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D E C I S I O N
of 13 April 2006

Case Number: T 0380/05 - 3.3.04

Application Number: 01913197.8

Publication Number: 1261363

IPC: A61K 38/09

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Title of invention:
Methods for treating FSH related conditions with GnRH antagonists

Applicant:
Praecis Pharmaceuticals incorporated

Headword:
GnRH Antagonists/PRAECIS

Relevant legal provisions:
EPC Art. 54, 56, 84

Keyword:
"Main request, auxiliary request 1 - novelty (yes), inventive step (no)"
"Auxiliary request 2 - clarity (no)"
"Auxiliary request 3 - clarity, novelty, inventive step (yes)"

Decisions cited:
G 0005/83, G 0001/03, T 0694/92, T 0149/93, T 0187/93, T 0333/97, T 0338/97, T 1045/98, T 0609/02, T 1020/03, T 0539/04

Catchword:
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Case Number: T 0380/05 - 3.3.04

D E C I S I O N
of the Technical Board of Appeal 3.3.04
of 13 April 2006

Appellant: (Applicant)
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Decision under appeal:
Decision of the Examining Division of the European Patent Office posted 8 November 2004 refusing European application No. 01913197.8 pursuant to Article 97(1) EPC.

Composition of the Board:

Chair: M. Wieser
Members: G. Alt
D. Rogers

Summary of Facts and Submissions

I. The appeal was lodged by the Applicant (Appellant) against the decision of the Examining Division to refuse under Article 97(1) EPC the patent application EP 01 913 197.8, international publication number WO 01/64 236. The patent application has the title: "Methods for treating FSH related conditions with GnRH antagonists".

II. Claim 1 of the only request before the Examining Division read as follows:

"Use of a GnRH antagonist suitable for in vivo administration to reduce both plasma FSH and LH levels in a subject in the manufacture of a medicament for treating hormone refractory prostate cancer in a subject."

III. The Examining Division decided that the subject-matter of this claim was not novel and did not involve an inventive step, contrary to the requirements of Articles 54 and 56 EPC.

IV. With the statement setting out the grounds for appeal, submitted on 15 March 2005, the Appellant filed two new documents:

(8) The Report to the Nation on Prostate Cancer 2004, Chapter 5, pages 45 to 53

(9) The Journal of Urology, vol.161, no.3, 1999, pages 970 to 976

V. The Board issued communications on 31 January 2006 and on 17 March 2006. Oral proceedings were held on 13 April 2006.

The Appellant requested to set aside the decision under appeal and to grant a patent on the basis of:

- claims 1 to 8 of the main request, filed on 12 August 2004, or

- claims 1 to 8 of auxiliary request 1, filed on 13 March 2006, or

- claims 1 to 7 of auxiliary request 2, filed at the oral proceedings, or

- claims 1 to 3 of auxiliary request 3, filed at the oral proceedings

VI. Claim 1 of the main request corresponded to claim 1 as considered by the Examining Division (see section (II) above).

Claim 1 of auxiliary request 1 read as follows:

"Use of a GnRH antagonist suitable for in vivo administration to reduce both plasma FSH and LH levels in a subject in the manufacture of a sustained-release formulation for treating hormone refractory prostate cancer in a subject, wherein the sustained-release formulation achieves sustained delivery of the GnRH antagonist for at least 28 days."

VII. Claims 1 and 6 of auxiliary request 2 read as follows:

"1. Use of a GnRH antagonist suitable for in vivo administration to reduce both plasma FSH and LH levels in a subject in the manufacture of a sustained-release formulation for treating hormone refractory prostate cancer in a subject, wherein the GnRH antagonist is a peptide compound comprising a structure:

A-B-C-D-E-F-G-H-I-J

wherein

A is pyro-Glu, Ac-D-Nal, Ac-D-Qal, Ac-Sar, or Ac-D-Pal, or an analogue thereof;
B is His or 4-Cl-D-Phe, or an analogue thereof;
C is Trp, D-Pal, D-Nal, L-Nal-D-Pal(N-O), or D-Trp, or an analogue thereof;
D is Ser, or an analogue thereof;
E is N-Me-Ala, Tyr, N-Me-Tyr, Ser, Lys(iPr), 4-Cl-Phe, His, Asn, Met, Ala, Arg or Ile, or an analogue thereof;
F is D-Asn or D-Gln;
G is Leu or Trp, or an analogue thereof;
H is Lys(iPr), Gln, Met, or Arg, or an analogue thereof;
I is Pro, or an analogue thereof ; and
J is Gly-NH_2 or D-Ala-NH_2, or an analogue thereof;

or a pharmaceutically acceptable salt thereof;
optionally wherein the GnRH antagonist is peptide compound comprising a structure:

Ac-D-Nal-4-Cl-D-Phe-D-Pal-Ser-N-Me-Tyr-D-Asn-Leu-Lys(iPr)-Pro-D-Ala-NH_2;

or a pharmaceutically acceptable salt thereof; or

Ac-D-Nal-4-Cl-D-Phe-D-Pal-Ser-Tyr-D-Asn-Leu-Lys(iPr)-Pro-D-Ala-NH_2;
or a pharmaceutically acceptable salt thereof, wherein the sustained-release formulation of GnRH antagonist comprises a solid ionic complex of a GnRH antagonist and a carrier macromolecule, wherein the carrier and GnRH antagonist used to form the complex are combined at a weight ratio of carrier:antagonist of 0.5:1 to 0.1:1 and wherein the sustained-release formulation achieves sustained delivery of the GnRH antagonist for at least 28 days, and wherein the dosage of the GnRH antagonist is 10-200 mg/month.

6. The use of any preceding claim, wherein the GnRH antagonist is administered at a dosage of about 5-500 µg/kg/day; or about 10-400 µg/kg/day, or about 10-100 µg/kg/day."

VIII. Claim 1 of auxiliary request 3 reads as follows:

"1. Use of a GnRH antagonist suitable for in vivo administration to reduce both plasma FSH and LH levels in a subject in the manufacture of a sustained-release formulation for treating hormone refractory prostate cancer in a subject, wherein the GnRH antagonist is a peptide compound comprising a structure:

A-B-C-D-E-F-G-H-I-J

wherein

A is pyro-Glu, Ac-D-Nal, Ac-D-Qal, Ac-Sar, or Ac-D-Pal, or an analogue thereof;
B is His or 4-Cl-D-Phe, or an analogue thereof;
C is Trp, D-Pal, D-Nal, L-Nal-D-Pal(N-O), or D-Trp, or an analogue thereof;
D is Ser, or an analogue thereof;
E is N-Me-Ala, Tyr, N-Me-Tyr, Ser, Lys(iPr), 4-Cl-Phe, His, Asn, Met, Ala, Arg or Ile, or an analogue thereof;
F is D-Asn or D-Gln;
G is Leu or Trp, or an analogue thereof;
H is Lys(iPr), Gln, Met, or Arg, or an analogue thereof;
I is Pro, or an analogue thereof ; and
J is Gly-NH_2 or D-Ala-NH_2, or an analogue thereof;

or a pharmaceutically acceptable salt thereof;
optionally wherein the GnRH antagonist is peptide compound comprising a structure:

Ac-D-Nal-4-Cl-D-Phe-D-Pal-Ser-N-Me-Tyr-D-Asn-Leu-Lys(iPr)-Pro-D-Ala-NH_2;

or a pharmaceutically acceptable salt thereof; or

Ac-D-Nal-4-Cl-D-Phe-D-Pal-Ser-Tyr-D-Asn-Leu-Lys(iPr)-Pro-D-Ala-NH_2;
or a pharmaceutically acceptable salt thereof, wherein the sustained-release formulation of GnRH antagonist comprises a solid ionic complex of a GnRH antagonist and a carrier macromolecule, wherein the carrier and GnRH antagonist used to form the complex are combined at a weight ratio of carrier:antagonist of 0.5:1 to 0.1:1, and wherein the dosage of the GnRH antagonist is 100-200 mg/month."

Claims 2 and 3 of this request referred to preferred embodiments of the use of claim 1.

IX. Besides the two documents mentioned in section (IV) above the following documents are referred to in this decision:

(1) US-5 843 901

(3) US-5 968 895

(5) Clinical Endocrinology, vol.40, no.2, 1994, pages 241 to 248

(6) The Journal of Urology, vol.159, no.5, 1998, supplement, page 334

(7) WO-97/44 037

X. The submissions made by the Appellant as far as they are relevant to the present decision may be summarised as follows:

None of documents (1), (3), (6) and (7), which were considered by the Examining Division as anticipating the subject-matter of claim 1 of the main request, referred to the treatment of prostate refractory prostate cancer. The claims of the main request, as well as of all other requests on file, were therefore novel (Article 54 EPC).

Document (9) did not provide the skilled person with a direct pointer to the invention according to claim 1 of

the main request or of auxiliary requests 1 to 3. Even though the document mentioned that FSH and/or its receptor might have been interesting therapeutic targets on which work could have been carried out to provide effective treatment for patients suffering from hormone refractory prostate cancer, which was contrary to the general knowledge in the art at the relevant date, a skilled person, without the benefit of the present application, could have had no reasonable expectation in arriving at the claimed invention. Therefore, this document either if taken alone or in combination with any other prior art document on file, would not have enabled a skilled person to arrive at the claimed subject-matter in an obvious way (Article 56 EPC).

Reasons for the decision

Main request
Novelty - Article 54 EPC

1. In point (2) of the decision under appeal the Examining Division came to the conclusion that the medical indication claimed, namely the treatment of hormone refractory prostate cancer, *"...merely refers to an advanced stage of prostate cancer. Any disease is characterised by different stages and the present examination division cannot accept that the definition in the present claims of a particular stage of the present disease can confer novelty to a well known treatment".*

In consequence, they decided that the disclosure in documents (1), (3), (6), and (7) anticipated the subject-matter of claim 1.

2. These documents disclose the use of GnRH antagonists (also designated as LHRH antagonists in documents (1), (3) and (7)) for the treatment of prostate cancer. They do not, however, mention hormone refractory prostate cancer or any method for its treatment.

3. Document (8) is a review article published after the filing date of the present application. The document describes hormone refractory prostate cancer (referred to as androgen-independent prostate cancer (AIPC)) as a stage of the disease, which is reached by nearly all patients suffering from advanced prostate cancer within 18 to 24 months (page 45, left column, first paragraph). The document discloses that patients, being in this late phase of the disease, need specific and different treatment and reports of the results of clinical trials, using Docetaxel-based Chemotherapy (page 46, right column, last paragraph and page 50, conclusions).

Document (9) describes that most prostate carcinomas, which initially respond to androgen-deprivation therapy, convert to a hormone-refractory state which typically is associated with an acceleration in disease pace resulting in a median survival of only 6 to 8 months (page 970, left column, first paragraph). The document is concerned with mechanism of this conversion and the regulation of the growth of hormone refractory prostate cancer.

4. The disclosure in these two documents, which were filed during the appeal procedure and which therefore were not available to the Examining Division, supports that hormone refractory prostate cancer, being a late stage of advanced prostate cancer, is distinct from hormone sensitive prostate cancer responding to androgen-deprivation therapy, and requires different treatment modalities than earlier disease stages.

5. According to the decision of the Enlarged Board of Appeal G 5/83 (OJ EPO 1985, 64; point (2) of the order, a European patent may be granted with claims directed to the use of a substance or composition for the manufacture of a medicament for a specified new and inventive therapeutic application.

The Enlarged Board derived the novelty of such claims from their sole new feature, that is the new pharmaceutical use of a known substance and considered that it was legitimate to allow claims directed to the use of a substance or composition for the manufacture of a medicament for a specified new and inventive therapeutic application, even where the process of manufacture as such did not differ from known processes using the same active ingredients (cf decision G 5/83, supra, points (11) to (19) of the reasons).

Thus, the Enlarged Board considered for the special case where the intended purpose of the preparation of the composition was for this composition then to be used for the treatment of the human or animal body by surgery or therapy or in diagnostic methods, that then Article 54(5) EPC allowed the preparation of the composition to be treated as notionally novel, even if

the medicament resulting from the preparation was not in any way different from a known medicament (cf decision G 5/83, supra, point (20) and decision T 1020/03 of 29 October 2004).

6. Thus, in consideration of what has been stated in point (4) above, namely that hormone refractory prostate cancer is distinct from hormone sensitive prostate cancer and requires different treatment modalities, the decision of the Examining Division regarding lack of novelty of claim 1 cannot be upheld in the light of decision G 5/83 (supra).

The subject-matter of claim 1, referring to the use of a GnRH antagonist in the manufacture of a medicament for treating hormone refractory prostate cancer, and of claims 2 to 8 dependent thereon, is therefore novel and meets the requirements of Article 54 EPC.

Inventive step - Article 56 EPC

7. The Examining Division decided that the claimed subject-matter did not involve an inventive step, based on the following considerations:

7.1 They considered it to be illogical that GnRH, being a hormone, should play a role in the treatment of a disease, which was designated as being no longer responsible to any hormonal manipulation. (point (3), second paragraph of the decision under appeal).

The Board notes that the Examining Division's assertion is purely speculative and not substantiated by any verifiable facts. It rather is based on the idea that

it is a logical consequence of the definition of the disease that GnRH has no efficacy anymore.

7.2 Moreover, the Examining Division was not satisfied that the technical problem posed, namely the treatment of hormone refractory prostate cancer, could indeed be solved by the use of an GnRH antagonist, since the application did not contain any evidence in this respect (point (3), third paragraph of the decision).

The Board notes that Article 56 EPC is not the correct provision of the EPC under which this objection should have been raised.

If an invention seems to lack reproducibility because its desired technical effect, which is expressed in the claim, is not achieved, then this results in a lack of sufficient disclosure which has to be objected under Article 83 EPC, cf decision of the Enlarged Board of Appeal G 1/03 (OJ EPO 2004, 413; point (2.5.2)).

Where a therapeutic application is claimed in the form of the use of a substance for the manufacture of a medicament for a defined therapeutic application, attaining the claimed therapeutic effect is a functional technical feature of the claim. As a consequence, under Article 83 EPC, the application must disclose the suitability of the product to be manufactured for the claimed therapeutic application.

According to the relevant case law of the Boards of Appeal, it has been accepted that for a sufficient disclosure of a therapeutic application, it is not always necessary that results of applying the claimed

composition in clinical trials or animal tests are reported. Showing that the claimed compound has a direct effect on a metabolic mechanism specifically involved in the disease to be treated may be sufficient, this mechanism being either known from the prior art or demonstrated in the application per se (cf decision T 609/02 of 27 October 2004; point (9) of the reasons).

The present application discloses that the FSH level in human subjects treated with a depot preparation of a GnRH antagonist remained at a nadir for a sustained period of time (see example 1 and figure 2). Document (9) discloses that hormone refractory prostate cancer cells express FSH and FSH-receptor, which are considered to play a role in the regulation of the growth of hormone refractory prostate cancer (see abstract, last paragraph).

Accordingly, as a direct effect of FSH and its receptor on a metabolic mechanism specifically involved in hormone refractory prostate cancer is discussed in the prior art, the Board judges that the requirement of sufficient disclosure (Article 83 EPC), which has been dealt with in the appealed decision under Article 56 EPC, is met.

8. Thus, the Board disagrees with the reasons given by the Examining Division in the decision under appeal with regard to lack of inventive step.

8.1 Document (9), page 976, left column, last paragraph reads:

"The observations presented in this study raise the possibility that FSH and its receptor may participate in regulating growth of hormone-refractory prostate cancer. Coupled with previous observations that prostate cancers synthesize biologically active FSH, our findings relate to our central hypothesis: FSH and its receptor may be part of an autocrine loop which participates in the regulation of the growth of hormone-refractory prostate cancer cells or in the transition from a hormone-dependent state to hormone-independent state. If this hypothesis is confirmed, FSH and/or its receptor may potentially serve as targets for therapeutic inventions."

8.2 In the light of this disclosure in document (9), which is considered to represent the closest state of the art, the problem underlying the present invention is considered to be the verification of the hypothesis made in document (9) by actually providing a medicament to treat hormone refractory prostate cancer.

8.3 Sustained suppression of serum FSH-level by GnRH antagonists is described in document (5) (see summary and passage bridging pages 244 to 245).

The use of GnRH antagonists in the treatment of conditions which require inhibition of FSH release, like prostate cancer, is described in document (7) (see page 1, lines 9 to 11 and claim 7).

Document (1) describes the mechanism of FSH release by the pituitary gland upon prior release of GnRH (LHRH) from the hypothalamus, which is considered to represent a control point in the physiological regulation of gonadal function (column 1, lines 11 to 21). Document (1) and document (3), both disclose the use of sustained release compositions containing a GnRH (LHRH) antagonist for the treatment of hormone dependent cancers, including prostate cancer (document (1), column 15, lines 48 to 52 and column 17, lines 15 to 17; document (3), column 3, lines 41 to 45, column 4, lines 55 to 65 and claims 1 to 5).

8.4 The Appellant argued that document (9) did not provide the skilled person with a direct pointer to the invention according to claim 1. The document suggested that FSH and/or its receptor might potentially serve as therapeutic targets. However, this was contrary to the common general knowledge at the relevant date and a skilled person had no reasonable expectation in arriving at the claimed invention in an obvious way by administering the medicaments known from documents (1), (3) or (7) for the treatment of prostate cancer to patients suffering from hormone refractory prostate cancer.

By referring to the case law of the Boards of Appeal the Appellant further argued that a reasonable expectation of success should not be confused with the understandable hope to succeed, and that even if an experiment is obvious to try for a skilled person it is not necessarily true that this person would have any reasonable expectation of success when embarking on it (decision T 187/93 of 5 March 1997; point (21) of the

reasons). Moreover, the more unexplored a technical field of research was, the more difficult it was to make predictions about its successful conclusion (decision T 694/92, OJ EPO 1997, 408; point (28.7) of the reasons). The Appellant also referred to decision T 539/04 of 28 June 2005, where the competent Board accepted the Appellant's arguments, namely that there was no reasonable expectation of success, "in the absence of any documents on file which could be regarded as raising doubts as to the soundness of these arguments" (point (14) of the reasons).

8.5 The present Board does not consider the case law cited by the Appellant to be applicable.

In the present case the closest state of the art, document (9), establishes that FSH and its receptor are expressed by hormone refractory prostate cancer cells, that they may play a role in the transition from a hormone-dependent to a hormone independent state of the disease and in the regulation of the growth of hormone refractory prostate cancer cells, and that they therefore may serve as targets for therapeutic interventions.

In the light of this disclosure and in the absence of any evidence in the cited prior art documents, from which it could be deduced that the hypothesis made in document (9) was wrong or that its realisation was asking for undue experimental effort, the skilled person would not have been deterred from testing the suitability of a GnRH antagonist, known to reduce the plasma FSH level (document (5)), and known to be useful in the treatment of conditions requiring inhibition of

FSH release, including hormone dependent cancers, such as prostate cancer (documents (1), (3) and (7)).

Obviousness is not only at hand when the results are clearly predictable but also when there is a reasonable expectation of success (cf. decision T 149/93 of 23 March 1995; point (5.2) of the reasons). A reasonable expectation of success does not require certainty (cf. decision T 338/97, of 7 February 2000; point (14) of the reasons).

Thus, in spite of the understandable uncertainties which always characterise experiments using biologic compounds the skilled person had no reason to adopt a sceptical attitude. He/she would have had either some expectations of success or, at worst, no particular expectations of any sort, but only a "try and see" attitude, which - as pointed out in decisions T 333/97 of 5 October 2000; point (13) of the reasons - does not equate with the absence of an reasonable expectation of success (cf. decision T 1045/98 of 22 October 2001; point (17) of the reasons).

8.6 The Board judges that a skilled person, trying to solve the problem underlying the invention according to claim 1 of the main request, would have combined the teaching in document (9) with the disclosure of either one of documents (1), (3), (5) or (7). In doing so he/she would have arrived at the claimed subject-matter in an obvious way. Claim 1 therefore does not involve an inventive step contrary to the requirements of Article 56 EPC.

Auxiliary request 1

9. Claim 1 of this request is distinguished from claim 1 of the main request in so far as the medicament is further defined as being a sustained release formulation which achieves sustained delivery of the GnRH antagonist for at least 28 days.

10. The reasons given in points (1) to (6) above with regard to novelty of the main request also apply to claims 1 to 8 of auxiliary request 1. The claims are therefore novel within the meaning of Article 54 EPC.

11. Document (3) discloses a pharmaceutical composition providing sustained delivery of a GnRH (LHRH) analogue to a subject for at least four weeks after the pharmaceutical composition is administered to the subject (claim 5). An GnRH (LHRH) analogue may be an agonist or an antagonist (column 3, lines 25 to 26).

In line with the Board's judgement with regard to the main request (see point (8) above), the subject-matter of claim 1 of auxiliary request 1 is obvious in the light of a combination of the teaching in documents (9) and (3). The claim, lacking an inventive step, does not meet the requirements of Article 56 EPC.

Auxiliary request 2

12. Claim 1 refers to the use of a GnRH antagonist in the manufacture of a sustained release formulation, wherein the dosage of the GnRH antagonist is 10-200 mg/month.

According to claim 6, the GnRH antagonist is administered at a dosage of about 5-500 µg/kg/day; or about 10-400 µg/kg/day, or about 10-100 µg/kg/day.

13. According to table 4 on page 27 of the present application, the average body weight of the study population receiving a GnRH containing sustained release formulation was 85 kg (188 lbs).

In the absence of any specific definition in the present application, the Board, for the following calculation, proceeds on the assumption that a month roughly consists of 30 days (365 divided by 12).

14. At its upper threshold claim 1 requires that 500 µg GnRH antagonist are delivered to a patient per kg body weight and per day. This means that the dosage of the GnRH antagonist in the sustained delivery formulation is 1 275 000 µg (500 x 85 x 30) or 1275 mg per month. This is far above the upper threshold indicated in claim 1, from which claim 6 is dependent, which is 200 mg per month.

15. The subject-matter of dependent claim 6 is contradictory to the subject-matter of independent claim 1. Therefore, the claims are not clear and concise. They do not define the matter for which protection is sought according to the requirements of Article 84 EPC.

Auxiliary request 3
Added subject-matter and clarity - Articles 123 and 84 EPC

16. Claim 1 is based on claims 41, 43 to 46 and on page 2, line 31 to page 3, line 3 and page 5, lines 7 to 12 of the published WO-application. Claim 2 is based on page 11, lines 6 to 8, claim 3 on claims 35 to 37 of the published WO-Application.

The claims are clear and precise and define the matter for which protection is sought.

Accordingly, the requirements of Articles 123(2) and 84 EPC are met.

Novelty - Article 54 EPC

17. The reasons given in points (1) to (6) above for the claims of the main request apply also to claims 1 to 3 of auxiliary request 3, whose subject-matter therefore is novel within the meaning of Article 54 EPC.

Inventive step - Article 56 EPC

18. Claim 1 refers to the use of a GnRH antagonist in the manufacture of a sustained-release formulation for treating hormone refractory prostate cancer. The decapeptide structure of the GnRH antagonist used is defined in the claim. An especially preferred antagonist having the structure disclosed in claim 1 is referred to in the present application as "Abarelix" (page 9, 27 to 29). The sustained release formulation comprises a solid ionic complex of a GnRH antagonist and a carrier which are present in a weight ratio of

0.5:1 to 0.1:1, and the dosage of the GnRH antagonist in the formulation is 100 to 200 mg/month.

19. Document (9), which is the only prior art document on file, which, at least on a hypothetical level, is concerned with the treatment of hormone refractory prostate cancer (see point (8.1) above), represents the closest state of the art for the assessment of an inventive step.

The problem to be solved by the invention according to claim 1 of auxiliary request 3 is identical to the problem as defined for the claims of the main request (point (8.2) above), namely the verification of the hypothesis made in document (9) by actually providing a medicament to treat hormone refractory prostate cancer.

20. The Board is convinced that this problem has been solved by the subject-matter of claim 1.

The question that has to be answered is whether a skilled person, in the light of the disclosure in the prior art documents on file, would have arrived at the solution according to claim 1 in an obvious way.

21. None of these prior art documents, except document (9) and post published document (8), refers to hormone refractory prostate cancer or a method for its treatment.

21.1 Document (3) discloses sustained-release formulations comprising a solid ionic complex of a GnRH antagonist, preferably Abarelix (PPI-149), and a carrier. The structure of the antagonist and the weight ratio

antagonist:carrier are as disclosed in present claim 1 (see document (3), claims 1 to 5, 30 and 31).

The present application describes in example 1 on page 28, lines 6 to 8 the delivery by intramuscular injection of "Abarelix depot (100mg)" to the participants of a study. It is said that delivered medicament was prepared as described in document (3). Document (3) describes in column 7, line 19 to column 8, line 34 in detail the preparation of the claimed complex and in example 3 in column 10 the preparation of a sustained delivery formulation.

The term "sustained release" or "sustained delivery" is identically defined in document (3) and in the present application, as referring to **continual** delivery of a pharmaceutical agent, a GnRH (LHRH) antagonist, in vivo over a period of time following administration (see document (3), column 4, lines 30 to 33 and the present application, page 23, lines 1 to 4).

Document (3) does not contain a disclosure referring to a sustained-release formulation wherein the dosage of the GnRH antagonist is 100-200 mg/month, as required by present claim 1.

21.2 The same holds true for the disclosure in document (1), which moreover does not disclose a complex of a GnRH antagonist and a carrier as used according to present claim 1.

21.3 Document (5) describes the sustained suppression of serum FSH level by daily injection of the GnRH antagonist Cetrorelix. This antagonist differs from the

antagonists used according to present claim 1, as can be seen from page 242, left column, third paragraph of document (5).

21.4 Document (6), describing the use of Abarelix (PPI-149) for the treatment of prostate cancer patients by daily subcutaneous injections, does not mention sustained-release formulations containing a carrier:GnRH antagonist complex as disclosed in present claim 1.

21.5 Document (7) does not refer to GnRH antagonists having the decapeptide structure disclosed in present claim 1.

22. Therefore, the Board judges that a skilled person, upon combining of the disclosure in document (9) with the disclosure in any other prior art document on file, would not have arrived at the subject-matter of claim 1 in an obvious way.

Claim 1 and claims 2 and 3 dependent thereon of Auxiliary Request 3 filed at the oral proceedings involve an inventive step and meet the requirements of Article 56 EPC.

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 grant a patent on the basis of claims 1 to 3 of Auxiliary Request 3 filed at the oral proceedings and a description to be adapted thereto.

Registrar: Chair:

P. Cremona M. Wieser