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Datasheet for the decision of 20 May 2009

Case Number: T 0251/07 - 3.3.04

Application Number: 95913644.1

Publication Number: 0754059

IPC: A61K 39/395

Language of the proceedings: EN

Title of invention:
Methods and compositions useful for inhibition of angiogenesis

Patentee:
THE SCRIPPS RESEARCH INSTITUTE

Opponent:
CENTOCOR, INC.

Headword:
Inhibition of angiogenesis/SCRIPPS

Relevant legal provisions:
EPC Art. 56

Relevant legal provisions (EPC 1973):
-

Keyword:
"Main request: inventive step (yes)"

Decisions cited:
-

Catchword:
-

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Case Number: T 0251/07 **-** 3.3.04

D E C I S I O N
of the Technical Board of Appeal 3.3.04
of 20 May 2009

Appellant: (Opponent)
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Decision under appeal:
Interlocutory decision of the Opposition Division of the European Patent Office posted dated 12 December 2006 concerning maintenance of European patent No. 0754059 in amended form.

Composition of the Board:

Chair: U. Kinkeldey
Members: R. Gramaglia
F. Blumer

Summary of Facts and Submissions

I. European patent No. EP-B-0 754059 (application No. 95 913 644.1, published as WO-A-95/025543) having the title "Methods and compositions useful for inhibition of angiogenesis" was granted with 22 claims.

II. Notice of opposition was filed by the opponent requesting the revocation of the European patent on the grounds of Article 100(a), (b) and (c) EPC on the grounds that the claims did not fulfil the requirements of Articles 54, 56, 83 and 123(2) EPC 1973.

III. The opposition division came to the conclusion that granted claim 1 lacked novelty and maintained the patent on the basis of the auxiliary request then on file.

IV. The appellant (opponent) filed an appeal against the decision of the opposition division. In reply thereto, the respondent (patentee) submitted with letter dated 10 September 2007 new claims in form of a Main Request and an Auxiliary Request.

V. Oral proceedings were held on 20 May 2009, during which the respondent filed an Amended Main Request, of which claim 1 read as follows:

"1. The use of an $\alpha_v\beta_3$ antagonist in the manufacture of a medicament for the treatment of arthritis, diabetic retinopathy, macular degeneration, a hemangioma or a solid tumour of breast or colon, said medicament comprising an angiogenesis—inhibiting amount of said $\alpha_v\beta_3$ antagonist."

Dependent claims 2 to 20 related to specific embodiments of the use according to claim 1.

VI. The following documents are cited in the present decision:

D5 Cheresh D.A., Proc. Natl. Acad. Sci. USA, Vol. 84, pages 6471-6475 (1987);

D6 W0-A-89/05155;

D7 WO-A-93/20229;

D9 EP-A-0578083;

D10 EP-A-0576898;

D11 Nicosia R.F. et al., Am. J. Pathol., Vol. 138, No. 4, pages 829-833 (1991);

D12 Saiki I. et al., Jpn. J. Cancer Res., Vol. 81, pages 668-675 (1990);

D13 Grant D.S. et al., Cell, Vol. 58, pages 933-943 (1989);

D14 Brooks P.C. et al., J. Clin. Invest., Vol. 96, pages 1815-1822 (1985);

D16 Folkman J. et al., Science, Vol. 235, pages 442-447 (1987);

D20 Pignatelli M. et al., Human Pathol., Vol. 23, pages 1159-1166 (1992);

D21 Schreiner C. et al., Clin. Expl. Metastasis, Vol. 9, No. 2, pages 163-178 (1991);

D22 Lafrenie R.M. et al., Cancer Res., Vol. 52, pages 2202-2208 (1992);

D23 Smith J.W. et al., J. Biol. Chem., Vol. 265, No. 21, pages 12267-12271 (1990).

VII. The submissions by the appellant, insofar as they are relevant to the present decision, can be summarized as follows:

Inventive step (Article 56 EPC 1973)
(Non-neoplastic) angiogenesis related diseases

- Document D16 could be viewed as the closest prior art. The problem to be solved could be formulated as the provision of alternative means (to those disclosed in this document) to treat the (non-cancer) angiogenesis-related diseases listed in claim 1.

- Departing from document D16, the solution to the problem above was obvious to the skilled person, in the light of documents D11, D12 or D13, which taught that RGD-containing peptides could be used as potent inhibitors of angiogenesis.

Treatment of solid tumours of breast or colon

- Document D6 was the closest prior art. The problem to be solved was the identification of further tumours that could be treated with an $\alpha_v\beta_3$ antagonist.

- The disclosure of document D6 was not limited to the teaching that antibodies reacting with $\alpha_v\beta_3$ could be used for inhibiting the growth of tumour cells expressing $\alpha_v\beta_3$. Rather it covered the inhibition of tumour growth in general. This is because the skilled person coming across document D6 would understand that the inhibition of tumour growth by monoclonal antibody (hereafter: "mAb") LM609 also involved blocking vascularization of the tumour tissue. Hence, the skilled person would have inferred from document D6 — either alone or in combination with document D5 or D7 - that it would be worthwhile applying the treatment concept described therein on various kinds of tumours, regardless of their $\alpha_v\beta_3$-status.

- The skilled person would have been motivated to apply the teaching of document D6 to solid tumour of the breast or colon, since there was evidence in documents D20 and D21 that cells derived from these tumours expressed the $\alpha_v\beta_3$ receptor.

- Document D9 disclosed cyclic adhesion inhibitors exhibiting the RGD motif for the treatment of several disease, including tumours. Document 10 dealt with linear RGD peptides for treating tumours. Starting from one of these documents as closest prior art, there was no reason why the skilled

person would not have used the RGD-containing peptides disclosed therein to treat breast or colon tumours, having regards to the fact that the target molecule of the inhibitory peptides referred to in these documents was not clearly identified.

VIII. The submissions by the respondent (patentee) can be summarized as follows:

Inventive step (Article 56 EPC)
(Non-neoplastic) angiogenesis related diseases

- Document D16 could be viewed as the closest prior art. The problem to be solved could be formulated as the provision of means to treat the (non-cancer) angiogenesis-related diseases listed in claim 1.

- However, no reference was made in document D16 to antagonists of integrin $\alpha_v\beta_3$. Nor could the teaching be derived from document D16 that inhibitors of angiogenesis were effective in the treatment of the non-neoplastic angiogenic diseases mentioned above.

- There was no evidence that the trails of migrating endothelial cells described in document D11 as "micro-vessels" contained a lumen.

- No further investigations were carried out by the authors of documents D11, D12 and D13 to establish that the effect of the RGD peptides was specific to the vitronectin receptor $\alpha_v\beta_3$.

- The combination of the teachings in documents D16 with that of any of documents D11, D12 or D13 by the

skilled person would not give rise to a reasonable expectation that an antagonist of $\alpha_v\beta_3$ could be used therapeutically to inhibit angiogenesis in vivo in order to achieve treatment of any of the non-cancer diseases listed in claim 1.

Treatment of solid tumours of breast or colon

- Document D6 was the closest prior art. The problem to be solved was the identification of further tumours that could be treated with an $\alpha_v\beta_3$ antagonist.

- The teaching of document D6 was that antibodies such as mAb LM609 which immunoreact with the ECr receptor (= $\alpha_v\beta_3$) were useful for inhibiting cell adhesion and hence the growth of tumours which express ECr. There was no disclosure in document D6 that the $\alpha_v\beta_3$ receptor was expressed by solid tumours of breast or colon. Therefore, $\alpha_v\beta_3$ antagonists would not be expected to be useful in the treatment of tumours which did not (or weakly) express the $\alpha_v\beta_3$ receptor.

- Moreover, the skilled person was aware of the fact that the inhibition of tumour growth observed in Example 11 of document D6 could not be the result of inhibiting angiogenesis.

- The teaching of documents D9 and D10 was that certain compounds could be used to treat tumours because they inhibited cell adhesion. These compounds would thus not be expected to be useful in the treatment of tumours which did not (or weakly) express the $\alpha_v\beta_3$ receptor.

IX. The appellant (opponent) requested that the decision under appeal be set aside and that the European patent No. 0 754 059 be revoked.

The respondent (patentee) requested that the decision under appeal be set aside and the patent be maintained on the basis of the Amended Main Request as filed on 20 May 2009 during the oral proceedings before the board, or, subsidiarily, on the basis of the Auxiliary Request as filed with letter dated 10 September 2007.

Reasons for the Decision

Main Request
Novelty (Article 54 EPC 1973)

1. It has not been disputed by the appellant, and the board agrees as well, that none of the documents presently before the board discloses the use of an $\alpha_v\beta_3$ antagonist as a medicament for the treatment of the angiogenesis related diseases arthritis, diabetic retinopathy, macular degeneration or hemangioma or the solid tumours of breast or colon. Therefore, the subject-matter of claim 1 satisfies the requirements of Article 54 EPC 1973. This conclusion extends to dependent claims 2 to 20.

Inventive step (Article 56 EPC 1973)
Introduction

2. According to the technical background reviewed in the patent in suit (see paragraphs [0002] to [0005]), the vitronectin receptor $\alpha_v\beta_3$ (integrin $\alpha_v\beta_3$) belongs to the

family of integrins, which are transmembrane heterodimers (i.e. made of two noncovalently linked protein subunits). The integrins on various cells were known at the earliest priority date of the patent in suit to mediate cell-cell and cell-extracellular matrix interactions ("cell adhesion events") and several integrins with different combinations of α and β subunits had been identified on various cells.

Claim 1

3. Claim 1 of this request is drafted in the form of a "second/further medical use" and relates to the use of an $\alpha_v\beta_3$ antagonist as a medicament for the treatment of two separate groups of diseases: (i) (non-neoplastic) angiogenesis-related diseases such as arthritis, diabetic retinopathy, macular degeneration and hemangioma and (ii) tumour-related diseases such as solid tumours of breast or colon. Since each group of diseases (i) and (ii) above has to be examined separately in the light of its own closest prior art (see points 4 and 13 infra), the inventive step will be dealt with in two distinct groups.

Closest prior art for disease group of (i)
Document D16

4. With respect to the non-neoplastic angiogenic diseases listed in claim 1, document D16 can be viewed as the closest prior art. The authors of this document summarize the knowledge by the year of publication (1987) with respect to certain angiogenesis—modulating molecules as well as the mechanism of angiogenesis and putative ways of its inhibition. It is stated on

page 446, r-h column, first full paragraph of this document that diabetic retinopathy, rheumatoid arthritis and hemangioma are non-neoplastic diseases arising from abnormal angiogenic processes. On page 445, l-h column, under the heading "Factors that modulate Angiogenesis" a series a agents inhibiting angiogenesis (such as protamine, heparin used in the presence of cortisone or hydrocortisone and fragments of heparin) are listed.

However, no reference is made to antagonists of integrin $\alpha_v\beta_3$. Nor can the teaching be derived from document D16 that inhibitors of angiogenesis were effective in the treatment of the non-neoplastic angiogenic diseases mentioned above. In fact, the authors of this document merely pose (but fail to provide an answer to) the question "Could the pathologic angiogenesis of diabetic retinopathy, rheumatoid arthritis [and the growth of tumors] be suppressed by specific inhibitors of capillary growth?" (see the final paragraph on page 446).

5. Starting from document D16 as closest prior art, the problem to be solved can thus be formulated as the provision of means to treat the (non-cancer) angiogenesis-related diseases listed in claim 1.

6. The solution proposed in claim 1 is the treatment of arthritis, diabetic retinopathy, macular degeneration and hemangioma with antagonists of integrin $\alpha_v\beta_3$. In view of paragraphs [0216] to [0225] and Fig. 16A-16E and its counterpart on page 5, lines 52-55 of the patent, showing the complete in vivo inhibition of βFGF-induced corneal angiogenesis by mAb LM609, which

is an antagonist of integrin $\alpha_v\beta_3$, the board is satisfied that the problem above has indeed been solved.

7. The appellant maintains that this solution was obvious to the skilled person departing from document D16, when turning to any of documents D11, D12 or D13, which taught that RGD-containing peptides could be used as potent inhibitors of angiogenesis.

8. The authors of document D11 used an in vitro rat aorta model involving rings of rat aorta embedded in gels of rat tail collagen (see page 829, r-h column, under "Materials and Methods"), and the ability to generate branching "micro-vessels" was observed in the presence or absence of the RGD-peptide GRGDS. The experiments reported in this document showed that the GRGDS inhibited migration of endothelial cells into collagen gel and inhibited branching of micro-vessels in this rat aorta model.

However, the serum-free collagen gel medium used by the authors of document D11 was an artificial environment which failed to reproduce the in vivo conditions of a complex organised tissue providing multiple integrin ligand targets for multiple integrin receptors. In view of this, the board finds it doubtful that the results reported in D11 could allow the skilled person to draw any reliable conclusion about inhibition of angiogenesis in vivo.

But even assuming in favour of the appellant that the skilled person considered it implicit that the in vitro results reported in document D11 could be extrapolated to the in vivo situation, the board observes that it

was well known that RGD-containing peptides inhibited integrins **as a broad class** (see paragraph [0004] and page 3, lines 36-40 of the patent), which integrins were to be found on vascular endothelial cells (see point 1 supra). But no further investigations were carried out by the authors of document D11 to establish that the effect of the GRGDS peptide was specific to the vitronectin receptor $\alpha_v\beta_3$. Hence, the experiment performed by the authors of document D11 merely showed that an RGD-peptide inhibited branching of micro-vessels in that model, without specifying **which** integrin receptor was being affected specifically. In other words, the authors of document D11 failed to demonstrate that angiogenesis could be inhibited in a tissue using $\alpha_v\beta_3$ antagonists and that the $\alpha_v\beta_3$ function was a fundamental requirement for angiogenesis in a tissue to occur.

Unlike document D11, the subject-matter of claim 1 supported by the description of the patent in suit do indeed overcome the conundrum above by demonstrating inter alia (see paragraphs [0216] to [0225]) that mAb LM609 (a specific antagonist of integrin $\alpha_v\beta_3$) completely inhibits in vivo βFGF-induced corneal angiogenesis **and** that mAb P1F6 (being an anti-$\alpha_v\beta_5$) is not effective in doing so because it has no such specificity for integrin $\alpha_v\beta_3$.

9. Document D12 discloses the effects of synthetic poly-RGD-peptides on tumour angiogenesis in mice. It is described that poly(RGD) significantly reduced the number of capillary vessels oriented towards the tumour mass (see page 673, r-h column, under "Discussion"). However, no such inhibition was observed with two other

RGD-containing molecules, namely the RGDS monomer and a random copolymer of arginine, glycine and aspartic acid. In view of these experimental results, the skilled person would assume that the presence of an RGD sequence could not be per se responsible for inhibiting the growth of capillaries. But accepting arguendo that the skilled person considered the equation "presence of RGD = reduction of the number of capillary vessels" as experimentally demonstrated, the investigations performed according to document D12 suffer from the same deficiency pointed out under point 8 supra that no further studies were done by the authors of document D12 to demonstrate that the effect of the poly(RGD) peptide was specific to the vitronectin receptor $\alpha_v\beta_3$.

10. Document D13 relates to YIGSR and PA 21 peptides (see Fig. 1 and page 941, under "Synthetic Laminin Peptides"). It is stated in the passage bridging pages 938 and 939 of this document that the authors had examined the effect of these peptides on capillaries in the developing chorioallontoic membrane (CAM) of the chick and that they found that these peptides blocked the growth of the capillary network. On page 940, l-h column, lines 3-5, it is confirmed that the peptides have shown the ability to reduce vascular growth and that they might be used to inhibit pathological vascularization.

11. However, in the board's view, the skilled person could not derive from document D13 the teaching that the YIGSR and PA 21 peptides targeted integrin $\alpha_v\beta_3$, let alone the teaching that it was sufficient to block (with an antagonist of integrin $\alpha_v\beta_3$) $\alpha_v\beta_3$ integrin and no other integrin in order to inhibit angiogenesis.

12. In summary, the board must conclude that the combination of the teachings in documents D16 with that of any of documents D11, D12 or D13 by the skilled person would not give rise to a reasonable expectation that an antagonist of $\alpha_v\beta_3$ could be used therapeutically to inhibit angiogenesis in vivo, thus opening the door to the successful treatment of any of the non-cancer diseases listed in claim 1.

Closest prior art for diseases of group (ii)
Document D6

13. As for the second aspect of claim 1 (i.e. the treatment of solid tumours of breast or colon), document D6 was identified by the parties as the closest prior art, and the board agrees as well. This document teaches that mAb LM609 immunoreacts with the RGD-directed adhesion receptor of endothelial cells (ECr) (see page 1, lines 6-8 and page 4, lines 15-16, respectively), found mainly on melanoma cells (see Fig. 7). The ECr receptor is now known to be identical to the $\alpha_v\beta_3$ receptor.

Example 11 of document D6 has the title "Inhibition of Tumor Growth by In Vivo Administration of Monoclonal Antibody LM609". According to this Example, human melanoma cells M21 were injected into mice, and the effect on tumour growth of injecting mAb LM609 was investigated. The tumours in those mice receiving mAb LM609 progressed "at a much slower rate" over those of the control (PBS) or the LM142-treated mice (see last line of page 47).

14. The therapeutic agent being the same (present claim 1: an $\alpha_v\beta_3$ antagonist; document D6: mAb LM609 blocking the ECr (= $\alpha_v\beta_3$) receptor and hence behaving as an $\alpha_v\beta_3$ antagonist), the difference between claim 1 (second group of diseases) and document D6 lies in the different tumours to be treated. The problem to be solved, thus, can be seen in the identification of further tumours that can be treated with an $\alpha_v\beta_3$ antagonist.

The solution proposed in claim 1 is the treatment of solid tumours of breast or colon. The board is satisfied that the problem above has indeed been solved in view of paragraphs [0228] and [0230] and Fig. 13A-13D and its counterpart on page 5, lines 33-39 of the patent, showing that antagonists of integrin $\alpha_v\beta_3$ inhibit tumour-induced angiogenesis, leading to the growth arrest and regression of numerous tumours types, inter alia the MDA 23.1 breast carcinoma cell line, regardless of their $\alpha_v\beta_3$-status (i.e., be they $\alpha_v\beta_3$-negative or $\alpha_v\beta_3$-positive).

Document D6 alone or taken in combination with documents D5 and/or D7 and/or D20 and/or D21

15. The appellant maintains that the disclosure of document D6 was not limited to the teaching that antibodies reacting with $\alpha_v\beta_3$ could be used for inhibiting the growth of tumour cells expressing $\alpha_v\beta_3$. Rather it covered any cancer (see the wording "all cell types" page 47, lines 2-6) and the inhibition of tumour growth in general (see claim 4 of document D6). This is because, in the appellant's view, the skilled person coming across document D6 would understand that the

inhibition of tumour growth by mAb LM609 also involved blocking vascularization of the tumour tissue. Hence the appellant concludes that the skilled person would have inferred from document D6 — either alone or in combination with document D5 - that it would be worthwhile applying the treatment concept described therein on various kinds of tumours, regardless of their $\alpha_v\beta_3$-status, including tumours of the breast and colon.

16. To buttress its view that it was already known before the priority date of the patent in suit that the $\alpha_v\beta_3$ antagonist LM609 had the capability to interfere with tissue vascularisation, the appellant relies on the following documents:

page 1, lines 18-22 of document D6:

"Cell adhesion is a critical process in tumor growth because it plays a role in the formation and vascularization of new tumor tissue. Therefore, agents that inhibit cell adhesion can be used therapeutically to inhibit tumor growth." (emphasis by the appellant)

page 20, line 31 to page 21, line 1 of document D6:

"... a monoclonal antibody of the present invention can be used to inhibit the binding interaction of ECr with vitronectin, fibrinogen and von Willebrand factor in vivo. For instance, a monoclonal antibody of the present invention contains antibody molecules that immunoreact with ECr to form an antibody molecule-ECr complex, present on the endothelial cell-surface, so

that the cell does not bind vitronectin, fibrinogen or von Willebrand factor." (emphasis by the appellant)

page 6471, l-h column, first paragraph of document D5:

"The molecular interactions that contribute to the proliferation, adhesion, and motility of endothelial cells are undoubtedly critical events associated with vessel wall repair in injured tissues and vascular proliferation in tumors"

page 6473, r-h column, last paragraph of document D5:

"Endothelial cells can interact with a number of proteins present in plasma and in the subendothelial matrix. These interactions are critical for events associated with wound healing, coagulation, lymphocyte infiltration at sites of inflammation, and tumor hematogenous spread"

page 2, lines 13-17 of document D7:

"Another monoclonal antibody, LM609 (produced by hybridoma LM609 ATCC HB 9537) disclosed in PCT Application Publication No. WO 89/05155 (published 15 June 1989) and Cheresh et al. J. Biol. Chem. 262: 17703-17711 (1987) was also found to bind to the αvβ3 complex and, due to its ability to inhibit the binding of ECr molecules present on the surface of tumor cells and blood vessel forming endothelial cells to vitronectin, fibrinogen and von Willebrand factor, was proposed for therapeutic use as tumor growth inhibitor."

17. In the board's judgement, however, the essence of the teaching of document D6 is that antibodies such as mAb LM609 which immunoreact with the ECr receptor (= $\alpha_v\beta_3$) are useful for inhibiting **cell adhesion** and hence the growth of tumours which express ECr (see pages 21, lines 13-16 and page 48, lines 2-6). It is confirmed on page 47, lines 2-6 of document D6 that the target for the therapeutic effect are any cell containing ECr on its surface, which exhibits significant immunoreaction with mAb LM609.

18. Moreover, the skilled person was aware of the fact that the inhibition of tumour growth observed in Example 11 of document D6 (see pages 47-48) could **not** be the result of inhibiting angiogenesis. According to this Example, human melanoma cells M21 were injected into mice and the effect on tumour growth of injecting monoclonal antibody LM609 was investigated (see point 14 supra). However, it was known to the skilled person that LM609 was a murine antibody specific for human $\alpha_v\beta_3$, which did not recognise murine $\alpha_v\beta_3$ (see document D14, page 570, l-h column, last paragraph: "LM609 [directed to chick (18) and human (9) $\alpha_v\beta_3$ (anti-$\alpha_v\beta_3$)]" and that, hence, mAb LM609 could not react with murine blood vessels. The skilled person would have thus understood that the effect seen (the tumours in those mice receiving mAb LM609 progressed "at a much slower rate" over those of the control) was due to inhibition of cell adhesion to the $\alpha_v\beta_3$ receptor expressed on the human melanoma cells themselves and not to inhibition of angiogenesis.

In conclusion, the appellant's view that the skilled person coming across document D6 (alone or taken in

combination with document D5 and/or D7) would understand that the inhibition of tumour growth by mAb LM609 also involved blocking vascularization of the tumour tissue, is not convincing.

19. In summary, document D6 could not teach/suggest inhibition of angiogenesis. Moreover, there was no disclosure in document D6 that the $\alpha_v\beta_3$ receptor was expressed by solid tumours of breast or colon. In view of this, the board must conclude that it was not obvious to the skilled person coming across document D6 (possibly supplemented by the teachings of document D5 and/or D7) that an $\alpha_v\beta_3$ antagonist would be useful for the treatment of breast or colon tumours.

20. The skilled person turning to document D6 would have faced further uncertainty arising from the fact that Example 11, designed for showing inhibition of tumour cell attachment and not inhibition of angiogenesis (see point 18 supra), did not lead to encouraging results (no tumour growth arrest or regression, but merely progression "at a much slower rate").

21. The appellant argues that the skilled person would still have been motivated to apply the teaching of document D6 to solid tumour of the breast or colon since there was evidence in documents D20 and D21 that cells derived from these tumours expressed $\alpha_v\beta_3$.

22. According to the abstract on page 1159, l-h column of document D20 the $\alpha_v\beta_3$ receptor was weakly expressed in 50 % of the invasive breast lobular carcinomas and in 10 % of the ductal breast carcinomas (see also Tables 2 and 3).

Example 11 of document D6 (see point 18 supra) shows that the results obtained starting from a M21 melanoma cell line are poor in spite of its significant immunoreaction with mAb LM609 (0.6 units: see histogram "M21" Vs "LM609" in Figure 7). Hence, in the board's judgement, the skilled person would not be encouraged to use mAb LM609 or any other $\alpha_v\beta_3$ antagonist for treating a solid breast tumour expressing the $\alpha_v\beta_3$ receptor only "weakly".

23. As regards, document D21, it is stated on page 174 of this document, under "Discussion", that HT29 colonic carcinoma cells exhibit an integrin which cross-reacts with an anti-vitronectin receptor antibody, which might be $\alpha_v\beta_3$, $\alpha_v\beta_x$ with a different binding specificity or the $\alpha_v\beta_1$ complex. The board is of the opinion that this vague information does not provide the skilled person with any reasonable expectation that using an $\alpha_v\beta_3$ antagonist will result in inhibition of colon tumour growth.

Documents D9 and D10

24. In a different line of argument, the appellant starts from documents D9 and D10 as closest prior art. Document D9 discloses cyclic adhesion inhibitors exhibiting the RGD motif for the treatment of several disease, including tumours. Document D10 deals with linear RGD peptides for treating tumours. The appellant argues that, since the target molecule of the inhibitory peptides referred to in these documents was not clearly identified, there was no reason why the skilled person would not have used the RGD-containing

peptides disclosed therein to treat breast or colon tumours.

25. As in the case of document D6 (see point 17 supra), the essence of the teaching of documents D9 (see page 5, lines 16-20) and D10 (see page 2, lines 28-31) was that certain compounds could be used to treat tumours because they inhibited cell adhesion.

Contrary to the appellant's opinion that the target molecule of the inhibitory peptides referred to in these documents was not clearly identified, it is stated in both documents D9 (see page 4, lines 6-7) and document 10 (see page 2, lines 32-34) that the cell adhesion inhibitory effect exerted by these compounds had to be measured by using the method described in document D23, which consisted in measuring binding of ligands to the $\alpha_v\beta_3$ receptor (see document D23, page 12268, r-h column, lines 6-11). Hence, the target molecule of the compounds referred to in documents D9 and D10 was clearly the $\alpha_v\beta_3$ receptor.

It follows that the skilled person would consider that the compounds described in documents D9 and D10 would not block cell adhesion in cells devoid of the $\alpha_v\beta_3$ receptor. These compound would thus not be expected to be useful in the treatment of tumours which did not express (or only weakly expressed) the $\alpha_v\beta_3$ receptor.

26. In summary, the subject-matter of claim 1 of the Amended Main Request satisfies the requirements of Article 56 EPC. This conclusion extends to dependent claims 2 to 20.

27. No need arises to deal with the Auxiliary Request.

Order

For these reasons it is decided that:

1. The decision under appeal is set aside.

2. The case is remitted to the department of first instance with the order to maintain the patent on the basis of claims 1 to 20 of the Amended Main Request as filed on 20 May 2009 before the Board and a description yet to be adapted thereto.

Registrar: Chair:

P. Cremona U. Kinkeldey