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Datasheet for the decision of 17 September 2024

Case Number: T 1262/22 - 3.3.04

Application Number: 16822941.7

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IPC: C07K14/54, C07K14/715, C12N15/113, C07K16/24, C07K16/28, A61K39/00

Language of the proceedings: EN

Title of invention:
Treatment of fibrosis

Patent Proprietor:
Singapore Health Services Pte Ltd
National University of Singapore

Opponent:
Bayer Aktiengesellschaft

Headword:
Fibrosis/SINGAPORE HEALTH SERVICES

Relevant legal provisions:
EPC R. 152(6)
EPC Art. 100(a), 56, 108

Keyword:
Appeal validly filed
Authorisation of the professional representative filing the notice of appeal
Inventive step - no

Decisions cited:
T 1685/08, T 1846/11, T 0924/17

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Case Number: T 1262/22 - 3.3.04

D E C I S I O N
of Technical Board of Appeal 3.3.04
of 17 September 2024

Appellant: (Opponent)	Bayer Aktiengesellschaft Kaiser-Wilhelm-Allee 1 51373 Leverkusen (DE)
Representative:	König Szynka Tilmann von Renesse Patentanwälte Partnerschaft mbB Düsseldorf Mönchenwerther Straße 11 40545 Düsseldorf (DE)
Respondent: (Patent Proprietor 1)	Singapore Health Services Pte Ltd 31 Third Hospital Avenue No 03-03 Bowyer Block Singapore 168753 (SG)
Respondent: (Patent Proprietor 2)	National University of Singapore 21 Lower Kent Ridge Road Singapore 119077 (SG)
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 2 February 2022 rejecting the opposition filed against European patent No. 3298040 pursuant to Article 101(2) EPC.**

Composition of the Board:

Chairwoman	M. Pregetter
Members:	O. Lechner
	A. Bacchin

Summary of Facts and Submissions

I. The appeal lodged by the opponent (appellant) lies from the opposition division's decision to reject the opposition against European patent No. 3 298 040.

II. With the statement of grounds of appeal, the appellant submitted arguments as to why the claims as granted were not novel, lacked an inventive step and were insufficiently disclosed.

III. The respondents (patent proprietors) resubmitted sets of claims according to a main request (claims as granted) and auxiliary requests 1 to 7 (first submitted on 27 March 2020) and auxiliary requests 8 to 15 (first submitted on 7 August 2020).

IV. The appellant submitted document D86 by letter dated 9 March 2023 and document D87 by letter dated 30 April 2024.

V. The respondents submitted documents D88 to D94 by letter dated 3 June 2024.

VI. The board issued a communication pursuant to Article 15(1) RPBA.

VII. By letter dated 9 September 2024, the respondents withdrew auxiliary requests 4 to 7 and 12 to 15 and resubmitted the remaining claim requests.

VIII. By letter dated 13 September 2024, the appellant withdrew its objections under Articles 100(b) and 83 EPC against the main request and all auxiliary requests

and also withdrew its request that document D87 be admitted.

IX. During the oral proceedings before the board:
- the appellant withdrew its inventive-step objections based on documents D18 and D19 as the closest prior art
- the respondents declared that they were withdrawing all auxiliary requests on file, leaving the main request as their only request

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

X. Claim 1 of the main request reads as follows.

"1. An antibody which is capable of binding to Interleukin 11 (IL-11) or IL-11 receptor a (IL-11Ra) and inhibiting IL-11 mediated signalling, for use in a method of treating or preventing fibrosis in a human."

XI. Reference is made to the following documents, which were relevant to the decision:

D1 US 2009/0202533 A1

D2 Q. Chen et al., J Immunol, 174(4), 2005, 2305-2313

D3 W. Tang et al., J Clin Invest, 98(12), 1996, 2845-2853

D5 T. Wynn, Nat Rev Immunol, 4(8), 2004, 583-594

D6 C. Lee et al., Am J Respir Cell Mol Biol, 39(6), 2008, 739-746

D14 M. Obana et al., Circulation, 121(5), 2010, 684-691

D15 M. Stangou et al., J Nephrol, 24(1), 2011, 106-111

D16 US 2010/0093976 A1

D17 A. Ham et al., Anesthesiology, 119(6), 2013, 1389-1401

D20 T. Wynn, J Pathol, 214(2), 2008, 199-210

D33 Expert Panel Report 3: Guidelines for the Diagnosis and Management of Asthma; Report No.: 07-4051; 28 August 2007; Section 2, Definition, Pathophysiology and Pathogenesis of Asthma, and Natural History of Asthma; pages 11 to 34

D34 Z. Zhu et al., J Clin Invest, 103(6), 1999, 779-788

D36 C. Redlich et al., J Immunol, 157, 1996, 1705-1710

D39 P. Ray et al., J Clin Invest, 100(10), 1997, 2501-2511

D41 V. Kumar, Robbins and Cotran, Pathologic Basis of Disease, Elsevier 2010, Chapter 15, The Lung, by Husain A., pages 677-737

D42 J. Mims, Int Forum Allergy Rhinol, 5(S1), 2015, S2-S6

D45 F. Marra et al., Semin Immunopathol, 31(3), 2009, 345-358

D46 M. Chiaramonte et al., J Clin Invest, 104(6), 1999, 777-785

D53 E. Lawitz et al., Am J Gastroenterol, 99(12), 2004, 2359-2364

D55 M. Boerma et al., Cancer Res, 67(19), 2007, 9501-9506

D56 W. Trepicchio et al., J Clin Invest, 104(11), 1999, 1527-1537

D58 A. Lentsch et al., J Leukoc Biol, 66(1), 1999, 151-157

D59 B. Sheridan et al., Am J Physiol, 277(5), 1999, L861-L867

D61 A. Waxman et al., J Clin Invest, 101(9), 1998, 1970-1982

D62 J. Wang et al., J Immunol, 165, 2000, 2222-2231

D86 Email dated 17 February 2022 from Bayer Intellectual Property GmbH to ksvr.net

XII. The appellant's arguments relevant to the decision can be summarised as follows.

(a) Filing of the appeal

The appeal had been validly filed within the time specified by Article 108 EPC. It was irrelevant that the notice of appeal had been filed without proper authorisation. Rule 152(2) EPC allowed for the authorisation to be submitted after the filing of the appeal. Reference was made to the Decision by the President of the EPO on the filing of authorisations

(12 July 2007) and decision T 924/17, which confirmed that an authorisation's date can be later than the notice of appeal date. König Szynka Tilmann von Renesse Partnerschaft mbB (KSTvR) had authorisation from Bayer AG as indicated in an email dated 17 February 2022 (document D86). The company's statement of representation in the notice of appeal, filed before the time limit for filing an appeal had expired, was sufficient. The notice of appeal had been correctly filed under Article 108 EPC and should not be dismissed.

(b) Main request – Inventive step – Article 100(a) EPC

Closest prior art

Document D1 represented the closest prior art.

Difference, its technical effect, and objective technical problem

The subject-matter of claim 1 differed from the disclosure in claims 5 and 8 of document D1, which already disclosed the use of antagonistic antibodies specific for IL-11 or IL-11Ra (claim 5) "[f]*or treating asthma (see D1, claim 3) in a human (see D1, claim 8 (referring back to claims 1 to 8))*" (point [93] of the statement of grounds of appeal), on account of the treatment of fibrosis.

The objective technical problem was to provide a further or alternative medical use of an antibody capable of binding to IL-11 or IL-11Ra and inhibiting IL-11-mediated signalling.

Obviousness

Fibrosis was an inherent feature of asthma. Even if it was accepted that fibrosis is not always associated with asthma, a strong link between these two conditions was evident from paragraph [0007] of document D1. Document D1 also discussed the pro-fibrotic role of IL-11, e.g. citing documents D2 ("Chen" in paragraph [0020]) and D3 ("Tang" in paragraph [0017]), which would have prompted a skilled person to use an IL-11 antagonist to treat fibrosis.

It was common knowledge that Th2-polarised responses promoted fibrosis, with IL-13 being the key pro-fibrotic cytokine (D5, page 585, right-hand column, chapter "IL-13 is the main pro-fibrotic mediator"; D20, paragraph bridging pages 5 and 6; D45, page 5, last paragraph and page 351, left-hand column, paragraph 1; D46, abstract). A skilled person could readily apply the concept from document D1 to treat fibrosis.

Although not explicitly stated in document D1, the reduction in surrogate fibrosis markers (IL-13, eosinophils, macrophages) in Examples 2 and 3 indicated that blocking IL-11 affects fibrogenesis and fibrosis.

The ovalbumin (OVA) sensitised mouse model used in document D1 as a model for asthma (paragraph [0009], Example 3), was also commonly known to model pulmonary fibrosis (D5, Box 2, first point under "Toxins and drugs"). Suitable anti-IL-11 and anti-IL-11Ra antibodies were already commercially available (paragraphs [0058] and [0076] of the patent).

The respondents' argument that only the patent resolved the uncertainty about IL-11's role was factually and

legally incorrect. Documents D2, D3, D6, D61 and D62 discussed the physiological role of IL-11. These documents showed a context-specific function, namely that exogenous high doses of IL-11 had anti-inflammatory effects, while endogenous IL-11 was pro-inflammatory (D6, page 744, right-hand column; D2, page 2310, left-hand column). Document D62 also suggested that IL-11 could induce tissue fibrosis (page 2230, right-hand column).
Documents D2 (page 2311, left-hand column, first full paragraph; page 2312, left-hand column, last sentence) and D6 (page 745, paragraph bridging the left-hand and right-hand columns) suggested blocking IL-11 signalling to treat IL-13-related fibrosis.

On the basis of the results of Examples 2 and 3 of document D1, either alone or in combination with documents D2 or D6, the claimed subject-matter would have been obvious to a skilled person.

XIII. The respondents' arguments relevant to the decision can be summarised as follows.

(a) Filing of the appeal

The appeal was inadmissible because the notice of appeal was filed by a representative who was not authorised at the time of filing, i.e. König Szynka Tilmann von Renesse Partnerschaft mbB (KSTvR). The decision rejecting the opposition was issued on 2 February 2022, making 12 April 2022 the deadline for filing the notice of appeal. On 17 March 2022, KSTvR filed the notice of appeal on behalf of Bayer AG, but the authorisation from Bayer AG was dated 25 March 2022, which was after the notice of appeal was filed. KSTvR officially confirmed that it was taking

over representation on 3 May 2022. Under Rule 152(6) EPC, actions taken by an unauthorised representative had to be considered not to have been taken. It was of fundamental importance that the EPO knew who was acting as a party's representative, so as not to be detrimental to legal certainty.
Since KSTvR was not authorised on the date of the notice of appeal, the appeal had not been filed within the period specified in Article 108 EPC and was therefore inadmissible.

(b) Main request – Inventive step – Articles 100(a) and 56 EPC

Closest prior art

Document D1 represented the closest prior art.

Difference, its technical effect, and objective technical problem

Starting from paragraph [0044] of document D1, the subject-matter of claim 1 differed in that it specifically addressed the treatment of fibrosis in humans.

The objective technical problem suggested in the communication of the Board of Appeal pursuant to Article 15(1) RPBA, namely to provide a further or alternative medical use of an antibody capable of binding to IL-11 or IL-11Ra and inhibiting IL-11-mediated signalling, could be adopted.

The claimed solution was the treatment of fibrosis in a human.

Obviousness

Starting from the disclosure of document D1, the skilled person would not have had a reasonable expectation of successfully treating fibrosis.

From the background section of document D1, particularly paragraphs [0007] and [0017] to [0021], which discussed the findings of documents D2, D3 and D62, it was evident that the data on IL-11 were contradictory. As explicitly stated in paragraph [0021] of document D1, the role of IL-11 remained unclear.

Fibrosis was not an inherent feature of asthma, as evidenced e.g. by documents D1, D33 (page 11, bullet point four), D41 (page 688, paragraph bridging the left-hand and right-hand columns) or D42 (page 1, right-hand column).

Neither D1 nor D6, both of which essentially provided the same data, demonstrated any effect on fibrosis. Furthermore, document D6 reported the context-specific, bidirectional effects of IL-11, further emphasising the unclear role of IL-11.

Document D2 used transgenic IL-13-overexpressing mice which not only showed fibrosis but also exhibited many other symptoms (see D2, page 2306, left-hand column, first full paragraph; see also D34, title). Document D3 involved transgenic IL-11-overexpressing mice. Neither D2 nor D3 investigated a fibrosis-specific model. Moreover, the data from these studies were unreliable and did not represent physiological models, as the constitutive expression of a transgene in tissue might cause developmental abnormalities that could confound the interpretation of the gene's effects in adult

organisms (document D39, page 2501, left-hand column, last paragraph to right-hand column, paragraph 2).

Document D62, which used the same OVA mouse model as document D1, presented entirely contradictory findings to those of documents D2, D3 and D6. Specifically, document D62 taught that IL-11 selectively inhibits OVA-induced eosinophilia and Th2 inflammation in pulmonary tissues (see title and final sentence of the abstract). The authors proposed that IL-11 has anti-inflammatory, fibrotic and cytoprotective properties, suggesting it could be a therapeutic agent for regulating Th2-dominated inflammatory disorders (document D62, page 2231, left-hand column, paragraph 1).

Several other documents, including D14, D15, D17, D36, D53, D55, D56, D58 and D59, had observed an anti-inflammatory effect of exogenously administered IL-11 in the lungs and other tissues, supporting the conclusions of document D62. Additionally, documents D16, D53 and D56 provided human data, showing that exogenous administration of IL-11 resulted in anti-inflammatory and/or anti-fibrotic effects.

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

(a) The appellant requested that:
- the opposition division's decision be set aside, and the patent be revoked
- document D86 be admitted
- documents D88 to D94 not be admitted

(b) The respondents requested that:
- the appeal be rejected as inadmissible

- in case the appeal be found admissible, the appeal be dismissed, and the patent be maintained as granted (main request)
- Annexes A to C as filed with the appellant's grounds of appeal not be admitted
- documents D88 to D94 be admitted

Reasons for the Decision

Filing of the appeal

1. The respondents submitted that at the time the notice of appeal was filed, the professional representative lacked the required authorisation. The appeal should therefore be deemed not to have been filed.

2. In accordance with Rule 152(1) EPC, the President of the EPO determines the cases in which a signed authorisation must be filed by representatives acting before the EPO.

3. Under Article 1(1) of the Decision of the President of the EPO dated 12 July 2007 on the filing of authorisations, in the version as applicable at the time the notice of appeal in question was filed (see Special edition No. 3, OJ EPO 2007, L.1, effective until 31 October 2024; cf. OJ EPO 2024, A75 and A77), a professional representative is required to file a signed authorisation only in the circumstances set out in Article 1(2) and (3) of said decision. This is the case if a change of professional representatives has occurred without the EPO being notified that the previous representative's authorisation has ended. In this case, the new representative must file (together with the notification of their appointment) an individual authorisation or a reference to an

authorisation already on file (Article 1(2) of the Decision of the President of the EPO); if they fail to do so, as in the case in hand, they will be requested to do so within a period to be specified by the EPO (Article 1(2) of the Decision of the President of the EPO and Rule 152(2) EPC).

4. If this invitation to file an authorisation within the given period is not fulfilled, any procedural steps taken by the representative, other than the filing of a European patent application, are deemed not to have been taken (Rule 152(6) EPC).

5. In the case in hand, the opponent, Bayer AG, filed notice of appeal on 17 March 2022, i.e. before the expiry of the time limit for filing a notice of appeal against the opposition division's decision dated 2 February 2022, said time limit expiring on 12 April 2022 (Article 108 EPC).

6. While representation during the opposition proceedings was undertaken by BIP Patents (in the following "BIP"), the notice of appeal was signed by a new professional representative, König Szynka Tilmann von Renesse Partnerschaft mbB (KSTvR). Since BIP had not informed the EPO of the termination of its authorisation, it was still deemed authorised before the EPO, as provided for by Rule 152(8) EPC. Hence, there was nothing unusual in the fact that the EPO continued to communicate with BIP, nor can it be concluded on this basis that KSTvR was not authorised, as submitted by the respondents.

7. From the legal framework indicated above, it follows that, pursuant to Rule 152(1) EPC and the Decision of the President of the EPO dated 12 July 2007 on the filing of authorisations, the new representative KSTvR

had to file an authorisation granted by the opponent/ appellant.

8. Although the EPO did not request the appellant to provide an authorisation after the notice of appeal was filed, the new representative KSTvR filed an individual authorisation of its own motion on 5 April 2022. The authorisation had been granted by the opponent, Bayer AG, on 25 March 2022.

9. In accordance with Rule 152(2) EPC, filing the authorisation on 5 April 2022 remedied the deficiency concerning the representation of the opponent/appellant before the relevant period for filing an appeal under Article 108 EPC expired, i.e. 12 April 2022.

10. Therefore, the consequence indicated in Rule 152(6) EPC, according to which if the required authorisation is not filed in due time any procedural step taken by the representative is deemed not to have been taken, did not materialise. The notice of appeal was thus validly filed.

11. This conclusion is not affected by the fact that at the time the notice of appeal was filed, BIP was also acting as the professional representative for this case, since the system of representation before the EPO permits representation by several representatives, as long as the above rules are respected.

12. Nor is this conclusion affected by the fact that KSTvR's authorisation bears a signature which is dated 25 March 2022, i.e. after the filing of the notice of appeal. Contrary to the respondents' submissions, the EPC does not express a requirement that the authorisation be signed before the filing of the notice

of appeal; this would even be inconsistent with the purpose of Rule 152(2) EPC, which allows for a deficiency concerning the filing of an authorisation to be remedied. An authorisation is an internal legal relationship between the representative and the party. Accordingly, the question of whether an authorisation was in existence at the time the notice of appeal was filed is irrelevant for the EPO, as long as any deficiency concerning the party's representation was remedied within the time limit under Article 108 EPC.

13. The respondents further submitted that the EPO's letter dated 11 April 2022, with which KSTvR was asked to confirm whether they intended to take over representation of Bayer AG, showed that there were doubts about the effectiveness of the authorisation filed on 5 April 2022. The respondents concluded that KSTvR did not actually take over representation until the reply of 3 May 2022, meaning that they clearly were not authorised when filing the notice of appeal.

14. The board does not agree. The EPO's letter of 11 April 2022 was aimed merely at clarifying if BIP was still a representative in addition to KSTvR, or whether KSTvR had taken over as the sole representative; there is certainly nothing in said letter to indicate a deficiency in the authorisation, which had already been validly filed on 5 April 2022.

15. Moreover, KSTvR's reply of 3 May 2022 cannot be understood as an actual taking over of representation for the first time, as submitted by the respondents. Such a conclusion would disregard the fact that KSTvR had already filed an authorisation granted by the opponent/appellant on 5 April 2022. Nothing more was actually required.

In any event, even though evidence of prior authorisation is not required under the circumstances in this case (see point 12 above), the board also finds that the email of 17 February 2022 (filed as document D86), in which KSTvR is clearly entrusted with taking over the case and filing the appeal, is unequivocal evidence that the opponent/appellant had authorised KSTvR to act on its behalf when the notice of appeal was filed. The email was issued by Bayer Intellectual Property GmbH, the previously appointed representative (BIP), which according to the general authorisation granted by Bayer AG on 29 April 2019 (Form 1004) also had the power to grant sub-authorisations. Therefore, there is no doubt that at the time the notice of appeal was filed, KSTvR was authorised to act on behalf of the opponent/appellant.

16. Both BIP and KSTvR were informed on 10 May 2022 that the appointment of a new representative for the opponent had been registered with effective date 5 April 2022, in accordance with the requests dated 5 April 2022 and 3 May 2022.

17. It also follows that the EPO's communication dated 17 May 2022, erroneously informing the patent proprietor that no appeal was pending, could not have originated from an assumption of a lack of authorisation. First, as indicated above, the registration of the appointment of the new representative had already been confirmed by the EPO's letter of 10 May 2022. Second, at that time a procedure to remedy the deficiency under Rule 152(2) EPC had not yet ended. Indeed, the communication of 17 May 2022 was immediately revoked by the EPO's letter dated 25 May 2022, which explained that the erroneous

information had been caused by a technical error and that a notice of appeal had been filed on 17 March 2022.

18. Decision T 1685/08, cited by the respondents, is not applicable to the case in hand since in that case the newly appointed representative never filed an authorisation.

19. Decision T 1846/11 is not applicable to the current situation either. In that case, the board considered the representative to be authorised only from the authorisation date. However, the representative was a legal practitioner, and at least until 1 November 2024 (see OJ EPO 2024, A75 and A77, for the introduction of equal treatment of legal practitioners and professional representatives regarding the filing of authorisations) legal practitioners always had to file an authorisation in order to act before the EPO. In this case, the representative is a professional representative, to whom the special regime of authorisations, in particular with regard to the possibility of remedying a deficiency pursuant to Rule 152(2) and (6) EPC, applies.

20. The board does not agree with the respondents' argument that decision T 924/17 was not applicable to this case particularly because under the circumstances in hand evidence was available contradicting the existence of an authorisation at the time the notice of appeal was filed, e.g. KSTvR's letter of 3 May 2022. As indicated above, said letter cannot be construed as the representation actually being taken over for the first time. An authorisation granted by the appellant was already on file and, although not required, the available evidence unequivocally shows that an actual

authorisation existed at the time the notice of appeal was filed.

21. It is therefore concluded that the notice of appeal was validly filed.

Admission of documents D88 to D94

22. Since the board acknowledged the anti-fibrotic effect of IL-11 as shown in document D53 without needing to consider the disclosure of document D88, there was no need to decide on the admission of the latter.

23. The request for admission of document D87 was withdrawn (see appellant's letter dated 13 September 2024), and the original request for admission of documents D89 to D94 was conditional upon the admission of document D87 (see respondent's letter dated 3 June 2024). Moreover, documents D87 and D89 to D94 were cited in support of arguments concerning disclosure of the invention which is not part of the present decision, Thus, there was no need to decide on the admission of documents D89 to D94.

Main request

Inventive step – Articles 100(a) and 56 EPC

Closest prior art

24. The parties agreed that document D1 represents the closest prior art.

25. Document D1 relates to the treatment and prophylaxis of Th2-mediated disorders with an antagonist of IL-11 or IL-11 receptor α (IL-11Ra). A murine OVA model of

allergic asthma is used as the animal model (paragraph [0044]). Paragraph [0007] mentions that asthmatic airways display lung hyperinflation, smooth muscle hypertrophy, fibrosis in the lamina reticularis, mucosal oedema, epithelial cell sloughing, cilia cell disruption and mucus gland hypersecretion.

26. The data in document D1 show (i) a significant increase in total cell number in the bronchoalveolar lavage fluid (BALF) and (ii) a reduction of mucin (protein) and IL-13 levels in the BALF, in IL-11Ra -/- mice (Example 2) or mice treated with an IL-11 antagonistic mutein (Example 3) when compared with controls.

Fibrosis was not directly assessed in these experiments.

27. Claims 5 and 8 of document D1 relate to the treatment of Th2-mediated disorders, selected from asthma, chronic obstructive pulmonary disease (COPD), rhinitis, allergies and atopic dermatitis, and define the use of an antibody specific for IL-11 or IL-11R (IL-11Ra in claim 8). Claim 9 defines the treatment of a human.

Difference, its technical effect, and objective technical problem

28. In agreement with the respondents, the board considers that the skilled person would not infer from the general statement in paragraph [0007] in the background section of document D1 that all asthma patients are affected by fibrosis. This is further supported by documents D33 (page 11, bullet point four), D41 (page 688, paragraph bridging the left-hand and right-hand columns) and D42 (page 1, right-hand column), which

confirm that fibrosis is not a universal feature among asthma patients.

29. Paragraph [0044] of document D1, suggested by the respondents as the starting point for the assessment of inventive step, provides only very general information. More specific information concerning the core of document D1, namely the treatment of Th2-mediated disorders in a subject, can be found in the claims. Starting from claim 8, which depends on claim 1 via claim 5, the subject-matter of claim 1 of the main request differs on account of the treatment of fibrosis in a human.

However, document D1 already makes it clear that humans are the relevant population to be treated (see claim 9 and paragraph [0009]). Thus, the subject-matter of claim 1 differs from the disclosure in document D1 in that fibrosis is treated.

30. The technical effect associated with this difference is the provision of a new medical use of anti-IL-11/ IL-11Ra antibody antagonists of IL-11-mediated signalling - specifically the treatment of fibrosis.

31. The treatment of fibrosis is made credible by the data provided in the examples of the application as filed, which are also present in the patent in suit.

32. As agreed by the parties, the objective technical problem is to provide a further or alternative medical use of an antibody capable of binding to IL-11 or IL-11Ra and inhibiting IL-11-mediated signalling.

The claimed solution is the treatment of fibrosis.

Obviousness

33. Starting from the disclosure of claim 8 of document D1 and taking into account the experimental evidence provided in document D1, especially Example 3, the skilled person knew that antagonising IL-11Ra in the OVA-induced model of asthma resulted in an increase in total cell numbers, specifically eosinophils, which are reported to be an indicator of airway inflammation and a feature of asthmatic airways (see paragraph [0007] of document D1), in bronchoalveolar lavage fluid (BALF) compared with controls. The reduction of eosinophils was highly significant ($p<0.01$). The levels of IL-13, a Th2 cytokine known to play a critical role in the pathogenesis of asthma and fibrosis (see points 36.,40. and 41. below), were also significantly reduced in the animals treated with the IL-11Ra antagonist.

34. The skilled person also knew from document D1 that asthmatic airways may display lung hyperinflation, smooth muscle hypertrophy, fibrosis in the lamina reticularis, mucosal oedema, epithelial cell sloughing, cilia cell disruption and mucus gland hypersecretion (paragraph [0007]).

35. While the respondents have questioned the data from the IL-11R null mouse model in Example 2 of document D1 in light of the disclosure of document D39 (page 2501, paragraph bridging left-hand and right-hand columns), the experimental evidence presented in Example 3 has not been challenged.

36. As argued by the appellant (see letter dated 9 March 2023, paragraphs 71, 72, 77 and 79), it was common general knowledge in the field that IL-13 was the main pro-fibrotic mediator (see e.g. documents D5, page 585,

right-hand column, chapter "IL-13 is the main pro-fibrotic mediator"; D20, paragraph bridging pages 5 and 6; D45, page 5, last paragraph and page 351, left-hand column, paragraph 1; D46, abstract).

37. Therefore, on the basis of the observed significant reduction in IL-13 levels and the number of eosinophils upon blockage of IL-11Ra, a skilled person had a reasonable expectation of success that neutralising the signalling of IL-11 – e.g. with antagonistic antibodies against IL-11 or IL-11Ra – could be successfully employed in the treatment or prevention of fibrosis in the context of asthma.

38. With reference to the background art discussion and the final statement in paragraph [0021] of document D1, as well as the reported anti-fibrotic and/or anti-inflammatory role of IL-11 in document D62, which was supported by many other documents such as D14, D15, D16, D17, D36, D53, D55, D56, D58 and D59, the respondents argued that a skilled person would have been discouraged from using an IL-11 antagonist for the treatment of fibrosis.

39. The statement in paragraph [0021] of document D1, which notes that the role of IL-11 in airway inflammation remained unclear, merely summarises prior art, including documents D2 (reference 22), D3 (reference 20) and D62 (reference 23), discussed in paragraphs [0017] to [0020], without considering the experimental data in document D1 itself.

On the basis of these data, the inventors of document D1 concluded that IL-11 antagonism could be used to treat Th2-mediated conditions, including inflammatory responses in the lungs, such as asthma. Document D6,

which stems from the same working group as document D62 and was published ten years later, addresses many of the documents discussed in document D1, including D2, D3, D61 (reference 13) and D62, while presenting the same experimental data as in document D1.

40. The content of documents D2, D3, D61 and D62 will be briefly summarised below.

Document D2 discloses that IL-13 is a major stimulator of inflammation and tissue remodelling at sites of Th2 inflammation. In Th2-dominant inflammatory disorders such as asthma, IL-11 is simultaneously induced. IL-13 is reported to be a potent stimulator of IL-11 and IL-11Ra, and IL-11 signalling is reported to play an important role in the pathogenesis of IL-13-induced inflammation, fibrosis, etc. (abstract, page 2310, page 2312, paragraph bridging the two columns).

Document D3 reports that transgenic overexpression of IL-11 induces asthma-like T and B cell-rich inflammation, airway fibrosis, myofibroblast accumulation and physiological dysregulation (abstract; page 2851, right-hand column, last paragraph).

Document D61 reports that in transgenic animals overexpressing IL-11, IL-11 diminished hyperoxia-induced expression of IL-1 and TNF and cell death response, diminishing hyperoxic lung injury (abstract).

Document D62 demonstrates that exogenous IL-11 selectively inhibits antigen-induced eosinophilia, Th2 inflammation and VCAM-1 gene expression in pulmonary tissues (abstract).

41. Considering the teaching in these prior-art documents and the contradictory reports on the role of IL-11 in e.g. documents D2 and D3 compared with documents like D61 or D62, along with new evidence, the authors of document D6 concluded that endogenous IL-11 signalling played an important role in the pathogenesis of Th2 antigen sensitisation and in the pathogenesis of Th2-mediated and IL-13-induced inflammatory and remodelling responses (page 745, paragraph bridging the left-hand and right-hand columns).

Moreover, on page 744, right-hand column, of document D6 the authors address the observed ambiguity concerning the role of IL-11. Accordingly, it was clear that IL-11 had complex, context-specific effects on Th2 inflammation. Endogenous IL-11 mediated pro-inflammatory and remodelling effects, while the exogenous administration of high concentrations of IL-11 activated compensatory pathways designed to provide feedback to and control the responses, leading to an anti-inflammatory effect.

42. The board notes that, like documents D2 and D3, documents D61 and D62, as well as D34, also rely on transgenic mouse models that constitutively overexpress IL-11 or IL-13 in the lungs. As highlighted by the respondents, constitutive overexpression was known to be problematic as it could cause various abnormalities in the lungs (document D39, page 2501, paragraph bridging the left-hand and right-hand columns). However, given the disclosures in documents D1 and D6, the board considers it unnecessary to discuss these transgenic mouse model data further.

43. Nonetheless, the potentially contradictory data identified by the respondent in document D62 are not

suitable to discourage the skilled person from using an IL-11 antagonist for the treatment of fibrosis. In this respect, the chronology of the publications has to be taken into account. More recent findings, such as presented in document D6 (see point 41. above), reflect the expertise gained and the development in the understanding of certain effects. The skilled person would have considered the findings of document D6 as representing the state of the art.

44. Thus, in view of the data of Example 3 of document D1, the skilled person would have reasonably expected that an IL-11 antagonist could treat fibrosis in the context of asthma.

45. The respondents also referred to several other documents as teaching away from the claimed invention, including document D14, D15, D17, D36, D53, D55, D56, D58 or D59, which reported an anti-inflammatory effect of (exogenously administered) IL-11 in the lung and other tissues, supporting the conclusions of document D62. Additionally, documents D16, D53 and D56 reported that exogenous administration of IL-11 resulted in both anti-inflammatory and/or anti-fibrotic effects.

As explained in document D6 (see point 41. above), while exogenous IL-11 may have anti-inflammatory and anti-fibrotic effects in certain contexts, it may also activate compensatory pathways leading to anti-inflammatory responses.
In contrast, the invention focuses on antagonising IL-11Ra to block endogenous IL-11 signalling, which, on the basis of the disclosure in documents D1 and D6, was known to promote inflammation and fibrosis in diseases such as asthma. Thus, the role of exogenous IL-11 disclosed in the prior art does not undermine the

potential therapeutic benefit of targeting endogenous IL-11 signalling with antagonists.

46. In conclusion, in view of the data in Example 3 of document D1, the skilled person would have used an IL-11 antagonist for the treatment of fibrosis in the context of asthma. An analysis of the other cited prior-art documents (see points 38. to 41. and 45. above) would not have taken away the expectation of success. The skilled person would thus have arrived at the claimed solution on the basis of the teaching of document D1 and common general knowledge.

Consequently, the subject-matter of claim 1 of the main request lacks an inventive step (Articles 100(a) and 56 EPC).

Admission of Annexes A to C as filed with the appellant's statement of grounds of appeal

47. The appellant attached to its statement of grounds of appeal Annexes A to C, which are copies of the arguments put forward by the appellant in various submissions during the opposition proceedings on disclosure of the invention (Annex A), novelty (Annex B), and inventive step (Annex C).

48. The board did not need to decide on the admission of Annexes A to C, because these Annexes did not have to be taken into account in order to reach the decision.

Order

For these reasons it is decided that:

1. The decision under appeal is set aside.

2. The patent is revoked.

The Registrar: The Chairwoman:

I. Aperribay M. Pregetter

Decision electronically authenticated