Unified Patent Court
Einheitliches Patentgericht
Juridiction unifiée du brevet

Local Division Munich
UPC_CFI_437/2024
UPC_CFI_681/2024

Decision

of the Court of First Instance of the Unified Patent Court
issued on 19 December 2025
concerning EP 3 346 403

CLAIMANT

GXD-Bio Corporation, B1, 13, Seoun-ro, Seocho-gu, Seoul 06732, Republic of Korea,

represented by: Dr Rauh, Vossius & Brinkhof UPC Litigators, Siebertstrasse 3, 81675 Munich, Germany.

DEFENDANTS

1. **Myriad International GmbH**, Nattermannallee 1, 50829 Cologne, Germany,
2. **Myriad GmbH**, Staffelseestraße 6, 81477 Munich, Germany,
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4. **Myriad Genetics GmbH**, Leutschenbachstraße 95, 8050 Zurich, Switzerland,
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8. **Myriad Genetics Inc.**, 322 North 2200 West, Salt Lake City 84116, United States of America,
9. **Eurobio Scientific**, 7 avenue de Scandinavie ZA de Courtaboeuf, 91940 Les Ulis, France,

represented by: Dr Hölder, Hoffmann Eitle, Patent- und Rechtsanwälte Partnerschaftsgesellschaft mdB, Arabellastraße 30, 81925 Munich, Germany.

PATENT AT ISSUE

European Patent n° EP 3 346 403

PANEL/DIVISION

Panel 2 of the Local Division Munich

DECIDING JUDGES

The decision is delivered by Presiding Judge U. Voß (Judge-rapporteur), by the legally qualified judge Dr D. Voß, the legally qualified judge Knijff and the technically qualified judge Schüller.

LANGUAGE OF THE PROCEEDINGS

English

SUBJECT-MATTER OF THE PROCEEDINGS

Infringement action and Counterclaim for revocation

ORAL HEARING

18 November 2025

SUMMARY OF FACTS

1 The Claimant has sued the Defendants for (direct and indirect) patent infringement of patent EP 3 346 403. (hereinafter “patent in suit” or “the patent”, Exhibit VB 4). The Defendants have filed a Counterclaim for revocation. In the respond to the Counterclaim for revocation the Claimant requests an Amendment of the patent in form of three Auxiliary claim requests`.

2 The patent in suit is titled “Data processing, analysis method of gene expression data to identify endogenous reference genes”. The application underlying the patent was filed on 5 October 2017 as a divisional application of EP 2 455 878 (Application no. 17194976.1, Exhibit HE 3), which in turn is a divisional application of EP 2 115 158, which is the EPO regional phase of the international patent application published as WO 2008/078969 (Exhibit HE 4). The patent in suit claims priority of KR 20060134883 of 27 December 2006 (Exhibit HE 5/5a). Date of filing was on 27 December 2007, date of publication and mention of the grant of the patent in suit was on 17 June 2020.

3 The patent is in force in Austria, Belgium, France, Germany, Italy, Luxembourg and The Netherlands.

4 Registered owner of the patent in suit was originally Albion, Inc., and Gencurix, Inc. (herein jointly referred to as “former patent owners” or “previous proprietor”). In May 2024, the former

patent owners and the Claimant concluded a “Patent Purchase Agreement” (Exhibit VB 29) with an “Patent Assignment Agreement” as Exhibit B.

5 Meanwhile, the Claimant is registered in the respective national registers in Austria, Belgium, France, Germany, Italy, Luxembourg and The Netherlands as the sole owner of the respective national parts of the patent (Exhibit VB 5/5a, VB 5.1, VB 5.2, VB 30 – VB 33).

6 Claims 1 to 3 of the patent in suit read as follows:

> “1. A method for quantifying expression level of a target gene in a FFPE (formalin-fixed, paraffin embedded) tissue sample of human breast cancer tissues, comprising:
>
> 1) synthesizing cDNA from RNA of a subject;
> 2) performing real-time PCR to amplify the target gene and Endogenous Reference Gene OAZ1 using a pair of primers and/or probes with the cDNA serving as a template; and
> 3) normalizing an expression level of the target gene to that of the endogenous reference gene of step 2).”
>
> 2. The method according to claim 1, wherein the Endogenous Reference Gene is amplified by a pair of primers and/or probes.
>
> 3. The method according to claim 1, wherein the Endogenous Reference Gene shows low expression levels, similar to most low-abundance intracellular transcripts.”

7 Defendant 8 is a US-based company that is specialized in genetic testing and precision medicine. One of its products is (or was) “EndoPredict”-Test (hereinafter “attacked embodiment” or “contested embodiment”). Defendants 1-7 are European subsidiaries of Defendant 8, which use, offer to use or offer, and supply the attacked embodiment in Austria, Belgium, France, Germany, Italy, Luxembourg and The Netherlands (Exhibits VB 16, VB 19, VB 24, VB 25, VB 26, VB 27).

8 Defendant 9 is a French biotech company that is specialized in in vitro medical diagnostics and life sciences. Defendant 8 sold and transferred its whole Endo-Predict-Test business to Defendant 9 in 2024 (Exhibit VB 1). Defendant 9 has taken over the entire European business for the attacked embodiment with effect from 1 August 2024.

9 The contested embodiment is a multi-gene expression test for ER positive/HER2 negative breast cancer. It can accurately predict the risk of recurrence of breast cancer in 15 years (second-generation) or in 5 years (first-generation) (Exhibit VB 13). It comprises a method and components for performing the method, including a Test-Kit.

10 The Test-Kit comprises reagents and other material for performing a quantitative reverse transcription real-time polymerase chain reaction (hereinafter “RT-PCR” or “RT-qPCR”). It contains primers and probes which are suitable for the amplification of eight target genes, i.e., BIRC5, RBBP8, UBE2C, IL6ST, AZGP1, DHCR7, MGP and STC2, and three reference genes for normalization, i.e., CALM2, OAZ1 and RPL37A, by RT-PCR (Exhibits VB 15, VB 16).

11 The method of the attacked embodiment contains four steps (Exhibits VB 14, VB 15, VB 16). First, a formalin-fixed, paraffin embedded (hereinafter “FFPE”) breast cancer tissue sample, e.g., from a biopsy of a breast cancer patient, is provided. Upon ordering the attacked embodiment, e.g., by a clinician or pathologist, the sample is then sent to a Myriad partner laboratory. As a second step, this laboratory performs RNA isolation. Third, the sample is analysed by the laboratory by using the Test-Kit and a suitable PCR platform. The PCR platforms generate RT-PCR data files comprising the expression levels of the eight target genes and the three reference genes in the sample. In the fourth step, the laboratory uploads the RT-qPCR data files to the EndoPredict Report Generator (hereinafter “EPRG”), a web application operated on a server in Switzerland (Exhibit HE 10). Upon receiving the uploaded data, the application generates the “EndoPredict test result” (“EPclin Risk Class”), which is based on the “EPclin Risk Score”. The report is transmitted to the user via webserver (Exhibit VB 16).

12 The “Epclin Risk Score” is a linear combination of a molecular signature (“12-Gene Molecular Score”) with the size of the tumour and the pathological nodal status. The 12-Gene Molecular Score consists of a linear combination of the relative expression values of the eight target genes normalized to three reference genes (CALM2, OAZ1, RPL37A) (Exhibit VB 13, VB 16). The expression levels of the target genes are normalized to an average expression level of CALM2, OAZ1 and RPL37A:

predict distant recurrence (Supplementary Fig. S4). Relative expression of each GOI was assessed as delta cycle threshold (ΔC_t) values based on normalization on the average of 3 reference genes (*CALM2*, *OAZ1*, and *RPL37A*):

$$\Delta C_t(\mathrm{GOI}) = 20 - C_t(\mathrm{GOI}) + [C_t(CALM2) + C_t(OAZ1) + C_t(RPL37A)]/3 \quad \text{(A)}$$

13 The C_t value is the number of cycles required for reaching the threshold during exponential amplification. With each cycle, the number of copies is, at least in theory, doubled. The C_t value can thus be understood as the logarithm of the number of copies to the base 2. Since the C_t value is the exponent of the potency 2^{Ct}, subtracting the C_t value of one gene from the C_t value of another gene corresponds to dividing the number of RNA copies of one gene by the number of copies of the other gene, i.e., the ratio of the expression levels of the two genes.

14 By subtracting the C_t value of the (breast cancer related) gene of interest from the average C_t value of the three reference genes OAZ1, CALM2, and RPL37A, the average expression level of the reference genes (the reference expression level) is divided by the expression level of the target gene. The difference (ΔC_t) thus represents the ratio of these two expression levels.

MAIN STEPS OF THE PROCEEDINGS

15 The preliminary objection raised by the Defendants pursuant to Rule 19 RoP was rejected by order of the Judge-rapporteur on 14 February 2025. By order of 27 February 2025, the Judge-rapporteur ordered the Claimant to provide security for legal costs and other expenses to the Defendants in the amount of EUR 112,000.

REQUESTS OF THE PARTIES

A Action

16 The Claimant requests

I. to order the Defendants in the territories of the Republic of Austria, the Kingdom of Belgium, the Federal Republic of Germany, the French Republic, the Italian Republic, the Grand Duchy of Luxembourg, and the Kingdom of The Netherlands,

subject to a recurring penalty payment of up to EUR 250,000 to be determined by the Court and payable to the Court for each case of infringement of this order, immediately from the date of service of the judgment referred to in Rule 118.8 of the Rules of Procedure,

to cease and desist from

1. using and/or offering for use, in the territory of one or more of the States mentioned in item I. above

   a method for quantifying expression level of a target gene in a FFPE (formalin-fixed, paraffin embedded) tissue sample of human breast cancer tissues, comprising:

   1) synthesizing cDNA from RNA of a subject;
   2) performing real-time PCR to amplify the target gene and Endogenous Reference Gene OAZ1 using a pair of primers and/or probes with the cDNA serving as a template; and
   3) normalizing an expression level of the target gene to that of the endogenous reference gene of step 2);

   (direct infringement of claim 1 of EP 3 346 403)

in particular, wherein the Endogenous Reference Gene is amplified by a pair of primers and/or probes;

(direct infringement of claim 2 of EP 3 346 403)

in particular, wherein the Endogenous Reference Gene shows low expression levels, similar to most low-abundance intracellular transcripts;

(direct infringement of claim 3 of EP 3 346 403)

in particular the EndoPredict Breast Cancer Prognostic Test;

2. offering and/or supplying in the territory of one or more of the States mentioned in item I. above for use in the territory of one or more of these States:

   a pair of primers and/or probes, suitable for performing a method for quantifying expression level of a target gene in a FFPE (formalin-fixed, paraffin embedded) tissue sample of human breast cancer tissues, comprising:

   1) synthesizing cDNA from RNA of a subject;
   2) performing real-time PCR to amplify the target gene and Endogenous Reference Gene OAZ1 using said pair of primers and/or probes with the cDNA serving as a template; and
   3) normalizing an expression level of the target gene to that of the endogenous reference gene of step 2);

   (indirect infringement of claim 1 of EP 3 346 403)

   in particular, wherein the Endogenous Reference Gene is amplified by a pair of primers and/or probes;

   (indirect infringement of claim 2 of EP 3 346 403)

   in particular, wherein the Endogenous Reference Gene shows low expression levels, similar to most low-abundance intracellular transcripts;

   (indirect infringement of claim 3 of EP 3 346 403)

   in particular the EndoPredict-Test-Kit;

II. to order Defendants 1-9,

subject to a recurring penalty payment of up to EUR 2,000 to be determined by the Court and payable to the Court for each day of delay, within a period of 30 days from the date of service of the judgment and the date when the requirements referred to in Rule 118.8 of the Rules of Procedure have been met, whatever is later,

to provide Claimant with information in a complete and orderly list in an electronic form that can be analysed by means of EDP, broken down by month of a calendar year and by infringing product and infringing process, as to the extent to which they

(the Defendants) have committed the acts referred to in items I.1. and I.2. above since 17 June 2020, specifying

1. the origin and distribution channels of the infringing products and processes;
2. the quantities produced, manufactured, delivered, received and/or ordered, as well as the price obtained for the infringing products; and
3. the identity of any third person involved in the production and/or distribution of the infringing products or in the use of the infringing process;
4. the individual offers, broken down by the quantities, dates, prices and type designations as well as the names and addresses of the commercial recipients of the offers;
5. the advertising carried out, broken down by advertising medium, its circulation, distribution period and distribution area, in the case of Internet advertising the domain, the access figures and the placement periods;
6. the actual costs broken down by individual cost factors and the profit made,
7. whereby as proof of the information provided the corresponding receipts (i.e., invoices, alternatively delivery notes) are to be submitted in copy with the proviso that data to which the information owed does not relate and with regard to which there is a justified interest in confidentiality on the part of the Defendants may be covered or blacked out;
8. whereby this obligation only applies to Defendant 9 from 1 August 2024 on;

III. to declare that Defendants 1-9 individually and jointly have infringed EP 3 346 403 by committing the acts as specified in items I.1. and I.2;

IV. to declare that Defendants 1-9 are individually and jointly liable to compensate Claimant for all damages that incurred and will incur due to the acts specified in items I.1. and I.2. above and committed since 17 June 2020 as to be specified in separate damage proceedings, whereby this obligation only applies to Defendant 9 from 1 August 2024 on.

V. to order Defendants to pay the reasonable and proportionate legal costs of these proceedings and other expenses in a provisional amount to be specified in the course of these proceedings and to declare that Defendants are to pay any further reasonable and proportionate legal costs of these proceedings and other expenses as to be further specified in separate cost proceedings.

17 The Defendants request

I. the infringement action be dismissed;

II. the Claimant bears all legal costs and other expenses incurred by Defendants.

As auxiliary measures, they request that

any order or measure by the Court be subjected to a security to be given by Claimant to Defendants (whether by deposit or bank guarantee) in an amount of no less than EUR 3,000,000.

B Counterclaim for revocation

18 The Defendants request

I. EP 3 346 403 be revoked with effect to the territories of Austria (AT), Belgium (BE), France (FR), Germany (DE), Italy (IT), Luxembourg (LU) and The Netherlands (NL);

II. the Claimant bears all legal costs and other expenses incurred by Defendants.

As auxiliary measures, they request that

any order or measure by the Court be subjected to a security to be given by Claimant to Defendants (whether by deposit or bank guarantee) in an amount of no less than EUR 3,000,000.

19 The Claimant requests

I. to dismiss Defendants' Counterclaim for revocation of EP 3 346 403 in its entirety and to maintain the patent in suit as granted ("main request");

II. as a subsidiary request to request I., to dismiss Defendants' Counterclaim for revocation of EP 3 346 403 in part and maintain the patent in suit

1. ("auxiliary request 1") based on the proposed amendment of independent claim 1 of the patent in suit as follows (proposed amendment underlined):

1. A method for quantifying expression level of a target gene in a FFPE (formalin-fixed, paraffin embedded) tissue sample of human breast cancer tis-sues, comprising:

1) synthesizing cDNA from RNA of a subject;
2) performing real-time PCR to amplify the target gene and Endogenous Reference Gene OAZ1 using a pair of primers and/or probes with the cDNA serving as a template; and
3) normalizing an expression level of the target gene to that of the endogenous reference gene of step 2);

wherein said Endogenous Reference Gene shows lower expression levels than GAPDH and ACTB.

2. The method according to claim 1, wherein the Endogenous Reference Gene is amplified by a pair of primers and/or probes.

3. The method according to claim 1, wherein the Endogenous Reference Gene shows low expression levels, similar to most low-abundance intracellular transcripts.

2. in the alternative ("auxiliary request 2") based on the proposed amendment of independent claim 1 of the patent in suit, i.e., claim 1 as granted in combination with claim 3 as granted, as follows (proposed amendment underlined, deletions crossed-out):

1. A method for quantifying expression level of a target gene in a FFPE (formalin-fixed, paraffin embedded) tissue sample of human breast cancer tis-sues, comprising:

1) synthesizing cDNA from RNA of a subject;
2) performing real-time PCR to amplify the target gene and endogenous reference gene OAZ1 using a pair of primers and/or probes with the cDNA serving as a template; and
3) normalizing an expression level of the target gene to that of the endogenous reference gene of step 2);

wherein the Endogenous Reference Gene shows low expression levels, similar to most low-abundance intracellular transcripts.

2. The method according to claim 1, wherein the endogenous reference gene is amplified by a pair of primers and/or probes.

~~3. The method according to claim 1, wherein the Endogenous Reference Gene shows low expression levels, similar to most low-abundance intracellular transcripts.~~

3. in the further alternative ("auxiliary request 3") based on the proposed amendment of independent claim 1 of the patent in suit, i.e., claim 1 in the proposed amendment according to auxiliary request 1 in combination with claim 3 as granted, as follows (proposed amendment underlined, deletions crossed-out):

1. A method for quantifying expression level of a target gene in a FFPE (formalin-fixed, paraffin embedded) tissue sample of human breast cancer tissues, comprising:

1) synthesizing cDNA from RNA of a subject;
2) performing real-time PCR to amplify the target gene and endogenous reference gene OAZ1 using a pair of primers and/or probes with the cDNA serving as a template; and
3) normalizing an expression level of the target gene to that of the endogenous reference gene of step 2);

wherein the Endogenous Reference Gene shows low expression levels, similar to most low-abundance intracellular transcripts, and shows lower expression levels than GAPDH and ACTB.

2. The method according to claim 1, wherein the Endogenous Reference Gene is amplified by a pair of primers and/or probes.

~~3. The method according to claim 1, wherein the Endogenous Reference Gene shows low expression levels, similar to most low-abundance intracellular transcripts.~~

4. The Claimant requests that auxiliary requests 1-3 be dealt with in the order as stated above and in accordance with their numbering.

5. In case the Court maintains the patent in suit in the form of one of the auxiliary requests, it hereby requests that:

a. the Counterclaim for revocation be dismissed to the extent that the patent in suit is upheld;

b. to render judgment against Defendants in the infringement action as requested in the Statement of claim, however, modified to align with the claim scope of the respective auxiliary request being upheld.

III. to order Defendants to pay the reasonable and proportionate legal costs of the Counterclaim for revocation and other expenses in a provisional amount to be specified in the course of these proceedings and to declare that Defendants are to bear any further reasonable and proportionate legal costs of the Counterclaim for revocation and other expenses as to be further specified in separate cost proceedings.

POINTS AT ISSUE

A Claim Construction

20 The parties disagree on the interpretation of feature 3 of claim 1.

21 In view of the Claimant, the (raw) target gene expression level obtained by the RT-PCR of step 2) is according to step 3) set in relation to a reference value that is partly or fully based on the expression level of OAZ1. The Claimant argues that the claim merely requires that OAZ1 is used as a reference gene for normalizing the target gene(s) expression level(s) but that it is not limited to the use of exclusively OAZ1 as a reference gene. The Claimant asserts that it is obvious to the skilled person that the use of OAZ1 in combination with further useful reference genes to normalize the expression level(s) of the target gene(s) is encompassed by the scope of claim 1 of the patent and that this can even provide advantages.

22 According to the Defendants, claim 1 requires that the expression level of the target gene is normalized by the expression level of a single gene, namely OAZ1, but not by using multiple reference genes or to an average expression level of an arbitrary – and unlimited – number of control genes.

B Infringement

23 In the opinion of the Claimant, the contested embodiment fulfils all features of claim 1 and subclaims 2 and 3 of the patent in suit. This also applies to feature 3 of claim 1. In the Claimant's view, the fact that the target genes are normalized not only by using OAZ1 but also by using other reference genes does not take the contested embodiment outside the scope of protection.

24 During the oral hearing, the Claimant argued that claim 1 should also be considered realised if feature 3 is understood to mean that only OAZ1 may be used as the sole reference gene. The calculation method of the contested embodiment corresponds mathematically to a calculation in which the bracket is resolved, meaning that the expression level of the target gene is first set in relation to the expression level of each individual reference gene before calculating the average value of the three normalised expression levels. According to the Claimant, this calculation leads to the same result.

25 The Defendants contest using the technical teaching of claim 1. When applying the attacked embodiment, the expression levels of the target genes are not normalized to the expression level of OAZ1. Instead, the levels are normalized to a different expression level, namely the arithmetic mean of the expression levels of OAZ1, CALM2, and RPL37A. According to the Defendants this expression level is different from the expression level of OAZ1. Regarding the argumentation of the Claimant in the oral hearing the Defendants replied that this is late filed and that they cannot respond. They stated that they are unable to assess whether the mathematical rule asserted by the Claimant was correct and would apply in the present case. The Defendants also pointed out that the contested embodiment performs only one step of normalizing.

26 The Defendants are further of the opinion that the realisation of claim 1 also fails because the contested embodiment does not fully carry out the claimed method in the territory of the

Contracted Member States because the step of normalizing is (undisputed) performed on a server in Switzerland.

27 In addition, the Defendants criticise that the Claimant's submission regarding the alleged infringements by the Defendant 8 is unsubstantiated. In the Defendants view, the mere control of a company group through corporate ownership and voting rights is not sufficient to be regarded as an “infringer”. The Defendants are of the opinion that the other circumstances put forward by the Claimant were all insufficient. According to the Defendants, there is no active (controlled) behaviour of Defendant 8 that could be considered an infringement.

C Legal consequences infringement action

28 In the Defendants' view, the legal consequences sought by the Claimant for the (alleged) use of the technical teaching of claim 1 go too far.

29 In the opinion of the Defendants, it would be disproportionate to grant an injunction preventing the marketing and use of the attacked embodiment because they are pursuing license negotiations in good faith and the effects of an injunction on patients speak against it.

30 The Defendants further assert that Claimant’s request for disclosure of material information is excessive and unfounded to the extent it goes beyond what is mandated by Art. 67 UPCA. According to the Defendants, in any event, Claimant lacks any legal or legitimate interest in obtaining an order to provide information on sales data which it already (undisputed) received from Defendant 8 (Exhibit HE 21).

31 Regarding the requested declaration of the obligation to compensate damages, the Defendants are of the opinion that the UPC has no competence to decide on (allegedly) assigned claims. In any case, at least to the extent the complaint concerns claims for alleged use made before Claimant was recorded as owner of the patent in suit in the national patent registers, Claimant cannot rely on any presumption arising from national patent registers, but will need to establish that not only the patent in suit but also any damages claims predating such assignment were indeed materially assigned. The Defendants dispute that the Claimant had acquired ownership of the patent in suit and the associated claims (for damages) through the Patent Purchase Agreement (Exhibit VB 29) and the “Patent Assignment Agreement”.

32 Furthermore, the Defendants contest a culpability before warning letters of June 2024 (Exhibit VB 2, VB 2.1, VB 2.2, VB 3). The Defendants started (uncontested) to market the attacked embodiment before the patent in suit was granted and before the application for the patent was filed (2018). Therefore – the Defendants – even a broad freedom-to-operate analysis before the launch of the product could have had no impact on the launch of the contested embodiment. According to the Defendants it is completely unrealistic to assume that even in a specialized technical field, market players would be able to constantly monitor patent applications for their grant date and assess their relevance on a recurrent basis.

33 Moreover, the Defendants are of the opinion that the five-year limitation stated in Art. 72 UPCA "without prejudice to Art. 24 (2) and (3) UPCA" leads in the present case to the application of the German and Austrian Law. Both stipulate a regular limitation period of three years. The Defendants are of the opinion that at least as far as any asserted infringement of the German or Austrian national part of the patent in suit is concerned, Claimant thus cannot claim any damages that may have arisen before 1 January 2021 or 24 July 2021, respectively. This also applies if considering that any potential hardship should be avoided regarding acts committed before the entry into force of the UPCA on 1 June 2023.

34 Finally, the Defendants submit that any preliminary enforcement of a judgment, in particular regarding an injunction, must be conditional on a provision of security. In the Defendants' view, the security for enforcement must amount to EUR 3 million.

35 The Claimant refutes all the Defendant's objections in detail.

D Counterclaim

Added Matter

36 The Defendants argue that the patent is invalid because its subject-matter extends beyond the content of the parent application as filed WO 2008/078969 (Exhibit HE 4).

37 The Defendants are of the opinion that Exhibit HE 4 does not disclose a method for quantifying the expression level of a target gene "in an FFPE tissue sample of human breast cancer tissues". According to the Defendants such a method is neither explicitly disclosed nor the clear and unambiguous consequence of what is explicitly mentioned in Exhibit HE 4. In the Defendants' view, the application as filed neither generically nor specifically refers to a target gene in a tissue sample of human breast cancer. Furthermore, the claimed method is not implicitly disclosed either.

38 Even if there was basis in Exhibit HE 4 for a method for quantifying the expression level of a target gene in an FFPE tissue sample of a human breast cancer, according to the Defendants, it would not be directly and unambiguously derivable from Exhibit HE 4 to normalize the expression level of such a target gene in this tissue to the expression level of OAZ1. In the Defendant's view, there is nothing to this regard in the description and experimental examples of the application as filed. Moreover, according to the Defendants, there is no pointer to OAZ1 for the use as reference gene in FFPE breast cancer samples.

39 In the Defendants´ view, the selection of OAZ1 in combination with FFPE breast cancer samples also constitutes an unallowable two-fold selection from independent lists, OAZ1 from the list of endogenous reference genes and FFPE breast cancer samples from the list of FFPE samples.

40 Finally, according to the Defendants, original claim 25 requires two separate reactions in step 2), i.e., (i) performing RT-PCT to amplify the target gene, (ii) and then performing RT-PCR to amplify the ERG. The same applies to original claim 24. However, claim 1 of the patent does not reflect these separate reactions and encompasses methods wherein the two reactions are performed simultaneously, e.g., in a multiplex PCR reaction. According to the Defendants, there is no basis for the generalization in the original application documents.

41 The Claimant argues that claims 25 and 16 and page 73, line 7, to page 74, line 1 of Exhibit HE 4 disclose all features of claim 1 of the patent in suit in combination other than the sample to be used in the claimed method. In view of the Claimant, the FFPE tissue sample of human breast cancer tissues employed in the method of granted claim 1 is directly and unambiguously disclosed on page 139, lines 1 to 4. Further, page 138, line 20, to page 139, line 15 discloses a qRT-PCR method to amplify the endogenous reference gene OAZ1 in FFPE tissue samples of human breast cancer tissues using a pair of primers and/or probes with the cDNA serving as a template. According to the Claimant it doesn´t matter that the feature “FFPE tissue samples of human breast cancer tissues” is not inextricably linked to the experimental details described on page 138, line 20, to page 139, line 15 of Exhibit HE 4. In its view, the skilled person will routinely adjust these experimental details.

42 The Claimant further takes the view that OAZ1 is singled out in the application as filed as the most suitable reference gene. According to the Claimant, this follows from the explanations on page 72, line 16 to page 73, line 5 in combination with the disclosure on page 141, lines 9-15 and Experimental Example 7 because it is emphasised that OAZ1 had a high expression stability and the lowest expression level. In conclusion, according to the Claimant, OAZ1 is singled out in the application as filed as the only novel endogenous reference gene showing a lower expression level than all traditional reference genes tested. Therefore, in Claimants opinion, the application as filed provides a clear pointer to use OAZ1 as a particularly preferred reference gene for normalizing target gene expression level(s). The Claimant asserts that Experimental Example 6 doesn´t contradict this. In its opinion it is not relevant to the claimed invention because it deals with gene amplification, which is a different matter than quantification of gene expression levels.

43 The Claimant further submits that “breast cancer” refers to one of three specific embodiments of FFPE tissues samples disclosed in Exhibit HE 4, i.e., breast cancer, stomach and ovary FFPE tissue samples Therefore, in Claimant´s view, the use of OAZ1 in the assessment of FFPE breast cancer tissue samples follows from the combination of a particularly preferred “singled out” embodiment with a further specific embodiment disclosed in the application as filed in the same technical context. Accordingly, in the opinion of the Claimant, the combination of OAZ1 and breast cancer does not result from a selection from two lists.

44 Regarding step 2) of original claim 25 the Claimant is of the opinion that the omission of the expression “and then” in step 2) of granted claim 1 and the corresponding linguistic adjustments do not add matter. According to the Claimant, the application as filed does not

present the performance of separate or consecutive PCR reactions as “essential”. There is – so the Claimant – also no described advantage or function of performing separate or consecutive PCRs to amplify the target gene(s) and the endogenous reference gene(s) in the application as filed. In Claimant´s view, the skilled person understands therefrom that a separation of PCRs does not contribute to, and is thus not relevant for, the technical teaching of the invention as disclosed in the original application. In other words, the skilled person would not consider performing separate or consecutive PCRs as necessary for achieving the overall aim and effect of the invention. The Claimant further argues that the order of events in step 2) in claim 25 of the application as filed is also not inextricably linked to the remaining features of this claim. Therefore, the Claimant is of the opinion that the skilled person immediately recognizes that it is irrelevant for normalizing the expression level of the target gene(s) in step 3) whether the expression levels of the target gene(s) and reference gene(s) have been determined in separate reactions or not.

Priority

45 The Defendants are of the opinion that the priority application (Exhibit HE 5) does not directly and unambiguously disclose the same invention as is claimed in granted claim 1 of the patent in suit. According to the Defendants, the priority claim therefore is invalid

46 The Claimant disagrees with Defendants’ allegation that the priority of the patent in suit is invalid. In its view any discussion on priority entitlement is obsolete and irrelevant because an invalid claim to priority is not a ground for revocation and none of the (alleged) grounds for invalidity put forward by the Defendants are valid.

Insufficient disclosure

47 According to the Defendants the patent in suit does not disclose the claimed subject matter in a manner sufficiently clear and complete for it to be carried out by a person skilled in the art.

48 The Defendants argue that there is no disclosure or example in the patent that would make it credible that OAZ1 is stably expressed in the relevant tissue, i.e., in FFPE human breast cancer tissues. In Defendants opinion, the severe lack of information in the patent throws serious doubts on the suitability of OAZ1 as a reference gene for normalizing of expression data of a target gene in FFPE breast cancer tissue. In the Defendant´s view, it is equally highly doubtful whether normalizing to OAZ1 as the only reference gene would provide any useful results due to copy number variations (CNVs).

49 The Claimant is of the opinion that an average skilled person has sufficiently clear and complete guidance on how to work the invention over the full scope as claimed. According to the Claimant, the patent provides ample evidence that OAZ1 is a suitable reference gene for normalizing gene expression levels in FFPE breast cancer tissue samples. In the opinion of the Claimant, the patent provides evidence that OAZ1 has ideal characteristics as reference gene for the claimed method. Firstly, it is demonstrated that OAZ1 is universally expressed and secondly that it even shows a particularly low variation in expression level (i.e., high expression stability) across a large spectrum of different tissues. The Claimant further states

that the use of OAZ1 as single reference gene provides useful results. OAZ1 shows invariant expression in FFPE breast cancer tissue samples. According to the Claimant, the expression of OAZ1 is not affected by potential genomic aberrations such as CNVs.

Inventive step

50 In view of the Defendants, the subject-matter of the patent lacks an inventive step. According to the Defendants the claimed teaching is obvious in a combination of [redacted] et al., Expression of glucocorticoid and progesterone nuclear receptor genes in archival breast cancer tissue. Breast Cancer Res. 2003; 5(1):R9-12 (Exhibit HE 14, hereinafter: [redacted] and [redacted] et al., Evidence based selection of housekeeping genes. PLoS One. 2007 Sep 19;2(9):e898 (Exhibit 16, hereinafter: de [redacted] Furthermore, the Defendants are of the opinion that the claimed teaching is obvious in light of Paik et al., A multigene assay to predict recurrence of tamoxifen-treated, node-negative breast cancer. N [redacted] J Med. 2004 Dec 30; 351(27):2817-26 (Exhibit HE 17, hereinafter [redacted] and [redacted] (Exhibit HE 16) and obvious from a combination of [redacted] et al., Agreement in breast cancer classification between microarray and quantitative reverse transcription PCR from fresh-frozen and formalin-fixed, paraffin-embedded tissues. Clin Chem. 2007 Jul;53(7):1273-9, and C (Exhibit HE 20) and [redacted] et al. (Exhibit HE 16).

51 According to the Claimant it was not obvious for the skilled person, seeking to provide improved means and methods for quantifying the expression level of a target gene in FFPE breast cancer tissue samples, to arrive at the invention as characterized in the claims of the patent in suit. In the opinion of the Claimant, the claimed subject-matter is inventive regardless of whether [redacted] (Exhibit HE 14), [redacted] (Exhibit HE 17) or [redacted] (Exhibit HE 20) are used as a starting point: (i) none of the cited prior art provides the skilled person with any incentive to use a weakly expressed gene, let alone OAZ1, as a reference gene in FFPE tissue samples; (ii) the skilled person had no reasonable expectation of success that OAZ1 would be a suitable or even advantageous reference gene for normalizing target gene expression level(s) in FFPE breast cancer samples, in particular, such expectation cannot be derived from [redacted] (Exhibit HE 16) because it fails to disclose OAZ1 as suitable for use with FFPE samples; (iii) moreover, the skilled person would not have implemented OAZ1 as a reference gene for normalizing and quantifying gene expression in FFPE breast cancer tissue samples, because the skilled person faced severe technical difficulties. The skilled person would not have used OAZ1 in FFPE breast cancer samples with a reasonable expectation of success to obtain useful results.

E Amendment of the Patent

52 If the Court does not dismiss the Counterclaim for revocation, the Claimant requests, in the alternative, that the patent be amended in accordance with the above-mentioned Auxiliary Requests 1- 3, Regel 30 RoP. The Claimant requests that auxiliary requests 1-3 be dealt with in the order as stated above and in accordance with their numbering.

53 Regarding each of the Auxiliary Requests, the Claimant argues that the requested amendments satisfy the requirements of Art. 84 and 123(2),(3) EPC and why the proposed amended claims are valid and why they are infringed.

54 According to the Defendants, the amendment introduced in claim 1 of Auxiliary Request 1 renders its subject matter unclear and is not supported by the application as filed. Furthermore, in Defendants´ view, the amendment of the Auxiliary Request 1 and 2 cannot overcome the objections raised against claim 1 of the Main Request on added matter, sufficiency of disclosure, and inventive step. The considerations as put forward for the claims as granted fully apply to Auxiliary Request 1 and 2. About Auxiliary Request 3 the Defendants argue that the combined features from both approaches are, already from Claimant's own submissions, inherent, and thus cannot contribute to the inventiveness of the alleged invention.

F Reference

55 In addition, reference is made to the submissions of the parties and the recording of the oral hearing.

GROUNDS FOR THE DECISION

A Scope of the patent in suit

I. Patent and its technical background

56 After the introductory words of the description, the patent in suit relates to a data processing and analysis method of gene expression data for identifying endogenous reference genes and a composition for the quantitative analysis of gene expression, comprising a pair of primers and/or probes useful in the amplification of the identified endogenous reference genes (para. [0001] of the patent description; hereinafter, only the paragraph numbers are cited).

57 A gene is the basic physical and functional unit that carries genetic information required for any organism. It is a DNA molecule which encodes a protein. For expressing the protein, a messenger RNA (hereinafter “mRNA”) molecule is transcribed from the gene and subsequently translated into the amino acid sequence of the protein encoded by the gene.

58 The activity of a gene is referred to as “gene expression”. The expression level of a gene therefore reflects the activity of the gene. Since certain genes have a different expression level in cancer cells than in healthy cells, quantifying their expression level is an important tool in cancer diagnostics or therapy. The expression level of a gene in a cell or a tissue can be determined by measuring the amount of mRNA molecules transcribed from the gene. In other words, the expression level of a gene in a cell/tissue corresponds to the amount of mRNA copies of the gene in the cell/tissue. As described in paragraphs [0003] and [0004] of the patent, several methods for measuring RNA were known, among others RT-qPCR or RT-PCR.

59 The expression level of a gene as measured by this method is influenced by several factors, in particular the size and condition of the sample and the experimental conditions, including sample treatment, developmental stage and pathological stage. Consequently, the gene expression levels measured in different samples or obtained in different laboratories cannot be simply compared to each other. However, it is desirable to measure or quantify the true expression level of a target gene independently of experimental variation and to enable comparability between different samples. Therefore, a normalization strategy is required to control for these experimental variations. A widely used normalization strategy for accurate comparison of gene expression between different samples is to use (endogenous) reference genes. The patent explicitly refers in paragraph [0003] to [redacted] et al., Genome Biol 3(7), p. RESEARCH0034, 2002”. According to the patent, it was known to use “housekeeping genes” as reference for normalization, i.e., genes that are involved in basic cellular functions and thus expressed in most cells/tissues (paras. [0002] – [0004]).

60 According to the patent, “traditional reference genes” such as glyceraldehyde-3-phosphate dehydrogenase (hereinafter "GAPDH") and β-actin (hereinafter "ACTB") have been used without proper validation, assuming that they are expressed at constant levels across different

samples, irrespectively cell or tissue type and are not regulated by experimental treatment (para. [0003]). However, as stated in the patent, it is necessary to select proper endogenous reference genes. Because they are essential for accurate measurement in qRT-PCR. In contrast, the use of inappropriate reference genes in the relative quantification of gene expression may result in biased expression profiles. This concern has, according to the patent in suit, already been raised by many researchers (para. [0004]).

61 The patent further states that with the acknowledgement of the importance of the proper validation of “traditional reference genes” and the identification of more suitable reference genes, a number of studies have been undertaken to select the most suitable genes among commonly used reference genes in specific experimental conditions, or to identify novel genes, which are superior to the traditional genes that are universally used for mRNA quantification. However, most of the previous studies have been focused on the selection (validation) of the most stable genes among commonly used reference genes in specific experimental systems or a given set of limited tissue samples (para. [0005]). In addition, novel endogenous reference genes have been found mostly based on microarray data. However, the patent in suit also considers these reference genes to be disadvantageous. As it is, according to the patent, well-known, the microarray technique has some problems and limitations (errors) due to the potential for inaccurate cross hybridization between probes and unintended transcripts, the potential for differences in hybridization efficiency between probe sets, and the potential for the incorrect annotation of transcripts (para. [0006]).

62 Furthermore, the patent states that, even if an ideal endogenous reference gene does not exist, it is possible to find a more ideal endogenous reference gene applicable to most experimental conditions than traditional reference genes through various, large gene expression data (para. [0007]).

63 In paragraph [0009] the patent concludes that it is therefore an object to provide a method of processing and analysing gene expression data, with a statistical concept introduced thereinto, to identify endogenous reference genes which are superior to “traditional reference genes” in terms of expression stability across a wide range of samples, thus being universally useful for the normalization of gene expression, and a composition for the quantitative analysis of gene expression, comprising a pair of primers and/or probes useful in the amplification of the identified endogenous reference genes.

64 Claim 1 protects a method having the following features:

0. Method for quantifying expression level of a target gene in a FFPE (formalin-fixed, paraffin embedded) tissue sample of human breast cancer tissues, comprising:

1. 1) synthesizing cDNA from RNA of a subject;

2. 2) performing real-time PCR to amplify the target gene and Endogenous Reference Gene OAZ1 using a pair of primers and/or probes with the cDNA serving as a template; and

3. 3) normalizing an expression level of the target gene to that of the endogenous reference gene of step 2).

II. Claim construction

65 Some of these features require explanation.

1. Legal framework for claim interpretation

66 In accordance with Art. 69 (1) EPC and the Protocol on its interpretation, a patent claim is not only the starting point, but the decisive basis for determining the scope of protection of a European patent. The interpretation of a patent claim does not depend solely on the strict, literal meaning of the wording used. Rather, the description and the drawings must always be used as explanatory aids for the interpretation of the patent claim and not only to resolve any ambiguities in the patent claim. However, this does not mean that the patent claim merely serves as a guideline and that its subject-matter also extends to what, after examination of the description and drawings, appears to be the subject-matter for which the patent proprietor seeks protection (Court of Appeal, UPC_CoA_335/2023, Decision of 26 February 2023 in conjunction with Decision of 11 March 2024 – NanoString v 10x Genomics; UPC_CoA_1/2024, Order of 13 May 2024 – VusionGroup v Hanshow; UPC_CoA_768/2024, Order of 30 April 2025 – Insulet v EOFlow, UPC_CoA_405/2024, 19 June 2025 – Alexion/Amgen; UPC_CoA_579/2025, Order of 7 November 2025 – OTEC/STEROS). Rather, Art. 69 EPC and its Protocol establish a primacy of the claims. The underlying legal principle is legal certainty.

67 These principles for interpreting a patent claim apply both to the question of patent infringement and to the question of validity. The understanding of a claim by the skilled person must be consistent for all purposes of the evaluation of infringement and validity (Court of Appeal, UPC_CoA_335/2023, Order of 26 February 2024 – NanoString v 10x Genomics).

68 The interpretation of a patent claim is a matter of law (Court of Appeal UPC_CoA_405/2024, 19 June 2025 – Alexion/Amgen). Therefore, the Court cannot leave the judicial task of interpreting the patent claim to an expert but must construe the claim independently (Court of Appeal, UPC_CoA_768/2024, Order of 30 April 2025 – Insulet v EOFlow). It is true that the understanding of the person skilled in the art of the terms used in the patent claim in the context of the patent claim as a whole and considering the description and drawings, is the basis for claim construction. But this does not mean that the Court must follow a party's expert´s opinion. The skilled person is a notional entity that cannot be equated with any real person in the technical field of the invention. The decisive factor is not the individual knowledge

and abilities of a person, but rather the general specialist knowledge that is customary in the relevant field of technology, as well as the average knowledge, experience, and abilities in this specialist field. It is for the Court, not the expert, to assess these circumstances (Court of Appeal, UPC_CoA_768/2024, Order of 30 April 2025 – Insulet v EOFlow).

2. Skilled person

69 The Court agrees with the Parties that the skilled person for the patent in dispute is a molecular biologist or a team of molecular biologists and/or a clinician or a team of clinician's familiar with genomic and/or prognostic testing, in particular of pathological samples with experience in gene expression analysis including the related statistical methods.

3. Claim 1

70 Based on this, the Court construes claim 1 as follows:

a) Feature 0

71 According to feature 0 the claimed method is a method for quantifying expression level of a target gene in a formalin-fixed, paraffin embedded (hereinafter: FFPE) tissue sample of human breast cancer tissues. The method therefore serves a specific purpose ("for").

72 FFPE tissue samples are well-known and broadly available. They are a very important tissue source for genomic prognostic or predictive tests. When a tumour from a patient is removed, a sample from the tumour is routinely fixed with formalin and embedded in paraffin to conserve the tissue for potential future analyses.

73 The target gene can be any gene of interest, such as, inter alia, a breast cancer-related gene that may serve as a predictive marker for breast cancer growth or recurrence. The human breast cancer is not particularly limited and includes any (sub)type of breast cancer as well as any stage of the various (sub)types of breast cancer. Accordingly, a FFPE tissue sample of human breast cancer tissues can be any sample comprising any amount or fraction of any human breast cancer tissue that has been removed from a human being.

74 In accordance with feature 0, the claimed method for quantifying expression level of a target gene comprises the following three steps.

b) Feature 1

75 Step 1) of the claimed method is synthesizing complementary DNA (cDNA) from RNA of a subject.

76 As already described, during gene expression, a gene is transcribed into RNA, for example, mRNA. Hence, the expression level of a gene can be quantified by measuring the amount of mRNA transcribed from the gene. A routine technique for measuring an RNA is RT-PCR (para. [0004]). In this technique, a reverse transcriptase enzyme is routinely used to first synthesize cDNA by using RNA as a template. The level of gene expression corresponds to the amount of RNA molecules transcribed from the gene which in turn corresponds to the amount of cDNA molecules synthesized from these RNA molecules.

c) Feature 2

77 Step 2) of the claimed method is performing RT-PCR to amplify the target gene and endogenous reference gene OAZ1 using a pair of primers and/or probes with the cDNA serving as a template.

78 In line with this step, the RT-PCR is used to amplify both target genes, i.e. a certain sequence within the cDNA molecules obtained in step 1), that is contained in a breast cancer-related gene, and OAZ1, i.e., a certain sequence within the cDNA molecules that is contained in the OAZ1 gene. In this way, an expression level of the target gene and an expression level of OAZ1 is obtained. As the term “endogenous reference gene” in feature 2 makes clear, obtaining the expression level of OAZ1 serves to use OAZ1 as an endogenous reference gene. This means that OAZ1 is used for normalization the expression level of the target gene according to feature 3 (see below).

79 A pair of primers (nucleic acid) and/or probes (nucleic acid) are routinely used for amplifying a target DNA in a RT-PCR (paras. [0048], [0088]), the first one to initiate the reaction and the latter for detecting the amplified product. Since the target gene can be any gene of interest (in a FFPE tissue sample of human breast cancer tissues), the pair of primers for amplifying the target gene are not structurally defined. The same applies regarding OAZ1. The primers for amplifying OAZ1 are not limited to a specific nucleotide sequence.

80 Feature 2 leaves open whether the amplification of the target gene and the endogenous reference gene OAZ1 by performing RT-PCR takes place “jointly” or parallel or whether the target gene is amplified first and then the endogenous reference OAZ1 by means of RT-PCR, so that separate or consecutive RT-PCR are performed.

d) Feature 3

81 Step 3) of the claimed method is normalizing an expression level of the target gene to that of the endogenous reference gene of step 2).

82 Normalization means compensating for variations and experimental errors or variable experimental factors by using an endogenous reference gene to determine the relative amount of a target gene and ensure the comparability of different tissue samples. Distortions that can

arise, for example, from different operating conditions or laboratory equipment are thus reduced to correctly quantify the actual gene expression of the target gene (paras. [0002] ff., [0023]). This is essential for accurate and robust measurement of an expression level of the target gene and - at the end - for a correct diagnostic and/or therapy.

83 The required normalizing should not be carried out in any way, but in accordance with feature 3 by normalizing the expression level of the target gene “to that of the endogenous reference gene of step 2)”. Feature 3 therefore refers to step 2) of the claimed method. As in step 2) only OAZ1 is expressly mentioned as endogenous reference gene, step 3) thus refers to OAZ1 as endogenous reference gene. According to the clear wording, its expression level must therefore be used for normalizing the expression level of the target gene. In principle, the parties also agree on this.

84 The Court cannot agree with the Claimant´s view that feature 3 suffices that the target gene expression level obtained by the RT-PCR of step 2) is set in relation to a reference value that is “partly based” on the expression level of the endogenous reference gene OAZ1. Rather, the technical teaching of claim 1 requires that the expression level of the target gene is normalized only to the expression level of OAZ1.

85 It is true that claim 1 is directed to a method for quantifying the expression level of a target gene in a FFPE tissue sample of human breast cancer tissues, “comprising” steps 1) to 3). The Court also agree with the Claimant that the term “comprising” in feature 0 in principle does not preclude further method steps being taken in the course of the claimed method. Finally, it is true that the claim is not limited to a specific calculation method.

86 However, the possibility of providing for further method steps does not alter the fact that the method steps specified in claim 1 must be carried out. Even if a further step involving a further reference gene may not excluded by claim 1, the endogenous reference gene of step 2) as referenced in step 3) would remain OAZ1 and OAZ1 only. No other reference gene is mentioned in step 2). Besides this, the singular is used in step 3), which requires normalizing of the expression level of the target gene to “that” of the endogenous reference gene. This is consistent with the fact that only a single endogenous reference gene is named in step 2), namely OAZ1. Consequently, there must be a normalization of the expression level of the target gene to the expression level of this endogenous reference gene OAZ1 only.

87 That several or multiple reference genes are not used to normalize the expression level of the target gene, but only OAZ1 is to be used as a reference gene in the claimed technical teaching can also be inferred by a person skilled in the art from the technical function of feature 3.

88 The use of reference genes for normalization was known in the prior art, with various genes having been used as reference genes, among others the “traditional reference genes” GAPDH and β-actin (paras. [0003], [0023]). However, about the “traditional reference genes” used, the patent in suit considers it disadvantageous that they have not been proper validated (para. [0003]) and may vary among different tissues and cell types and can be regulated by

experimental conditions (para. [0004]). This is particularly problematic because the use of inappropriate reference genes is known to lead to incorrect results or biased expression profiles. The patent in suit emphasises in that regard that the selection of a proper gene is essential for accurate measurement in qRT-PCR (para. [0004]). It also points out that several studies have already been undertaken to select the most suitable genes among commonly used reference genes in specific experimental conditions, or to identify novel genes, which are superior to the "traditional reference genes" that are universally used for mRNA quantification (para. [0005]). Although the patent criticises previous studies, this criticism does not relate to the aim of the studies as such. On the contrary, the patent explicitly states that it is interested in the use of a "more ideal" endogenous reference gene applicable to most experimental conditions (para. [0007]) or the use of reference genes which are "superior" to previously used genes and show more stable expression across a wide range of samples, thus being universally useful for the normalization of gene expression, rather than being limited for use on specific tissue samples or in specific studies (paras. [0008], [0009]).

89 On this basis, the objective technical problem of claim 1 is to provide a method for quantifying expression level of a target gene in FFPE human breast cancer tissues in which a reference gene with higher expression stability than "traditional reference gene" across a wide range of samples is used.

90 The description of the patent in suit states that there are several genes known from public databases which are more suitable for the normalizing in this sense. The patent identifies (among 2,0887 genes) 13 novel endogenous reference genes and explains that they show higher expression stability with lower expression levels across a wide range of samples than "traditional reference genes" and that they therefore are suitable for the normalization of universal genes having relatively low expression levels (para. [0017], see also paras. [0037], [0038], [0039], [0042], [0044], [0047], [0096], Table 9). In consideration of the fact that the majority of intracellular transcripts are expressed in low abundance, the patent recommends a reference gene with an expression level similar to that of a target gene, so that the measurement can be carried out on the same linear scale (paras. [0039], [0045]). The patent concludes that therefore the endogenous reference genes identified in the patent are believed to be more suitable and widely used because they show relatively lower expression and lower variability than the "traditional reference genes" (para. [0045]). Furthermore, the patent describes that the 13 novel endogenous reference genes were analysed for expression in 60 FFPE samples using qRT-PCR in order to examine the possibility of applying them to tissues in which high RNA degradation occurs (para. [0098]). All the genes, except for one (DIMTL), were found to be expressed in all samples. Despite difference in the type of samples used in the experiments, almost all genes, except for several genes, were observed to be expressed in a pattern similar to that observed in 48 samples, including frozen human tissue and cancer cell lines. According to the patent, these results indicate that the novel endogenous reference genes disclosed in the patent can be applied to gene expression in FFPE samples (para. [0098]).

91 Although the patent identifies in its description 13 (or 12) novel endogenous reference genes which, according to the patent, are more stably expressed than the “traditional reference genes”, claim 1 mentions only one of them, namely OAZ1. Consequently, a selection from the identified novel endogenous reference gens has been made in claim 1 in favour of a specific endogenous reference gene, OAZ1. However, the use of the other endogenous reference genes identified in the description has no bearing on the claim.

92 This leads the person skilled in the art to understand that, according to the teaching of the patent, the sole use of OAZ1 in normalizing the expression level of the target gene is the solution to the above-mentioned technical objective. OAZ1 is the “superior” reference gene in the sense of the patent, the use of which achieves the technical purpose of normalization according to feature 3. Its use serves to obtain the true expression level of a target gene independently of experimental variation and to enable comparability between different samples. It leads to more reliable and unbiased measurement results. The use of other or additional endogenous reference genes is not necessary to achieve this according to the claimed teaching.

93 In accordance with the selection in claim 1, OAZ1 is described in the patent specification as “The endogenous reference gene used in the present invention is OAZ1.” (par. [0030], see also paras. [0038], [0040], [0042], [0044], [0045], [0047]). The other identified genes, however, are not named in this way. Furthermore, OAZ1 is explicitly mentioned in connection with expression stability (paras. [0042], [0044], [0045], Fig 7) and low expression level (para. [0040], Fig. 6). Further, the patent states that OAZ1 had the lowest expression level in the above mentioned 48 samples (para. [0092]). The person skilled in the art recognises that the selection and use of OAZ1 is linked to this circumstance. This means that OAZ1 also fulfils the requirement for the above-mentioned recommendation. It is described as the endogenous reference gene with a low expression level that is similar to the expression level of a target gene.

94 Another point should be noted. In the general description of the state of the art, the patent refers to [redacted] et al., Genome Biol 3(7), p. RESEARCH0034, 2002” (para. [0003]). This paper not only describes that the use of the expression level of a single control gene as reference value for normalisation purposes is known. It is also shown that normalizing an expression value of a target gene to a reference expression level calculated based on the geometric mean of the expression levels of multiple control genes provides – according to the researchers – more accurate results. Hence, in the state of the art both approaches were known. Even though the patent does not deal with this prior art in detail and neither criticises nor describes either approach as advantageous, it cannot be ignored that in light of this prior art, only a single reference gene is mentioned in claim 1. This circumstance will reinforce the person skilled in the art's understanding that claim 1 requires that the expression level of a target gene is determined relative to the expression level of OAZ1 as a single reference gene.

95 In addition, the skilled person notices that the patent does not describe an embodiment in which the expression level of multiple reference genes is used for control within the

normalization according to step 3) of the claimed method. Even though it is not necessary for a patent specification to describe all embodiments that may fall within the scope of the patent claim, the person skilled in the art considers the absence of a description of such an embodiment, in conjunction with the explicit wording of claim 1, as further indication that the claimed teaching provides for normalization only by means of the expression level of OAZ1.

96 Finally, it must be considered that normalizing ultimately conceals a calculation, whereby – as already mentioned – the specific calculation is not specified in claim 1. However, by selecting OAZ1 as the endogenous reference gene, the patent consequently requires the use of a specific value, namely the measured value of the expression level of OAZ1. The use of multiple reference genes and their expression levels for normalization is associated with the use of other expression values and, as a result, also with differing normalization results. However, there is no indication in the patent in suit as to whether and under what conditions such differing values solve the technical problem and deliver reliable results. OAZ1 is highlighted in the patent specification precisely because of its low expression level. Ultimately, the patent is not simply about using OAZ1 in some way for normalization but about normalizing the expression level of a target gene in relation to a specific value which is the expression level of OAZ1.

97 In this context, the following should also be born in mind. Any further steps must not counteract the technical purpose of the steps identified in the claim. However, adding further process steps or steps of normalizing with further genes would not only be irreconcilable with the selection decision made by the patent and would counteract the technical purpose of process step 3).

B Counterclaim for revocation

98 The Counterclaim for revocation is successful. Regarding the claims as granted (“Main Request”), the patent in suit contains added matter. Therefore, the patent must be revoked based on Art. 138(1)(c) EPC, Art. 65(2) UPCA.

99 The application to amend the patent in suit based on Auxiliary Request 1, Auxiliary Request 2 or Auxiliary Request 3 is refused because each of these Auxiliary Requests extends beyond the content of the application as filed, Art. 138(1)(c) EPC, Art. 65(2) UPCA.

I. Claim as granted (Main Request)

1. Legal considerations of the Court regarding added matter

100 According to Art. 138(1)(c) EPC, the subject matter of the European patent shall not extend beyond the content of the application as originally filed or, if the patent is based on a divisional

application or a new application filed pursuant to Art. 61 EPC, beyond the content of the earlier application as originally filed (added matter).

101 In order to ascertain whether there is added matter, the Court must ascertain what the skilled person would derive directly and unambiguously using his/her common general knowledge and seen objectively and relative to the date of filing, from the whole of the application as filed, whereby implicitly disclosed subject-matter, i.e. matter that is a clear and unambiguous consequence of what is explicitly mentioned, shall also be considered as part of its content (Court of Appeal, UPC_CoA_764/2024, UPC_CoA_774/2024, 2 October 2025 – expert e-Commerce/Seoul Viosys; UPC_CoA_382/2024, 14 February 2025 – Abbott/Sibio) .

102 Where the patent results from a divisional application, this requirement applies to each earlier application. The subject matter of the granted claim thus may not extend beyond (1) the disclosure of the application as filed for the patent in suit and (2) the disclosure of the original PCT application that entered the regional phase and is the parent application for the divisional application (Court of Appeal, UPC_CoA_764/2024, UPC_CoA_774/2024, 2 October 2025 – expert e-Commerce/Seoul Viosys).

2. Findings on added matter

103 It is not in dispute that the claimed subject-matter of the patent in suit is directly and unambiguously disclosed in the present (divisional) application as filed (Exhibit HE 3). However, the parties argue about whether the granted claims of the patent in suit do extend beyond the content of the parental application as filed (Exhibit HE 4).

a) Claim 1

104 Claim 1 as granted extends beyond the content of the parental application as filed (Exhibit HE 4). The skilled person does not directly and unambiguously derive from the application as filed that the claimed method for quantifying an expression level of a target gene refers to a target gene “in a FFPE tissue sample of human breast cancer tissues” and that the endogenous reference gene for the normalisation of the target gene is OAZ1.

105 Claim 25 of Exhibit HE 4 which is according to the Claimant the basis of clam 1 of the granted patent reads:

> “A method for quantifying an expression level of a target gene, comprising:
>
> 1) synthesizing cDNA from RNA of a subject;
>
> 2) performing real-time PCR to amplify the target gene using a pair of primers and/or probes with the cDNA serving as a template and then performing real-time PCR to amplify the endogenous reference gene using the composition of claim 16; and

3) normalizing an expression level of the target gene to that of the endogenous reference gene of step 2).”

106 Claim 16 of Exhibit HE 4 reads as follows:

> “A composition for detecting at least one of the guide genes identified using the method of claim 12, comprising a detection reagent applicable to amplification of the guide gene.”

107 Claim 12 of Exhibit HE 4 reads as follows:

> “A method for selecting guide genes, comprising: measuring the candidate endogenous reference genes selected using the method of claim 1 for coefficient of variation (CV); and ranking the candidate endogenous reference genes in an ascending order of CV.”

108 Claim 1 of Exhibit HE 4 reads as follows:

> “A method for selecting candidate endogenous reference genes (ERG), comprising:
>
> 1) computing expression levels of genes from EST, SAGE and microarray datasets; and
>
> 2) identifying genes which are constitutively expressed across a wide range of tissues using the computed gene expression levels of step 1) and zero(0)'s proportions thereof.”

(i) <u>FFPE tissue sample of human breast cancer tissues</u>

109 Claim 25 therefore discloses a method for quantifying an expression level of a target gene, comprising the three mentioned steps. However, claim 25 refers to such a method without mentioning that the target gene is “in a FFPE tissue sample of human breast cancer tissues”. The other claims that must be observed because of the respective references also contain no indication that the method according to claim 25 refers to a method for quantifying an expression level of a target gene “in a FFPE tissue sample of human breast cancer tissues”.

110 Nor can the person skilled in the art derive directly and unambiguously from the other disclosure content of the application as filed that this belongs to the invention.

111 The application Exhibit HE 4 discloses on page 6, line 15 ff.:

> “Leading to the present invention, intensive and thorough research on accurate comparison of gene expression among different samples, conducted by the present inventors, resulted in the finding that gene expression datasets constructed from

microarray data, in addition to EST and SAGE data, are useful in searching for endogenous reference genes, and that novel reference genes identified using the datasets are superior to previously used genes and show more stable expression across a wide range of samples, thus being universally useful for the normalization of gene expression, rather than being limited for use on specific tissue samples or in specific studies."

112 The description continues page 7, line 5 under the heading "Technical problem":

> "Therefore, it is an object of the present invention to provide a method of processing and analyzing gene expression data, with a statistical concept introduced thereinto, to identify endogenous reference genes which are superior to traditional reference genes in terms of expression stability across a wide range of samples, thus being universally useful for the normalization of gene expression, and a composition for the quantitative analysis of gene expression, comprising a pair of primers and/or probes useful in the amplification of the identified endogenous reference genes."

113 These paragraphs make it clear that the objective of the invention is to find universal genes which are not limited to use on specific tissue samples or in specific studies. Rather, the application states that available (public) gene expression data were analysed to identify genes that are expressed in many different human tissues. With this background in mind the person skilled in the art will set out to read the application.

114 On page 138, line 20, to page 139, line 15 of Exhibit HE 4, the following is taught to the skilled person under the heading "EXPERIMENTAL EXAMPLE 7: Validation of Reference gene, <7-1> Validation of Expression Level of ERG by Quantitative RT-PCR (qRT-PCR)":

> "For use in validating the expression stability of the ERGs identified from the datasets, a total of 108 human samples, including 26 frozen human tissues, 60 formalin-fixed, paraffin embedded (FFPE) human tissues, and 22 human cancer cell lines were obtained (Table 6). The 60 FFPE tissues were composed of 10 breast cancer tissues, 8 normal stomach tissues, 9 stomach cancer tissues, 10 normal ovary tissues, 4 ovarian dropsy tissues, 9 borderline ovarian tumors, and 10 ovarian cancer tissues. Total RNA was isolated from these tissues and cell lines. For frozen human tissues and human cancer cell line samples, RNA which met the requirements of A260/2802:l. 80 and rRNA (28S/18S) >1.0 was used in qRT-PCR. cDNA was synthesized from the RNA using a standard technique and then diluted in distilled water (1:3 cDNA:DW) before qRT-PCR. PCR primers are summarized, together with the Universal Probe Library (UPL) thereof, in Table 7, below."

115 On page 145, line 12 to page 146, line 5 of Exhibit HE 4 it says under the heading "<7-2> Validation of ERG using Expression Stability-Based on qRT-PCR data":

> “Furthermore, the 13 novel ERGs were analysed for expression in 60 FFPE samples using qRT-PCR in order to examine the possibility of applying them to the tissues in which high RNA degradation occurs. All of the genes, except for DIMT1L, were found to be expressed in all 60 samples. Cp was observed to range from 18.85 to 33.02 for traditional ERGs and from 23.33 to 31.38 for the novel ERGs (FIG. 9). Because of the lack of amplification in 5 samples, DIMT1L was omitted from subsequent stability analyses. Despite difference in the type of samples used in the experiments, almost all genes, except for several genes, were observed to be expressed in a pattern similar to that observed in the previous 48 samples. These results indicate that the novel ERGs of the present invention can be applied to gene expression in FFPE samples. geNorm and NormFinder analyses demonstrate that most of the novel ERGs are more stably expressed with lower Cp values in FFPE samples, as well as in the 48 samples, than are traditional 5 ERGs (Table 9).”

116 With the understanding mentioned above, the person skilled in the art can directly and unambiguously conclude from the Experimental Example 7 that the expression stability of the 13 identified novel endogenous reference genes has been analyzed, including in FFPE samples using qRT-PCR and that the results of the analyses indicate that the novel endogenous reference genes of the present invention can be applied to gene expression in FFPE samples in general.

117 This is the only thing that can be inferred from the passages quoted. The fact that the composition of the 60 FFPE samples is explained on page 138, line 20 ff. and that breast cancer tissue samples are also listed there, does not change this. In the context under discussion here, it is not sufficient that breast cancer tissue samples are disclosed. Rather, they must also be disclosed as belonging directly and unambiguously to the invention. However, this cannot be established as the application teaches the person skilled in the art that the technical problem is to find universal genes which are not limited to use on specific tissue samples. The person skilled in the art therefore does not derive from the quoted passages that the use of the identified novel endogenous reference genes is limited to the FFPE breast cancer tissue sample.

118 Apart from that, there are no indications as to why the identified novel endogenous reference genes should only be used in a sample with this type of cancer and not in a sample of one of the other types of cancer mentioned. There is no pointer in the application Exhibit HE 4 that the FFPE breast cancer tissue samples are particularly preferred. The data do not show that the expression of any of the novel endogenous reference genes is particular stable in FFPE breast cancer tissue samples.

119 Finally, Experimental Example 7 deals with the validation of 13 novel endogenous reference genes. A method for quantifying an expression level of a target gene is not directly and clearly disclosed here.

(ii) OAZ1 as a reference gene of a target gene in a FFPE breast cancer sample

120 The application as filed (Exhibit HE 4) also does not clearly and unambiguously disclose that OAZ1 is used as the (sole) reference gene for normalizing the expression level of a target gene in a FFPE breast cancer sample.

121 Although Exhibit HE 4 discloses OAZ1 as one of the 13 novel endogenous reference genes (e.g. p. 46, 69, 70, 73, 132, 133, 138, 141, 186, Table 9, Fig. 8) or as a "guide gene" in the sense of Claim 16 (see claim 17, p. 208, line 19 Exhibit HE 4), neither claim 25 nor the other claims in the chain of reference specify OAZ1 as the endogenous reference gene which should be used for normalizing in the mentioned method. Nor does this follow from the disclosure content of the application as a whole. In particular, the application as filed does not contain any example or experiment in which OAZ1 is used in a method as a reference gene for normalizing the expression level of a target gene in a FFPE breast cancer sample.

122 The skilled person notices that although OAZ1 is described as one of the 13 novel reference genes or as a "guide gene" in the application, it is not mentioned as a reference gene in claim 25 or in claims 16, 12 or 1. For this reason alone, it cannot be derived from the claims of the application that OAZ1 is to be used as an endogenous reference gene for normalizing the expression level of a target gene in a FFPE breast cancer tissue sample. This does also not follow from the overall disclosure content of the application as filed (Exhibit HE 4).

123 In this respect, it must first be taken into account that the objective of the claimed invention is stated to identify a universally applicable reference gene, whereby the application as filed identifies 13 novel reference genes. On page 9, line 17 ff., it states:

> "By the method, 2,087 genes were first found as housekeeping genes which are expressed in most tissues, and the usefulness thereof in the relative quantification of different target genes was determined by analyzing their expression stability. Out of the 2,087 genes, 13 genes were found to show higher expression stability with lower expression levels across a wide range of samples than traditional reference genes such as GAPDH and ACTB and therefore are suitable for the normalization of universal genes having relatively low expression levels."

124 Therefore, the criteria for finding the 13 novel reference genes are higher expression stability (meaning: presence in a wide range of samples and tissues) and relatively low expression levels (meaning: expression levels of the same magnitude as the target genes). Regarding the 13 novel endogenous reference genes the application as filed describes the analyses performed on these novel reference genes, whereby only general conclusions regarding the expression level of these reference genes are drawn (Exhibit HE 4, p. 69, lines 25 ff.). OAZ1 is not singled out in this respect. Therefore, this part of the description cannot be a base for a direct and unambiguous disclosure of OAZ1 as a sole reference gene in the claimed method.

125 On page 70, lines 18 ff., the application as filed deals with the existence of copy number variations, having previously emphasised that the higher the coefficient of variation (CV) is, the more greatly the gene expression varies from one tissue to another (Exhibit HE 4, p. 69, lines 2 f.). In this context, the application as filed states:

> "In order to validate the suitability of the 13 genes for reference genes, they were examined for gene copy number variation with reference to the Database of Genomic Variants (//projects. tcag.ca/variation/) (see Table 5). As a result, only OAZ1 and DIMT1L, among the 13 genes of the present invention, were found on chromosome regions known for gene copy variation, whereas many (ACTB, GAPDH, PGK1, B2M, TBP, TFRC, ALAS1) of the traditional reference genes were located in such chromosome regions."

126 This is repeated in Experimental Example 6, where is also stated that:

> "These results suggest that almost all of the identified reference genes of the present invention, except for the two genes, can be used as guide genes for the measurement of gene amplification because they might be highly unlikely to show variation in gene copy number."

127 Even if the skilled person will recognise that Experimental Example 6 does not refer to quantification of gene expression levels, but rather to "measurement of gene amplification" and that these are different biological processes, this does not alter the fact that the passages quoted suggest that OAZ1 (like DIMT1L) is not a suitable reference gene as it is located on chromosome regions known for copy number variation like 7 of the "traditional reference genes" for which the invention sets out to find better genes. Therefore, nothing can be inferred from this part of the description that directly and unambiguously indicates that OAZ1 is to be used as a reference gene for normalizing the expression level of a target gene (in a FFPE breast cancer tissue sample)

128 Insofar as the Claimant refers to Experimental Example 7 and seeks to establish therein a direct and unambiguous disclosure of the teaching protected by Claim 1 as granted, the Court cannot agree.

129 It is true that already quoted Experimental Experiment 7 explains that the expression level of the 13 endogenous reference genes was validated in 60 FFPE tissues and that this FFPE tissues were composed of 10 breast cancer tissues, 8 normal stomach tissues, 9 stomach cancer tissues, 10 normal ovary tissues, 4 ovarian dropsy tissues, 9 borderline ovarian tumours, and 10 ovarian cancer tissues. It is also true that OAZ1 is one of the 13 endogenous reference genes and that it belongs to the 12 genes which were to be found to expressed in all 60 FFPE samples. Therefore, OAZ1 was (reliably) detected in all 60 FFPE samples (see also Fig. 9.) and in the 10 FFPE breast cancer tissues samples. It also means that OAZ1, among other genes, has low variability across a variety of different tissues.

130 However, this is not sufficient for direct and unambiguous disclosure. It should be noted that the disclosure of a feature as such is not sufficient. Rather, it is necessary that it be directly and unambiguously disclosed as belonging to the invention. This is not apparent in the present case.

131 Firstly, it is not apparent that Experimental Example 7 is an embodiment of Claim 25 of the application as filed. Example 7 deals with the validation of the 13 novel reference genes, but there is no disclosure of a method for quantifying the expression level of a target gene in an FFPE tissue, nor a method for quantifying the expression level of a target gene in a sample of a human breast cancer.

132 Secondly, OAZ1 is not singled out in this Example regarding FFPE tissue samples. In Experimental Example 7-1, the statement that OAZ1 has the lowest expression level refers to the analysis of 48 samples, 26 frozen samples and 22 cancer cell lines, but not to FFPE samples (Exhibit HE 4, p. 141, line 5 ff.). Furthermore, this statement is relative. Such a level is only relevant if the target gene has a similar level. However, the invention is not limited to a specific target gene with a typically low expression level. Besides that, Table 9 shows that OAZ1 does not have the best expression stability in FFPE samples. For example, ARL8B and LUC7L2 performed better. These genes also showed lower expression levels than OAZ1 in the FFPE samples.

133 Thirdly, Experimental Example 7 does not demonstrate expression stability of OAZ1 in breast cancer FFPE tissues. As mentioned, the 60 FFPE tissues comprised 7 sample types of cancer. The expression variability of the 13 endogenous reference genes was not analysed separately in each tissue or regarding each kind of cancer, but – in accordance with the objective of the invention of the application – universally, in a wide range of tissue samples. Table 9 of the application provides the expression stability for the average of the 60 FFPE tissues in terms of "M" and "S" values, calculated by the programs geNorm and NormFinder, respectively. It shows (only) expression values across all 60 FFPE tissues, thus (only) for the entire pool of FFPE samples. The data provided therefore cannot directly and unambiguously reveal the expression stability of OAZ1 in FFPE breast cancer tissue samples. The overall expression level of a gene – in this case, OAZ1 – in 60 FFPE tissue samples does not allow conclusions to be drawn about the expression level of this gene in a specific sample – in this case, FFPE human breast cancer tissue.

134 In this respect, no implicit disclosure can be assumed either. It is not apparent that the expression stability of OAZ1 required for normalization is a clear and unambiguous consequence of what is explicitly mentioned. It is not directly and unambiguously derivable from such expression stability values obtained over a variety of tissues whether a specific reference gene is also stably expressed in one specific tissue type such as breast cancer tissue.

b) Claim 2 and 3

135 Subclaims 2 and 3 as granted extend also beyond the content of the parental application as filed (Exhibit HE 4). The statements made in relation to claim 1 apply accordingly. The dependent claims also contain added matter.

3. Other grounds for revocation

136 Since the ground for revocation according to Art. 138(1)(c) EPC applies, there is no need to clarify whether the other revocation grounds raised by the Defendants are valid.

4. Refusal of the Main Request

137 The Main Request of the Claimant to maintain the patent as granted must therefore be refused because the granted claims contain added matter. The patent in suit must be revoked because the ground for revocation of Art. 138(1)(c) EPC is justified.

II. Auxiliary Requests

138 Since all three auxiliary requests relate to a method of quantifying the expression level of a target gene in a FFPE tissue sample of human breast cancer and use OAZ1 as the reference gene for normalizing the target gene, each of the auxiliary requests also contains an inadmissible extension under Article 138(1)(c) EPC. The auxiliary requests for amendment of the patent must therefore be rejected. It is irrelevant whether any further grounds for invalidity asserted by the Defendants are valid.

C Infringement action

139 The infringement action is not justified. It must be dismissed.

140 Apart from the fact that the infringement action cannot succeed due to the revocation of the patent, based on the above-mentioned claim construction, the contested embodiment does not fulfil the technical teaching of claim 1, neither directly nor (as Test-Kit) indirectly. Feature 3 is not realised. The expression level of the target gene is not normalized to that of the endogenous reference gene of step 2), namely OAZ1.

141 In the attacked embodiment the expression levels of the target genes are normalized to an average expression level of the three reference genes CALM2, OAZ1, and RPL37A. By subtracting the C_t of the breast cancer related target genes from the average C_t of the three reference genes OAZ1, CALM2, and RPL37A, the average expression level of the reference genes is divided by the expression level of the target genes. OAZ1 is therefore not used as the sole reference gene for normalisation.

142 In the calculation method presented by the Defendants, which was not contested, there is also no (intermediate) calculation step in which the expression level of the target gene is normalized against the expression level of OAZ1 alone. There is no three-step normalization against each reference gene. Rather, only one normalization (calculation) takes place, in which the average value of the expression levels of the three reference genes is used. However, the average expression level is not identical to the measured value of the expression level of OAZ1.

143 Insofar as the Claimant submits in the oral hearing for the first time that the calculation method of the contested embodiment corresponds mathematically to a calculation in which the bracket is resolved, this is late filed. The Defendants were unable to respond to this. They also complained about this. For this reason, the Claimant's new submission or argument must be disregarded in accordance with Rule 9.2 RoP. However, even if it were to be taken into account and it were assumed in favour of the Claimant that its submission regarding mathematical consistency is correct, this would not help it to succeed. The actual construction/configuration of the contested embodiment is decisive for assessing whether it embodies the technical teaching. The uncontested calculation method must therefore be taken as a basis. And this calculation method does not make use of the teaching of the patent in suit. It is not acceptable to assume an infringement because the same result as that achieved by the attacked embodiment can also be hypothetically achieved by a method that complies with the patent, especially if this requires further steps to be carried out after obtaining the normalization value according to the patent (calculation of the average with several normalization values of other reference genes) in order to achieve the same result. Even if the methods are mathematically identical in terms of the result, they are in fact different.

144 Finally, it should be noted that the realisation of feature 3 is not apparent even if the claim would allow the use of further reference genes for normalization. It is in any case not covered by the claim to use as further or multiplex reference genes those which are not considered by the patent to be sufficiently stable or more suitable reference genes. However, this is precisely the case for genes CALM2 and RPL37A. They are identified in the description of the patent as “candidate reference genes”, which, however, were not even selected as “guide genes” and thus not added to the 13 reference genes because their expression stability was insufficient (para. [0030], [0038]).

145 The Claimant has not argued that, despite the materials and reagents it contains, the Test-Kit is suitable and intended for use in a method for quantifying the expression level of a target gene in a FFPE breast cancer tissue sample in which normalization is carried out using OAZ1 alone. An indirect infringement is therefore also ruled out from this point of view.

146 Since the realisation of claim 1 is not given for the reasons stated above, there is no need to address the other points of dispute between the parties in the infringement action.

D Legal consequences

147 As a result of the revocation action, European Patent EP 3 346 403 is revoked with effect to the requested territories.

148 The infringement action is dismissed.

149 The Claimant shall bear the costs of the infringement action and the Counterclaim for revocation, Art. 69(1) UPCA.

DECISION

1. The European patent EP 3 346 403 is revoked with effect to the territories of Austria (AT), Belgium (BE), France (FR), Germany (DE), Italy (IT), Luxembourg (LU) and The Netherlands (NL).
2. The Application to amend the patent in suit is dismissed.
3. The infringement action is dismissed.
4. The costs of the infringement action and the Counterclaim for revocation are to be borne by the Claimant.
5. The value in dispute for the infringement action is set at EUR 1,000,000. The value in dispute for the Counterclaim for revocation is set at EUR 1,500,000.

Presiding Judge U. Voß	Ulrike Voß Digital unterschrieben von Ulrike Voß Datum: 2025.12.05 10:50:44 +01'00'
Legally qualified judge Dr D. Voß	Daniel Voß Digital unterschrieben von Daniel Voß Datum: 2025.12.05 11:07:32 +01'00'
Legally qualified judge Knijff	Marije Knijff Digitaal ondertekend door Marije Knijff Datum: 2025.12.05 17:07:04 +01'00'

Technically qualified judge Schüller	Cornelis Schuller Digitally signed by Cornelis Schuller Date: 2025.12.05 17:29:50 +01'00'
For the sub-registrar	Veronika Ruisinger Digital unterschrieben von Veronika Ruisinger Datum: 2025.12.08 12:38:42 +01'00'

INFORMATION ON APPEAL

An appeal against this decision may be brought before the Court of Appeal by any party whose claims have been unsuccessful, in whole or in part, within two months of service of the decision (Art. 73(1) UPCA, R. 220.1 (a) RoP, 224.1 (a) RoP).

INFORMATION ON ENFORCEMENT (Art. 82 UPCA, Art. 37(2) UPCS, R. 118.8, 158.2, 354, 355.4 RoP):

An authentic copy of the enforceable order will be issued by the Deputy-Registrar upon request of the enforcing party, R. 69 RegR.

INSTRUCTION TO THE REGISTRY

A certified copy of the decision shall be sent to the European Patent Office and the national Patent and Trademark offices as soon as the decision on the revocation action has become legally binding.

This decision was read in open court on 19 December 2025.

Presiding Judge U. Voß

Ulrike Voß
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Datum: 2025.12.19 10:14:01 +01'00'