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Datasheet for the decision of 29 September 2022

Case Number: T 0335/20 - 3.3.08

Application Number: 13174869.1

Publication Number: 2687223

IPC: C12Q1/6809, C12Q1/6883

Language of the proceedings: EN

Title of invention:
Detecting and treating dementia

Patent Proprietors:
Mayo foundation for medical education and research
The University of Manchester
University Of British Columbia
VIB VZW
Universiteit Antwerpen

Opponent:
James Poole Limited

Headword:
Progranulin for use in treating dementia/MAYO FOUNDATION

Relevant legal provisions:
EPC Art. 88(3), 56
RPBA 2020 Art. 13(2)

Keyword:
Auxiliary request 1: priority - partial priority (yes);
inventive step (no)
auxiliary request 2: allowable (yes)

Decisions cited:
G 0001/15, T 0609/02

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Case Number: T 0335/20 - 3.3.08

D E C I S I O N
of Technical Board of Appeal 3.3.08
of 29 September 2022

Respondents : (Patent Proprietor 1)	MAYO FOUNDATION FOR MEDICAL EDUCATION AND RESEARCH 200 First Street S.W. Rochester, MN 55905 (US)
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Appellant: (Opponent)	James Poole Limited One Southampton Row London WC1B 5HA (GB)

Representative: Carpmaels & Ransford LLP
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Decision under appeal: **Interlocutory decision of the Opposition Division of the European Patent Office posted on 29 November 2019 concerning maintenance of the European Patent No. 2687223 in amended form**

Composition of the Board:

Chairwoman T. Sommerfeld
Members: R. Morawetz
L. Bühler

Summary of Facts and Submissions

I. European patent No. 2 678 223 (the patent) is based on European patent application No. 13 174 869.1, which was filed as a divisional application in respect of earlier European patent application No. 07 840 211.2, having a date of filing of 30 May 2007 and claiming priority from, *inter alia,* European patent application No. 06 116 589.0 (P3) filed on 4 July 2006. The patent is entitled "*Detecting and treating dementia*".

II. One opposition to the granted patent was filed. The opposition proceedings were based on the grounds for opposition in Article 100(a) EPC, in relation to inventive step (Article 56 EPC), and in Article 100(b) and 100(c) EPC.

III. By an interlocutory decision, the opposition division decided that the patent in amended form on the basis of auxiliary request 2, and the invention to which it relates met the requirements of the EPC. The opposition division also held that the subject-matter of claim 1 of the main request (patent as granted) was not sufficiently disclosed for it to be carried out (Article 100(b) EPC) and that claim 1 of auxiliary request 1 lacked clarity (Article 84 EPC).

IV. The patent proprietors and the opponent both filed notice of appeal against the opposition division's decision.

V. With their statement of grounds of appeal, the patent proprietors submitted sets of claims of a main request and auxiliary requests I to III. Auxiliary request II was identical to auxiliary request 2 considered in the

decision under appeal. Auxiliary request III was identical to auxiliary request 4, which had been filed during the opposition proceedings, on 24 July 2019.

VI. In its statement of grounds of appeal, the opponent submitted arguments to the effect that the subject-matter of claim 1 of auxiliary request 2 underlying the decision under appeal was only entitled to partial priority from P3, and did not comply with the requirements of Article 56 EPC.

VII. In their reply to the opponent's appeal, the patent proprietors presented arguments to the effect that the subject-matter of claim 1 of auxiliary request II was entitled to the priority of P3, and that document D9 could not serve as the closest prior art. As for auxiliary request III, the patent proprietors submitted that it was limited to the subject-matter of "claim 1A" as identified by the opponent, and hence was entitled to the priority of P3.

VIII. In reply to the patent proprietors' appeal, the opponent submitted that the claims of the main request and auxiliary request I lacked inventive step for the same reasons as auxiliary request II. No objections were raised to the claims of auxiliary request III.

IX. The board scheduled oral proceedings in accordance with the parties' requests and subsequently issued a communication pursuant to Article 15(1) RPBA. In this communication, the board informed the parties that it was inclined to agree with the opponent that claim 1 of auxiliary request II enjoyed partial priority from P3, and that it was inclined to disagree with the patent proprietors that the whole of claim 1 of auxiliary

request III was entitled to the priority of P3.

X. With a further letter dated 29 July 2022, the patent proprietors submitted a set of claims of auxiliary request IV.

XI. Oral proceedings before the board took place as scheduled. During the oral proceedings, the patent proprietors withdrew the main request and renumbered the pending claim requests such that auxiliary request I became the main request, auxiliary request II became auxiliary request 1, auxiliary request III became auxiliary request 2 and auxiliary request IV became auxiliary request 3. The patent proprietors later withdrew their appeal and thus became the respondents to the appeal by the opponent (hereinafter "appellant"). At the end of the oral proceedings the Chairwoman announced the board's decision.

XII. Claim 1 of auxiliary request 1 reads as follows:

"1. A PGRN polypeptide for use in treating a mammal having a neurodegenerative disorder or suspected to develop a neurodegenerative disorder, wherein said neurodegenerative disorder is frontotemporal dementia, wherein the PGRN polypeptide is a full-length PGRN polypeptide."

Claim 1 of auxiliary request 2 reads as follows:

"1. A PGRN polypeptide for use in treating a mammal having a neurodegenerative disorder or suspected to develop a neurodegenerative disorder, wherein said neurodegenerative disorder is frontotemporal dementia, wherein said PGRN polypeptide comprises the amino acid

sequence set forth in SEQ ID NO:1."

XIII. The following documents are referred to in this decision:

D3 Huey E.D. *et al.*, Neurology 66, 2006, 17-22

D9 Baker M. *et al.*, Nature 442, 24 August 2006, 916-919

D11 Klein R.L. *et al.*, Neurosci Lett. 401, 2006, 130-135

D12 Lo Blanco C. *et al.*, PNAS 101, 2004, 17510-17515

D23 Bard F. *et al.*, Nature Medicine 6, 2000, 916-919

D24 Hong C-S. *et al.*, Gene Therapy 13, 2006, 1068-1079

D25 Immonen A. *et al.*, Molecular Therapy 10, 2004, 967-972

D26 Tuszynski M.H. *et al.*, Nature Medicine 11, 2005, 551-555

D27 Zhang Y. *et al.*, Molecular Therapy 6, 2002, 67-72

D28 Zhang Y. *et al.*, Clinical Cancer Research 10, 2004, 3667-3677

D29 Alignment of human PGRN polypeptide amino acid sequences

D31 GenBank GI number 183612, 1994

D32 GenBank GI number 4504151, 2006

XIV. The appellant's arguments, insofar as they are relevant to the decision, are summarised below.

Auxiliary request 1 - claim 1

Priority

The term "PGRN polypeptide" was a generic term in the sense of decision G 1/15 and its meaning was broadened from P3 to the patent.

As for human progranulin (PGRN), in P3 this meant a polypeptide of SEQ ID NO:2 (identical to SEQ ID NO:1 in the patent) and nothing else (see page 3, lines 15 to 17). No isoforms were mentioned on page 3 of P3. Page 27 of P3 disclosed nothing about using the isoform disclosed in document D32 for medical use, and did not change the definition given on page 3 of P3. Although the authors of P3 were aware of the sequence from document D32, they had not included it in the definition of human PGRN on page 3 of P3.

In contrast, the same term in the claims of auxiliary request 1 meant this sequence (SEQ ID NO:1) and other full-length human PGRN polypeptide sequences. The patent explicitly expanded this term to encompass the sequence identified as GenBank GI number 4504151 (see paragraph [0006]), which was distinct from SEQ ID NO:1 (see documents D29, D31 and D32). A PGRN polypeptide having the sequence of GI number 4504151 was therefore an example of a full-length PGRN polypeptide which fell within the scope of the upheld claims but was not

entitled to the priority of P3. Accordingly, claim 1, which represented a generic "OR"-claim, could be separated into two claim parts A and B. Of these two part-claims, claim 1A was entitled to the priority of P3, whereas claim 1B was not.

Inventive step

Closest prior art

Document D9 reported studies showing that PGRN deficiency was the underlying mechanism of frontotemporal dementia (FTD). It provided the same data as Example 1 of the patent, on which the claimed medical use was predicated. Figures 1 and 3 of document D9 were identical to Figures 1 and 2 of the patent. On the basis of this data, document D9 proposed the use of PGRN replacement as a therapeutic strategy to treat FTD (page 918, left-hand column, last paragraph to page 919, left-hand column, first paragraph). Therefore, document D9 was directed to the same purpose as the claim, the treatment of FTD.

The opposition division was incorrect to select the closest prior art on the basis of enablement of the medical use, which would, if anything, be relevant for novelty but was not a criterion for selecting the closest prior art. Document D9 did provide a plausible disclosure because it taught that reduced levels of PGRN led to FTD, which in turn allowed the conclusion that PGRN therapy was suitable for treating FTD.

Document D9, rather than document D3, was the closest prior art because it was the most promising springboard to the invention.

Objective technical problem

By suggesting replacement therapy, document D9 disclosed a novel therapeutic strategy but did not explicitly disclose specific sequences of PGRN, and therefore did not teach which PGRN polypeptide or polynucleotide sequence to use for the proposed PGRN replacement therapy. The difference between document D9 and claim 1B was the identification of a particular PGRN sequence, such as GI number 4504151.

The claim merely represented putting document D9's proposal into effect. The patent did not contain any direct evidence that PGRN polypeptides had a therapeutic effect on FTD. There were no clinical assays in patients nor proof-of-concept experiments in animals. There was no technical effect associated with any specific sequence; each PGRN sequence was just one way to implement the teaching of document D9. Therapy had to be recited in the problem, because document D9 talked about therapy.

The objective technical problem to be solved was the provision of a way to implement the PGRN replacement therapy proposed in document D9.

Obviousness

Document D9 proposed replacement therapy, which the skilled person knew could be achieved by administration of a PGRN polypeptide or polynucleotide, e.g. in an expression vector. The skilled person would have used the protein for replacement because reduced levels of this protein were found to be a cause of FTD. To do so, the skilled person would have needed to identify a PGRN sequence to deliver. In the absence of any sequence

information in document D9, the skilled person would, as a matter of routine, have looked for sequences in standard sequence databases, such as GenBank. Only two human PGRN sequences were known at the relevant date. Both sequences were equally obvious. The sequence of GI number 4504151 was available at least from 7 May 2006 (see document D32). Therefore, the skilled person looking up a sequence for PGRN at the filing date would have found the sequence of GI number 4504151 in an obvious manner.

Implementation of the PGRN replacement therapy was simple. The skilled person knew how to administer a PGRN polypeptide at the filing date, because methods for administration were well known in the art, see documents D23 to D28. Documents D11 and D12 each confirmed that adeno-associated virus delivery of polypeptides had been shown to treat neurodegenerative disorders successfully.

Based on the data and the mechanism underlying FTD disclosed in document D9, the skilled person would have had a reasonable expectation of successfully treating FTD according to the claim.

It was irrelevant that document D9 did not teach the use of a polypeptide. It disclosed that an absence of PGRN led to FTD, and in suggesting replacement of the missing factor it suggested giving the PGRN polypeptide. Another way would have been to use the polynucleotide encoding the polypeptide. The administration of a PGRN polynucleotide or of a polypeptide were both obvious.

In putting the teaching of document D9 into effect by using the PGRN amino acid sequence of document D32, the

skilled person would have arrived at the medical use of claim 1B. Accordingly, claim 1 as a whole lacked an inventive step.

Auxiliary request 2

Admittance of an objection under Article 56 EPC (Article 13(2) RPBA)

The objection was that the claimed subject-matter was not entitled to the priority of P3 and lacked an inventive step over the teaching of document D9 in combination with common general knowledge regarding the use of affinity tags in the purification of therapeutic proteins. Evidence of this common general knowledge was provided by P3 (see page 21, lines 11 to 16) and the patent (see page 24, paragraph [0085]). The addition of affinity tags would have led the skilled person to a polypeptide comprising the amino acid sequence of SEQ ID NO:1.

This objection was not an amendment of the appellant's appeal case but a further development of the argument made against auxiliary request 1.

The board had raised the issue of the lack of priority of claim 1 of auxiliary request 2 in the preliminary opinion, and the appellant's objection merely addressed this lack of priority.

XV. The respondents' (patent proprietors') arguments, insofar as they are relevant to the decision, are summarised below.

Auxiliary request 1

Priority

The term "progranulin" was a general term that had the same meaning in P3 and in the patent. Neither claim 1 of auxiliary request 1 nor claim 1 of P3 was limited to human PGRN.

The passage on page 3 of P3 gave an example of a PGRN that could be used, but was not an exhaustive definition of the invention of P3. P3 disclosed both human isoforms known at the time, SEQ ID NO:1 (see page 3, lines 15 to 17) and the sequence of document D32 (see page 27, lines 7 to 9). It would have been immediately clear to the skilled person that the sequence of document D32 was also an embodiment of the invention of P3. P3 used the sequence of document D32 as a reference sequence for identifying deleterious mutations, a fact that would already lead the skilled person to the conclusion that this is a sequence that must be present in order to prevent the disease. Furthermore, the sequence of document D32 was identified as a PGRN isoform, indicating that there were several isoforms of the functional protein. PGRN and functional fragments thereof were further disclosed in P3 on page 3, lines 25 to 30 and page 6, lines 9 to 10. Page 5, lines 1 to 3 of P3 mentioned the molecules of the invention. P3 even included the murine orthologue (see page 21, lines 29, 32 and 33). Page 3, line 9 was valid for all human PGRNs. Accordingly, all the claimed subject-matter was entitled to the priority date of P3.

However, if valid priority was to be denied to part of the subject-matter of claim 1, that part was only the single PGRN sequence of document D32. This was the

"relevant subject-matter", since only this was open to inventive-step objections involving document D9.

Inventive step

Closest prior art

Document D9 was not an enabling disclosure of a therapeutic application because there was no disclosure of the specific therapeutics or the technical teaching for reducing a therapeutic application to practice. Since document D9 was not an enabling disclosure of a therapeutic application, it was not a disclosure of such an application at all. The closest prior art could not be a teaching in a document that could not be reduced to practice by the skilled person on the basis of that document.

Document D9 could not serve as closest prior art, as it was not directed at the treatment of FTD but at the elucidation of its aetiology. The single sentence at the end of the document did not change the general purpose of the document.

Objective technical problem

The claimed subject-matter differed from document D9 in that it (i) related to therapy and (ii) involved a protein, which (iii) had a specific sequence, which was not entitled to the priority of P3. As therapy was not disclosed in document D9 it could not be mentioned in the problem, but rather was part of the solution.

The objective technical problem to be solved was the provision of a practical application of the genome data findings of document D9.

Obviousness

The claimed invention was not obvious even if document D9 was considered to be a suitable starting point. Starting from document D9, the skilled person would have first had to transfer the teaching of that document to a therapeutic setting and then select the correct agent in that setting, the polypeptide of document D32. Document D9 provided a pointer to therapy but not to how it should be carried out. Replacement therapy could be carried out in many ways, e.g. by giving the protein, by gene therapy or by using a therapeutic agent that would increase production of the protein. Document D9 did not state that the protein should be replaced, and provided no pointer to the sequence of document D32. Nor was a full-length protein mentioned in document D9.

Auxiliary request 2

Admittance of an objection under Article 56 EPC (Article 13(2) RPBA)

No substantive objections had been raised against the subject-matter of auxiliary request 2 before. The fact that claim 1 was not entitled to the priority of P3 did not mean that its subject-matter was obvious. The combination of document D9 and document D32 could not render the claimed subject-matter obvious, because document D32 did not disclose the sequence of SEQ ID NO:1.

The reasoning submitted by the appellant for claim 1 of this request differed from the reasoning submitted for auxiliary request 1, and was a new line of argument

based on factual allegations presented at the oral proceedings for the first time. The objection had therefore to be considered an amendment of the appellant's case within the meaning of Article 13(2) RPBA. No justification had been provided for only raising it at the oral proceedings. The new line of argument should not be admitted into the appeal proceedings.

XVI. The appellant requested that the decision under appeal be set aside and that the patent be revoked.

The respondents requested that the opponent's appeal be dismissed (i.e. that the patent be maintained on the basis of the set of claims of auxiliary request 1 filed as auxiliary request II with the statement of grounds of appeal) or, alternatively, that the patent be maintained in amended form on the basis of the set of claims of auxiliary request 2 filed as auxiliary request III with the statement of grounds of appeal.

Reasons for the Decision

Auxiliary request 1 - claim 1

Priority

1. The disclosure of document D9, relied on by the appellant in the context of inventive step, is part of the state of the art as defined in Article 54(2) EPC only in respect of subject-matter that is not entitled to the priority of P3. Whether or not the subject-matter of claim 1 is entitled to the priority of P3

therefore needs to be determined.

2. The opposition division held that the use of a progranulin (PGRN) polypeptide having an amino acid sequence other than SEQ ID NO:1 was not entitled to the priority of P3. In the appeal proceedings, the appellant asserted that claim 1 was only entitled to partial priority from P3, while the respondents submitted that the entire subject-matter of claim 1 was entitled to the priority of P3.

3. Claim 1 relates to the medical use of "*a PGRN polypeptide*". The term "*a PGRN polypeptide*" is not further defined in claim 1. The board considers that since the term is a generic term which has no accepted and unambiguous definition in the art it is to be construed in accordance with paragraph [0006] of the patent, which provides the following definition: "*The term 'PGRN polypeptide' as used herein includes, without limitation, human PGRN polypeptides (e.g., human PGRN polypeptides set forth in GenBank® under GI numbers 183612, 4504151, and 77416865), mouse PGRN polypeptides (e.g., the mouse PGRN polypeptide set forth in GenBank® under GI number 6680107), zebrafish PGRN polypeptides (e.g., zebrafish PGRN polypeptides set forth in GenBank® under GI numbers 66472848, 77797837, 47086569, and 47086537), ... and granulin P*".

4. Therefore, the expression "*a PGRN polypeptide*" in claim 1 does not denote a single specific PGRN polypeptide but is a generic expression covering different PGRN polypeptides. Claim 1, where it is directed to the use of a PGRN polypeptide, may thus be seen as a claim which encompasses "alternative subject-matter by virtue of one or more generic expressions or

otherwise", i.e. a generic "OR"-claim as referred to in G 1/15 (see OJ EPO 2017, A82, Order).

5. In line with the principles set out in G 1/15 (see Reasons, point 6.4), in assessing whether subject-matter within claim 1 may enjoy partial priority from P3 the subject-matter disclosed in P3 that is relevant, i.e. relevant in respect of prior art disclosed in the priority interval - in this case document D9 - needs to be determined.

6. Disclosed subject-matter that is relevant in view of document D9 is that relating to the use of a human PGRN polypeptide in the treatment of FTD. In accordance with G 1/15 (*ibid*), to the extent that P3 discloses any such subject-matter falling within claim 1, claim 1 is entitled to priority in respect of that subject-matter.

7. P3 discloses the "*use of an effective amount of a pharmaceutical composition of progranulin or a functional fragment thereof for the manufacture of a medicament to treat neurodegenerative diseases*" (see claim 1). According to dependent claim 3, the neurodegenerative disease can be frontotemporal dementia (FTD), and according to dependent claim 6, the PGRN can be a polypeptide. On page 3, line 1 of P3, under the heading *"Aims and detailed description of the invention*" PGRN is described in detail. It is disclosed that "*the human PGRN gene is located at chromosome 17q21 and it*[s] *sequence is available in GenBank (Accession Number M75161)*" (see page 3, lines 6 to 8); that "*human progranulin is 593 amino acids long*" (see page 3, line 9); that *"each of the five human granulins* [granulins A, B, C, D and F] *that have, to date, been isolated as individual peptides is represented in the common precursor*" (see page 3, lines 11 to 13); and

that "*the nucleotide sequence of human progranulin is depicted in SEQ ID NO:1, the amino acid sequence of human progranulin is depicted in SEQ ID NO:2*" (see page 3, lines 15 to 17). Finally, P3 states that "*progranulin a functional fragment thereof, such as granulin A or granulin B or granulin C or granulin D or granulin F are herein further designated as the molecules of the invention*" (see page 3, lines 31 to 32).

8. It is evident from the preceding point that P3 unequivocally discloses that the human PGRN polypeptide has a single amino acid sequence, SEQ ID NO:2, which corresponds to the amino acid sequence of SEQ ID NO:1 of the patent. While granulin fragments are also disclosed as being molecules of the invention, PGRN isoforms are not mentioned on page 3 of P3.

9. The respondent's arguments to the effect that P3 and the patent disclose the same human PGRN amino acid sequences and hence the same subject-matter are not persuasive.

10. First, the fact that the patent and P3 use the same terms, progranulin or PGRN, does not support the respondents' case, because these are generic terms and different meanings are attributed to these terms as regards human PGRN polypeptide by the patent (see paragraph [0006] and point 3. above) and P3 (see page 3, lines 1 to 32 and point 7. above).

11. Secondly, because "PGRN polypeptide" is a generic term encompassing human PGRN polypeptides (see paragraph [0006] and point 3. above), it is irrelevant that claim 1 of auxiliary request 1 and claim 1 of P3 do not

refer explicitly to a human PGRN polypeptide.

12. Thirdly, while the board accepts that P3 provides the sequence of the second full-length variant of the human PGRN polypeptide known at the filing date of P3, i.e. the sequence having GenPept Accession Number NP_002078.1, which is disclosed in document D32, this does not alter the definition provided on page 3 of P3. In brief, Table 1 of P3 summarises the PGRN mutations identified in Belgian FTD patients and provides information about the predicted RNA and protein in these patients. The legend below the table explains that the numbering of the predicted RNA is "*according to transcript of largest PGRN transcript (GenBank Accession Number NM_002087.2) and starting at translation initiation codon*" (see page 27, lines 7 to 9) and that the numbering of the predicted protein is "*according to the largest PGRN isoform (GenPept Accession Number NP_002078.1*" (see page 27, lines 9 to 10).

13. The skilled person would directly and unambiguously, derive from the disclosure on page 27 of P3 that the PGRN polypeptide amino acid sequence of document D32 was used as the reference sequence for the identification of mutation sites because it was the largest PGRN isoform. However, page 27, lines 4 to 10, of P3 is silent on a possible use of this isoform in the therapy of FTD. The skilled person would furthermore realise that the applicant of P3 was aware of the existence of the amino acid sequence of document D32 and did not include it in the definition of the human PGRN polypeptide provided on page 3 of P3. They would not therefore have directly and unambiguously derived from page 27, lines 4 to 10, of P3 that a human PGRN polypeptide having the amino acid

sequence of document D32 was also to be used in the treatment of FTD.

14. Fourthly, the fact that P3 also mentions murine or mouse PGRN polypeptides does not change the definition of PGRN as it relates to the human PGRN polypeptide in P3. In particular, the denomination of the murine orthologue of human PGRN as "progranulin" instead of "granulin" in the context of describing the generation of PGRN knock-out mice (see P3, page 21, lines 31 to 35) is for "the sake of simplicity" only and does not change the relevant definition on page 3 of P3.

15. To summarise, in the patent, the meaning of the human PGRN polypeptide includes polypeptides having the amino acid sequence of SEQ ID NO:1 and other full-length polypeptides, e.g. a polypeptide having the amino acid sequence defined by GenBank GI number 4504151 which is distinct from SEQ ID NO:1 (see paragraph [0006] and point 3. above; documents D29, D31 and D32), whereas in P3 human PGRN polypeptide is explicitly limited to mean a polypeptide having the amino acid sequence of SEQ ID NO:2 (SEQ ID NO:1 in the patent). Therefore, the meaning of human PGRN polypeptide was broadened from P3 to the patent.

16. Accordingly, claim 1 of auxiliary request 1 can be conceptually divided into two parts (see decision G 1/15, Reasons, point 6.4 and point 6. above). The first part (called "claim 1A" below) corresponds to the invention disclosed directly and unambiguously in P3 and is limited, as regards the use of human PGRN polypeptides, to a human PGRN polypeptide having the amino acid sequence set forth in SEQ ID NO:1. The second part (called "claim 1B" below) is the rest of the subject-matter of the claim and, as

regards the use of human PGRN polypeptides, embraces the human PGRN polypeptide set forth in GenBank GI number 4504151 and disclosed in document D32 (see paragraph [0006] of the patent and point 3. above). Claim 1A is entitled to the priority of P3, while claim 1B is not.

17. The patent proprietor did not dispute that the subject-matter of claim 1B was not entitled to priority from any other document.

18. The board concludes that the effective date of claim 1B is the filing date of the patent, and that the disclosure of document D9 is part of the state of the art as defined in Article 54(2) EPC in respect of the subject-matter of claim 1B.

Inventive step

Closest prior art

19. In accordance with the established case law of the Boards of Appeal, the closest prior art for assessing inventive step is normally a prior art disclosing subject-matter conceived for the same purpose or aiming at the same objective as the claimed invention and having the most relevant technical features in common, i.e. requiring the minimum of structural modifications (see also Case Law of the Boards of Appeal of the European Patent Office, "CLBA", 10th edition 2022, section I.D.3.1).

20. Claim 1B is a purpose-limited product claim under Article 54(5) EPC, directed to a PGRN polypeptide for use in treating FTD. The purpose or objective of a purpose-limited product claim under Article 54(5) EPC

is, generally, the therapeutic indication recited in the claim. In the case at hand, this is the treatment of FTD.

21. In the decision under appeal, the opposition division held that document D3, a review article on neurotransmitter deficits and treatments in FTD, represented the closest prior art. Document D9 was considered to be unsuitable as the starting point for the assessment of inventive step because it was held not to relate to the same, or to a similar, purpose as the claim.

22. On appeal, the appellant maintained that document D9 was directed to the same purpose as claim 1 and was the closest prior art, while the respondents maintained that document D9 could not serve as the closest prior art.

23. Document D9 reports studies that identify mutations in the *PGRN* gene as the underlying mechanism involved in FTD. In particular, document D9 discloses that mutations in *PGRN* that result in null alleles cause reduced levels of PGRN which in turn cause FTD (see Figures 1 and 3). On the basis of these findings, document D9 proposes PGRN replacement as a therapeutic strategy to treat FTD (see page 918, left-hand column, last paragraph to page 919, left-hand column, first paragraph). The therapeutic strategy proposed in document D9 to treat FTD is thus based on the elucidation of the mechanism underlying FTD. In agreement with the appellant the board considers that document D9 credibly discloses that PGRN replacement therapy is suitable for treating FTD. Accordingly, document D9 provides an enabling disclosure of the suitability of PGRN replacement for the treatment of

FTD (see also T 609/02; Reasons, point 9). Since document D9 deals with the same disease as claim 1, identifies low levels of PGRN as the cause of the disease and provides an enabling disclosure of the suitability of PGRN replacement for the treatment of FTD, it is considered to be a suitable starting point for the assessment of inventive step in claim 1.

24. It is undisputed that document D9 does not provide any information on the specific therapeutics to be used for the replacement of PGRN or any technical teaching for reducing the therapeutic application to practice.

25. The opposition division held that this lack of information as to how to reduce the therapeutic application to practice meant that the "therapeutic use" was not directly and unambiguously derivable from the disclosure of document D9, with the result that this document did not disclose "in an enabling manner, a method of treating FTD", and therefore was not directed to the same, or to a similar, purpose as claim 1. The respondents furthermore submitted that, since document D9 was not an enabling disclosure of a therapeutic application, it was not a disclosure of such an application at all, and that the closest prior art could not be a teaching in a document that could not be reduced to practice by the skilled person on the basis of that document.

26. Document D9 is considered to provide an enabling disclosure of what it proposes, i.e. PGRN replacement therapy as a therapeutic strategy to treat FTD (see point 23. above). It is not necessary for document D9 to provide an enabling disclosure of what is claimed. When applying the problem-and-solution approach in the assessment of inventive step, information that is not

disclosed in the prior art is considered in determining the distinguishing features, the resulting technical effect, and the formulation of the objective technical problem to be solved. To what extent the claimed subject-matter differs from the disclosure in document D9 is thus relevant when determining the distinguishing features (see also point 30. below). The teaching towards the distinguishing features may then come from another prior-art document or from the common general knowledge of the skilled person (see also point 34. below).

27. Document D9's lack of disclosure as regards implementation of the proposed PGRN replacement therapy does not therefore disqualify it from being the starting point for the assessment of inventive step. Accordingly, the opposition division's reasoning cannot hold, and the respondents' first line of argument as to why document D9 could not be the closest prior art likewise fails.

28. The respondents' further line of argument, that document D9 could not serve as the closest prior art because it was not directed at the treatment of FTD but at the elucidation of its aetiology, is not persuasive either. Document D9 not only elucidates FTD's aetiology but goes on to propose a therapeutic strategy for the treatment of FTD that is predicated on this elucidation of FTD's aetiology (see page 918, left-hand column, last paragraph to page 919, left-hand column, first paragraph). It is this disclosure in document D9 that relates to the same purpose as the claim and is taken as a suitable starting point for the assessment of inventive step in claim 1 (see point 23. above).

29. As regards document D3, which is considered the closest prior art in the decision under appeal and which the respondents propose as the closest prior art in the appeal proceedings, the board notes as follows. Pursuant to Article 56 EPC, the claimed invention must not be obvious to the person skilled in the art having regard to any prior art, subject to Article 56, second sentence, EPC. Where there are several reasonable starting points for the assessment of inventive step, if the invention is obvious to the skilled person from the prior art in the light of one of these starting points that is enough to conclude that there is a lack of inventive step. This was not disputed by the respondents.

Objective technical problem

30. Document D9 does not disclose which molecule to use for the proposed PGRN replacement therapy or how to implement it. Therefore, the subject-matter of claim 1B under consideration (see point 16. above) differs from the disclosure in document D9 in that human PGRN polypeptides having defined amino acid sequences are used to treat FTD.

31. The respondents' assertion that therapy was not disclosed in document D9 and that this constituted a further difference of the claimed subject-matter is not persuasive, for the reasons set out in point 23. above. The objective technical problem cannot therefore be formulated as suggested by the respondents, i.e. as the finding of a practical application of the genome data findings of document D9, because it ignores the fact that document D9 already proposes PGRN replacement therapy as a therapeutic strategy to treat FTD.

32. The patent provides neither clinical assays in patients nor proof-of-concept experiments in animal models: thus, the patent contains no evidence of PGRN administration in any form. The respondents did not dispute that the patent contained no evidence that any specific PGRN polypeptide had a surprising effect in the therapy of FTD. Accordingly, no surprising technical effect(s) are linked to the distinguishing features.

33. In agreement with the appellant, the objective technical problem can be formulated as the provision of a way to implement the PGRN replacement therapy proposed in document D9 for treating FTD.

Obviousness

34. In the assessment of obviousness, the question to be answered is whether or not a person skilled in the art starting from the disclosure in document D9 and seeking a solution to the technical problem formulated above would have provided a PGRN polypeptide falling within the scope of claim 1B for use in treating FTD.

35. As explained in point 23. above, document D9 discloses that reduced levels of PGRN protein cause FTD, and proposes PGRN replacement as a therapeutic strategy to treat FTD. In agreement with the appellant the board considers that this teaching would have prompted the skilled person to use a human PGRN polypeptide for the replacement therapy, because it was this that was lacking, given that reduced levels of PGRN protein caused FTD. To provide the human PGRN polypeptide, the skilled person would have consulted databases known to provide information on proteins including their amino acid sequence, such as GenBank. In doing so, on the day

before the effective date of the claimed invention, the skilled person would have found two full-length human PGRN polypeptides having different amino acid sequences in GenBank, see documents D29, D31 and D32. Based on the teaching in document D9 (see point 23. above), the skilled person would have had a reasonable expectation that a PGRN replacement therapy with either one of these human PGRN polypeptides would be suitable for the treatment of FTD. In these circumstances, either of the available human PGRN polypeptide constituted an equally obvious solution to the objective technical problem, so it was obvious to choose one of these. It is established in the case law of the Boards of Appeal that an arbitrary choice from a number of possible solutions which were available to the skilled person, in the absence of a hint to do so, is not inventive (see CLBA, I.D.9.21.9).

36. For the same reason, the respondents' argument as to the existence of other possible solutions, such as PGRN polynucleotides or agents capable of increasing the production of PGRN, is not persuasive. In the absence of a technical effect that would distinguish the use of a human PGRN polypeptide from these other possible solutions, its use is considered an arbitrary selection from a number of possible solutions and hence not inventive. In any case, as explained above, the board considers that document D9's disclosure of the mechanism underlying FTD would have prompted the skilled person to use a human PGRN polypeptide for the treatment of FTD.

37. It was not contested by the respondents that implementation of the replacement therapy involved only routine methods which were known to the person skilled in the art before the effective date of the claimed

invention and had already been shown to treat neurodegenerative disorders successfully, as evidenced by the disclosures in documents D11, D12, D23, D24, D25, D26, D27 and D28.

38. The board concludes that the skilled person faced with the objective technical problem of providing a way to implement the PGRN replacement therapy proposed in document D9 would, in an obvious manner, have provided the human PGRN polypeptide of document D32 and used it in the treatment of FTD with a reasonable expectation of success. They would thus have arrived at an embodiment of claim 1B without the need for inventive activity.

39. The subject-matter of claim 1B of auxiliary request 1 does not meet the requirements of Article 56 EPC. Accordingly, claim 1 as a whole does not meet the requirements of Article 56 EPC.

Auxiliary request 2

Admittance of the appellant's objection under Article 56 EPC (Article 13(2) RPBA)

40. During the oral proceedings, the appellant submitted that the subject-matter of claim 1 of auxiliary request 2 lacked inventive step over document D9 in combination with common general knowledge regarding the purification of therapeutic proteins. In brief, the appellant submitted that the addition of affinity tags was a commonly known modification in the purification of therapeutic proteins and that such a modification would result in a polypeptide comprising SEQ ID NO:1. As evidence of the common general knowledge regarding the use of tags in the purification of therapeutic

proteins, the appellant relied on statements in paragraph [0085] of the patent and on page 21, lines 11 to 16 in P3.

41. Auxiliary request 2 has been on file since the beginning of the appeal proceedings (see section V.) and the appellant has not raised any objection to the subject-matter of the claims of auxiliary request 2 in the course of the written appeal proceedings (see sections VI. and VIII.).

42. The appellant's new line of argument involved new facts (see point 40. above), and was an amendment of the appellant's case and not a further development of the argument put forward for the subject-matter of claim 1 of auxiliary request 1. Indeed, it was not disputed by the appellant that the argument put forward for claim 1 of auxiliary request 1 did not apply to claim 1 of auxiliary request 2.

43. According to Article 13(2) RPBA, which applies in the case at hand, any amendment to a party's appeal case after notification of a summons to oral proceedings is, in principle, not to be taken into account unless there are exceptional circumstances, which have been justified with cogent reasons by the party concerned.

44. The appellant submitted that it was the board that had raised the issue of the lack of priority of claim 1 of auxiliary request 2 in its preliminary opinion, and the appellant's objection merely addressed this lack of priority.

45. However, the fact that the board observed that it was inclined to disagree with the respondents as regards entitlement to the priority of P3 of the subject-matter

of claim 1 (see section IX.) does not mean that the appellant was entitled to raise a new objection to this claim, involving new facts, at the oral proceedings.

46. The appellant did not submit that there were any exceptional circumstances which would justify admitting the new objection.

47. The board therefore decided to not admit into the appeal proceedings the appellant's new objections under Article 56 EPC to the subject-matter of claim 1 of auxiliary request 2 (Article 13(2) RPBA).

48. Consequently, the set of claims of auxiliary request 2 is allowable.

Order

For these reasons it is decided that:

1. The decision under appeal is set aside.

2. The case is remitted to the opposition division with the order to maintain the patent with the following claims and a description and drawings to be adapted thereto:
Claims 1 to 6 of auxiliary request 2 filed as auxiliary request III with the patent proprietors' statement of grounds of appeal dated 2 June 2020.

The Registrar: The Chairwoman:

L. Malécot-Grob T. Sommerfeld

Decision electronically authenticated