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Datasheet for the decision of 21 February 2025

Case Number: T 1004/22 - 3.3.08

Application Number: 11781200.8

Publication Number: 2569419

IPC: C12N5/071, C12Q1/68, C12N5/0735, C12N5/02, C07K14/47, C07K14/50, A61K35/12

Language of the proceedings: EN

Title of invention:
Differentiation of human embryonic stemm cells

Patent Proprietor:
Janssen Biotech, Inc.

Opponent:
SANOFI

Headword:
Embryonic stem cell differentiation/JANSSEN BIOTECH

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

Keyword:
Inventive step - "try and see" situation
Main request, Auxiliary requests 1-48 - inventive step (no)
Amendment after communication - taken into account (no)

Decisions cited:
T 0418/07, T 1014/07, T 1480/16, T 0995/18, T 1792/19, T 1857/19, T 0424/21

Catchword:
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Case Number: T 1004/22 - 3.3.08

D E C I S I O N
of Technical Board of Appeal 3.3.08
of 21 February 2025

Appellant I: (Patent Proprietor)	Janssen Biotech, Inc. 800/850 Ridgeview Drive Horsham, PA 19044 (US)
Representative:	Vossius & Partner Patentanwälte Rechtsanwälte mbB Siebertstrasse 3 81675 München (DE)
Appellant II: (Opponent)	SANOFI 54 rue La Boétie 75008 Paris (FR)
Representative:	Gaentzsch, Peer Christian Zwicker Schnappauf & Partner Patentanwälte Part mbB Hansastraße 32 80686 München (DE)
Decision under appeal:	**Interlocutory decision of the Opposition Division of the European Patent Office posted on 15 February 2022 concerning maintenance of the European Patent No. 2569419 in amended form**

Composition of the Board:

Chair	T. Sommerfeld
Members:	B. Claes
	A. Bacchin

Summary of Facts and Submissions

I. The appeals lodged by the patent proprietor (appellant I) and the opponent (appellant II) lie from the interlocutory decision of the opposition division on European patent No. 2 569 419, entitled "*Differentiation of human embryonic stem cells*", granted on European patent application No. 11781200.8, which was filed as an international application under the PCT and published as WO 2011/143299.

II. The opposition proceedings were based on the grounds for opposition in Article 100(a) EPC, in relation to novelty (Article 54 EPC) and inventive step (Article 56 EPC), and in Article 100(b) EPC.
The opposition division held, *inter alia*, that, while the subject-matter of claims 1 and 2 of the main request did not meet the requirement of novelty, the set of claims of auxiliary request 1 and the invention to which it relates met the requirements of the EPC.

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

D5: Chen S. *et al.*, Nature Chemical Biology, 2009, Vol. 5(4), pages 258-265

D6: Mfopou J.K. *et al.*, Gastroenterology, 2010 June; 138(7):2233-45, 2245.e1-14., published online on 3 March 2010 (doi:10.1053/j.gastro.2010.02.056)

IV. With the grounds of appeal, appellant I re-submitted the set of claims of the main request as well as sets of claims of auxiliary requests 1 to 39 (all filed in the opposition proceedings with the submission of

22 July 2022) and submitted sets of claims for new auxiliary requests 40 to 47. Auxiliary request 1 dealt with in the decision under appeal was maintained and re-submitted as auxiliary request 48.

Independent claims 1 and 3 of the main request read:

"1. A population of cells expressing markers characteristic of the pancreatic endoderm lineage, wherein greater than 80% of cells in the population co-express PDX1 and NKX6.1."

"3. A method to generate a population of cells expressing markers characteristic of the pancreatic endoderm lineage, wherein greater than 50% of the cells in the population co-express PDX1 and NKX6.1, comprising the steps of:

a. culturing a population of pluripotent stem cells,
b. differentiating the population of pluripotent stem cells into a population of cells expressing markers characteristic of the definitive endoderm lineage,
c. differentiating the population of cells expressing markers characteristic of the definitive endoderm lineage into a population of cells expressing markers characteristic of the pancreatic endoderm lineage, in a medium supplemented with noggin and a protein kinase C activator selected from the group consisting of (2S,5S)-(E,E)-8-(5-(4-(Trifluoromethyl)phenyl)-2,4-pentadiemoylamino) benzolactam, Indolactam V, phorbol-12-myristate-13-acetate, and phorbol-12,13 -dibutyrate, with the proviso that said medium is not supplemented with 1 µM ALK5 inhibitor II." (emphasis added by the board, indicating amendment by insertion compared to claim 3 of the patent as granted)

Claim 2 of the main request is dependent on product claim 1. Claims 4 to 12 are dependent on method claim 3.

The set of claims of auxiliary request 1 dealt with in the decision under appeal (and re-submitted as auxiliary request 48; claims 1 to 10) was filed during the oral proceedings and consists of method claims 3 to 12 of the main request.

V. With the grounds of appeal, appellant II submitted objections concerning auxiliary request 1 dealt with in the decision under appeal against, *inter alia*, the subject-matter of claim 1 for lack of inventive step (Article 56 EPC).

VI. Each appellant replied to the other party's appeal.

VII. After the parties were summoned to oral proceedings, the board issued a communication pursuant to Article 15(1) RPBA providing the board's preliminary opinion and noting, *inter alia*, that appellant I, as the respondent to the appeal of appellant II, had not filed requests in defence against appellant II's appeal that the subject-matter of claim 1 of auxiliary request 1 dealt with in the decision under appeal lacked an inventive step.

VIII. On 21 January 2025, appellant I made a further submission and submitted new auxiliary requests 49 to 54.

IX. The parties' submissions and arguments on appeal relevant for the decision are taken into consideration in the reasons for the decision by the board set out below.

X. The parties' requests relevant for the decision of the board were as follows.

Appellant I (patent proprietor) requested
- that the decision under appeal be set aside to the extent that the subject-matter of claims 1 and 2 of the main request was not novel over the disclosure in document D2and the case subsequently be remitted to the opposition division for further prosecution,
or alternatively,
- that the decision under appeal be set aside and that novelty of the subject-matter of claims 1 and 2 of one of auxiliary requests 1 to 47, filed with the statement of grounds of appeal, be acknowledged in view of document D2 and the case subsequently be remitted to the opposition division for further prosecution,
or further alternatively,
- that the decision under appeal be set aside and the patent be maintained with the set of claims of one of auxiliary requests 1 to 47,
or further alternatively,
- that the appeal of the opponent (appellant II) be dismissed (auxiliary request 48),
or further alternatively,
- that the decision under appeal be set aside and the patent be maintained with the set of claims of one of auxiliary requests 49 to 54, filed with letter of 21 January 2025.

Appellant II (opponent) requested that the decision under appeal be set aside and the patent be revoked. Appellant II also requested that auxiliary requests 1 to 47 and 49 to 54 not be admitted into the proceedings.

Reasons for the Decision

Appellant I's appeal

The invention

1. The invention is in the field of cell biology and medicine and relates to cell-replacement therapy for type I diabetes mellitus. The invention provides methods to promote the differentiation of pluripotent stem cells - which have the potential to produce differentiated cell types that include all somatic tissues and organs - into pancreatic cells producing insulin that are able to function similarly to pancreatic islets of Langerhans.

Main request

The claimed invention

2. The claimed invention entails both (see section IV.) a method for generating from pluripotent stem cells a population of cells expressing markers characteristic of the pancreatic endoderm lineage (independent claim 3) and a population of such cells expressing markers characteristic of the pancreatic endoderm lineage (independent claim 1).

3. Claim 3 defines a method for generating a population of cells which express markers characteristic of the pancreatic endoderm lineage (i.e. a so-called embryonic stem cell differentiation protocol) comprising three steps:

a. culturing a population of pluripotent stem cells

b. differentiating the cell population of step a. into a "population of cells expressing markers characteristic of the definitive endoderm lineage" (see paragraph [0036] of the patent)

c. differentiating the cell population of step b. into a "population of cells expressing markers characteristic of the pancreatic endoderm lineage" (see paragraph [0037] of the patent) in a medium supplemented with noggin and a particular protein kinase C (PKC) activator, e.g. Indolactam V (ILV)

Inventive step (Article 56 EPC) - claim 3

4. Although the opposition division did not specifically deal in the decision under appeal with claim 3 of the main request since it came to the conclusion that the subject-matter of claim 1 lacked novelty, it did decide on inventive step of the subject-matter of the identical claim 1 of auxiliary request 1. On appeal, appellant II disagreed with the decision in this respect and reiterated that the claimed method lacked inventive step in light of the disclosure of protocol P3 in document D6, representing the closest prior art, when combined with the teaching in document D5.

5. Since claim 3 of the main request is identical to claim 1 of auxiliary request 1 dealt with in the decision under appeal, the board could consider the objection of appellant II in the context of the main request.

Closest prior art, difference, technical effect

6. Document D6 discloses differentiation protocols for generating pancreatic progenitor cells starting from human embryonic stem cell (hESCs) lines including the well-established D'Amour protocol from which experimental protocols P1 to P3 are essentially derived. The first stage of each disclosed experimental protocol (stage 1, lasting three to four days) is identical to stage 1 of the D'Amour protocol and aims to differentiate a population of pluripotent hESCs into definite endoderm cells. It is undisputed that stage 1 corresponds to steps a. and b. in the method of claim 3 resulting in "a population of cells expressing markers characteristic of the definitive endoderm lineage".

7. The medium in stages 2 and 3 (each lasting four days) in protocols P2 and P3 is supplemented with noggin, replacing FGF10 as used in the D'Amour protocol, a measure aiming at inducing a pancreatic fate and blocking a hepatic fate in the cells (hepatocyte blockade and pancreas induction (HBPI), see Supplementary Table 1 on page 2245.e2 and page 2241, left-hand column, lines 5 to 14). Protocols P2 and P3 result in large $PDX1^+$ cell clusters (20 to 30%) at the HBPI stages 2 and 3 and up to 50 to 80% $PDX1^+$ cell at the $PDX1^+$ progenitor stage 4 (see page 2241, left-hand column, lines 23 to 30) lasting four days, in which the medium is supplemented with FGF10 but lacks noggin.

8. The board agrees with the parties and the opposition division that protocol P3 of document D6 (see page 2245.e2, Supplementary Table 1) constitutes a **suitable starting point** for the assessment of inventive step.

9. There was also consensus among the parties that the **difference** between experimental protocol P3 disclosed in document D6 and the claimed method is that the latter, in step c., aims to differentiate the definitive endoderm lineage resulting from stage 1 of the D'Amour protocol (see point 6. above) into a population of cells expressing markers characteristic of the pancreatic endoderm lineage by the use of a medium containing noggin which is supplemented with a PKC activator (e.g. ILV).

10. It was also undisputed that this difference results in the **technical effect** of a more complete specification of $PDX1^+$ pancreatic endoderm cells, here co-expressing (at least) also NKX6.1, both markers being characteristic of pancreatic endoderm in the resulting cells (see patent paragraph [0037]), this being intended to generate a population of cells suitable as a source for β-cells.

Formulation of the objective technical problem

11. The opposition division considered that the objective technical problem was the provision of an improved method for generating a cell population of pancreatic endoderm lineage co-expressing higher levels of PDX1 and NKX6.1. However, co-expression of the PDX1 and NKX6.1 markers was not determined in document D6. Accordingly, formulating the objective technical problem as providing an improvement in terms of a higher proportion of co-expression of these markers is not appropriate.

12. During the oral proceedings, appellant I formulated the objective technical problem as the provision of a

method that allows generating a population of cells that is a suitable source for β-cells.

13. Appellant II has argued neither that this objective technical problem was wrongly formulated nor that the patent fails to disclose that the claimed invention solves this problem. In fact, the board agrees and is also satisfied that the patent demonstrates that, compared to the population of cells resulting from the P3 protocol of document D6, the claimed method, including step c. of supplementing the medium with a combination of noggin and ILV, allows for the generation of a population of cells with a more complete specification of $PDX1^+$ pancreatic endoderm cells in terms of their co-expression of the NKX6.1 marker.

Obviousness

14. For coming to a conclusion on obviousness, the question is whether the skilled person, when starting from protocol P3 disclosed in document D6, would add to the noggin containing medium in the protocol's HBPI stage 2 and/or 3 a PKC activator such as ILV with a view to generating a population of cells with a more complete specification of $PDX1^+$ pancreatic endoderm cells, in this case co-expressing the NKX6.1 marker.

15. The opposition division and appellant I were in agreement that document D6 did not provide the skilled person with a pointer to the use of a PKC activator. The board concurs with this position. If such a pointer had been derivable by the skilled person from the disclosure in document D6, the claimed solution would likely have lacked an inventive step (or even novelty) based on the disclosure in document D6 alone. There is,

however, consensus among the parties, and the board agrees, that this is not the case.

16. Nevertheless, and thus contrary to the position of appellant I, the board agrees with appellant II that document D6 *does* provide **a pointer** for the skilled person to certain aspects of the claimed solution in the concluding remarks reading:

"*Our findings support the statement that beta-cell derivation from hES cells should follow developmental pathways, and confirm the need for further optimization of current protocols. We presume that this efficient derivation of early pancreas progenitors opens new perspectives for diabetes cell therapy, and provide material for investigating pancreatic differentiation* in vitro. (...) *In light of progress in pancreas biology, our challenges focus on unraveling molecular cues required in protocol P3 for strong induction and/or coexpression of PTF1a and NKX6.1, which together with PDX1 mark the fully specified pancreas progenitor.*" (see page 2244, left-hand column, last paragraph, emphasis added by the board)

and in the last sentence of the abstract reading:

"*Although additional signals appear to be required for full specification of PDX1$^+$ early pancreatic progenitors (via PTF1a and NKX6.1 coexpression), these findings indicate the signaling pathways required for differentiation of bipotential progenitors*." (emphasis added by the board)

17. These statements provide a pointer for the skilled person, that, in order to obtain "fully specified pancreas progenitor" cells - which in fact corresponds

to the very aim of the claimed method to generate a mor e complete specification of $PDX1^+$ pancreatic endoderm cells (see point 9. above) - additional differentiation factors (cues, signals) are needed which increase expression of pancreatic endoderm markers, in particular and explicitly referring in this context to improved NKX6.1 co-expression in $PDX1^+$ cells.

18. In view of this pointer in the disclosure of document D6, the question in point 14. needs to be clarified: namely, whether additional differentiation factors (cues, signals) which improve co-expression of the NKX6.1 marker in $PDX1^+$ cells were known to the skilled person and implementable in protocol P3 disclosed in document D6

19. **Document D5** is in the same technical field as document D6 and the claimed invention. It aims to differentiate hESCs with the goal of providing insulin-secreting β-cells ("*generation of a cell population that is a key milepost on the path to making beta cells*", see abstract, lines 7 to 9). Molecules were screened to identify those that increased the number of $PDX1^+$ pancreatic cells when starting from a definitive endoderm lineage derived from hESCs (see page 259, left-hand column, lines 13 to 22), obtained, as in document D6, by the first stage 1 of the D'Amour protocol (see point 6. above). The most effective compound identified in generating $PDX1^+$ cells from the definitive endoderm lineage was ILV resulting in up to 26.9% $PDX1^+$ cells (see page 260, left-hand column, lines 12 to 39 and also Figure 1f) and in 45.8% $PDX1^+$ cells when ILV was combined with FGF10 (see page 260, left-hand column, lines 40 to 49). Most of the $PDX1^+$ cells following ILV treatment showed substantial expression of other pancreatic progenitor markers. In

particular, 83.5% of the $PDX1^+$ cells co-expressed NKX6.1 (page 260, right-hand column, lines 1 to 8). Document D5 explains that the supplemented ILV activates PKC signalling, this being needed for induction of $PDX1^+$ cells (page 263, left-hand column, lines 14 to 31).

19.1 Hence, because document D6 disclosed PDX1 expression in up to 80% of the cells generated by protocol P3 (see point 7. above) and document D5 taught the skilled person the means, i.e. PKC activation by ILV, to achieve what document D6 desired, i.e. pointed to, namely, significant NKX6.1 co-expression in $PDX1^+$ cells (83.5% of the resulting $PDX1^+$ cells obtained in document D5 co-express NKX6.1; see point 19. above), the skilled person would have been prompted by the teaching of document D5 to implement a PKC activator such as ILV in protocol P3 disclosed in document D6.

19.2 Appellant II submitted and the board agrees that since the abstract of document D5 stated that "*(-)-indolactam V works specifically at one stage of pancreatic development, inducing pancreatic progenitors from definitive endoderm*" (lines 6 and 7), the administered **ILV acted on definitive endoderm** to differentiate it towards pancreatic progenitors (while, at the same time, hepatic induction was blocked). Similarly, in protocol P3 of document D6, noggin was used to induce pancreas differentiation from definitive endoderm in stages 2 and 3 (see Supplementary Table 1 on page 2245.e2 and point 6. above). Therefore, the skilled person would supplement protocol P3 of document D6 with ILV in the stages in which the medium contains noggin. This straightforwardly resulted in the combination of the two differentiation factors in the same medium as required by claim 1.

19.3 The board also agrees with appellant II that the skilled person would adopt a "try and see" approach (see Case Law of the Boards of Appeal of the EPO, 10th edn. 2022, referred to in the following as CLBA, I.D.7.2). Indeed, in view of the teaching in the state of the art, the skilled person had either some expectation that when noggin and ILV were combined in protocol P3, a high co-expression of both pancreatic progenitor markers (more than 50%) could be achieved, or, at worst, no expectations of any sort, but only with such a "try and see" attitude, which, however, does not equate to an absence of a reasonable expectation of success. A "try and see" situation is considered to occur basically in the presence of two criteria, namely, if the skilled person, in view of the teaching in the state of the art, has clearly envisaged the claimed subject-matter and determined by routine tests whether the subject-matter has the desired effect.

20. Appellant I argued that the skilled person would not have arrived at the claimed invention, essentially because of a lack of a reasonable expectation of success, and referred to decision T 1014/07 (Reasons 10) to submit that the mere existence of teachings in the state of the art is not a conclusive reason for concluding that the skilled person would have combined these teachings to solve the problem that they are confronted with if any prompting to make such a combination is missing in the state of the art. Appellant I further referred to decision T 418/07 (Reasons 43) and submitted that a necessary distinction, which is made in evaluating the attitude of the skilled person, had to be made between a "hope to succeed", which is linked to the wish that a result

be achieved, and a "reasonable expectation of success", which is linked to the ability to predict reasonably, based on the technical circumstances, a successful conclusion of the project within acceptable time limits.

21. The board does not find these arguments convincing, and the cited decisions are not applicable to the case in hand for the following reasons.

22. In a first line of argument, appellant I submitted that the highest percentage of $PDX1^+$ cells in the populations disclosed in document D5 was obtained after administration of ILV in combination with FGF10 but that this only resulted in 45.8% $PDX1^+$ cells(see page 260, left-hand column, lines 46 to 49, see also point 19. above). Since only 83.5% of these $PDX1^+$ cells co-expressed NKX6.1 (see page 260, right-hand column, line 7), document D5 in fact disclosed that only 38.2% of the resulting cells in the culture treated with ILV and FGF10 co-expressed PDX1 and NKX6.1. Taking into account that administration of the combination of ILV and FGF10 was superior to the administration of ILV alone, the skilled person would thus not be motivated by the disclosure of document D5 to reasonably expect more than 50% of cells as obtained with the claimed method to co-express the two markers when treated with ILV alone. The skilled person would therefore not have combined the disclosure in documents D6 and D5 with a reasonable expectation of solving the formulated objective technical problem.

23. However, the board agrees with appellant II that this consideration is not pertinent when considering obviousness in the case at hand. In fact, the objective technical problem as formulated by appellant I (see

point 12. above) does *not* aim to increase the level of PDX1-expressing cells in the population but rather to increase the number of NKX6.1$^+$ cells in the PDX1$^+$ cell population obtained by protocol P3 of document D6, thus the aim is to provide a more complete specification of PDX1$^+$ pancreatic endoderm cells, here co-expressing (at least) also NKX6.1, that is a suitable source for β-cells. Rather, what the skilled person is accordingly interested in is that 83.5% of the resulting PDX1$^+$ cells co-express NKX6.1, as noted by appellant II.

24. In a second line of argument, appellant I submitted that even when combining the teachings in documents D6 and D5, the conservative skilled person would be hesitant to make any modifications to the initial protocol P3 and would not have arrived at the claimed method. Indeed, the skilled person would have added ILV to the medium at a stage in protocol P3 in which noggin was not present, i.e. the protocol's stage 4.

24.1 In a first aspect of this second line of argument, appellant I agreed with the decision under appeal that the skilled person would add ILV in stage 4 of the protocol P3, i.e. the stage in which FGF10 is present and not to stages 2 or 3 in which noggin is present, because document D5 taught that ILV treatment worked better in terms of induction of PDX1 expression in the presence of FGF10.

24.2 However, as noted in point 23. above, the formulated objective technical problem (see point 12. above) does *not* aim to increase the level of PDX1 expressing cells in the population but rather to increase the number of NKX6.1$^+$ cells in the PDX1$^+$ cell population obtained by protocol P3 of document D6. Therefore, also in this

aspect, appellant I's consideration is not pertinent when considering obviousness.

24.3 In a second aspect of the second line of argument, appellant I submitted that the screenings in document D5 were undertaken on a population of cells derived from defined endoderm generated by a stepwise differentiation protocol based on the D'Amour protocol (see page 264, paragraph spanning the columns) which corresponded almost perfectly to stages 1, 2 and 3 of the D'Amour protocol. Thus, document D5 only disclosed that endoderm cells resulting from stage 3, corresponding to the same stage in the D'Amour protocol, were treated with ILV, i.e. during stage 4.

24.4 Furthermore, as a third aspect of the second line of argument, appellant I submitted that since the skilled person knew that expression of PDX1 and NKX6.1 was absent in cells resulting from stage 1, i.e. in the "definitive endoderm" cells, when starting from document D6 and desiring to obtain a more complete specification of $PDX1^+$ pancreatic endoderm cells, i.e. which co-express also NKX6.1, the skilled person would have considered modifying protocol P3 only from a stage in which some NKX6.1 was expressed, i.e. during stage 4 of the protocol.

25. The board is, however, not persuaded by appellant I's submissions on aspects two and three, that, having regard to the teaching in document D5, the skilled person would only supplement ILV in the medium used in stage 4 of protocol P3 of document D6 and not in the media applied in stages 2 and 3 in the protocol P3 comprising noggin.

26. Firstly, the omission of FGF10 and the replacement with noggin in stages 2 and 3 of protocol P3 of document D6 was a deliberate measure aimed at inducing a pancreatic fate and blocking a hepatic fate of the cells (HBPI, see point 7. above) while at the same time resulting in high PDX1 expression in the differentiating population of cells. The fact that Figure 2 of document D5 demonstrates that, besides the administration of ILV alone, the combined administration of ILV and FGF10 also increases NKX6.1 expression does not necessarily mean that the skilled person would, in view of these facts, only implement adding ILV at the stage(s) in protocol P3 of document D6 in which FGF10 is administered (i.e. stage 4) and not at earlier stages where noggin is present.

27. Indeed, as noted in points 23. and 24.2 above, the skilled person in the case in hand does not primarily aim to further increase the level of PDX1 expressing cells in the population, but rather they aim to increase the number of $NKX6.1^+$ co-expressing cells in the $PDX1^+$ cell population obtained by protocol P3 of document D6. Since the general teaching in document D5 is that ILV induces pancreatic progenitors from definitive endoderm (see abstract, lines 6 and 7), the board agrees with appellant II that the skilled person would have considered, and certainly would not have dismissed, in addition to adding ILV in stage 4 of protocol P3, the option to add ILV in the earlier stages (i.e. 2 and 3) designed to provide HBPI with noggin present in the medium.

28. Secondly and furthermore, the screening tests disclosed in document D5 were conducted on the cells obtained after nine days of differentiation of hESCs in stages 1, 2 and 3 of the slightly modified version of the

D'Amour protocol, resulting in a heterogeneous population of endoderm in which already 5.6% of cells were $PDX1^+$ (see page 259, left-hand column, line 20, to right-hand column, line 20). The skilled person would therefore not be prompted by the disclosure in document D5 to wait to add ILV until after completion of stage 3 in protocol P3 of document D6, lasting four days and ending at day 11 or 12 after the start of stage 1, but would understand that already after nine days markers characteristic of pancreatic endoderm will have appeared in the differentiating population. Thus, when following the teaching in document D5, the skilled person would add ILV after nine days in protocol P3 of document D6, i.e. during stage 3, to the medium comprising noggin, and would thus arrive at the claimed invention. The board can thus agree with appellant II's argument that document D5 does *not* suggest only adding ILV to cells corresponding to the cells resulting from a step corresponding to step 3 of the D'Amour protocol, i.e. thus only in step 4 and thus only in a medium in which noggin was not present in protocol P3 disclosed in document D6.

29. Appellant I disagreed that a "try and see" situation applied in the case in hand. Indeed, the approach only applied in exceptional cases. Here, however, the skilled person could not envisage the claimed solution from the state of the art, nor did the state of the art point to or suggest the claimed approach. Hence, the first criterion for accepting that a "try and see" approach would be adopted by the skilled person under the circumstances failed to be met (see CLBA, I.D. 7.2).

30. However, despite contrary (unconvincing) arguments of appellant I, the board concluded above that i) document

D6 does provide the skilled person with a pointer for solving the formulated objective problem, i.e. high co-expression of the PDX1 and NKX6.1 markers (see points 16. to 18.), ii) the skilled person would consider document D5 to present an approach for obtaining such high co-expression (see points 23. and 24.2) and iii), when applying this approach to protocol P3 disclosed in document D6, the skilled person would add ILV to a noggin containing medium in stage 3 of the protocol (see points 25. to 28.). Therefore, the first criterion for accepting that a "try and see" approach would be adopted under the circumstances of the case in hand, i.e. that in view of the teaching in the state of the art, the skilled person had clearly envisaged the claimed subject-matter (see point 19.3 above), is fulfilled.

31. Furthermore, also the second criterion for adopting a "try and see" situation (see CLBA, I.D.7.2), i.e. requiring that only routine methods are necessary to achieve the claimed subject-matter, is fulfilled. In fact, appellant I has not argued that adding ILV to a medium used in protocol P3 disclosed in document D6 went beyond routine experimentation for the skilled person, but rather that the skilled person would not have been motivated to adapt protocol P3 by adding ILV in stage 3.

32. In view of the above considerations, the skilled person would have had no reasons to adopt a conservative approach, nor would they have had a mere "hope to succeed", as submitted by appellant I. Rather, the skilled person would have been in a **"try and see"** situation and would have obtained a population of cells as defined in claim 1 with a high degree of co-expression of the PDX1 and NKX6.1 markers when

combining the teachings of documents D6 and D5. The claimed subject-matter hence fails to involve an inventive step (Article 56 EPC).

Auxiliary requests 1 to 47 - inventive step (Article 56 EPC)

33. Appellant I re-submitted auxiliary requests 1 to 39 and filed new auxiliary requests 40 to 47 on appeal. Appellant I considered the amendments in these requests to address the opposition division's finding that the subject-matter of product claims 1 and 2 of the main request was not novel.

34. Claim 3 of each of auxiliary requests 1 to 4 and 40 is identical to claim 3 of the main request (see section IV.).

Claim 3 of auxiliary requests 5 to 9 and 41 differs from claim 3 of the main request in that also supplementation with FGF10 is disclaimed: "with the proviso that said medium is neither supplemented with FGF10 nor with 1 µM ALK5 inhibitor II".

Claim 3 of auxiliary requests 10 to 14, 20 to 24 and 44 differs from claim 3 of the main request in that the disclaimer reads: "with the proviso that said medium is not supplemented with an inhibitor of ALK5".

Claim 3 of auxiliary request 42 differs from claim 3 of the main request in that the disclaimer reads: "with the proviso that said medium is not supplemented with ALK5 inhibitor II".

Claim 3 of auxiliary requests 15 to 19 and 43 differs from claim 3 of the main request in that the disclaimer reads: "with the proviso that said medium is neither

supplemented with FGF10 nor with ALK5 inhibitor II".

Claim 3 of auxiliary requests 25 to 29 and 45 differs from claim 3 of the main request in that the disclaimer reads: "with the proviso that said medium is neither supplemented with FGF10 nor with an inhibitor of ALK5".

Claim 3 of auxiliary requests 30 to 34 and 46 differs from claim 3 of the main request in that the disclaimer reads: "with the proviso that said medium is not supplemented with a TGFβ receptor signaling inhibitor".

Claim 3 of auxiliary requests 35 to 39 and 47 differs from claim 3 of the main request in that the disclaimer reads: "with the proviso that said medium is neither supplemented with FGF10 nor with a TGFβ receptor signaling inhibitor".

35. Appellant I has not argued that the subject-matter of claim 3 of these requests overcame the board's negative finding on lack of inventive step of claim 3 of the main request (see point 32. above) and, in fact, expressed its understanding at the oral proceedings that the subject-matter lacked inventive step for the same reasons as claim 3 of the main request. Accordingly, the board can only conclude that the subject-matter of claim 3 of each of the auxiliary requests 1 to 47 lacks an inventive step.

36. In view of the above finding, the board also saw no necessity to take a stance on the admittance of auxiliary requests 40 to 47 into the appeal proceedings, as requested by appellant II.

Summary on the appeal of appellant I

37. In view of the above considerations, the board decided to dismiss appellant I's appeal.

Appellant II's appeal

Auxiliary request 48 - inventive step (Article 56 EPC)

38. Claim 1 of auxiliary request 48 (identical to auxiliary request 1 dealt with in the decision under appeal) is identical to claim 3 of the main request (see section II.). Accordingly, the board's negative conclusion on inventive step for claim 3 of the main request (see point 32. above) applies also to this claim.

Auxiliary requests 49 to 54 - admittance (Article 13(2) RPBA

39. These sets of claims are limited to the product claims 1 and 2 of the main request and of auxiliary requests 40 and 1 to 4, respectively, and thus are devoid of method claims. They were submitted by appellant I about one month before the date of the oral proceedings with a submission sent in reply to the board's communication under Article 15(1) RPBA (see section VIII.).

40. Article 13(2) RPBA implements the third level of the convergent approach applicable in appeal proceedings and thus imposes the most stringent limitations on a party wishing to amend its appeal case at an advanced stage of the proceedings. It provides that any amendment to a party's appeal case made at this stage of the proceedings must, as a rule, not be taken into

account unless there are exceptional circumstances justified with cogent reasons.

41. The board sees no option but to consider the filing of these auxiliary requests an amendment to appellant I's appeal case. Therefore, like any newly filed claim request, this filing represents a new line of defence against the opposition. By adding this new line of defence to its case, appellant I, as the respondent to appellant II's appeal, has changed its case (see also decision T 424/21, Reasons 16). The provisions of Article 13(2) RPBA hence apply.

42. No exceptional circumstances are apparent in the case in hand which could allow the board to consider the requests in the appeal proceedings.

42.1 Appellant II's objection of lack of inventive step of the subject-matter of method claim 3 of the main request (and claim 1 of auxiliary request 1 dealt with in the decision under appeal) were already raised and addressed in the opposition proceedings. Despite the fact that a positive conclusion had been reached in that respect in the decision under appeal (see the appealed decision, Reasons 18), on appeal, appellant II reiterated the inventive-step objection against the method claims in its grounds of appeal (see section 4), and specifically addressed why it disagreed with the reasons in the appealed decision (see section 4.3).

42.2 Thus, appellant I had reasons to file new auxiliary requests addressing the inventive-step objection against the method claims earlier than one month before the oral proceedings, namely with the reply to the appeal of appellant II, instead of awaiting the board's negative opinion on inventive step of those claims, as

provided in the communication under Article 15(1) RPBA. The fact that the board in its preliminary opinion, agreeing with an objection of a party raised in opposition proceedings, came to a different conclusion than the opposition division on inventive step of the subject-matter of the method claims does not constitute exceptional circumstances. Indeed, it is a possible outcome that appellant I, as the respondent to appellant II's appeal, could have expected. However, appellant I, as the respondent in that appeal, chose not to file any requests in defence of appellant II's appeal.

42.3 In view of the above circumstances, appellant I's arguments that the newly filed auxiliary requests addressed and rendered moot the board's concerns, expressed in the communication pursuant to Article 15(1) RPBA, that the method claims lacked an inventive step fail to constitute cogent reasons to justify its filing about one month before the oral proceedings.

42.4 Appellant I's argument that the newly filed auxiliary requests constituted a serious attempt to streamline the appeal proceedings and thus contributed to a reduction of the complexity of the case because they focus its appeal case on the sole negative issue in the decision under appeal, i.e. lack of novelty of claims 1 and 2 of the main request, must also fail as a cogent reason.

42.5 In fact, contrary to appellant I's arguments, taking into account the newly filed auxiliary requests would change the factual and legal framework of the appeal case before the board and would not lead to a simplification of the appeal proceedings. Indeed,

having regard to the framework that was presented by appellant I in appeal, all requests before the board contained the method claims, for which inventive step was the common relevant issue. On that basis, the board in its preliminary observations and comments in the communication pursuant to Article 15(1) RPBA did not see reasons to take a conclusive stance on the complex issue of novelty of the subject-matter of the product claims, which included new facts on sufficiency of disclosure of allegedly novelty-destroying prior art. With auxiliary requests 49 to 54, appellant I instead presented for the first time amendments containing a deletion of the entire category of the method claims. Their consideration in the proceedings would require the board to assess the complex issue of novelty of the product claims, together with a new discussion on sufficiency of disclosure of the state of the art on account of new documentary evidence, or to remit the case to the opposition division, both of which are detrimental to procedural economy.

42.6 Furthermore, when drafting the communication, the board also had no reason to assume that a defence in the form of a limitation to the product claims would still be a realistic option for appellant I in view of its conduct in the opposition proceedings, in particular at the initial stage of the appeal proceedings. Indeed, in response to the opposition division's finding during the oral proceedings that claims 1 and 2 of the main request lacked novelty, the patent proprietor filed a new auxiliary request 1 limited to method claims, hence consciously choosing not to obtain a decision of the opposition division on the amended product claims in, for example, auxiliary requests 1 to 4, pending at the beginning of oral proceedings before the opposition division (see Minutes, point 7.), which now form part

of auxiliary requests 51 to 54. Unlike for the method claims, a fall-back position requiring a *separate* discussion of the product claims was not pursued in the statement of grounds of appeal or in the reply to appellant II's statement of grounds of appeal. It was only after receipt of the board's communication under Article 15(1) RPBA that this position was introduced. It was therefore legitimate to rely on the assumption that other alternatives would not be pursued.

42.7 Also here, therefore, had appellant I wanted to focus its appeal on the sole negative issue in the decision under appeal, as argued, i.e. lack of novelty of the subject-matter of the product claims, it should have filed these auxiliary requests with its reply to appellant II's appeal or at the latest before the board issued the communication. The board fails to see any reason why these requests could not have been submitted at that point of the appeal.

42.8 In view of the above considerations, the board cannot concur with appellant I that the deletion of the method claims did not change the factual and legal framework of the appeal.

42.9 In addition, the case law referred to by appellant I fails to justify a different stance in the case in hand. Indeed, the circumstances of the case at hand differed from the case law as follows.

- In decision T 1857/19, the amendment by the deletion of claims addressed and overcame objections under Article 123(2) EPC newly raised by the board in the communication pursuant to Article 15(1) RPBA and thus enhanced procedural economy (see Reasons 1.1).

- In decisions T 424/21 (Reasons 22) and T 995/18 (Reasons 2), the amendment concerned the deletion of dependent claims and was considered by the board to not substantially shift the case.

- In decisions T 1480/16 (Reasons 2.3) and T 1792/19 (Reasons 2.2), the board considered the deletion of method claims from a claim request not to change the framework of that case and therefore not to constitute a change of the party's appeal case because, contrary to the case in hand, no new discussion on novelty or inventive step, respectively, was required.

43. In view of the above, the board decided that no exceptional circumstances presented themselves for taking into account auxiliary requests 49 to 54 on appeal. The auxiliary requests were accordingly not considered in the proceedings.

Order

For these reasons it is decided that:

1. The appealed decision is set aside.

2. The patent is revoked.

The Registrar: The Chair:

C. Rodríguez Rodríguez T. Sommerfeld

Decision electronically authenticated