeller 1 domain of LRP6 and are capable of antagonising Wnt signaling pathway "by preventing Wnt1, Wnt2, Wnt6, Wnt7a, Wnt7b and Wnt10 from binding to LRP6" as recited in the claim.

55. The board therefore cannot identify in the cited passages of the application, alone or in combination, any direct and unambiguous disclosure of an LRP6-binding molecule comprising an antigen-binding portion of a monoclonal antibody that binds an epitope within the propeller 1 domain of human LRP6 and is capable of antagonising Wnt signaling pathway by preventing Wnt1, Wnt2, Wnt6, Wnt7a, Wnt7b and Wnt10 from binding to LRP6.

56. The same reasoning applies to the subject-matter of claim 1 of each of auxiliary request 9 to 11, which also relates to an LRP6-binding molecule that binds an epitope within the propeller 1 domain of human LRP6 and is capable of antagonising Wnt signaling pathway by preventing Wnt1, Wnt2, Wnt6, Wnt7a, Wnt7b and Wnt10 from binding to LRP6 (see section X.).

57. Consequently, claim 1 of each of auxiliary requests 8 to 11 comprises subject-matter which extends beyond the content of the application (Article 123(2) EPC).

Order

For these reasons it is decided that:

1. The appeal is dismissed.

The Registrar: On behalf of the Chair (according to Art. 8(3) RPBA):

I. Aperribay L. Bühler

Decision electronically authenticated