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Datasheet for the decision of 20 November 2020

Case Number: T 2099/15 - 3.3.02

Application Number: 06825074.5

Publication Number: 1928879

IPC: C07D487/04, A61K31/437, A61P29/00

Language of the proceedings: EN

Title of invention:
FUSED HETEROCYCLIC COMPOUNDS USEFUL AS KINASE MODULATORS

Patent Proprietor:
Bristol-Myers Squibb Company

Opponent:
Bayer Pharma Aktiengesellschaft

Headword:

Relevant legal provisions:
EPC Art. 100(c), 56
EPC R. 99(2)
RPBA Art. 12(4)
RPBA 2020 Art. 25(2)

Keyword:
Grounds for opposition - amendments
Admissibility of appeal
Late-filed evidence - documents not admitted in first instance proceedings
Inventive step

Decisions cited:
G 0001/03, G 0003/14, G 0001/91, G 0007/93

Catchword:

Europäisches Patentamt
European Patent Office
Office européen des brevets

Beschwerdekammern

Boards of Appeal

Chambres de recours

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Case Number: T 2099/15 - 3.3.02

D E C I S I O N
of Technical Board of Appeal 3.3.02
of 20 November 2020

Appellant: (Opponent)	Bayer Pharma Aktiengesellschaft Müllerstrasse 178 13353 Berlin (DE)
Representative:	BIP Patents c/o Bayer Intellectual Property GmbH Alfred-Nobel-Straße 10 40789 Monheim am Rhein (DE)
Respondent: (Patent Proprietor)	Bristol-Myers Squibb Company Route 206 and Province Line Road Princeton, NJ 08543 (US)
Representative:	Mewburn Ellis LLP Aurora Building Counterslip Bristol BS1 6BX (GB)
Decision under appeal:	**Decision of the Opposition Division of the European Patent Office posted on 15 October 2015 rejecting the opposition filed against European patent No. 1928879 pursuant to Article 101(2) EPC.**

Composition of the Board:

Chairman	M. O. Müller
Members:	A. Lenzen
	L. Bühler

Summary of Facts and Submissions

I. This decision concerns the appeal filed by the opponent (appellant) against the opposition division's decision (decision under appeal) to reject the opposition against European patent No. 1 928 879 (patent in suit).

II. During opposition proceedings, the appellant requested the revocation of the patent in suit in its entirety, on the basis of following grounds for opposition: Article 100(a) EPC (lack of novelty and inventive step), Article 100(b) EPC and Article 100(c) EPC.

The opposition division decided, *inter alia*, not to admit D16 to D18 into the proceedings.

III. The following documents, cited during the opposition proceedings, are relevant for the present decision:

D1 WO 2004/081013 A1
D15 Results of MK2 inhibition
D16 Polanc, S., Stanovnik, B., Tišler, M., Synthesis, 1975, 3, pages 175 to 176
D17 Stanovnik, B., Tišler, M., Žigon, V., Monatshefte für Chemie, 1972, 103, pages 1624 to 1631
D18 Barlin, G. B., Brown, I. L., Golič, L., Kaučič, V., Aust. J. Chem., 1982, 35, pages 423 to 430
D19 WO 98/08847 A1
D20 Böhm, H.-J., Flohr, A., Stahl, M., Drug Discovery Today: Technologies, 2004, 1, pages 217 to 224

IV. In the course of the appeal proceedings, the board issued a communication pursuant to Article 15(1) RPBA 2020 in preparation for the oral proceedings, which had been scheduled as per the parties' requests. In this communication, the board set out why the appeal was likely to be dismissed.

V. By letter of 30 October 2020, the appellant informed the EPO that it would not be attending the oral proceedings.

VI. By letter of 20 November 2020, the oral proceedings were cancelled.

VII. The parties' requests relevant for this decision were as follows.

The appellant requested that the decision under appeal be set aside and the patent in suit be revoked in its entirety.

The patent proprietor (respondent) requested:

(i) that the appeal be held inadmissible,
(ii) that the appeal be dismissed if it was held admissible,
(iii) that oral proceedings be arranged if neither of the two previous requests could be granted,
(iv) that D16 to D18 not be admitted into the appeal proceedings.

VIII. The appellant's arguments, in so far as they are relevant for the present decision, can be summarised as follows.

Disclaimer (1) contained the feature "*$N(Me)_2$*". The corresponding definition in the application as filed, however, referred to "*$NH(Me)_2$*". Thus, a hydrogen atom had been deleted compared with the application as filed. However, it was also conceivable that the substituent "*$NH(Me)_2$*" was an ammonium group or that it contained one methyl group too many. The amendment related to disclaimer (1) was therefore not a correction of an obvious error pursuant to Rule 139 EPC. Undisclosed disclaimer (2) related, *inter alia*, to imidazo[1,2-b]pyridazine-8-amine. This compound, however, did not even fall under the subject-matter of claim 1 without disclaimer (2). Disclaimer (2) therefore excluded more than was necessary to restore novelty, contravening G 1/03. Therefore, the subject-matter claimed by the patent as granted extended beyond the content of the application as filed, contrary to Article 100(c) EPC.

The opposition division's decision not to admit D16, D17 and D18 was wrong. These documents were novelty-destroying for at least some of the claims of the patent as granted.

D1 was the closest prior art. The compounds referred to in claims 1 to 6, 12, 13 and 15 to 19 differed from those in D1 in that they were based on a different scaffold: whereas the compounds in D1 were based on pyrazolo[1,5-a]pyrimidines, those in the patent in suit were derived from imidazo[1,2-b]pyridazines. The structural definition in the claims as granted was very broad and it was not credible that activity inhibiting MAPKAP kinase-2 (MK2) was achieved over the whole breadth of the claims as granted. This was also evident from D12. Even if the MK2-inhibiting effect were to be acknowledged over the whole breadth of the claimed

compounds, and thus the objective technical problem were to be considered the provision of further MK2 inhibitors, the solution to this problem would have been obvious on the basis of either D1 alone or a combination of D1 with D19. As was evident from D20, scaffold hopping was a well-established approach for providing alternative compounds. Furthermore, D1 indicated that the compounds it disclosed could be used to treat allergies and Alzheimer's disease. The skilled person would have looked for compounds for the treatment of these conditions because compounds of this type could be MK2 inhibitors. In the course of this search, the skilled person would have come across D19 as it dealt with compounds for treating those conditions. The scaffold of the compounds in D19 was the same as that in the patent in suit. The substitution patterns of the compounds in D1 and D19 overlapped to a great extent. The skilled person would therefore have tested the compounds of D19 for their anti-MK2 activity and in so doing would have arrived at the subject-matter of claims 1 to 6, 12, 13 and 15 to 19 of the patent as granted in an obvious manner.

IX. The respondent's arguments, in so far as they are relevant for the present decision, can be summarised as follows.

In its statement of grounds of appeal, the appellant failed to deal with the reasons for the decision in a manner specific enough to put the board and the respondent in a position to immediately understand the reasons why the decision under appeal was alleged to be incorrect. The appeal was therefore not admissible.

The decision under appeal was correct where disclaimer (1) was concerned. The related amendment was a

correction of an obvious error pursuant to Rule 139 EPC. The appellant's objection against disclaimer (2) was at best an objection for an alleged lack of clarity.

The appellant's novelty objections were based on D16 to D18 only, i.e. documents which the opposition division had not admitted into the proceedings. The appellant did not request the admission of these documents nor did it provide any arguments as to why they should now be admitted on appeal. Furthermore, the opposition division had applied the right principle of *prima facie* relevance. D16 to D18 should therefore not be admitted.

D1 was the closest prior art. The compounds referred to in claims 1 to 6, 12, 13 and 15 to 19 differed from those in D1 on account of the use of a different scaffold. The patent in suit listed a large number of compounds that satisfied the structural definition in the claims. Most of them were tested according to one of the assays described in the patent in suit and, as was evident from D15, each of the tested compounds showed MK2-inhibiting activity. The opposition division had acknowledged that D15 provided sufficient evidence to confirm that the claimed compounds were MK2 inhibitors. The appellant had not discharged its burden of proof. Thus, the objective technical problem was the provision of further MK2 inhibitors. Scaffold hopping might have been one avenue that the skilled person could have pursued, but there would have been no reasonable expectation of success in retaining the activity of the compounds disclosed in D1. D19 was concerned with a different mode of action from that in the patent in suit. It was therefore irrelevant to the solution of the objective technical problem. The

subject-matter of the claims as granted therefore involved an inventive step.

Reasons for the Decision

Admissibility of the appeal (Article 110 EPC in conjunction with Rule 101(1) EPC and Rule 99(2) EPC)

1. The respondent requested that the appeal be held inadmissible because "*it fails to deal with the reasons for the decision in a manner specific enough to put the Board and Patentee in a position to immediately understand the reasons why the decision is alleged to be incorrect*" (page 4, paragraph 3 in its reply to the statement of grounds of appeal).

2. In opposition proceedings, the appellant had objected to claim 1 as granted under Article 100(c) EPC because the definition of disclaimer (1), i.e. the feature

> "*(1) if X is NH(Me), **$N(Me)_2$**, NH(unsubstituted phenyl), or $NHNH_2$, then Y is other than hydrogen or halogen*" (emphasis added),

differed from the corresponding definition in the application as filed, which referred to "$NH(Me)_2$" instead of "$N(Me)_2$". The opposition division held that this amendment was a correction under Rule 139 EPC and hence allowable (decision under appeal, point 3.3.2 on page 4). In its statement of grounds of appeal (point 1.1 on pages 3 et seq.), the appellant reiterated this objection and set out why it did not agree with the opposition division's conclusion. This alone is enough to render the appeal admissible from a substantive point of view (Rule 99(2) EPC).

3. The appellant also set out in detail why the claimed subject-matter lacked novelty and in doing so addressed the reasoning in the opposition division's decision (see in particular the two last paragraphs on page 10, the paragraph bridging pages 14 and 15 and the first full paragraph of page 15 of the statement of grounds of appeal). Furthermore, the statement of grounds of appeal contains detailed arguments as regards lack of inventive step. The respondent was able to deal with each of these objections in detail in its reply to the statement of grounds of appeal.

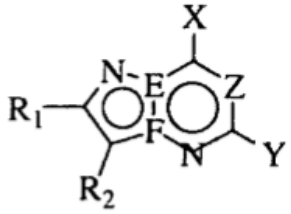
4. Therefore, it had to be concluded that the appellant had sufficiently substantiated each ground for opposition invoked by it in its statement of grounds of appeal. Consequently, the board decides that the appeal is admissible.

Patent in suit as granted

5. The patent in suit as granted contains 19 claims.

5.1 Independent claim 1 reads as follows:

"*A compound according to formula (I),*



(I)

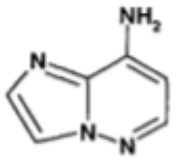
or an enantiomer, diastereomer, or a pharmaceutically-acceptable salt, thereof, wherein:

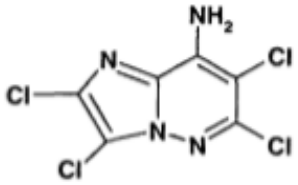
E is C; F is N;
X is NR_4R_5;
Z is CR_3;
Y is selected from hydrogen, halogen, nitro, cyano, SR_8, $S(O)_pR_8$, OR_8, NR_6R_7, CO_2R_8, $C(=O)R_8$, $O-C(=O)R_8$, $C(=O)NR_8R_9$, cycloalkyl, cycloalkenyl, cycloalkynyl, heterocyclo, aryl, and heteroaryl, provided that if Y is hydrogen then R_4 is phenyl substituted with a carboxamido group;
R_1 and R_2 are independently selected from (i) hydrogen, alkyl, halogen, nitro, cyano, SR_{10}, OR_{10}, $NR_{10}R_{11}$, $NR_{10}C(=O)R_{11}$, CO_2R_{10}, $C(=O)R_{10}$, $-O-C(=O)R_{10}$, $C(=O)NR_{10}R_{11}$;
R_3 is selected from hydrogen, halogen, alkyl, substituted alkyl, alkenyl, substituted alkenyl alkynyl, substituted alkynyl, nitro, cyano, SR_{13}, OR_{13}, $NR_{13}R_{14}$, $NR_{13}C(=O)R_{14}$, CO_2R_{13}, $C(=O)R_{13}$, $-O-C(=O)R_{13}$, $-C(=O)NR_{13}R_{14}$, cycloalkyl, heterocyclo, aryl, and heteroaryl;
R_4, R_5, R_6, and R_7 are independently selected from hydrogen, alkyl, substituted alkyl, alkenyl, substituted alkenyl, alkynyl, substituted alkynyl, OR_{15}, SR_{15}, $C(=O)R_{15}$, CO_2R_{15}, $C(=O)NR_{15}R_{16}$, $C(W)OR_{16}$, $S(O)_pR_{17}$, $SO_2NR_{15}R_{16}$, cycloalkyl, heterocyclo, aryl, and heteroaryl; or (ii) R_4 is taken together with R_5 and the nitrogen atom to which they are both attached and/ or R_6 is taken together with R_7 and the nitrogen atom to which they are both attached to form a heteroaryl or heterocyclo;
R_8, R_9, R_{10}, R_{11}, R_{13}, R_{14}, R_{15}, and R_{16} at each occurrence are independently selected from (i) hydrogen, alkyl, substituted alkyl, alkenyl, substituted alkenyl, alkynyl, substituted alkynyl, cycloalkyl, aryl, heteroaryl, and heterocyclo; or (ii) together with the nitrogen atom to which they are

attached, R_8 is taken together with R_9, and/or R_{10} is taken together with R_{11}, and/or R_{13} is taken together with R_{14}, and/or R_{15} is taken together with R_{16} to form a heteroaryl or heterocyclo;
R_{17} is selected from alkyl, substituted alkyl, alkenyl, substituted alkenyl, alkynyl, substituted alkynyl, cycloalkyl, aryl, heteroaryl, and heterocyclo;
W at each occurrence is O, S, N, CN, or NH; and
p is 1 or 2,
with the following provisos:

(1) if X is NH(Me), $N(Me)_2$, NH(unsubstituted phenyl), or $NHNH_2$, then Y is other than hydrogen or halogen; and

(2) the following compounds are excluded:





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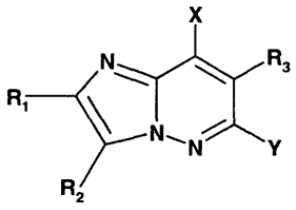
5.2 Claims 2 to 4 are dependent on claim 1.

5.3 Independent claim 5 reads as follows:

"*A compound of formula (Ia):*



(Ia)

or an enantiomer, diastereomer, or a pharmaceutically-acceptable salt, thereof, wherein:

X is NR_4R_5;
Y is hydrogen, halogen, OR_8, or NR_6R_7;
R_1 and R_2 are independently selected from (i) hydrogen, alkyl, halogen, nitro, cyano, SR_{10}, OR_{10}, $NR_{10}R_{11}$, $NR_{10}C(=O)R_{11}$, CO_2R_{10}, $C(=O)R_{10}$, $-O-C(=O)R_{10}$, $C(=O)NR_{10}R_{11}$;
R_3 is selected from hydrogen, halogen, alkyl, substituted alkyl, alkenyl, substituted alkenyl, alkynyl, substituted alkynyl, nitro, cyano, SR_{13}, OR_{13}, $NR_{13}R_{14}$, $NR_{13}C(=O)R_{14}$, CO_2R_{13}, $C(=O)R_{13}$, $-O-C(=O)R_{13}$, $-C(=O)NR_{13}R_{14}$, cycloalkyl, heterocyclo, aryl, and heteroaryl;
R_4 is -AM;
R_5 is hydrogen or C_{1-4}alkyl;
or R_4 and R_5 together with the nitrogen atom to which they are attached form a 5-, 6- or 7-membered monocyclic heteroaryl or heterocyclo ring, or a 7- to 11-membered bicyclic heteroaryl or heterocyclo ring, each ring optionally substituted with one to three groups, T_1, T_2; and/or T_3;
A is a bond, C_{1-3}alkylene, C_{2-4}alkenylene, C_{2-4}alkynylene, -C(O)-, or $-SO_2-$; M is (i) hydrogen, $NR_{15}R_{16}$, alkyl, alkoxy, or alkenyl; or (ii) cycloalkyl, heterocyclo, aryl, or heteroaryl, each ring optionally substituted by one to three groups, T_1, T_2, and/or T_3;
R_6 is selected from hydrogen or C_{1-4}alkyl optionally substituted by one to three groups selected from halogen, C_{1-4}alkyl, nitro, cyano, amino, C_{1-4}alkoxy, and OH;
R_7 is selected from alkyl, cycloalkyl, heterocyclo, aryl, and heteroaryl, each group of which is optionally substituted by one to three groups, T_4, T_5, and/or T_6;
or R_6 and R_7 together with the nitrogen atom to which they are attached form a heteroaryl or heterocyclo

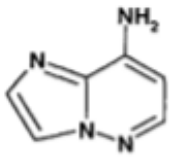
ring, each ring is optionally substituted by one to three groups, T_4, T_5, and/or T_6;
R_8 is selected from alkyl, cycloalkyl, heterocyclo, aryl, and heteroaryl, each group of which is optionally substituted by one to three groups, T_4, T_5, and/or T_6;
R_{10}, R_{11}, R_{13}, and R_{14} at each occurrence are independently selected from (i) hydrogen, C_{1-4}alkyl, and substituted C_{1-4}alkyl; or (ii) R_{10} and R_{11} together with the nitrogen atom they are both attached, and/or R_{13} and R_{14} together with the nitrogen atom they are both attached combine to form an optionally substituted 5-, 6-, or 7-membered heteroaryl or heterocyclo;
R_{15} and R_{16} are independently selected from (i) hydrogen, alkyl, substituted alkyl, alkenyl, substituted alkenyl, alkynyl, substituted alkynyl, cycloalkyl, aryl, heteroaryl, and heterocyclo; or (ii) together with the nitrogen atom to which they are attached R_{15} is taken together with R_{16} to form a heteroaryl or heterocyclo;
T_1, T_2, and T_3 are independently selected from (i) halogen, alkyl, substituted alkyl, alkenyl, substituted alkenyl, alkynyl, substituted alkynyl, nitro, cyano, SO_3H SR_{19}, $S(O)_pR_{21}$, $S(O)_pNR_{19}R_{20}$, $NR_{19}S(O)_pR_{21}$, OR_{19}, $NR_{19}R_{20}$, $NR_{19}C(=O)_{20}$, $NR_{19}C(=O)NR_{19}R_{20}$, CO_2R_{19}, $C(=O)R_{19}$, $-O-C(=O)R_{19}$, $-C(=O)NR_{19}R_{20}$, cycloalkyl, heterocyclo, aryl, and heteroaryl, wherein p is one or 2; and/or (ii) two groups, T_1 and T_2, located on adjacent ring atoms are taken together with the ring atoms to which they are attached to form a fused cycloalkyl, aryl, heteroaryl, or heterocyclo;
T_4, T_5 and T_6 are independently selected from (i) halogen, alkyl, substituted alkyl, alkenyl, substituted alkenyl, alkynyl, substituted alkynyl, nitro, cyano, SR_{19}, OR_{19}, $NR_{19}R_{20}$, $NR_{19}C(=O)R_{20}$, CO_2R_{19}, $C(=O)R_{19}$, $-O-C(=O)R_{19}$, $-C(=O)NR_{19}R_{20}$, cycloalkyl, heterocyclo,

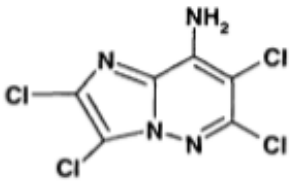
aryl, and heteroaryl; and/or (ii) two groups, T_4 and T_5, substituted on adjacent ring atoms are taken together with the ring atoms to which they are attached to form a fused cyclalkyl, heterocyclo, aryl, or heteroaryl; and
R_{19} and R_{20} at each occurrence are selected independently from (i) hydrogen, alkyl, substituted alkyl, alkenyl, substituted alkenyl, cycloalkyl, aryl, heteroaryl, and heterocyclo; or (ii) R_{19} and R_{20} together with the nitrogen atom to which they are both attached form a heteroaryl or heterocyclo ring; and
R_{21} at each occurrence, is selected from alkyl, substituted alkyl, alkenyl, substituted alkenyl, alkynyl, substituted alkynyl, cycloalkyl, aryl, heteroaryl, and heterocyclo;

with the following provisos:

(1) if X is NH(Me), $N(Me)_2$, NH(unsubstituted phenyl), or $NHNH_2$, then Y is other than hydrogen or halogen; and

(2) the following compounds are excluded:





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5.4 Claims 6 to 13 are dependent on claims 1 and/or 5.

5.5 Independent claim 14 is a product claim directed at different specific compounds.

5.6 Independent claim 15 reads as follows:

"*A pharmaceutical composition comprising one or more compounds according claim 1 or 14 and a pharmaceutically acceptable carrier or diluent.*"

5.7 Independent claim 16 is a second medical use claim relating to the treatment of various conditions. It may be reproduced in abridged form as follows:

"*A compound according to claim 1 or 14 for use in the treatment, in a mammal, of* [various conditions]."

5.8 Claims 17 to 19 are dependent on claim 16.

6. Amendments (Article 100(c) EPC)

6.1 According to the appellant, the two provisos at the end of claim 1, i.e.

> "*(1) if X is NH(Me), $N(Me)_2$, NH(unsubstituted phenyl), or $NHNH_2$, then Y is other than hydrogen or halogen; and*
>
> *(2) the following compounds are excluded:*
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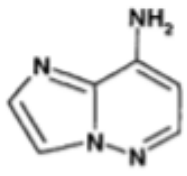
> 
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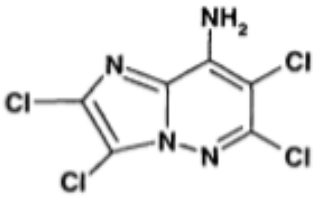
> 
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gave rise to objections under Article 100(c) EPC. In line with the appellant's wording, the two provisos are referred to as "disclaimer (1)" and "disclaimer (2)".

6.2 Disclaimer (1)

The appellant argued that the application as filed (page 4, line 23; page 29, line 26; page 122, line 19; page 127, line 13) defined disclaimer (1) differently, namely as follows (emphasis added):

> "*(1) if E is C, F is N, Z is CR_3, and X is NH(Me),* ***$NH(Me)_2$,*** *NH(unsubstituted phenyl), or $NHNH_2$, then Y is other than hydrogen or halogen*".

The replacement of "*$NH(Me)_2$*" (application as filed) with "*$N(Me)_2$*" (claim 1 as granted) was not a correction of an obvious error pursuant to Rule 139 EPC as held by the opposition division, and was not allowable.

This is not convincing. "Me" is a well-known abbreviation for a methyl group ($-CH_3$) and is also defined as such in the application as filed (page 54, line 28). When reading disclaimer (1) in the application as filed it is immediately obvious that the mention of "*$NH(Me)_2$*" for the substituent X must be incorrect. The first possibility is that this group lacks the indication of a positive charge and/or a corresponding counter-anion. This is because the nitrogen would be bound to four moieties (1x H, 2x Me, 1x the characteristic imidazo[1,2-b]pyridazine) and thus would only have four valency electrons (whereas it needs five in an uncharged state). The second possibility is that the nitrogen atom is in an uncharged state and one of the moieties H and Me in "*$NH(Me)_2$*" is superfluous. In the latter case, the nitrogen would be bound to three moieties and would have one non-bonded electron pair, resulting in five valency electrons.

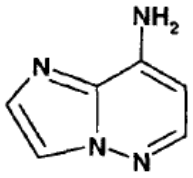
The skilled person would rule out the first possibility because all the other alternatives mentioned for X in disclaimer (1) in the application as filed result in molecules with an uncharged amino group, and because salts in the form R-$N^{+}H(Me)_2$ (with R being the characteristic imidazo[1,2-b]pyridazine moiety, and with whichever counter-anion) are already accounted for by the fact that claim 1 relates to "*pharmaceutically-acceptable salts*" of compounds of formula (I).

When considering the second possibility, the skilled person would further recognise that it is the hydrogen atom in "*$NH(Me)_2$*" that is superfluous, not one of the two methyl groups. This is simply because leaving out one methyl group would lead to "*NHMe*", i.e. to the group mentioned just before "*$NH(Me)_2$*" in the passages of the application as filed, which would obviously make no sense.

In summary, when reading the definition of disclaimer (1) in the application as filed the skilled person would recognise not only that the mention of "*$NH(Me)_2$*" must be erroneous, but also that what was actually intended was $N(Me)_2$. Therefore, the amendment in disclaimer (1) is a correction of an obvious error pursuant to Rule 139 EPC and hence allowable.

6.3 Disclaimer (2)

Disclaimer (2) is an undisclosed disclaimer according to G 1/03 (OJ 2004, 413). Therefore, it should not remove more than necessary to restore novelty. According to the appellant, however, the exclusion of compound



did not meet this condition "*da diese Verbindung auch ohne den Disclaimer (2) nicht vom Anspruch 1 erfasst wird*" (statement of grounds of appeal, page 8, paragraph 1).

This argument is not convincing as it is a contradiction in itself. If a given compound does not fall within the subject-matter of a claim, e.g. because it is not encompassed by a structural definition, it cannot be excluded from it by means of a disclaimer. To put it another way, a disclaimer directed at this compound does not actually remove anything from the subject-matter before the addition of said disclaimer. The disclaimer therefore cannot remove more than necessary e.g. to restore novelty. For the sake of completeness, it is pointed out that an objection under Article 84 EPC against claim 1 in view of such an apparent contradiction would not have been admissible as this contradiction was already present in the claims as granted (G 3/14, OJ 2015, A102).

6.4 The reasoning above also applies to claim 5 of the patent as granted, which recites the same disclaimers (1) and (2), and, *mutatis mutandis*, to claims 2 to 4, 6 to 13 and 15 to 19. The appellant's objections are not relevant for claim 14 because this claim does not recite disclaimers (1) and (2). It must therefore be concluded that the ground for opposition pursuant to Article 100(c) EPC does not prejudice maintenance of the patent as granted.

7. Clarity (Article 84 EPC), unity (Article 82 EPC), scope of protection (Article 123(3) EPC)

Under the last point of its statement of grounds of appeal (point 4, starting on page 27) the appellant made further remarks about the patent as granted. In its communication pursuant to Article 15(1) RPBA 2020, the board explained that these remarks related to an alleged lack of clarity of the claims as granted or to an alleged lack of unity and/or extension of the scope of protection of the patent as granted. The board also set out why objections based on those remarks were either not admissible (objections relating to an alleged lack of clarity; see G 3/14, OJ 2015, A102) or not relevant (objections relating to an alleged lack of unity; see G 1/91, OJ 1992, 253; objections relating to an alleged extension of the scope of protection of a granted patent cannot be relevant where the patent in its granted form is at issue). The appellant did not comment on this in the further course of the appeal proceedings. It is therefore to be concluded that none of these remarks prejudices maintenance of the patent as granted.

8. Novelty (Articles 100(a) and 54 EPC)

The opposition division had decided not to admit D16 to D18 into the proceedings because they were not *prima facie* relevant (decision under appeal, point 2.2 on page 3). Nevertheless, in its statement of grounds of appeal, the appellant put forward novelty objections based on these documents - and on these documents only.

A board of appeal should only overrule the way in which a department of first instance has exercised its discretion when deciding on a particular case if it

concludes that that department has done so according to the wrong principles, or without taking into account the right principles, or in an unreasonable way, and has thus exceeded the proper limits of its discretion (G 7/93, OJ 1994, 775; point 2.6 of the reasons). However, the appellant did not even assert that the opposition division had taken into account the wrong principles or that it had taken into account the right principles but in an unreasonable way. As a matter of fact, the appellant merely stated that it did not share the opposition division's opinion. In its communication pursuant to Article 15(1) RPBA 2020, the board expressed its preliminary view that the opposition division seemed to have exercised its discretion according to the right principle (*prima facie* relevance) and in a reasonable manner. The appellant did not make any other comments in this respect in the further course of the appeal proceedings.

Therefore, the board decides to not admit D16 to D18 into the proceedings pursuant to Article 12(4) RPBA 2007, which is applicable pursuant to Article 25(2) RPBA 2020. In view of this, the merits of the appellant's objections need not be assessed. It is to be concluded that the ground for opposition pursuant to Article 100(a) EPC - lack of novelty - does not prejudice maintenance of the patent as granted either.

9. Inventive step (Articles 100(a) and 56 EPC)

9.1 Like the patent in suit (paragraph [0002]), D1 (page 1, lines 6 to 10) relates to compounds that inhibit MK2. On this basis, both parties agreed that D1 was the closest prior art.

9.2 The compounds in claims 1 and 5 of the patent in suit differ from those in D1 in that the central scaffold is different. More specifically, claims 1 and 5 of the patent in suit relate to imidazo[1,2-b]pyridazines while D1 refers to pyrazolo[1,5-a]pyrimidines. The difference between these scaffolds is that the nitrogen and carbon bridgehead atoms (bridging the two nitrogen heterocycles) are interchanged.

9.3 In its example section (paragraphs [0114] to [0189]), the patent in suit lists a large number of compounds which satisfy claims 1 and 5. Most of these compounds were tested according to one of the assays described in the patent in suit (paragraphs [0111] and [0112]). The results are summarised in D15 and show that the tested compounds have MK2-inhibiting activity.

In this context, the appellant argued that the structural definition in the claims as granted was very broad and that the compounds actually illustrated in the patent in suit represented only a very small fraction of them, with the claims also covering oligomeric and polymeric compounds, for example. Consequently, it was not credible that MK2-inhibiting activity was achieved over the whole breadth of the claims. D12 (page 1247, left-hand column, paragraph 2) also made it clear that the structural breadth of active compounds was much narrower than what was claimed in the patent in suit.

This is not convincing. It may be true that the compounds illustrated in the patent in suit do not cover the entire breadth of the structural definition in the claims and that they instead form "subgroups" of the broader Markush formulae, as argued by the appellant. However, this alone does not lead to the

conclusion that MK2-inhibiting activity would not be credible for compounds which meet the structural definition in the claims but do not, in the appellant's view, fall within one of the subgroups formulated by the appellant. In the case in hand, it is down to the appellant to demonstrate that not all of the compounds actually covered by the structural definition in the claims as granted have MK2-inhibiting activity. This is all the more the case in this appeal case because the opposition division had already decided that this line of argument was not convincing (decision under appeal, point 7.5 on page 8) and the board addressed this point specifically in its communication pursuant to Article 15(1) RPBA 2020. The appellant did not discharge its burden of proof simply by making this allegation. Furthermore, there is nothing in D12 to indicate that the objective technical problem was not solved over the entire breadth of the claims.

Thus, the objective technical problem is the provision of further (i.e. alternative) MK2 inhibitors.

9.4 The solution to this objective technical problem in the form of the compounds defined in claims 1 and 5 as granted is not suggested by either D1 alone or a combination of D1 with D19.

9.4.1 It may well be true that structural modifications such as "scaffold hopping" are routine practice for the skilled person trying to provide alternative compounds that still have the same activity as the starting compounds, as argued by the appellant. But at the same time it is also well known that structural modifications of this kind may have a big impact on the activity of a given compound (D20: page 217, right-hand column, lines 7 to 12). Therefore, if the skilled

person were to modify the scaffold of a particular chemical compound, they would not normally have any reasonable expectation of success in retaining its activity.

9.4.2 The appellant also argued that D1 (page 33, lines 4 to 30, in particular lines 8 and 14) stated that the MK2 inhibitors it disclosed were effective at treating e.g. allergies and Alzheimer's disease. These conditions could also be treated with the compounds in D19, some of which were based on the same imidazo[1,2-b]pyridazine scaffold as the compounds in claims 1 and 5 of the patent in suit (D19: page 19, line 26 to page 20, line 23, in particular page 19, line 30 and page 20, line 6; page 6, formula I-B together with page 11, lines 1 to 2). The skilled person would have recognised the overlap between the substitution pattern of the pyrazolo[1,5-a]pyrimidine scaffold in D1 and that of the imidazo[1,2-b]pyridazine scaffold in D19. The skilled person would therefore have also tested the compounds in D19 for their activity towards MK2 and in so doing would have arrived at the subject-matter of claims 1 and 5 as granted in an obvious manner.

This is not convincing. D19 is concerned with compounds that block the receptor sites for corticotropin-releasing factor (CRF), i.e. with CRF antagonists (page 1, lines 7 to 12). This mode of action is different from that underlying the compounds of claims 1 and 5 as granted, namely the inhibition of MK2 (paragraph [0010]). Thus, when faced with the objective technical problem of providing further MK2 inhibitors, the skilled person would have had no reason to turn to a document which is concerned with a completely different mode of action.

9.5 On the basis of above, the subject-matter of claims 1 and 5 involves an inventive step. The same reasoning applies *mutatis mutandis* to independent claims 15 and 16 and dependent claims 2 to 4, 6, 12, 13 and 17 to 19. Because the appellant only objected to claims 1 to 6, 12, 13 and 15 to 19, it is to be concluded that the ground for opposition pursuant to Article 100(a) EPC - lack of inventive step - does not prejudice maintenance of the patent as granted either.

Order

For these reasons it is decided that:

The appeal is dismissed.

The Registrar: The Chairman:

N. Maslin M. O. Müller

Decision electronically authenticated