Local Division Munich
UPC_CFI_846/2024
UPC_CFI_485/2025
UPC_CFI_535/2025

Decision

of the Court of First Instance of the Unified Patent Court
Local Division Munich
delivered on 7 July 2026

HEADNOTES

1. To assess whether a party is the holder of an “exclusive licence” within the meaning of Art. 47(2) UPCA, it is decisive whether a licensee is entitled to solely use and to exclude others, including the patent proprietor, from using the patented invention, which includes, in the case of an infringement, the right to assert claims. This does not necessarily mean that the right to use the patented invention can only be licensed to one exclusive licensee in its entirety and without limitations. An exclusive licence may, for instance, be limited in terms of its geographical scope, field of use or duration.

2. In order for a prior art disclosure to be relevant for novelty, the disclosure must be such that the skilled person can reproduce it using common general knowledge, i.e. the skilled person must be able to carry out the teaching of the prior art. Absent such an enabling disclosure, there is no (complete) technical teaching in the prior art and hence no potentially novelty-destroying disclosure.

3. In case of a mere aggregation of two independent methods, whereby the features of these methods do not interact functionally to produce an effect that goes beyond mere addition in solving the objective problem but are simply juxtaposed, the combination of these two methods, both being not novel or at least non-inventive, cannot be held inventive. The skilled person would, as a matter of routine, combine these two methods.

CLAIMANT IN THE INFRINGEMENT PROCEEDINGS:

1. **Promosome LLC,** 48 Gurley Road, 06902 Stamford, Connecticut, United States of America.

DEFENDANTS IN THE COUNTERCLAIMS:

1. **Promosome LLC,** 48 Gurley Road, 06902 Stamford, Connecticut, United States of America.

2. **The Scripps Research Institute**, 10550 North Torrey Pines Road, La Jolla, California 92037, United States of America, proprietor of the patent.

represented by: Georg A. Rauh of Vossius & Partner Patentanwälte Rechtsanwälte mbB, Siebertstr. 3, 81675 Munich, DE (for both parties).

DEFENDANTS IN THE INFRINGEMENT PROCEEDINGS, COUNTERCLAIMANTS:

1. **BioNTech SE,** An der Goldgrube 12, 55131 Mainz, Germany,

2. **BioNTech Manufacturing GmbH**, An der Goldgrube 12, 55131 Mainz, Germany,

3. **BioNTech Manufacturing Marburg GmbH,** Emil-von-Bering-Straße 76, 35041 Marburg, Germany,

4. **BioNTech Innovative Manufacturing Services GmbH,** Vollmersbachstraße 66, 55743 Idar-Oberstein, Germany,

5. **BioNTech Europe GmbH,** An der Goldgrube 12, c/o BioNTech SE, 55131 Mainz, Germany,

represented by: Christine Kanz of HOYNG ROKH MONEGIER, Steinstrasse 20, 40212 Duesseldorf, Germany (for Defendants 1-5).

6. **Pfizer Manufacturing Belgium NV,** Rijksweg 12, 2870 Puurs-Sint-Amands, Belgium,

7. **Pfizer SAS,** 23-25 Avenue du Docteur Lannelongue, 75014 Paris, France,

8. **Pfizer AB,** Solnavägen 3h, 11363 Stockholm, Sweden,

9. **Pfizer, Inc.,** 66 Hudson Boulevard East, 10001-2192, New York, United States of America.

represented by: Tobias J. Hessel of Clifford Chance Partnerschaft mbB
Königsallee 59, 40215 Düsseldorf, Germany (for Defendants 6-9).

PATENT AT ISSUE:

European patent EP 2 401 365.

PANEL/DIVISION:

Panel 2 of the Local Division Munich.

DECIDING JUDGES:

This Decision has been issued by the Presiding Judge Dr Daniel Voß, the legally qualified Judge Dr Georg Werner, the legally qualified Judge András Kupecz (Judge-rapporteur) and the technically qualified Judge Dr. Martin Schmidt.

LANGUAGE OF THE PROCEEDINGS:

English.

SUBJECT-MATTER OF THE PROCEEDINGS

Infringement action and counterclaims for revocation.

DATE OF THE ORAL HEARING

12 May 2026

BACKGROUND AND FACTS

1. On 30 December 2024, the Claimant brought an infringement action before the Unified Patent Court (´UPC´) before the Local Division Munich (´LD Munich´) against two groups of Defendants (Defendants 1-4 and 5-9, respectively, jointly referred to as "Defendants"). The Defendants brought counterclaims for revocation on 18 June 2025 against the Claimant and the patent proprietor "The Scripps Research Institute", also referred to as "Counterdefendant 2" and jointly as "Counterdefendants".

2. The Claimant is a biotechnology company based in the United States of America.

3. Defendants 1) to 5) are pharmaceutical companies based in Germany and belong to the BioNTech Group, whereby Defendant 1) is the parent company (controlling company) and Defendants 2-5) are its subsidiaries.

4. Defendants 6) to 9) are pharmaceutical companies based in Belgium, France, Sweden and the USA and belong to the Pfizer Group. Defendants 6) to 8) are subsidiaries of Defendant 9), which is the parent company of the Pfizer Group.

5. The partnership of the Defendants resulted in the Coronavirus vaccine with the trade name “Comirnaty”.

6. The patent in suit is EP 2 401 365 (“the Patent”) which is entitled “Reengineering of an mRNA primary structure for increased protein production”. The Patent was filed on 24 February 2010 and claims the priority of US 155049 P, dated 24 February 2009. The application was published on 4 January 2012. The mention of the grant of the European Patent was published on 27 April 2016.

7. The Patent is in force in the UPC Contracting Member States France, the Federal Republic of Germany and Sweden.

8. The proprietor of the Patent is Counterdefendant 2. The patent proprietor is a medical research institute located in La Jolla, California, United States of America. The patent proprietor was served a copy of the counterclaim for revocation on 10 July 2025.

9. The Patent, which was granted in the English language, has the following claims:

   1. A method of improving full-length protein expression efficiency comprising:

      a) providing a polynucleotide comprising:

         i) a coding sequence for the full-length protein;
         ii) a primary initiation codon that is upstream of the coding sequence of the full-length protein, said primary initiation codon encoding the first amino acid of the coding sequence of the full-length protein; and
         iii) one or more secondary initiation codons, located within the coding sequence of the full-length protein downstream of the primary initiation codon; and

      b) mutating the one or more secondary initiation codons located within the coding sequence of the full-length protein downstream of the primary initiation codon, wherein the mutation results in a decrease in initiation of protein synthesis at the one or more secondary initiation codons resulting in a reduction of ribosomal diversion away from the primary initiation codon,

   thereby increasing expression efficiency of the full-length protein initiated at the primary initiation codon, wherein mutating the one or more secondary initiation codons located within the coding sequence of the full-length protein downstream of the primary initiation codon comprises mutating one or more nucleotides such that the amino acid sequence of the protein remains unaltered.

2. The method of claim 1, wherein the one or more secondary initiation codons is in the same reading frame as the coding sequence and is not AUG, or wherein the one or more secondary initiation codons is out-of-frame with the coding sequence.

3. The method of claim 1, wherein the one or more secondary initiation codons is located one or more nucleotides upstream or downstream from a ribosomal recruitment site, preferably wherein the ribosomal recruitment site comprises a cap or an IRES.

4. The method of claim 1, wherein the one or more secondary initiation codons is selected from the group consisting of ACG, GUG, UUG, CUG, AUA, AUC, AUU, AAG and AGG.

5. The method of claim 1, wherein more than one secondary initiation codon within the coding sequence is mutated, or wherein all secondary initiation codons within the coding sequence are mutated.

6. The method of claim 1, wherein mutating the one or more secondary initiation codons comprises mutating one or more nucleotides flanking the one or more secondary initiation codons to diminish the efficiency of the one or more secondary initiation codons.

7. The method of claim 1, wherein mutating the one or more secondary initiation codons does not introduce new initiation codons, or wherein mutating the one or more secondary initiation codons does not alter usage bias of mutated codons.

8. The method of claim 1, wherein the generation of truncated proteins, polypeptide, or peptides other than the full-length encoded protein is decreased.

9. The method of claim 1, wherein mutating one or more secondary initiation codons does not introduce miRNA seed sequences, splice donor site, splice acceptor site, or mRNA destabilization elements.

10. The method of claim 1, wherein the polynucleotide sequence further comprises one or more miRNA binding sites located within the coding sequence, and said method further comprises the step of mutating the one or more miRNA binding sites, wherein the mutation results in a decrease in miRNA binding at the one or more miRNA binding sites resulting in a reduction of miRNA-mediated down regulation of protein translation.

11. The method of claim 10, wherein mutating the one or more miRNA binding sites comprises: mutating one or more nucleotides in a miRNA seed sequence; mutating the one or more miRNA binding sites comprises mutating one or more nucleotides such that initiation codons are not introduced into the polynucleotide sequence; mutating one or more nucleotides such that rare codons are not introduced into the polynucleotide sequence; or mutating one or more nucleotides such that additional miRNA seed sequences are not introduced into the polynucleotide sequence.

10. On the basis of claims 1, and otherwise, claims 2 (second alternative), 4, 5 (first alternative), 7 (first alternative), 8 and 10 in the form of "especially, when" requests,

the Claimant attacks the following embodiments which are, according to the Claimant, all products directly produced by the manufacturing process according to the Patent. Attacked embodiments 2a-2e are so-called mRNA vaccines against the SARS-CoV-2 virus (“severe-acute-respiratory-syndrome-related coronavirus type 2”, also known as “corona virus”):

- mutated cDNA obtained by the method according to the Patent which is then cloned into plasmid vectors and the plasmid vectors are propagated to obtain plasmid DNA (both, cDNA and plasmid DNA, are referred to as “**attacked embodiment 1a”**);
- Mutated mRNA produced from the plasmid DNA (“**attacked embodiment 1b**”);
- “Comirnaty Original” or also “BNT162b2” (with the active substance tozinameran) against the wild type of SARS-CoV-2 (hereinafter also referred to as “**attacked embodiment 2a**”).
- “Comirnaty Original/Omicron BA.1” (with the active substances tozinameran and riltozinameran) against the wild type of SARS-CoV-2 and the sub-variant BA.1 of the SARS-CoV-2 variant Omicron (hereinafter also referred to as “**attacked embodiment 2b**”).
- “Comirnaty Original/Omicron BA.4-5” (with the active substances tozinameran and famtozinameran) against the wild type of SARS-CoV-2 and the subvariants BA.4 and BA.5 of the SARS-CoV-2 variant Omicron (hereinafter also referred to as “**attacked embodiment 2c**”).
- “Comirnaty Omicron XBB 1.5” (with the active substance raxtozinameran) against the sub-variant XBB 1.5 of the SARS-CoV-2 variant Omicron (hereinafter also referred to as “**attacked embodiment 2d**”).
- “Comirnaty JN.1” (with the active substance bretovameran) against the sub-variant JN.1 of the SARS-CoV-2 variant Omicron (hereinafter also referred to as “**attacked embodiment 2e**”).

Requests

11. The Defendants have raised a Preliminary Objection (“PO”) in which they request:

    the Court to dismiss the infringement action insofar as it relates to Comirnaty® variants sold only before 1 June 2023 due to a lack of (temporal) jurisdiction.

12. The Claimant requests in the PO:

    to dismiss Defendants’ Preliminary Objection.

13. The Claimant requests in the infringement action:

I. to declare that Defendants infringed European Patent No. 2 401 365 by way of

1. using within the territories of Germany, France and Sweden a method of improving full-length protein expression efficiency comprising,

a) providing a polynucleotide comprising: i) a coding sequence for the full-length protein; ii) a primary initiation codon that is upstream of the coding sequence of the full-length protein, said primary initiation codon encoding the first amino acid of the coding sequence of the full-length protein; and iii) one or more secondary initiation codons located within the coding sequence of the full-length protein downstream of the primary initiation codon, and

b) mutating the one or more secondary initiation codons located within the coding sequence of the full-length protein downstream of the primary initiation codon, wherein the mutation results in a decrease in initiation of protein synthesis at the one or more secondary initiation codons resulting in a reduction of ribosome diversion away from the primary initiation codon;

thereby increasing the expression efficiency of the full-length protein initiated at the primary initiation codon, wherein mutating the one or more secondary initiation codons located within the coding sequence of the full-length protein downstream of the primary initiation codon comprises mutating one or more nucleotides such that the amino acid sequence of the protein remains unaltered;

(independent claim 1 of Patent)

<u>especially, when</u>

the one or more secondary initiation codons is out-of-frame with the coding sequence;

(Claim 2 Alt. 2)

and/or

the one or more secondary initiation codons is selected from the group consisting of ACG, GUG, UUG, CUG, AUA, AUC, AUU, AAG and AGG;

(Claim 4)

and/or

more than one secondary initiation codon within the coding sequence is mutated;

(Claim 5 Alt. 1)

and/or

mutating the one or more secondary initiation codons does not introduce new initiation codons;

(Claim 7 Alt. 1)

and/or

the generation of truncated proteins, polypeptide or peptides other than the full-length encoded protein is decreased;

(claim 8)

and/or the polynucleotide sequence further comprises one or more miRNA binding sites located within the coding sequence, and said method further comprises the step of mutating the one or more miRNA binding sites, wherein the mutation results in a decrease in miRNA binding at the one or more miRNA binding sites resulting in a reduction of miRNA-mediated down regulation of protein translation;

(Claim 10)

(**infringement of method claims**)

2. offering, putting on the market, using, or importing or storing for the aforementioned purposes in Germany, France and Sweden products obtained directly by the process according to 1) above,

in particular

a. <u>so-called complementary DNA (cDNA), isolated as well as inserted into a plasmid vector (so-called pDNA or plasmid DNA) having the following sequences</u>

   [in relation to attacked embodiment 2a – Comirnaty Original]

[ATG…[]...TGA], shortened for readability, see the full sequence in the Annex to this Decision.

and

[in relation to attacked embodiment 2b - Comirnaty Original/Omicron BA.1]

[ATG...[]...AAA], shortened for readability, see the full sequence in the Annex to this Decision.

and

[in relation to attacked embodiment 2c - Comirnaty Original/Omicron BA.4-5]

[ATG...[]…TGA], shortened for readability, see the full sequence in the Annex to this Decision.

and

[in relation to attacked embodiment 2d - Comirnaty Omicron XBB 1.5]

[ATG…[]…AAA], shortened for readability, see the full sequence in the Annex to this Decision.

and

[in relation to attacked embodiment 2e - Comirnaty JN.1]

[ATG…[]…TAG] , shortened for readability, see the full sequence in the Annex to this Decision.

b. RNA *in-vitro* transcribed from the DNA sequences according to lit. a. having the following sequences

[in relation to attacked embodiment 2a – Comirnaty Original]

[AUG…[]...UGA], shortened for readability, see the full sequence in the Annex to this Decision.

and

[in relation to attacked embodiment 2b - Comirnaty Original/Omicron BA.1]

[AUG...[]...AAA], shortened for readability, see the full sequence in the Annex to this Decision.

and

[in relation to attacked embodiment 2c - Comirnaty Original/Omicron BA.4-5]

[AUG...[]…UGA], shortened for readability, see the full sequence in the Annex to this Decision.

and

[in relation to attacked embodiment 2d - Comirnaty Omicron XBB 1.5]

[AUG…[]…AAA], shortened for readability, see the full sequence in the Annex to this Decision.

and

[in relation to attacked embodiment 2e - Comirnaty JN.1]

[AUG…[]…UAG], shortened for readability, see the full sequence in the Annex to this Decision.

c. <u>Vaccines including the RNA according to lit b., marketed and distributed under the following brand names:</u>

“Comirnaty Original”, “Comirnaty Original/Omicron BA.1”, “Comirnaty Original/Omicron BA.4-5”, “Comirnaty Omicron XBB.1.5”, “Comirnaty JN.1”;

(infringement of directly obtained process products)

II. to order the Defendants under the forfeiture of a recurring penalty payment of EUR 10,000 EUR for each day of delay, within a period of 1 month from the date of service of the judgment, subject to Rule 118.8 of the Rules of Procedure,

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

Defendants) have committed the acts referred to in item I above since 27 April 2016, specifying

1. the origin and distribution channels of the infringing products;

2. the quantities produced, manufactured, delivered, received and/or ordered, as well as the price obtained for the infringing products;

3. the identity of any third person involved in the production and/or distribution of the infringing products;

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; and

6. the actual costs broken down by individual cost factors and the profit made,

whereby as proof of the information provided the corresponding receipts (i.e., invoices, alternatively delivery notes) are to be submitted in electronic 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;

III. to declare that Defendants are liable to compensate Claimant for all damages that incurred (including interest) and will incur due to the acts specified in item I. above and committed since 27 April 2016, as to be specified in separate damage proceedings;

IV. to order Defendants to pay interim damages, whereby at a minimum, Claimant's expected costs of the proceedings for the award of damages and compensation must be covered, whereby an amount of at least EUR 832,485.00 is suggested;

V. to order Defendants to pay the reasonable and proportionate legal costs of these proceedings and other expenses;

VI. to declare that the orders according to items II. and IV. are immediately enforceable notwithstanding any appeal,

<u>alternatively</u>,

in the event that a security is ordered, to permit Claimant to provide it by bank or savings institution guarantee and determines the amount of the security separately for each claim awarded and for the decision of cost liability;

VII. to issue a decision by default in the event that Defendants fail to take a step within the time limit foreseen in the UPC Rules of Procedure or set by the Court or fail to appear at an oral hearing after having been duly summoned.

14. The Defendants request in the infringement action (using the Defendants' numerals):

IV. the Court orders that the infringement action is dismissed (R. 23, 24(g) RoP),

V. the Court orders the Claimant to bear the costs of the infringement action,

VI. the Claimant be ordered to reimburse the costs of the infringement action on a provisional basis (R. 150.2 RoP) in the amount of EUR 1,500,000.

In the alternative, the Defendants request that

VII. enforcement of the decision is made subject to the prior provision of security by the Claimant to the other parties in the amount of at least EUR 1,000,000.00 (R. 352.1, 354.2 RoP), which may be provided by a written, irrevocable, unconditional and unlimited guarantee from a credit institution authorized to do business in the territory of a member state of the Unified Patent Court ("UPC"),

VIII. the Defendants be allowed to avert the enforcement of the decision by providing security, which can be provided by a written, irrevocable, unconditional and unlimited guarantee from a credit institution authorized to do business in the territory of a member state of the UPC, without regard to the provision of security by the Claimant (R. 9.1 RoP).

15. In response to the requests from the Defendants, the Claimant, in addition to the above, requests the Court:

1. Defendants' request to make enforcement of the decision subject to security is dismissed.

2. Defendants' request to allow aversion of the enforcement of the decision by providing security is dismissed.

3. Defendants' request to order the Claimant to reimburse the costs of the infringement action on a provisional basis (R. 150.2 RoP) in the amount of EUR 1,500,000.00 is dismissed.

16. In the Counterclaim for revocation, the Defendants (as counterclaimants) request (using the Defendant's numerals):

I. European patent EP 2 401 365 B1 is revoked entirely with effect to the territory of Germany (DE), France (FR) and Sweden (SE),

II. the Claimant and the Patent Proprietor bear the costs of the Counterclaim for revocation. Both the Claimant and the Patent Proprietor are jointly and severally liable for all costs of the Counterclaim for revocation incurred by the Defendants.

III. the Claimant and the Patent Proprietor be ordered to reimburse the costs of the Counterclaim for revocation on a provisional basis (R. 150.2 RoP) in the amount of EUR 1,500,000.00. Both the Claimant and the Patent Proprietor are jointly and severally liable for such provisional cost reimbursement.

17. In the Counterclaim for revocation, the Counterdefendants request:

I.

1. The counterclaim for revocation of EP 2 401 365 B1 is dismissed in its entirety and the patent in suit is maintained as granted ("main request").

2. Counterclaimants' requests to order the Counterdefendants to reimburse the costs of the Counterclaim for revocation on a provisional basis (R. 150.2 RoP) in the amount of EUR 1,500,000.00 is dismissed.

II. In the alternative to request I.1. above, the Counterdefendants request the Court ("**auxiliary requests**"):

1. The counterclaim for revocation of EP 2 401 365 B1 is dismissed in part to the extent it goes beyond the version of EP 2 401 365 B1 according to the following auxiliary requests:

a-y, auxiliary requests 1-25, all submitted in the English language as Exhibits VB AR 1 – VB AR 25, respectively,

with auxiliary requests 1 and 5 as corrected with the Reply to the Defence to the Application to Amend (Exhibits VB AR 1 (corrected) and VB AR 5 (corrected)).

2. that auxiliary requests VB AR 1 – 25 be dealt with in the order as stated above and in accordance with their numbering, and that the patent in suit is maintained respectively.

3. In case the Court maintains the patent in suit in the form of one of the auxiliary requests, that judgment is rendered 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. Further, the Counterdefendants request the Court to order Counterclaimants 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.

18. In the <u>Counterclaim</u> for revocation, the <u>Defendants</u> (as counterclaimants) further request:

to dismiss Auxiliary Requests 1-25.

POINTS AT ISSUE

Preliminary Objection ("PO")

19. The Defendants raised a PO against the jurisdiction of the Court insofar as in the Statement of Claim relief is sought for Comirnaty® Original/Omicron BA.1 (attacked embodiment 2b) which has been produced and sold *only before* 1 June 2023, i.e. where the alleged infringing acts have concluded before establishment of the UPC. Assuming jurisdiction for such concluded act would be contrary to the principle of international law that treaties have no retrospective effect as set out in Art. 28 of the Vienna Convention on the Law of Treaties ("VCLT").

20. In accordance with Art. 28 of the VCLT "Unless a different intention appears from the treaty or is otherwise established, its provisions do not bind a party in relation to any act or fact which took place or any situation which ceased to exist before the date of the entry into force of the treaty with respect to that party." According to the Defendants, not only is the UPCA silent on retroactivity, i.e. it does not expressly provide for it, but it also contains no provisions which would allow such an interpretation. Comirnaty® Original/Omicron BA.1 was not sold on/after 1 June 2023 in France, Germany, and Sweden, i.e., the UPC member states concerned by this action. Art. 28 VCLT mandates that a treaty does not bind a party in respect of any act or fact that occurred or any situation that ceased to exist before the date of entry into force of the treaty. In the present case, the production/sale of each of the Comirnaty® variants is to be seen as one "act" within the meaning of Art. 28 VCLT.

21. According to the Claimant in its comments to the PO, there are no infringing acts that may have already terminated before 1 June 2023, because infringement of the patent protected method of claim 1 of EP365 is undisputedly ongoing since before and after 1 June 2023. The fact that the application of the protected method of claim 1 results in different directly obtained process products neither "interrupts" such general ongoing infringement nor leads to different infringing activities that may require individual treatment as to the application of the jurisdiction of this Court. Rather, all of the attacked activities relate back to the same act/will of Defendants. The Claimant further contests the Defendants' assertion that attacked embodiment 2b has not been produced or sold on or after 1 June 2023 on the basis of lack of knowledge. Irrespectively of this, the Court generally has jurisdiction to rule on acts of infringement committed by Defendants only before 1 June 2023.

Standing to sue

22. The Claimant asserts its claims for patent infringement against the Defendants on the basis that the Claimant is the exclusive licensee of the patent proprietor (Counterdefendant 2). The underlying licensing agreement has been submitted as

Exhibits VB 4a and VB 4b. […] Counterdefendant 2 has at all times understood and treated the licences granted under Exhibit VB 04a to Claimant as exclusive for all commercial exploitation. In an auxiliary way, the Claimant argues that it is at least entitled to assert the claims as a non-exclusive licensee.

23. According to the Defendants, the Claimant has no standing to sue. First of all, the agreement between the parties of the contract does not cover an exclusive licence, which the amendment agreement did not resolve. Furthermore, the licence agreement had neither been validly concluded under US law nor would it have been validly concluded under French, Swedish or German law. The Defendants argue that a valid licence agreement does not exist because the licence agreement and its amendment exhibits VB4a and VB4b were not validly executed. In particular, the Defendants have challenged the identities of the persons signing the agreements and their authority to sign the agreement on behalf of the parties entering into the agreement. Even if this was assessed differently, the licence agreement could not transfer the patent rights, since the patent at issue did not yet exist at the time the licence agreement was concluded and is therefore not covered by the agreement at all. Finally, according to the Defendants, the Claimant failed to notify the patentee or to provide evidence of such notification of the action at hand.

Claim construction

24. According to the Claimant, the aim of the proprietary process is to adapt or mutate DNA or mRNA in such a way as to maximize the production of functional full-length proteins expressed or produced from it, while minimizing the production of in-frame and out-of-frame peptides. A full-length protein essentially comprises all amino acids that are encoded by the correct reading frame of the gene that encodes the protein. The polynucleotide to be provided is either DNA (deoxyribonucleotide) or mRNA (messenger ribonucleotide). This is further confirmed by the technical necessities of mutating an mRNA. mRNA itself is not feasible to be mutated because mRNA is single-stranded, unstable and not self-replicable unlike a plasmid DNA. Rather, the starting point for mutating mRNA is DNA, or to be more accurate, complementary DNA (cDNA) which can be mutated before being transcribed into mRNA. Accordingly, there is no difference whether a mutated DNA or a mutated mRNA is to be produced. The coding sequence for the full-length protein (i.e. the blueprint for the protein) comprises a primary start codon and at least one secondary start codon. A start codon can be the usual start codon (ATG for DNA and AUG for mRNA, also called “canonical codon”). However, start codons can also be ACG, GUG, UUG, CUG, AUA, AUC, and AUU. These are the so-called secondary, non-canonical start codons. The primary start codon is located upstream of the coding sequence and at the same time forms the first amino acid (methionine) of the coding sequence. In contrast, the secondary start codons are located downstream of the primary start codon, i.e. towards the 3’-end in relation to the primary start codon.

25. The technical effect of the invention is described in the claim. Due to the mutation of at least one secondary start codon, this is no longer recognized by the ribosomes as a possible false start codon. This inevitably leads to the ribosomes being less able to be diverted from the actual primary start codon AUG. As a result, the ribosomes begin the translation process more reliably and more frequently at the primary start codon, so that in comparison more full-length proteins (and fewer unwanted by-products) are expressed. According to Patent [0040], "increased protein expression" refers to translation of a modified mRNA where one or more secondary initiation codons are mutated that generates polypeptide concentration that is at least about 5%, 10%, 20%, 30%, 40%, 50% or greater over the polypeptide concentration obtained from the wild-type mRNA where the one or more secondary initiation codons have not been mutated. Increased protein expression can also refer to protein expression of a mutated mRNA that is 1.5-fold, 2-fold, 3-fold, 5-fold, 10-fold or more over the wild-type mRNA. In the claimed method these functional limitations are technical limitations of the method and the claimed method must be applied in that manner to achieve these technical limitations.

26. The <u>Defendants</u> argue that the Patent in suit does not define the term "coding sequence". When looking at the examples of the patent in suit, it is evident that the coding sequence can be a wild-type sequence, i.e., the sequence as it occurs in nature, or a codon optimised sequence. Codon optimisation is generally used to select the codons used most frequently in an organism for a given amino acid, which *inter alia* results in higher protein expression efficiency.

27. A codon is only defined as a "(secondary) initiation codon" if protein synthesis actually starts at this codon. The Patent also uses the term "putative [or potential] (secondary) initiation codon". This term describes an AUG codon or, alternatively, one of the non-AUG initiation codons listed in claim 4, which can be identified by *in silico* methods in any given sequence. However, these codons only constitute secondary initiation codons within the meaning of the claim if protein synthesis actually starts at the respective codon, i.e., if a ribosome binds to this codon and subsequently translates the mRNA into a protein. The Defendants refer to such codons at which protein synthesis actually starts as "actual secondary initiation codons".

28. The claimed effects can only be achieved if (at least) one actual secondary initiation codon is in fact mutated. Not all actual secondary initiation codons automatically result in the effects claimed. In fact, it has never been experimentally shown that a mutation of an actual secondary initiation codon would result in a decrease in initiation of protein synthesis at the one or more secondary initiation codons resulting in a reduction of ribosomal diversion away from the primary initiation codon, as claimed.

29. For the interpretation of claim 10, the Defendants submit that the wording of the claim is quite clear in that it is not sufficient to simply identify and mutate known or predicted

miRNA binding site(s), but that such mutation must result in an actual decrease of miRNA binding at a miRNA binding site; and a higher protein translation because of such decrease in binding.

Counterclaim for revocation

30. The Defendants (counterclaimants) are of the opinion that the Patent is invalid. They submit that the Patent lacks novelty over WO 91/01374, a PCT patent application titled "Prevention of Internal Initiation" (document "**D1**"). D1 identifies the exact same issue that is addressed in the Patent as the problem to be solved by the alleged invention, but also proposes the exact same solution to this problem, namely mutating secondary initiation codons such that the resulting amino acid sequence remains unaltered. D1, therefore, anticipates claim 1 of the Patent in a novelty destroying manner. Matsuda et al. (2006) – "Close spacing of AUG initiation codons confers dicistronic character on a eukaryotic mRNA", RNA, vol. 12, p. 1338-13 (document "**D2**") also takes away the novelty of claim 1 of the Patent since it discloses mutation of a downstream secondary initiation codon, thereby increasing the expression efficiency of the full-length protein of interest. WO 2006/011966 A1 – a PCT patent application titled "OPTIMIZING EXPRESSION OF ACTIVE BOTULINUM TOXIN TYPE E" (document "**D3**") is also novelty destroying according to the Defendants.

31. Furthermore, the Defendants argue that claim 1 lacks novelty in view of the well-known concept of "codon optimisation". D3 also anticipates the subject matter of claim 1 since the codon optimisation suggested therein leads to a mutation of (out-of-frame) putative secondary initiation codons as claimed. Such codon optimised sequences are explicitly characterized as "providing increased expression of the encoded active BoNT/E in a primate cell line". At least when applying the same approach the Claimant applied in its infringement allegations, such increased expression can be attributed to the mutation of secondary initiation codons. In addition, if the Claimant's approach to establishing infringement (an *in silico* analysis) is applied in an equal manner to the codon optimised DNA sequence of Babcock et al. (2004) – "Amino Acids 270 to 510 of the Severe Acute Respiratory Syndrome Coronavirus Spike Protein Are Required for Interaction with Receptor", Journal of Virology, vol. 78 (9), p. 4552-456 (document "**D4**"), this would also disclose the features of claim 1.

32. If a lack of novelty were not accepted over the above references, claim 1 is according to the Defendants at least obvious. Over D3 and D4, any mutation of (putative) secondary initiation codon(s) and an alleged technical effect as claimed would be a mere bonus effect of the codon optimisation expressly disclosed in those references.

33. Furthermore, the combined teaching of Das et al. (2006) – "Copious production of SARS-CoV nucleocapsid protein employing codon optimized synthetic gene", Journal of Virological Methods, vol. 137, p. 343-346 (document "**D5**") and Grote et al. (2005) –

"JCat: a novel tool to adapt codon usage of a target gene to its potential expression host", Nucleic Acids Research,vol. 33, p. W526-W531 (document "**D6**") would have led the skilled person to carry out a codon optimisation that also mutated one actual secondary initiation codon, as demonstrated by reference to Kopecky-Bromberg et al. (2007) – "Severe Acute Respiratory Syndrome Coronavirus Open Reading Frame (ORF) 3b, ORF 6, and Nucleocapsid Proteins Function as Interferon Antagonists", Journal of Virology, vol. 81 (2), p. 548-557 (document "**D7**").

34. The Defendants furthermore submit that the claimed invention is insufficiently disclosed, because the Patent does not provide any guidance on how to identify actual (as opposed to merely putative) secondary initiation codons and claims a method which does not achieve the claimed effect over the full scope of the claims, inter alia because the patent in suit does not provide any evidence and/or guidance to the skilled person to conclude that mutating secondary initiation codons located farther away than ~19 nucleotides downstream of the primary initiation codon will achieve an increase in expression of the full-length protein of interest. Finally, the Patent does not disclose how to implement the alleged invention if claim 1 is construed to require mutation of (putative) secondary initiation codons starting from an already codon optimised sequence nor does it provide any information on its effectiveness.

35. If the Claimant's interpretation of claim 10 is followed, D3 and D4 also disclose the additional features of claim 10. Moreover, Claim 10 lacks inventive step. The subject matter of claims 10 and 11 represents at best an amalgamation of independent and unrelated features (here method steps). Accordingly, when assessing patentability, and in particular inventive step, it must be established whether each set of features is on its own obvious in the light of the prior art.

36. The additional features/method steps of dependent claim 10, which are not also in claim 1, are fully anticipated by Forman et al. (2008) – "A search for conserved sequences in coding regions reveals that the let-7 microRNA targets Dicer within its coding sequence", PNAS, vol. 105 (39), p. 14879 (document "**D9**") and Tay *et al*. (2008) – "MicroRNAs to Nanog, Oct4 and Sox2 coding regions modulate embryonic stem cell differentiation", Nature, vol. 455, p. 112 (document "**D10**"). The additional method steps outlined in claim 10 were therefore known from the prior art and cannot provide an independent contribution to inventive step. The subject matter of claim 10 is also insufficiently disclosed as the Patent does not provide any guidance on how to identify actual miRNA binding sites as opposed to merely predicted miRNA binding sites. Finally, claims 10 and 11 are invalid since they contain added matter contrary to Art. 123(2) EPC. The combination of the two alternative methods into a single (combined) method leads to new technical information not disclosed or derivable from the application as filed.

37. The other subclaims are according to the Defendants also invalid for lack of novelty, inventive step, sufficiency and/or added matter.

38. The Counterdefendants defend the validity of the Patent. According to the Counterdefendants, D1 fails to disclose the functional limitation of granted claim 1 that the change of the one or more secondary initiation codons must result in increased expression efficiency of the full-length protein as well as the functional limitation that the change of the one or more secondary initiation codons must result in a reduction of ribosomal diversion away from the primary initiation codon. D2 does not disclose the mutation of any secondary initiation codon (but the mutation of two primary initiation codons). D3 fails to disclose secondary initiation codons and *a fortiori* their mutation, in particular thereby increasing expression of the full-length protein as required by granted claim 1. Furthermore, still according to the Counterdefendants codon-optimisation as discussed in D4 is distinct from mutating one or more secondary initiation codons as stipulated by granted claim 1.

39. The Counterdefendants further submit that the claimed subject-matter of the Patent also involves an inventive step. It was not obvious based on the description of codon-optimisation to mutate one or more secondary initiation codons as according to granted claim 1. Codon-optimisation does not inevitably result in the removal of secondary initiation codons and *a fortiori* not in increasing expression of the full-length protein as required by granted claim 1.

40. The claimed subject-matter is according to the Counterdefendants also sufficiently disclosed in an enabling manner in the Patent. Whether the mutation of one more secondary start codons increases full-length protein expression can be tested by routine means, including routine means being illustrated in the Patent. The Defendant's position that secondary start codons can only be functional secondary start codons if they are present within approximately 19 nucleotides of the primary start codon by relying on D2 is incorrect. In addition, based on concrete practical examples it will become evident that the removal of secondary initiation codons from a codon-optimised sequence is possible.

41. Finally, there is no added subject-matter as claims 10 and 11 as granted do not extend beyond the contents of the application as filed. The skilled person is certainly not confronted with any information which is not directly and unambiguously derivable from the original application as a whole.

42. By way of a (conditional) application to amend the Patent, the Counterdefendants request the Court to uphold the Patent in the form of Auxiliary Requests ("ARs") 1-25, to be dealt with in that order. The Counterdefendants have explained why in their view the amendments to the ARs satisfy the requirements of Articles 84 and 123(2), (3) EPC and why the proposed amended claims are valid and infringed.

43. The Defendants have lodged a defence against the application to amend. They are of the opinion that the ARs are inadmissible and fail to overcome the reasons why the claimed subject matter is not patentable over the cited prior art.

Infringement

44. The Claimant has had an analysis carried out by of the University of Maryland which, together with publicly available information, confirms that the Defendants 1) to 4) use the process for producing the cDNA in Germany in accordance with the patent in suit (Exhibits VB6 and VB35). Particularly, Defendant 4) manufactures the cDNA in Germany under the control of Defendant 1) which is then cloned and propagated using a plasmid vector to produce cDNA. Defendants 1) to 4) also use the patented process for the manufacture of mRNA for subsequent use in the attacked embodiments 2a to 2e). The Defendants proceed in a division of labour in the large-scale production of the vaccine (from the mutated DNA of origin to the vaccine).

45. The attacked embodiments are products directly produced by the manufacturing process according to the patent in suit. This is confirmed not least by the analysis of All of the attacked embodiments have the material and technical properties which have been imprinted on them by the patent protected process. The attacked embodiments 2a-2e carry the blueprint (genetic code) in the form of mRNA for the so-called spike protein. The mRNA used by the Defendants (attacked embodiment 1b) for the attacked embodiments 2a-2e is not merely a blueprint of the spike protein of SARS-CoV-2 (see above). Rather, the codons of the mRNA encoding a full-length spike protein were "optimised" to improve the immune response.

46. extracted the respective RNA sequence of the corresponding SARS-CoV-2 variants from publicly accessible gene banks. These sequences then served as a reference. He then extracted the RNA sequence of the respective vaccine variant of the Defendants, also from publicly available sources. Using these sequences, he performed alignments for each of the vaccine variants with the reference sequence. On this basis, he compared the codons of interest in the reference sequence with the respective vaccine sequences. Finally, he determined the total number of changes for each codon in the vaccine sequence compared to the reference. Based on this analysis, comes to the conclusion that in all attacked embodiments 2a-2e, a plurality of secondary non-canonical and out-of-frame start codons are mutated downstream of the primary start codon within the coding sequence which does not change the amino acid sequence of the full-length protein. In all attacked embodiments 2a-2e, the most potent miRNA binding sites were mutated in such a way that the number of miRNA binding sites in the mRNA was reduced. Subsequently, experiments were carried out that confirm that minimizing out-of-frame start codons stabilizes mRNA and enhances protein production, a strategy employed in the attacked

embodiments to maximize Spike protein expression and, consequently, the immune response.

47. In addition, [redacted] has shown the deliberate mutation of the binding sites for the six miRNAs by the Defendants (in accordance with Exhibit VB 18) leads to a reduction in miRNA-mediated downregulation of Spike protein translation (see also Exhibit VB 6, marginal no. 53) and thereby to an increase of the desired protective immune response to the Spike protein. Given that there are almost 500 relevant miRNA binding sites on the respective spike protein, the mutation of exactly these binding sites cannot be coincidental but must have been done on purpose.

48. The <u>Defendants</u> contest that the attacked embodiments make use of the method as claimed in the Patent. The Claimant does not base its infringement allegations on identifying of mutations of actual secondary initiation codon(s) and providing evidence that these achieve the effects as claimed. Rather, the Claimant only relies on alleged mutations of out-of-frame putative secondary initiation codons. In fact, the Claimant has analysed only a subset of secondary initiation codons mentioned in claim 4. Nowhere was it shown that any of these putative secondary initiation codons were actual secondary initiation codons in the Sars-CoV-2 spike protein sequence, meaning that there are any such codons at which translation initiation actually occurs.

49. There is no evidence whatsoever that any improved expression could be attributed to a mutation of secondary initiation codons or, more precisely, to mutations of actual secondary initiation codons causing the effects claimed. The experimental evidence presented by the Claimant in the [redacted] reports only involved an: (i) *in silico* analysis to identify mutations over the "wild-type" SARS-CoV-2 sequence; and (ii) measuring protein expression and stability compared to the unmutated (wild-type) sequence, without even trying to ascertain that the observed effects are actually due to the mutation of actual secondary initiation codons (and/or miRNA binding sites for that matter). Moreover, the experimental setup chosen by the Claimant is at any rate severely flawed. Even if one were to ignore this and accept that the Claimant has demonstrated an effect of the mutations in the allegedly infringing embodiments on protein expression, this would be an expected effect that cannot be linked to the claimed invention, but is rather due to codon optimisation of the overall sequence. In fact, codon optimisation has long been known to increase translation efficiency, expression and stability, and was widely used before the priority date of the patent in suit. The Claimant did not provide any tangible evidence that Comirnaty achieves the effects explicitly claimed, because the experiments were designed in such a way that does not allow any distinction between effects caused by codon optimisation, as opposed to the claimed method of mutating away secondary initiation codons.

50. Further arguments and defences, in particular also relating to the Auxiliary Requests will be, to the extent relevant for this decision, discussed below.

GROUNDS FOR THE DECISION

51. The infringement action and the counterclaim for revocation are admissible. The counterclaim for revocation is successful on the merits. The infringement action is unfounded.

I. International jurisdiction

52. The international jurisdiction of the UPC, specifically the LD Munich, has not been challenged by the Defendants and are therefore to be assumed (cf. Rule 19.7 RoP and Article 26 of EU Regulation 1215/2012 of the European Parliament and of the Council of 12 December 2012 on jurisdiction and the recognition and enforcement of judgments in civil and commercial matters ("the Brussels recast Regulation")).

53. The UPC, specifically the LD Munich, further has international jurisdiction and competence to decide on the counterclaim for revocation on the basis of Art. 24(4) in conjunction with Article 71b(1) and 71a(2) sub a of the Brussels recast Regulation and Art. 32(1)(e) UPCA.

II. Preliminary Objection

54. The PO is admissible but unfounded.

55. The PO has been brought within one month of service of the Statement of claim. A temporary lack of jurisdiction and competence can also be the subject-matter of a preliminary objection under R. 19.1(a) RoP (cf. UPC_CoA_156/2025 order of 2 June 2025, XSYS/ESKO). The PO is therefore admissible.

56. Contrary to the Defendants' arguments in the PO, the UPC is competent to decide on alleged acts of infringement which have occurred prior to the entry into force of the UPCA.

57. It is (rightly) undisputed between the parties that the Court has (exclusive) competence as far as the action relates to an action for an infringement of a patent (Art. 32(1)(a) UPCA) as defined under Art. 2(g) UPCA.

58. As held by the Court of Appeal in the XSYS/ESKO case cited above (with reference to UPC_CoA_30/2024, APL_4000/2024, 16 January 2025, in Fives/Reel), the UPCA (in particular Art. 3 and 32(1) UPCA) does not provide for any temporal limitation of the exclusive competence of the Court concerning the acts of alleged infringements, whether acts have taken place before or after the entry into force of the UPCA. The Court of Appeal also held that, in the absence of any provision contrary thereto, the object and purpose of the UPCA – to create a court common to the UPC Member

States integrated into their judicial systems and to transfer (exclusive) competence to said court for those actions and counterclaims listed under Art. 32(1) UPCA, in order to prevent the difficulties caused by a fragmented market for patents in Europe and the variations between national court systems – do not suggest or imply any temporal limitation of the Court's competence.

59. The fact that there is a transitional period of seven years after the entry into force of the UPCA during which an action for infringement or for revocation of a European patent […] may still be brought before national courts or other competent national authorities does not change the above. The concurrent jurisdiction of the UPC and the national courts during the transitional period also applies to infringements that occurred prior to the entry into force of the Agreement.

60. As the Court of Appeal also held in XSYS/ESKO, the competence of the UPC for acts of infringement that have occurred before the entry into force of the UPCA does not contradict the principle of non-retroactivity of treaties under the principles of customary international law and Art. 28 VCLT. The Court is applying the relevant applicable provisions on the competence of the Court, namely Art. 32 UPCA. This does not raise a question of retroactivity. Even if retroactivity were (in favour of the Defendants) assumed for those (alleged) infringements that occurred prior to the date of entry into force of the UPCA, this would not be incompatible with Art. 28 VCLT since it appears from the Agreement that the Court shall have competence on infringement also in respect of acts having occurred prior to the entry into force of the Agreement.

61. Neither the relevant provisions nor the interpretation thereof by the Court of Appeal distinguish, for the purposes of establishing competence, between acts that were *only* carried out before the entry into force of the UPCA, i.e. allegedly infringing acts that were already completed before 1 June 2023, and continuous acts that started before 1 June 2023 and continued thereafter. There is no legal basis for making this distinction, at least not for establishing the competence of this Court (cf. CoA in Fives/Reel, cited above).

62. In conclusion, the Court is competent to hear this action, also for the alleged infringement by Comirnaty® Original/Omicron BA.1 (attacked embodiment 2b), even if it were accepted that this product was produced and sold only before 1 June 2023.

III. Standing to sue

63. Article 47(2) UPCA provides that, unless the licensing agreement provides otherwise, the holder of an exclusive licence in respect of a patent shall be entitled to bring actions before the Court under the same circumstances as the patent proprietor, provided that the patent proprietor is given prior notice. According to Article 47(3) UPCA, the holder of a non-exclusive licence shall not be entitled to bring actions before the Court, unless

the patent proprietor is given prior notice and is so far as expressly permitted by the licence agreement.

64. These provisions of the UPCA are independent and must therefore be interpreted autonomously (cf. UPC_CoA_365/2025_UPC_CoA_413/2025, order of 17 June 2025, Knaus Tabbert/Yellow Sphere and Härtwich). Art. 47 UPCA shall be interpreted in good faith in accordance with the ordinary meaning to be given to the terms of the Agreement and in the light of its object and purpose bearing in mind the legal context, including any applicable European Union law (cf. UPC_CoA_30/2024, APL_4000/2024, 16 January 2025, in Fives/Reel). Evidence that a claimant, who is not the patent proprietor, is entitled to commence proceedings has to be provided by the claimant in the Statement of Claim (Rule 13.1(f)) RoP).

65. Applying these principles to the case at hand, the Court is satisfied that the Claimant is entitled to bring this action.

Validity of the licence agreement

66. In the Statement of Claim, the Claimant provided exhibits VB4a and VB4b as evidence for the assertion that it is the exclusive licensee of the Patent.

67. The Court notes at the outset that the Defendants do not challenge that licence agreements VB4a and VB4b exist and that these agreements have been signed. The dispute centres on whether the signatures are valid and whether the individuals had the authority to sign the agreement. In that respect, the Claimant has provided an exemplary signature of ███ ███ ███ and an affidavit by him that he signed exhibit VB4a on behalf of the patent proprietor, i.e. the licensor and Counterdefendant 2 in these proceedings, (Exhibit VB28b). For the Claimant, exhibit VB4a was signed by ███ ███ Apart from the signature on VB4a, this is confirmed in VB29a by the Board of Managers of the Claimant who declare that ███ ███ signed the agreement. For ███ ███ who signed VB4b, the Claimant submitted a Citrix Signature Certificate identifying him as signatory of Exhibit VB4b (Exhibit VB29c). On behalf of the licensor and Counterdefendant 2, the Claimant submits that Exhibit 29c identifies ███ ███ as signatory of Exhibit VB4b. He confirms this in his affidavit (Exhibit VB26).

68. In relation to the authorities of ███ ███ and ███ ███ to execute Exhibit VB04a or, respectively, Exhibit VB 04b, in VB29a […].

69. The Court is sufficiently convinced by the evidence provided by the Claimant. In any event, nothing concrete has been presented by the Defendants that could challenge the evidence provided by the Claimant. In particular, the fact that the Claimant did not submit a Citrix Signature Certificate for ███ ███ ███ does, in the absence of concrete indications to the contrary, not cast doubt on the veracity of his affidavit.

Likewise, in view of the confirmation by the Board of Managers of the Claimant, it would have been up to the Defendant to provide concrete indications that [redacted] did not sign the agreement and/or did not have the authority to do so on behalf of the Claimant. Against this background, it has to be accepted that VB4a and VB4b were signed by the individuals identified by the Claimant and that these individuals had the authority to sign these agreements on behalf of the parties entering into the agreements.

70. To the extent that the Defendants maintain their argument that […].

71. Finally, [redacted] as General Counsel of Counterdefendant 2 confirms in his affidavit (Exhibit VB26) that Counterdefendant 2 has been given prior notice by the Claimant of its intention to initiate legal proceedings in relation to the Patent before the UPC against the Defendants. Since the form in which prior notice is to be given pursuant to Article 47(2) UPCA is not specified in that provision and no concrete facts or arguments that cast doubt on the proof of notification provided by the Claimant in the form of the declaration by [redacted] have been brought forward by the Defendants, the Court accepts the statement by the Claimant that prior notice has been given.

72. The Court also accepts that the Claimant is an exclusive licensee. […].

73. Art. 47(2) UPCA does not define the term "exclusive licence". Giving a good faith interpretation of this provision in the context of the UPCA, it is according to the Court decisive whether a licensee is entitled to solely use and to exclude others, including the patent proprietor, from using the patent, which includes, in the case of an infringement, the right to assert claims. Against this background, the Court follows the Claimant that read together, these clauses transfer to the Claimant all rights of commercial exploitation, while at the same time barring Counterdefendant 2 from granting rights to any other party in that field. […].

74. Also the fact that […] does not make the licence non-exclusive in the sense of Art. 47(2) UPCA. These provisions do not detract from the exclusive position of the Claimant to commercially exploit and prosecute the subject matter of the licence. This is sufficient to satisfy the requirements of Art. 47(2) where it concerns the exclusivity of the licence, whereby the Court notes that upon a good faith interpretation, "exclusive" does not necessarily mean that the right to use the patented invention can only be licensed to one exclusive licensee in its entirety and without limitations. It is commonly accepted that an exclusive licence may, for instance, be limited in terms of its geographical scope, field of use or duration. Moreover, the Claimant, […] (also see exhibit VB26, the statement from the general counsel of Counterdefendant 2, [redacted] who declares that the […] provision is common for research and educational institutions like Counterdefendant 2 and was never viewed as impacting the exclusivity of an exclusive licence).

75. Finally, the Court does not have doubts that the Claimant is a party to both VB4a and VB4b. The "Statement of Relocation" provided as exhibit VB27, the existence and contents of which has not been challenged by the Defendants, shows that Promosome LLC relocated its principal place of business from New York to the State of Connecticut on 12 July 2017. There is no reason to assume that the legal entity changed as a result of the relocation process.

76. Based on the above, the Court comes to the conclusion that the Claimant has standing to sue as an exclusive licensee.

IV. Technical background (common general knowledge)

77. By way of technical background to this case and to set out the common general knowledge that the skilled person (see definition below) possessed at the relevant date, the Court considers it useful to provide the following summary of what the parties have helpfully submitted as technical background information. The Court understands that parties' submissions such that this information belonged to the common general knowledge at the relevant date and that this is not in dispute between the parties. Accordingly, the following has been taken from the (undisputed parts of) the parties' submissions.

The genetic code

78. The genetic material in the nucleus of a cell consists of a macromolecule called DNA. DNA is a polymer consisting of many smaller units called deoxyribonucleotides („nucleotides"). A nucleotide consists of a sugar and a phosphate group linked to one of four different bases, A (adenine), C (cytosine), T (thymine) or G (guanine).

79. The coding region of protein-encoding genes specifies a polypeptide sequence composed of a string of individual amino acids. Each amino acid is encoded by three consecutive nucleotides called a "codon" or "base triplet".

80. The nucleotides of the DNA in the cell nucleus join together and form two strands (double-stranded DNA).

81. A DNA single strand is a linear and unbranched chain of nucleotides. In these chains, the deoxyribose sugars of the individual nucleotides are each linked via a phosphate group by means of a so-called phosphodiester bond. The first and last nucleotide of the chain are each linked to only one other nucleotide. The two ends of the DNA single strand can be distinguished from each other based on the numbering convention of the deoxyribose sugar. The two ends are referred to as the "5'-end" and the "3'-end". There is a phosphate residue at the 5'-end and an OH group at the 3'-end.

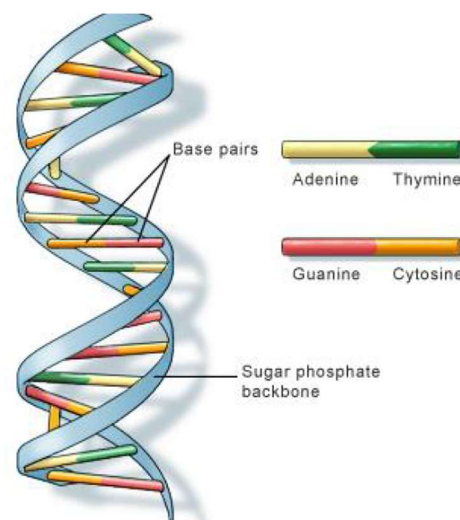
82. The DNA sequence of a single strand could look like this, for example (this sequence consisting of six different codons):

5'- ...ATG CGC AAT GCG ATA TAC... -3'

83. A DNA double strand is a twisted ladder-like structure formed from two antiparallel strands of DNA, the sequence of which could look like this, for example:

5'- …ATG CGC AAT GCG ATA TAC... 3'
3'- ...TAC GCG TTA CGC TAT ATG... 5'

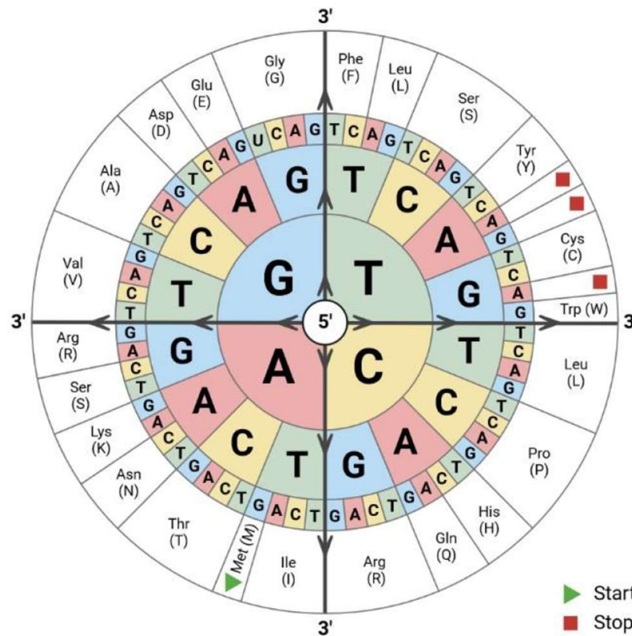
84. The "rungs" of the strands are formed by the interacting bases of the two individual strands. Only certain, so-called complementary bases can interact with each other, A with T or C with G. Consequently, a DNA double strand consists of two antiparallel DNA single strands with a complementary sequence of nucleotides. As mentioned above, double-stranded DNA ("dsDNA") is present in a helical conformation (i.e. a twisted rope ladder). This structure is called a DNA double helix. It carries the genetic code that determines the characteristics of a living organism.



85. A gene is a section of DNA that contains the information to produce an RNA ("ribonucleic acid"). The step from DNA to RNA is called "transcription" and is explained in more detail below. One class of RNAs, messenger RNAs (mRNAs), serves as a blueprint for proteins. The step from mRNA to protein is called "translation". A gene thus contains the genetic code for the formation of a specific protein (via the mRNA as an intermediate stage) in the form of "codons" or "base triplets". Each "codon" or "base triplet" codes for a specific amino acid (with the exception of the stop codons). The coding sequence of consecutive codons is also referred to as an open reading frame ("ORF"). An open reading frame is the area of DNA that is located between a start (or "initiation") codon and a stop codon. The start codon typically codes for the amino acid

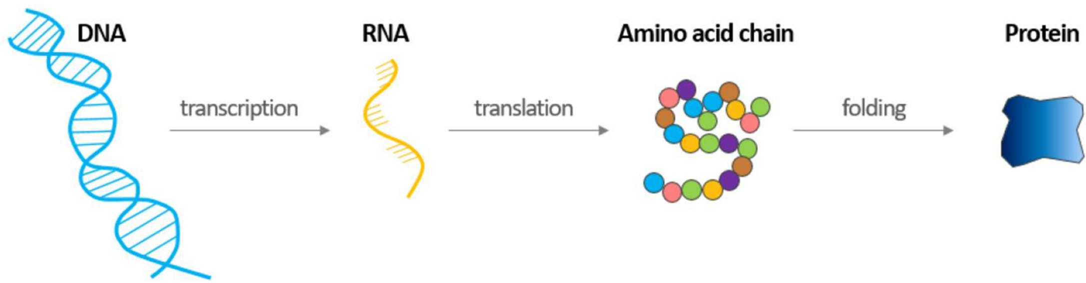
methionine and the stop codon ends the reading frame without coding for an amino acid itself. The open reading frame thus encodes the amino acid sequence of a protein.

86. In humans, there are 64 (i.e. 4^3 possible combinations) codons. 61 of these encode the 20 different amino acids. In addition, there are three stop codons (or terminators). The different codons can be depicted schematically as follows (whereby it should be noted that the illustration below refers to the 4 nucleotide bases used in DNA, namely A, G, T and C; in mRNA, T is replaced by U):



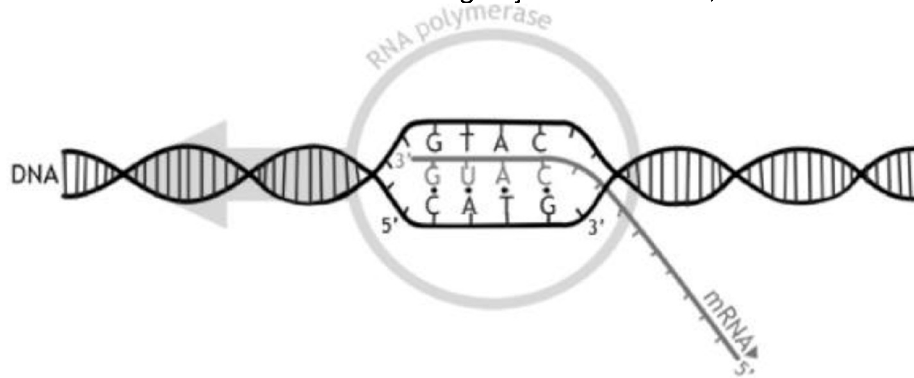
87. As can be seen above, except for methionine and tryptophan, each amino acid is encoded by multiple codons. This is known as "degeneration of the genetic code". For example, the amino acid serine is encoded by either UCU, UCC, UCA, UCG, AGC, or AGU. As another example, tyrosine is encoded by either UAU or UAC. This degeneration means that different codon sequences can encode instructions for the same amino acid chain. Consequently, one codon can be mutated or substituted for another codon without changing the encoded amino acid sequence. Methionine is only encoded by ATG (AUG in mRNA). As mentioned above, this is also typically the translation initiation codon in a coding sequence.

88. The translated proteins are finally folded into a three-dimensional spatial structure in a cell to make them functional. This process takes place during or after the synthesis of the amino acid chain in the endoplasmic reticulum (ER), in the Golgi apparatus and partly also in the cytosol of the cell. The process of transcription, translation and eventually folding into a functional protein is schematically depicted below:



Transcription in more detail

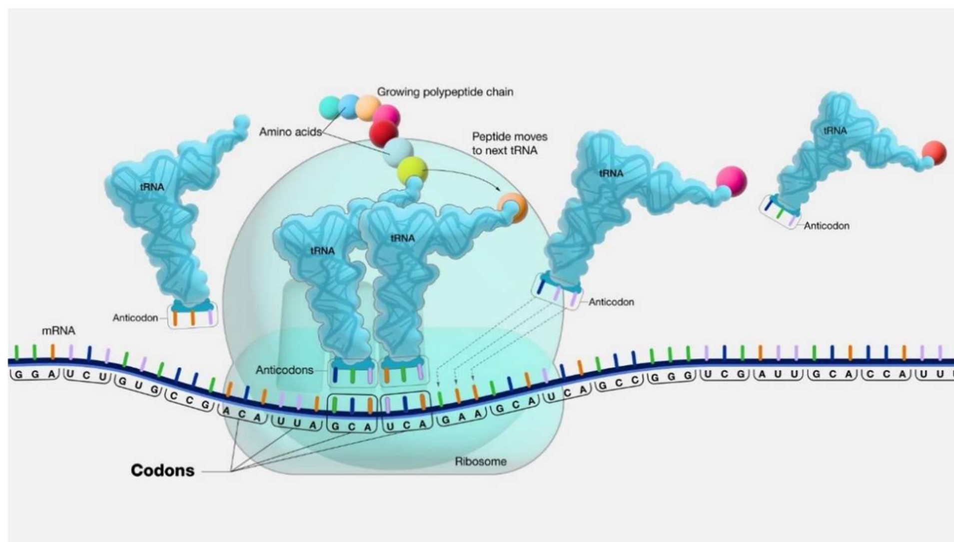
89. As mentioned above, protein expression begins with the transcription step. The DNA double helix is first unwound and a protein-coding DNA strand is transcribed into mRNA. At the beginning of a gene there is a special series of bases - the "promoter" - to which an enzyme complex consisting of "RNA polymerase" and other transcription factors attaches itself. The RNA polymerase produces a copy of the DNA section in the form of another nucleic acid consisting of just one strand, the mRNA:



90. The base G pairs with the unpaired base C in the DNA, a free base U (uracil, which, as mentioned above, occurs in the mRNA instead of base T and is complementary to base A) pairs with the unpaired base A.

Translation in more detail

91. Once transcription is complete, the mRNA is subject to modification in the nucleus, *e.g.* splicing and base modification, to become a mature mRNA. The mature mRNA is transported out of the cell nucleus and reaches so-called "ribosomes" in the cytoplasm of the cell. This is where translation takes place - the translation of the information contained in the mRNA nucleotide sequence into the amino acid sequence of the expressed protein. This process is schematically depicted in the below figure.



92. As shown above, the ribosomes bring an mRNA together with the appropriate *transfer RNA* (tRNA). Put simply, the tRNAs carry a specific amino acid on one side and three bases (the anticodon) on the other side that match a codon on the mRNA. If the codon of the mRNA and the anticodon of a tRNA match (i.e. are complementary to each other), the tRNA unloads its amino acid. The amino acids are linked together in the order of the codons of the mRNA bases to form a chain that leaves the ribosome until a "stop codon" (the sign for terminating translation) is reached on the mRNA. The amino acid chain then generally folds into a specific three-dimensional structure, which is the active protein.

mRNA structure and translation initiation

93. The sub-structures of an mRNA include a cap, the 5′-untranslated region (5′-UTR), the coding sequence ("CDS") with one or more open reading frames ("ORF") and the 3′-untranslated region ("3′-UTR") followed by a poly-A tail.

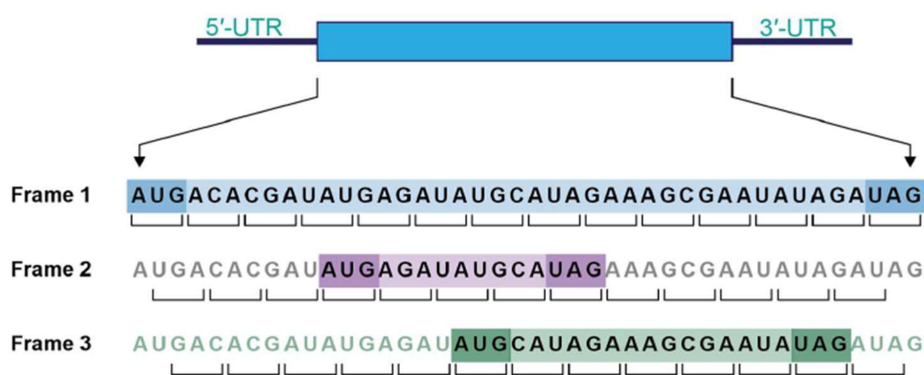
94. The 5′-cap consists of a modified guanine (G) nucleotide at the 5′-end of the mRNA and has several functions: it protects the mRNA from degradation and facilitates the binding of the ribosome, enabling the initiation of protein synthesis.

95. Untranslated regions (UTRs) are segments of mRNA that do not code for proteins but serve important functions. In particular, these regions play a key role in the regulation of translation efficiency and mRNA stability. The 5′ UTR is located at the 5′-end of the mRNA, starting immediately after the 5′-cap and ending just before the coding sequence begins. The 3′-UTR comes after the coding sequence and continues until the polyA tail.

96. The polyA tail at the 3′-end of the mRNA is a stretch of adenine (A) nucleotides that is added in the cell nucleus and assists in transporting the mRNA from the cell nucleus into the cytoplasm, as well as protecting the mRNA against degradation by RNases (ribonucleases), cellular enzymes that degrade mRNA for different reasons such as the control of protein level or removal of faulty mRNAs.

97. The coding sequence of the mRNA starts with an initiation codon (as mentioned above, this is most commonly an "AUG" codon; "initiation codon" and "start codon" are terms that are used interchangeably), at which the process of translation commences. In prokaryotes, the 5′-UTR contains a sequence called the "Shine-Dalgarno sequence" (5′- AGGAGGU-3′, "SD"), which is found 3-10 base pairs upstream (i.e., 5′) from the initiation codon which provides the "context" for ribosome binding near the initiation codon. In eukaryotes, the AUG initiation codon is embedded into a "Kozak consensus sequence", i.e., a specific sequence surrounding the AUG initiation codon. However, the start codon AUG can also occur at other, secondary sites of the mRNA. Thus, it can also happen that the ribosomes do not start the translation process at the actual and correct (primary) start codon, but at an incorrect (secondary) codon which can for example be located downstream on the mRNA nucleotide sequence. In addition to the usual start codon AUG (so-called "canonical start codon"), there are also other ("non-canonical") start codons such as CUG, ACG and GUG as secondary start codons.

98. The coding sequence following the 5′-UTR contains the genetic information required to translate the mRNA into a protein. In such a coding sequence there can be, in theory, more than one ORF, i.e., ORFs theoretically beginning and ending at different initiation and stop codons, see below, with the initiation codon "AUG" and the stop codon ("UAG" in the following diagram):



99. The primary and a different (secondary) start codon can occur within the same reading frame ("in-frame"), i.e. within the same sequence of groupings of three nucleotides (so-called triplet code):

... ***AUG*** CGC ***ACG*** GCG AUA UAC...

or in different reading frames ("out-of-frame"), i.e. within a different sequence of groupings of three nucleotides:

... ***AUG*** CG***A*** ***CG***U GCG AUA UAC...

100. Secondary, downstream "in-frame" start codons can lead to incomplete, truncated proteins or peptides, while secondary, upstream "in-frame" start codons can lead to longer proteins than the actual protein to be read. Finally, secondary "out-of-frame" start codons can lead to completely different proteins, as the reading frame and thus the sequence of amino acids in the protein is completely changed.

Codon optimisation

101. The efficiency of protein translation depends, inter alia, on the availability of the specific (complementary) tRNA carrying the corresponding amino acid in a given cell type. The more matching tRNAs are available in a cell, the quicker the corresponding tRNA (with its amino acid attached) can be transported to the ribosome and the quicker translation can progress. Organisms have developed different preferences regarding the anti-codon used in a tRNA for a specific amino acid, meaning that some tRNAs (for a specific amino acid) are more abundant than others in the cells of the specific organism.

102. These observations have been used in designing DNA templates employing codons that lead to increased protein translation efficiency of mRNAs produced using such DNA templates. More specifically, the optimisation involves considering whether the polynucleotide sequence contains codons that match the optimal codons for the target organism. This is of particular importance when the sequence to be expressed comes from an organism that is different to the target organism, as such a sequence is more likely to have sub-optimal codons for expression in the (heterologous) target organism. If this is the case, e.g. when a viral sequence is to be optimised for expression in human cells, one would have to consider the most commonly used codon for each amino acid in human cells during such a sequence optimisation by adjusting the codon usage of the DNA/mRNA template accordingly.

103. To evaluate how well the codon usage of a sequence aligns with the most frequently used codons in a particular organism, the "Codon Adaptation Index" (CAI) is a commonly used method to evaluate the degree of codon optimisation of a gene with respect to a specific organism. CAI values can range from 0 to 1, where the closer a value is to 1, the higher the degree of codon optimisation for the relevant organism. Therefore, genes with a higher CAI value would be expected to be expressed more efficiently in the relevant organism than genes with a low CAI value.

miRNA

104. MicroRNAs (miRNAs) are short, highly conserved, non-coding ribonucleic acids that play an important role in the complex network of cellular gene expression regulation. They are widely distributed and regulate a variety of biological functions. They act by modulating transcription and translation programs and therefore control both physiological and pathological processes such as cell development, cell differentiation, proliferation (cell division), apoptosis (cell self-destruction) and tumor growth. miRNAs act as small guide molecules in so-called "RNA silencing" by negatively influencing the expression of various genes at both mRNA and protein level by degrading (i.e. destroying) the mRNA or sterically suppressing the translation process by binding to the mRNA. This regulation occurs after transcription and is known as post-transcriptional regulation.

105. An miRNA binding site is a specific sequence on the mRNA where an miRNA can bind. This binding is guided primarily by a short sequence within the miRNA called the "seed sequence," which usually consists of nucleotides 2-7 or 8 from the miRNAs 5′-end. The nature of the pairing between the miRNA and its target determines the effectiveness of regulation.

V. The Patent and its interpretation

106. In par. [0001] of the description of the Patent, it is described that translation initiation in eukaryotes involves recruitment by mRNAs of the 40S ribosomal subunit and other components of the translation machinery at either the 5' cap-structure or an internal ribosome entry site (IRES). Following its recruitment, the 40S subunit moves to an initiation codon. It is stated that one widely held notion of translation initiation postulates that the 40S subunit moves from the site of recruitment to the initiation codon by scanning through the 5' leader in a 5' to 3' direction until the first AUG codon that resides in a good nucleotide context is encountered (Kozak "The Scanning Model for Translation: An Update" J. Cell Biol. 108:229-241 (1989)). According to the description, more recently, it has been postulated that translation initiation does not involve scanning, but may involve tethering of ribosomal subunits at either the cap-structure or an IRES, or clustering of ribosomal subunits at internal sites (Chappell et al. "Ribosomal shunting mediated by a translational enhancer element that base pairs to 18S rRNA" PNAS USA 103(25):9488-9493 (2006); Chappell et al., "Ribosomal tethering and clustering as mechanisms for translation initiation", PNAS USA 103(48):18077-82 (2006)). The 40S subunit moves to an accessible AUG codon that is not necessarily the first AUG codon in the mRNA. Once the subunit reaches the initiation codon by whatever mechanism, the initiator Methionine-tRNA, which is associated with the subunit, base pairs to the initiation codon, the large (60S) ribosomal subunit attaches, and peptide synthesis begins.

107. Par. [0002] adds that as translation is generally thought to initiate by a scanning mechanism, the effects on translation of AUG codons contained within 5' leaders, termed upstream AUG codons, have been considered, and it is known that an AUG codon in the 5' leader can have either a positive or a negative effect on protein synthesis depending on the gene, the nucleotide context, and cellular conditions. For example, an upstream AUG codon can inhibit translation initiation by diverting ribosomes from the authentic initiation codon. However, the notion that translation initiates by a scanning mechanism does not consider the effects of potential initiation codons in coding sequences on protein synthesis. In contrast, the tethering/clustering mechanisms of translation initiation suggests that putative initiation codons in coding sequences, which include both AUG codons and non-canonical codons, may be utilized, consequentially lowering the rate of protein synthesis by competing with the authentic initiation codon for ribosomes.

108. According to par. [0003] miRNA-mediated down-regulation can also negatively impact translation efficiency. Although miRNAs generally mediate their effects by base-pairing to binding sites in the 3' untranslated sequences (UTRs) of mRNAs, they have been shown to have similar repressive effects from binding sites contained within coding sequences and 5' leader sequences. There may be more than 1,000 different miRNAs in humans.

109. Par. [0004] states that the negative impact of putative initiation codons in mRNA coding sequences and miRNA-binding sites in mRNAs pose challenges to the pharmaceutical industry. For example, the industrial production of protein drugs, DNA vaccines for antigen production, general research purposes and for gene therapy applications are all affected by a sub-optimal rate of protein synthesis or sequence stability. Improving protein yields and higher protein concentration can minimize the costs associated with industrial scale cultures, reduce costs of producing drugs and can facilitate protein purification. Poor protein expression limits the large-scale use of certain technologies, for example, problems in expressing enough antigen from a DAN [sic] vaccine to generate an immune response to conduct a phase 3 clinical trial.

110. Against this background, the Patent in par. [0005] states that there is a need in the art for improving the efficiency and stability of protein translation and improving protein yield and concentration, for example, in the industrial production of protein drugs.

111. This need is purportedly met by a method as claimed in independent claim 1 of the Patent. This claim can be broken down into features as follows, largely corresponding to the feature breakdown adopted by the parties:

[1] A method of improving full-length protein expression efficiency comprising:

[1.1] a) providing a polynucleotide comprising:

[1.1.1] i) a coding sequence for the full-length protein;

[1.1.2] ii) a primary initiation codon,

[1.1.2.1] that is upstream of the coding sequence of the full-length protein, and

[1.1.2.2] encodes the first amino acid of the coding sequence of the full-length protein,

[1.1.3] iii) one or more secondary initiation codons,

[1.1.3.1] located within the coding sequence of the full-length protein downstream of the primary initiation codon, and

[1.2] b) mutating the one or more secondary initiation codons,

[1.2.1] located within the coding sequence of the full-length protein downstream of the primary initiation codon,

[1.3] The mutation results in a decrease in initiation of protein synthesis at the one or more secondary initiation codons,

[1.3.1] resulting in a reduction of ribosomal diversion away from the primary initiation codon;

[1.3.2] thereby increasing expression efficiency of the full-length protein initiated at the primary initiation codon,

[1.4] wherein mutating the one or more secondary initiation codons comprises mutating one or more nucleotides such that the amino acid sequence of the protein remains unaltered.

112. The parties debated about the interpretation of some of these features, which therefore requires discussion.

113. The principles applicable to claim interpretation have been set out by the UPC Court of Appeal in its final order in UPC_CoA_335/2023 (Order of 26 February 2024, as rectified, Nanostring/10x Genomics). The patent claim is not only the starting point, but the decisive basis for determining the protective scope of a European patent under Art. 69 EPC in conjunction with the Protocol on the Interpretation of Art. 69 EPC. 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. The patent claim is to be interpreted from the point of view of a person skilled in the art. In applying these principles, the aim is to combine adequate protection for the patent proprietor with sufficient legal certainty for third parties. These principles for the interpretation of a patent claim apply equally to the assessment of the infringement and the validity of a European patent.

114. The skilled person always interprets features in the light of the claim as a whole (see UPC_CoA_1/2024, order of 13 May 2024, VusionGroup/Hanshow, UPC_CoA_768/2024, order of 30 April 2025, Insulet/EOFlow). From the function of the individual features in the context of the patent claim as a whole, the skilled person will deduce which technical function these features actually have individually and as a whole. With regard to the terminology used in a patent, this can lead to the skilled person attributing a meaning to a term that differs from its general usage. The patent specification can define terms independently and may thus represent its own lexicon, see e.g. LD Munich, UPC_CFI_248/2024, decision dated 22 August 2025 (Brita SE/AQUASHIELD); CD Munich, UPC_CFI_836/2024, decision dated 20 November 2025 (BAUSSMANN/Raimund Beck); CD Paris seat, UPC_CFI_309/2023, decision dated 5 November 2024 (NJOY/Juul).

The skilled person

115. The parties did not expressly define the skilled person. In the view of the Court, the person skilled in the art is a person having a PhD degree in molecular biology or biochemistry and having several years of professional experience with molecular cloning techniques and protein expression systems.

116. As follows from the above, the skilled person has as their common general knowledge the information provided in the “technical background” section.

Claim interpretation from the perspective of the skilled person

117. Claim 1 of the Patent is a method claim. The claimed method is defined by a number of concrete method steps (**feature groups 1.1**, **1.2** and **1.4**) and specifies a particular technical effect that is achieved by the method, i.e. improving full-length protein expression efficiency (**feature 1**). This technical effect is repeated in **feature group 1.3**, in particular **feature 1.3.2**, as the result to be achieved by the claimed method (i.e., again, increasing the expression efficiency of the full-length protein).

118. According to **feature 1.1**, the first method step of the claimed method is providing a polynucleotide. Par. [0022] defines the term "polynucleotide sequence" as a deoxyribonucleotide or ribonucleotide polymer in either single- or double-stranded form, and unless otherwise limited, encompasses known analogues of natural nucleotides that hybridize to nucleic acids in a manner similar to naturally occurring nucleotides. Nucleic acid sequences can be, e.g., prokaryotic sequences, eukaryotic mRNA sequences, cDNA sequences from eukaryotic mRNA, genomic DNA sequences from eukaryotic DNA (e.g., mammalian DNA), and synthetic DNA or RNA sequences, but are not limited thereto. Accordingly, the polynucleotide to be provided is either DNA (deoxyribonucleotide) or mRNA (messenger ribonucleotide). The skilled person knows that, from a technical perspective, an mRNA itself is not feasible to be mutated because mRNA is single-stranded, unstable and not self-replicable, unlike e.g. a plasmid DNA. Rather, the starting point for mutating mRNA is typically a DNA sequence which can be mutated before being transcribed into mRNA. Accordingly, there is no difference whether a mutated DNA or a mutated mRNA is to be produced because in both cases, the generation of a mutated DNA is required (that can then further be transcribed into the mutated RNA).

119. According to **feature 1.1.1**, the DNA/RNA comprises a coding sequence for the full-length protein (i.e. a polynucleotide sequence which codes for a protein product (protein of interest) whose production is to be modulated, par. [0016]). The coding sequence can be a wild-type sequence, i.e., a sequence as it occurs in nature, but the claim is not limited to the coding sequence being a wild-type sequence. In particular, the skilled person understands, using the description as an explanatory aid and their common general knowledge, that the coding sequence may be codon optimised, e.g. for higher expression in mammalian cells (see par. [0042] which discusses "codon usage bias" in a particular organism and [0075] which gives an example of a HcRed1 coding sequence that was human codon-optimised for higher expression in mammalian cells after generating it by mutagenesis of a non-fluorescent chromoprotein from the reef coral *Heteractis crispa*, but before identifying potential initiation codons and generating modified sequences). Such codon optimised sequences are, in principle, not excluded from the claim.

120. The full-length protein that is encoded by the coding sequence can be any protein of interest. Par. [0016] of the description mentions as examples therapeutic proteins, nutritional proteins, industrial useful proteins, reporters or selectable markers genes such as enhanced green fluorescent protein (EGFP) or luciferase. The claimed subject matter is, however, not limited to any of those examples.

121. **Features 1.1.2 and 1.1.3** require that the polynucleotide comprises a primary initiation codon and one or more secondary initiation codons. An "initiation codon" or "initiation triplet" is defined in the description (par. [0036]) as the position within a cistron (a unit of DNA that encodes a single polypeptide or protein, par. [0014]) where protein

synthesis starts. According to par. [0039] the term "primary initiation codon" refers to the initiation codon of a cistron that encodes the first amino acid of the coding sequence of the encoded protein of interest whose production is to be modulated. This codon is also referred to in the Patent as the "authentic initiation codon". In the same paragraph, the term "secondary initiation codon" is defined as an initiation codon that is other than the primary or authentic initiation codon for the encoded protein of interest (see further discussion below).

122. The primary initiation codon is characterised in the claim as being located upstream of the coding sequence (**feature 1.1.2.1**), i.e. in the direction of the 5'-end of the nucleotide sequence (par. [0038]), and at the same time as encoding the first amino acid (i.e. methionine) of the coding sequence of the full-length protein, i.e. the protein of interest (**feature 1.1.2.2**). In contrast, the one or more secondary initiation codons are located within the coding sequence of the full-length protein, downstream of the primary initiation codon (**feature 1.1.3.1**), i.e. towards the 3'-end of the (mRNA) sequence in relation to the primary initiation codon (par. [0038]).

123. In eukaryotic mRNAs, an initiation codon typically consists of three nucleotides (the Adenine, Uracil, and Guanine (AUG) nucleotides) which encode the amino acid Methionine (Met) (see par. [0036]) and [0046], also called "canonical" start codon). However, translation can sometimes also initiate at other codons: ACG, GUG, UUG, CUG, AUA, AUC, and AUU (see par. [0046] and claim 4). These are the so-called non-canonical start codons. According to the description, this was known from the prior art (par. [0046]). This understanding is in-line with the agreed common general knowledge of the skilled person as set out above.

124. According to **feature group 1.2** at least one secondary initiation codon located downstream of the primary initiation codon within the coding sequence of the full-length protein should be mutated (**feature 1.2.1**). According to the (undisputed) understanding of the person skilled in the art, "mutating" means altering the nucleic acid sequence of the given genome, e.g. altering at least one nucleotide in at least one of the codons: e.g. AC<u>G</u> → AC<u>A</u>. **Feature 1.4** further requires that the amino acid sequence of the protein to be expressed remains unchanged despite the mutation. I.e. the same amino acid should remain encoded with a different codon. This is made possible by the degeneracy of the genetic code. The claim is, however, not limited to mutations of the one or more secondary initiation codons that do not introduce any new initiation codons, nor does the claim require that the at least one secondary initiation codon is mutated into a non-initiation codon. These are preferred embodiments to which claim 1 of the Patent is not limited (cf. par. [0047] and claim 7, first alternative).

125. The parties have discussed at length whether in the claimed method, the term “secondary initiation codon” (**feature 1.1.3**) refers to an *actual* secondary initiation codon, in the sense that protein synthesis is actually initiated at that codon.

126. First of all, the definition of an initiation codon provided in the description, discussed above, is that protein synthesis starts there (see par. [0036]). It can thus already be inferred from this definition that the claim requires the mutation of one or more actual secondary initiation codons. This interpretation is confirmed by the claim as a whole. **Features 1.1.3 and 1.2** will not be read by the skilled person in isolation, but together with **feature group 1.3** which specifies the result (technical effect) achieved by these features (see discussion above). According to **feature 1.3**, <u>the mutation of</u> the one or more secondary initiation codon <u>results</u> in a <u>decrease in the initiation</u> of protein synthesis <u>at the one or more secondary initiation</u> codons. According to **feature 1.3.1**, this decrease in initiation results in a reduction of <u>ribosomal diversion away</u> from the primary initiation codon. <u>Thereby</u> the expression efficiency is increased. In the wording of the claim, even though it speaks generally of a “secondary initiation codon”, which might at first glance be perceived broadly as to include any codon that could putatively be a secondary initiation codon, it is therefore at least implicit to the skilled person that at least one actual secondary initiation codon must be mutated; otherwise, there can be no reduced initiation of protein synthesis at such codon (and consequently none of the effects resulting therefrom).

127. The interpretation of the claim as requiring the mutation of one or more actual secondary initiation codons is supported by the description. Par. [0048] explains that the claimed method reduces the competition between various initiation codons for the translation machinery. By eliminating downstream initiation codons, coding sequences that are in the same reading frame as the encoded protein, the generation of truncated proteins, with potential altered function, will be eliminated. In addition, by eliminating downstream initiation codons that are out-of-frame with the coding sequence, the generation of various peptides, some of which may have negative effects on cell physiology or protein production, will also be eliminated. As a result, the method allows for improved and more efficient expression of the full-length protein, i.e. the protein of interest (**features 1.1 and feature group 1.3**).

128. The description mentions *putative* (or potential) secondary initiation codons. These are codons having the nucleotide sequence of an initiation codon and where translation *could* initiate. All putative initiation codons in a polynucleotide sequence can readily be identified, for instance using a computer program. Such a program can subsequently “recode an mRNA to eliminate potential initiation codons” (cf. par. [0057]).

129. The skilled person realises that a putative secondary initiation codon may be an actual secondary initiation codon. This insight lies at the core of the invention (par. [0047]). However, the skilled person also knows that not all putative secondary initiation codons are actual secondary initiation codons. Whether a putative initiation codon is an actual

initiation codon is a matter of fact. It depends on whether protein synthesis is actually initiated at that codon (see above). The skilled person knows on the basis of their common general knowledge that whether a putative secondary initiation codon is in fact an actual secondary initiation codon will be determined by the circumstances, including for example the nucleotide context of that codon within the polynucleotide sequence (also see par. [0057]).

130. In summary, the claimed method requires the mutation of one or more actual secondary initiation codons in order to achieve the effects as claimed. Put differently, the claim requires a causal link between mutating the one or more secondary initiation codons (**feature 1.2**) and the resulting increase in protein expression efficiency (**feature group 1.3**). In this respect, feature group 1.3 has a limiting effect, as it links the specific requirements for the secondary start codon to the effects of the mutation.

131. To the extent the Claimant argues anything different by emphasising that features 1 and 1.3 are a "technical limitation" of the claim by drawing an analogy to method claims having a "use feature" or a "stated purpose", the Court notes that a purpose stated in a method claim can define the specific application of a method and thus regularly requires certain steps that are at least implicit in the claimed method. For example, in LD Munich 19 December 2025, UPC_CFI_437/2024 and UPC_CFI_681/2024, GXD-Bio/Myriad), the claimed method was "for quantifying expression level of a target gene in a formalin-fixed, paraffin embedded (hereinafter: FFPE) tissue sample of human breast cancer tissues", thus defining the technical context of that claim. Likewise, in CD Munich 24 February 2026, UPC_CFI_337/2025, TCL/Corning, the claimed method was "for producing alkali-free glass sheets", thus defining and limiting the claimed subject matter to the production of such glass sheets.

132. Here, the situation is rather different: the features referred to by the Claimant as "technical limitation" neither further define the technical context of the claimed method, nor do these features convey technical information to the skilled person on how a concrete method step is to be carried out. These features only make concrete what the result must be when a secondary initiation codon is mutated and therefore (implicitly) presuppose that the secondary initiation codon within the meaning of feature 1.2 is an actual secondary initiation codon.

133. A different claim interpretation does not follow from the Case Law of the Boards of Appeal of the EPO that the Claimant has referred to. On the contrary, this case law distinguishes between different types of statements of purpose in method claims, namely those that define the application or use of a method and those that define the effect arising from the steps of a method and implicit therein. Where the purpose merely states a technical effect which inevitably arises when carrying out the other remaining steps of the claimed method and is thus inherent in those steps, such a

technical effect has no limiting effect because it is not suitable for distinguishing the claimed method (see Case Law of the Boards of Appeal of the EPO, section I-C-5.2.5).

134. The claimed method does, however, not comprise a step of identifying or ascertaining beforehand, i.e. before the step of mutating, whether any particular putative secondary initiation codon is an actual secondary initiation codon. For the claimed method it suffices, but is also required, that one or more actual secondary initiation codons are mutated leading to the effects claimed, regardless of whether the mutated codon was previously known to be an actual secondary initiation codon or can only be identified as such retrospectively.

135. This understanding is consistent with the teaching of the examples in the description. For instance, in Example 1 (paras. [0061]–[0069], Figures 2–4), multiple potential secondary initiation codons were removed from the CAT and CD5 ORFs without pre-identifying which were "actual." Western blot analyses then revealed an increase in full-length protein expression. This teaching is furthermore in line with par. [0047], according to which putative initiation codons in coding sequences may also be utilized (see above). Against this background, there is no need for the Court to reach a final conclusion as to whether, in view of the experimental conditions of the examples in the Patent, the skilled person would assume that one or all of the putative secondary start codons that were mutated in Example 1 are actual secondary initiation codons.

136. In addition, the Court notes that the claim does not require that <u>only</u> actual secondary initiation codons are mutated. From the use of the word "comprising" in feature 1, it already follows that mutating putative secondary initiation codons, or other (mutation) steps, such as a step of routine codon optimisation, are not excluded from the claim, nor is it excluded that such other mutations are carried out at the same time as mutating the one or more actual secondary initiation codons. There is also no technical functional reason why the claimed method would exclude other mutations or mutation steps. It should nevertheless always be required that the effects of feature group 1.3 are achieved and are specifically attributable to the mutation of actual secondary initiation codons.

137. In view of the further discussion, the Court considers it helpful to note already here that from the above it follows that, depending on the concrete facts and circumstances, it may be reasonable to assume on the basis of available evidence that one or more actual secondary initiation codons have been mutated resulting in the claimed effects. This is, however, a matter of evidence rather than claim construction.

138. Finally, the Court notes that the claim does not specify any degree with which the expression efficiency of the full-length protein is to be increased. According to par. [0040], "increased protein expression" refers to translation of a modified mRNA where one or more secondary initiation codons are mutated that generates a polypeptide concentration that is at least about 5%, 10%, 20%, 30%, 40%, 50% or greater over the

polypeptide concentration obtained from the wild-type mRNA where the one or more secondary initiation codons have not been mutated. Increased protein expression can also refer to protein expression of a mutated mRNA that is 1.5-fold, 2-fold, 3-fold, 5-fold, 10-fold or more over the wild-type mRNA. However, these definitions have not been included in the claim. Nevertheless, the claim does require an increase in expression efficiency and, using the description for guidance, the skilled person will understand the claim feature "increased protein expression efficiency" such that there must be at least a very small (such as "about 5%"), but measurable increase in protein expression compared to the starting polynucleotide sequence without the mutation of the one or more secondary initiation codons.

In the Counterclaim for Revocation:

139. The counterclaim for revocation is admissible and is successful on the merits.

140. The LD Munich has jurisdiction to hear the counterclaim for revocation (see above) and the patent proprietor ("PP") has become a party to the proceedings (as a defendant in the counterclaim) as required by Rule 25.2 RoP. No admissibility concerns have been raised by the Counterdefendants nor are these apparent.

VI. Novelty

141. The Defendants have argued that the subject matter claimed in the Patent lacks novelty over several prior art disclosures. The attack succeeds. The Court finds that claim 1 as granted is not novel.

Principles

142. For the purposes of Article 54 EPC, an invention shall be considered to be new if it does not form part of the state of the art.

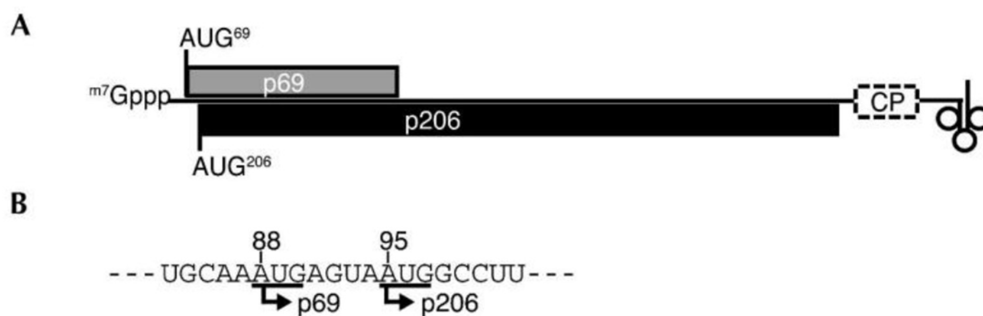
143. The assessment of novelty within the meaning of Art. 54(1) EPC requires the determination of the whole content of the prior publication. However, the content of a prior art document must not be treated as a reservoir from which features may be drawn to create a particular embodiment, but rather different passages in a document may only be combined if there is a clear and unmistakable teaching suggesting this. A feature may also be disclosed implicitly, but this requires that the skilled person would objectively consider such feature to be necessarily implied in the explicitly disclosed content, i.e. matter that is a clear and unambiguous consequence of what is explicitly mentioned, shall also be considered as part of its content. Knowledge that a skilled person only acquires as a result of further deliberation beyond this cannot be considered a direct and unambiguous disclosure. It is decisive whether the subject-matter of the claim with all its features is directly and unambiguously disclosed in the

prior art citation (see UPC_CoA_312/2025, UPC_CoA_333/2025, UPC_CoA_880/2025 UPC_CoA_882/2025, decision of 2 June 2026, *Kodak/Fujifilm*, UPC_CoA_182/2024, order of 25 September 2024, App 21143/2024, *Mammut/Ortovox*).

Lack of novelty vis-à-vis document D2 (Matsuda et al)

144. D2 is a scientific paper published in the year 2006, authored by D. Matsuda and T. Dreher entitled “Close spacing of AUG initiation codons confers dicistronic character on a eukaryotic mRNA” that was published in the journal “RNA”. It forms part of the state of the art for the Patent.

145. D2 studies the translation of two proteins from overlapping open reading frames encoded by a bicistronic mRNA derived from Turnip Yellow Mosaic Virus (TYMV) genomic RNA. The parties agree that a bicistronic nucleic acid is characterized by the fact that it encodes two distinct proteins, each of which can be translated using different open reading frames for translation and each of which has its own initiation codon. This is, for instance, shown in Fig. 1 of D2:



146. D2 describes at page 1340, right column, second paragraph:

> “We have previously reported that knockout of the downstream AUG^{206} by mutation to ACG resulted in a 2.5-fold higher expression rate from the upstream AUG^{69} (Matsuda et al. 2004). This mutation did not alter the coding of ORF69 and did not alter the predicted secondary structure of the RNA”.

147. Figure 4 of D2 and the legend to Figure 4 shows the following:

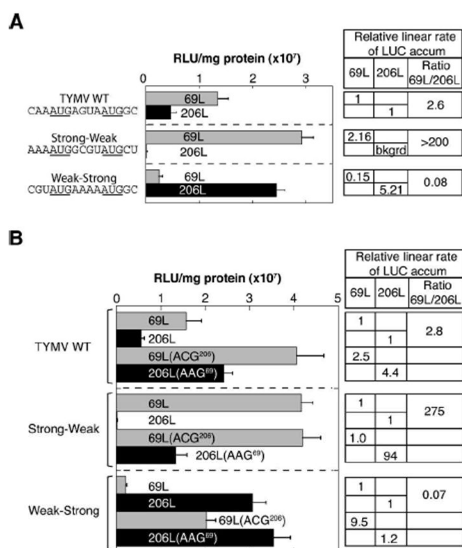


FIGURE 4. Changes in the initiation codon sequence contexts lead to altered ratios of 69L to 206L, but translational coupling is retained. (*A*) Expression in cowpea protoplasts of 69L and 206L is shown for reporter mRNAs with wild-type or variant initiation cassette (nt 85–99). Note that in dicot plants, AAAAUGGC appears to be the optimal context for translation initiation (Joshi et al. 1997; Lukaszewicz et al. 2000; Kawaguchi and Bailey-Serres 2005). (*B*) Expression in cowpea protoplasts of 69L and 206L is shown for reporter mRNAs with knockout mutations of AUG^{69} or AUG^{206} as indicated. The knockout mutations do not alter the encoded amino acid sequence. Loss of expression by both AUG mutations was previously confirmed in the wild-type context by in vitro translation of full-length TYMV RNA transcripts (Weiland and Dreher 1989).

<u>Features 1, 1.1.1, 1.1.2, 1.4</u>

148. Based on the above teachings, D2 discloses a method of improving full-length protein expression efficiency comprising providing a polynucleotide comprising a coding sequence for the full-length protein (i.e. the p69 protein), a primary initiation codon (i.e. the AUG^{69} codon), that is upstream of the coding sequence of the full-length protein, and that encodes the first amino acid of the coding sequence of the full- length protein (features 1 and 1.1.1 and 1.1.2 of claim 1 of the Patent, respectively). This was never in dispute between the parties.

149. Initially, there was discussion between the parties as to whether D2, in particular Figure 4, disclosed feature 1.4 of claim 1 which requires mutating one or more nucleotides such that the amino acid sequence of the protein remains unaltered. Eventually, the Counterdefendants did not provide any further response to the Defendants´ explanation that D2 describes two sets of experiments: one set of experiments addressing the sequence context of the start codon (not altering the start codon itself, the “Strong-Weak” / “Weak-Strong” experiments) and another set of experiments which involves mutating the start codon. In the latter experiments, which are the relevant ones for novelty (see below), the amino acid sequence of the protein does in fact remain unaltered. This is disclosed explicitly in D2 on p. 1340, cited above, and in the legend to Figure 4B, where it is stated that “the knockout mutations do not alter the encoded amino acid sequence”. Feature 1.4 is thus also disclosed in Matsuda.

Features 1.1.3, 1.2 and 1.3

150. The remaining point of dispute between the parties is whether Matsuda discloses features 1.1.3, 1.2 and 1.3 of claim 1, in particular whether Matsuda discloses the mutation of one or more secondary initiation codons.

151. The Counterdefendants take the position that Matsuda discloses the mutation of a second primary initiation codon, i.e. the primary initiation codon for the "second" protein encoded by the bicistronic RNA. The Defendants are of the opinion that the Counterdefendants are making an artificial distinction between multicistronic constructs and constructs that have more than one start site. In reality, they say, there is no difference.

152. In the Court's view, the Counterdefendants´ argumentation is based on a wrong interpretation of claim 1 of the Patent. The claim is not limited to "monocistronic" polynucleotide sequences encoding only one single protein product. As discussed above under claim interpretation, the claimed subject matter is directed at improving the expression efficiency of a (full length) "protein of interest". The primary initiation codon refers to – and is defined by being – an initiation codon that encodes the first amino acid of the encoded protein of interest (also see claim feature 1.1.2.2). A secondary initiation codon is defined as being an initiation codon other than the primary initiation codon (see claim construction above). According to these definitions, the initiation codon of a "second" protein encoded by a bi- or multicistronic RNA is to be regarded as a secondary initiation codon within the meaning of feature 1.1.3. There is no technically sensible reason why the skilled person would consider the claim to be limited to monocistronic sequences in the Counterdefendants' sense of the word. Put differently, the claims cover bi- (or multi-) cistronic polynucleotides expressing more than one polypeptide (protein), the translation initiation of which, according to the claim, is to be decreased so that the expression efficiency of the protein of interest is increased.

153. The reference made by the Counterdefendants to par. [0016] of the description of the Patent does not show that the "gene of interest" shall evidently not be part of a bi- or polycistronic mRNA comprising two or multiple primary initiation codons. According to par. [0016]: "a "gene of interest" is intended to include a cistron, an open reading frame (ORF), or a polynucleotide sequence which codes for a protein product (protein of interest) whose production is to be modulated. Contrary to the view of the Counterdefendants, par. [0016] rather confirms to the skilled person that the "gene of interest" is (only) defined by the protein product whose expression is to be increased. The fact that the terms "cistron", "ORF" or "polynucleotide sequence" are used in singular implies nothing more than that there is according to the invention only one protein of interest.

154. This, of course, does not mean that there cannot be any "second protein" in the method according to (claim 1 of) the Patent. On the contrary, as discussed above, the very concept underlying the claimed subject matter is to mutate an (actual) secondary initiation codon which is located within the coding sequence of the full-length protein of interest downstream of the primary initiation codon, i.e. a codon that initiates translation of a second (unwanted) protein product. The mutation results in a decrease in initiation of protein synthesis of that second product in favour of the translation of the protein of interest which is ("thereby") increased (feature group 1.3). This is fully consistent with and anticipated by the teaching of D2 whereby the expression of the p69 protein is increased by mutating away (knocking-out) the start codon of another ("second") protein, i.e. the p206 protein. The fact that these proteins are part of a bicistronic construct does not change the fact that the (initiation codon for the) second protein lies downstream, within the coding sequence of the protein of interest, which is all that is required by the claims of the Patent.

155. Against the background of this interpretation, the skilled person understands D2 to clearly and unambiguously disclose the mutation of AUG codon number 206 ("AUG^{206}"). This is a secondary initiation codon as the translation of p206 starts here, which has not been disputed by the Counterdefendants (also see e.g. D2, p. 1339, rh. col., 3rd par., first sentence). The secondary initiation codon lies downstream of the primary initiation codon. Features 1.1.3 and 1.2, respectively, are thus disclosed in D2.

156. D2 further discloses that mutating the secondary initiation codon increases the expression of the p69 protein (the protein of interest of which the primary initiation codon is AUG^{69}) 2.5-fold (p. 1340, cited above) at the "expense" of the p206 product ("knock-out"). This has also not been disputed. Feature group 1.3 is thus also disclosed in D2.

157. The skilled person is clearly and unambiguously taught by D2 that p69 is the protein of interest, the expression efficiency of which is increased by mutating away a start codon other than the primary initiation codon, i.e. a secondary initiation codon, leading to a decrease in production of the unwanted p206 protein thereby increasing the expression efficiency of the p69 protein of interest. As a consequence, all the features of claim 1 of the Patent are disclosed in D2.

158. The subject matter claimed in claim 1 of the Patent is therefore not novel.

Lack of novelty vis-à-vis document D1 (WO '374)

159. Document D1 also takes away the novelty of the claimed subject matter. Document D1 is an international PCT-application published as WO 91/01374 on 7 February 1991, i.e. well before the priority date of the Patent. D1 is therefore part of the state of the art for the Patent.

160. D1 describes a method of preventing undesired initiation of translation at an internal initiator codon in a DNA sequence encoding a polypeptide, wherein a Shine-Dalgarno ("SD") sequence is located upstream of the internal initiator codon; see e.g. the abstract of D1:

(57) Abstract

Described is a method of preventing undesired initiation of translation at an internal initiator codon in a DNA sequence encoding a polypeptide, wherein a Shine-Dalgarno sequence is located upstream from the internal initiator codon. The method includes altering either the internal initiator codon or the Shine-Dalgarno sequence, or both, such that inappropriate initiation of translation and/or ribosome binding is prevented.

161. As follows from D1, see p.1, l. 3-5, D1 aims to "maximize the expression and purity of useful polypeptides":

This invention relates to the use of recombinant DNA techniques to maximize the expression and purity of
5 useful polypeptides.

162. It is noted that the terms "polypeptide" and "protein" are used interchangeably both in D1 and the Patent, which is, undisputed, in line with the skilled person's understanding that a "protein" consists of one or more polypeptide chains. D1 thus discloses features 1 and 1.1.

163. D1 teaches that a critical stage in the expression of a protein is the initiation of translation (p. 1, l. 6-7). Further on p. 1, D1 describes that initiation of translation starts at an initiator codon. In prokaryotes, a ribosomal binding site (with at its core the Shine Dalgarno sequence) usually precedes the initiator codon. D1 then goes on to explain that the codons that serve as prokaryotic initiator codons are found not only at the initial position but also at other positions in the coding region (p.2, l. 28-30). Such "internal initiator codons" can result in second site or internal initiation. Second site or internal initiation results in the production of a protein corresponding to the sequence between the second site start codon and the first in-frame stop codon encountered. D1 aims to prevent this undesirable initiation of translation (p.3, l. 30-p.4, line 2). D1 thus discloses feature 1 and features 1.1.1, 1.1.2 and 1.1.3 of claim 1 of the Patent. This is as such not in dispute between the parties (except for the Counterdefendants's argument that D1 does not, in an enabling way, disclose the technical effect of actually improving full-length protein expression, see discussion below).

164. According to the method disclosed in D1, the expression and purity of the protein of interest is to be achieved by altering (by substituting one or more base pairs) the internal initiation codon such that the inappropriate initiation of translation and/or ribosome binding is prevented, see e.g. claims 1 and 2 of D1:

1. A method of preventing undesired initiation of translation at an internal initiator codon in a DNA sequence encoding a polypeptide, wherein there is located upstream of said internal initiator codon a Shine-Dalgarno sequence, said method comprising altering either said internal initiator codon or said Shine-Dalgarno sequence, or both, such that inappropriate initiation of translation and/or ribosome binding is prevented.

2. The method of claim 1, wherein said internal initiator codon is altered by a substitution of one or more base pairs.

165. Thus, D1 also discloses feature 1.1.3, 1.2 and 1.2.1 of claim 1 of the Patent.

166. D1 furthermore discloses that it is most preferred that the second site initiation codon is altered such that internal initiation and ribosome binding is eliminated without changing the (amino acid) sequence of the desired translation product, i.e. the protein of interest. See, p.7, l. 22-34 of D1:

Second site or internal initiation can be eliminated according to the invention by effecting an appropriate alteration in the sequence of either the codon being used
25 as the second site initiator codon or in the nearest adjacent Shine-Dalgarno sequence or in both. The most preferred alteration is one that, without altering the sequence of the desired translation product, is known unambiguously to be capable of eliminating internal
30 initiation and ribosome binding. If only a single change

167. Feature 1.4 of claim 1 of the Patent is thus also disclosed in D1.

168. D1 furthermore gives an explanation as to why translation initiation at a secondary initiation codon is undesirable, see claim 1 above or p. 7, l. 7-21:

Second site initiation is undesirable for a number of reasons. Second site starts may disrupt translation from properly initiated ribosomes, as well as compete with
10 initiation at the true initiation site for ribosomes, initiation factors, charged tRNAs, and any other factors needed for production of the final protein product. Thus second site initiators may reduce the overall yield of a desired product of protein synthesis. The product of the
15 second site starts may also result in the need for additional purification steps. Products of internal initiation, when in the same reading frame, can be very similar e.g., in size, physical properties and immunological specificity, to the desired product. These
20 similarities can present particularly difficult purification problems.

169. D1 further discloses on p1., l. 3-5

This invention relates to the use of recombinant DNA techniques to maximize the expression and purity of
5 useful polypeptides.

and on p. 5, l. 10-13:

10 The invention improves yield of recombinant proteins and facilitates purification by preventing the production of non-functional truncated protein fragments beginning at internal initiation sites.

170. The aim and technical effects disclosed in D1 (improving the expression (yield) of recombinant proteins corresponds to increasing translation efficiency) thus correspond to the effects claimed in (feature 1 and) feature group 1.3 of claim 1 of the Patent, thereby disclosing to the skilled person all the features of claim 1 of the Patent in a direct and unambiguous way.

171. This is nevertheless contested by the Counterdefendants on the ground that, according to the Counterdefendants, D1 suffers from a number of disclosure deficiencies. As D1, still according to the Counterdefendants, fails to provide an enabling disclosure, it cannot be novelty destroying.

172. The Court notes, firstly, that the assessment of novelty is to be carried out vis-à-vis the state of the art (Art. 54 EPC). Pursuant to Article 54(2) EPC, the state of the art shall

be held to comprise everything made available to the public by means of a written or oral description, by use, or in any other way.

173. The question of *what* has been made available to the public depends on the facts and circumstances of the individual case. This must be assessed from the perspective of the skilled person, including the common general knowledge available to the skilled person at the relevant date. In this context, it should be noted that novelty is to be assessed differently from inventive step: technical information directly corresponding to a claimed invention may be “made available” in the prior art (lack of novelty), or the claimed subject matter may not have been made available but still be obvious for the skilled person (novel, but lack of inventive step), or not made available and not obvious (novel and inventive). Thus, in particular, what is “hidden” in the prior art may still be obvious (See EPO Enlarged Board of Appeal, decisions G2/88 and G6/88, Reasons 10 and 8).

174. Against this background, the Court in principle agrees with the Counterdefendants that in order for a prior art disclosure to be relevant for novelty, the disclosure must be such that the skilled person can reproduce it using common general knowledge, i.e. the skilled person must be able to carry out the teaching of the prior art. Absent such an enabling disclosure, there is no (complete) technical teaching in the prior art and hence no potentially novelty-destroying disclosure. The need for an enabling disclosure is also in conformity with the principle expressed in Art. 83 EPC for patent applications which have to "disclose the invention in a manner sufficiently clear and complete for it to be carried out by a person skilled in the art" (cf. Case Law of the Boards of Appeal Ch. I.C.4.12). Applying this “disclosure test” to the prior art, a prior art disclosure relied upon for novelty must be reproducible for the skilled person without undue burden. The disclosure content of a prior art disclosure has to be examined on the basis of the prior art document as a whole (cf. by analogy Court of Appeal in Amgen/Sanofi, Headnote 5 in relation to sufficiency of disclosure).

175. The burden of substantiation and proof for lack of novelty lies on the Defendants as the party invoking the lack of novelty. However, where a party contests that a prior art method, even though it has been argued in a substantiated way that all of the method steps of a claim are as such disclosed, is relevant for novelty because it cannot be reproduced by the skilled person, it is for that party to at least substantiate why this is the case.

176. Applying the above principles to the present case, the Court comes to the conclusion, different from the Counterdefendants, that all of the features of the method claimed in claim 1 of the Patent are disclosed in D1 in an enabling way.

177. As follows from the above discussion, D1 discloses all of the concrete method steps that have to be performed by the skilled person to achieve the aim of increasing the expression of a protein of interest as a coherent technical concept.

178. The Counterdefendants have not disputed the correctness and/or technical feasibility of any of the method steps provided in document D1 for the skilled person using their common general knowledge. It is not in dispute that D1 discloses the mutation of a secondary initiation codon with the aim of increasing the expression of a protein of interest and that the skilled person who performs those steps will in fact be able to achieve that result without any undue burden. The Counterdefendants have not argued (in a substantiated way) that there are any "gaps" in or any other serious doubts concerning the disclosure of D1 in relation to the method steps to be taken. Nor is it in dispute that D1 discloses in sufficient detail how to mutate the secondary start codons such that the amino acid sequence of the protein whose expression is to be increased stays unchanged (also see Fig. 2, the "codon dictionary").

179. The doubts that are raised by the Counterdefendants regarding the accuracy and credibility of the scientific explanation provided by the inventors of D1 underlying the result to be achieved are not considered to be relevant for the technical teaching of D1 where it concerns the concrete method steps that are to be followed by the skilled person including the end result achieved when carrying out these steps, i.e. improving the yield of the protein of interest, nor has this been argued by the Counterdefendants. In general, a correct scientific explanation for or theory underlying a particular technical effect or step is not required for enablement, as long as the technical teaching in a prior art document is reproducible by the skilled person without undue burden. Likewise, there is no requirement in the EPC that the prior art provides experimental evidence that a method disclosed therein has been carried out, as long as at least one way of performing the method has been disclosed in the prior art.

180. That said, the Court notes that the underlying mechanism explained in D1 for the increased expression of the protein of interest seems to correspond to the explanations provided in the Patent, see p. 7 of D1, depicted above. In particular, it is stated there that "second start sites…may compete with initiation at the true initiation site for ribosomes" (cf. feature 1.3.1 of claim 1). Especially against the background that, at the priority date, it was known that translation can initiate at other codons than the usual translation initiation codon (cf. par. [0047] of the Patent), no convincing reasons have been provided why this explanation would not be credible for the skilled person.

Preferred embodiment: IL-2 Toxin (59 kD contamination)

181. In a preferred embodiment, the inventors of D1 describe that the purification of IL-2-toxin (a 68,170 dalton fusion protein, p. 5, l. 28 et seq.) yields a 59,000 dalton polypeptide as a contaminant (p.6, line 5-6). This 59 kD protein is believed to be derived from an internal initiation of translation at codon 84 in the IL-2-toxin mRNA (p.6, line 24-25). The inventors further state that "any substitution at the third nucleotide of the GUG codon at position 84 of IL-2-toxin will eliminate internal initiation at position 84 without effecting a change in the amino acid sequence of IL-2-toxin." The

Counterdefendants have argued that the existence of the 59 kDa product is only stated but not shown in D1 and in particular no experimental data on the 59 kDa product is disclosed in D1 and that the source of the alleged 59 kDa product - i.e., expression initiated at the suggested GUG or a degradation product is not disclosed in D1. Because of these deficiencies, the disclosure of D1 would not be enabling.

182. To the extent that this argument can even be decisive for the question of what has been made available to the public by D1 (which has to be determined on the basis of the whole contents of D1 and not just a preferred embodiment, see principles and reasoning above), the Court has seen no evidence that invalidates the clear statement in D1 that the 59 kD protein was in fact produced. Under these circumstances, i.e. a clear and not obviously erroneous (at least, this has not been brought forward by any party) statement in D1 that the 59 kD protein was found, it would have been up to the Counterdefendants to provide further substantiation, convincing facts and arguments why the teaching is in fact non-reproducible. The facts and evidence relied upon by the Counterdefendants do not qualify as such.

183. Document D12, a scientific article that was published before the filing of D1, and which is authored by Frank Genbauffe, who is listed as the inventor of D1, is by its nature unsuitable to cast doubt on the findings of D1. First of all, D12 does not disclose that the 59 kD protein was not found or does not exist. Moreover, as rightly pointed out by the Defendants, Figure 4 (lane B) of D12 relating to a cell extract shows many bands in the 50 to 62 kDa range, which may well include a 59 kD protein product. Figure 3 (lane B) of D12 likewise appears to show a 59 kDa band. The statement from the Claimant that the additional bands in D12 are likely to have been the result of the purification process, for example by degradation, is not supported by verifiable facts and in any event does not justify the conclusion that the disclosure of the 59 kD product in D1 is not enabling.

184. D1 clearly states that the invention improves yield of recombinant proteins and facilitates purification by preventing the production of non-functional truncated protein fragments beginning at internal initiation sites. Against the concrete teachings in D1 of how to perform the method disclosed therein, the result achieved when those steps are carried out, and the (credible) explanations provided therefor, there stands no teaching in D1 itself or in the prior art that casts doubt on this statement of effect of the method taught in D1. The effect is therefore disclosed to the skilled person.

185. From the above it follows that D1 discloses all the features of claim 1 of the Patent directly and unambiguously.

Interim conclusion and consequences

186. The conclusion based on the above is that the subject matter of claim 1 is not novel. As a consequence, the Patent cannot be maintained as granted ("main request") of the Counterdefendants.

187. In the alternative to their main request, the Counterdefendants request that the counterclaim for revocation of EP 2 401 365 B1 is dismissed in part to the extent it goes beyond the version of EP 2 401 365 B1 according to ARs 1-25, to be dealt with in that order. The Court understands these requests, in light of the Counterdefendants' submissions, as a conditional application to amend the Patent in accordance with one of the Auxiliary Requests, the condition being that the Patent as granted cannot be maintained (also see heading B. and par. 246 DtCC).

188. As was made explicit during the oral hearing, the Court furthermore understands the requests of the Counterdefendants in the Defence to the Counterclaim for revocation as pertaining to "closed claim sets", meaning that if one claim of any claim set is held to be invalid, the entire claim set is unallowable. This follows from the wording of the requests and is confirmed by the contents of the Counterdefendants' defence. Under these circumstances, it follows from Art. 76(1) UPCA, according to which the Court shall decide in accordance with the requests submitted by the parties, that the (dependent) subclaims 2-11 of the Patent as granted will not be examined by the Court (see e.g. LD Munich, UPC_CFI_248/2024, decision dated 22 August 2025, Brita SE/AQUASHIELD). To the extent that the Counterdefendants submitted, for the first time at the oral hearing, that the last auxiliary request (number 25) should be regarded as an open claim set in that it could allow the combination with further subclaims if there was a need to do so, the Court does not have to decide on this, if only for the reason that the Counterdefendants did not indicate or propose any further such combination.

189. In addition, except for claim 10 (and 11 which depends on claim 10), and apparently different from the situation in UPC_CoA_622/2025 and UPC_CoA_623/2025, decision dated 27 May 2026, Hefei/Grundfos, mn. 109, the Claimant did not defend the subclaims of the Patent as granted in a substantiated way. As claim 10 (and 11) are the subject of a dedicated auxiliary request (AR4, see below), the Court sees no need to separately examine these subclaims here as the result is the same.

190. Against this background, the Court will now turn to the Auxiliary Requests in the order they were submitted, as requested by the Counterdefendants.

VII. Auxiliary Requests

191. The conditional application to amend is admissible but cannot save the Patent.

192. The application is admissible on the basis of Rule 30 RoP, as the application was made timely, i.e. together with the Statement of Defence, the requirements of Rule 30.1(b)

and (c) are met and the proposals are not considered to be unreasonable in number (Rule 30.1(c)). In relation to the latter requirement, the Court notes that 25 is a high number of ARs. However, given the number of validity attacks on the Patent and the way the ARs have been structured and defended by the Counterdefendants (see table and further discussion below), their number is not considered to be unreasonable.

193. The Counterdefendants structured the ARs as follows:

	AR 1	**AR2**	**AR 3**	**AR 4**	**AR 5**
	(“more than one secondary initiation codon”)	(“secondary initiation codons comprise at least one of each of ACG, GUG, UUG, CUG, AUA, AUC, and AUU”)	(“eukaryotic cells and bacteria”)	(“mutating the one or more miRNA binding sites”)	(“out-of-frame with the coding sequence”)

194. ARs 6-25 each comprise different permutations of the above features as indicated in a reference table.

AR1

195. In AR1, the <u>one or more</u> secondary initiation codon(s) has been further defined as <u>more than one</u> secondary initiation codon. The subject matter of claim 1 of AR1 essentially corresponds to the subject matter of claim 5 as granted. In addition, feature 1.4 has been amended such that mutating the more than one secondary initiation codon comprises mutating <u>more than one nucleotide</u> (such that the amino acid sequence of the protein remains unaltered).

196. Notwithstanding the clarity arguments brought forward by the Defendants, the requirement to mutate more than one secondary initiation codon cannot make the subject matter of AR1 inventive over document D1, considered alone or in combination with document D3.

Principles

197. The approach to assessment of inventive step taken by the UPC has been provided by the Court of Appeal in its decisions dated 25 November 2025 in

UPC_CoA_528/2024, UPC_CoA_529/2024, Amgen/Sanofi and CoA_464/2024 (and other numbers), Meril/Edwards.

198. A European patent is only validly granted for an invention if – apart from other requirements – it involves an inventive step. An invention shall be considered as involving an inventive step if, having regard to the state of the art, it is not obvious to a person skilled in the art (Art. 56 EPC).

199. In the UPC approach, it first has to be established what the object of the invention is, i.e. the objective problem. This must be assessed from the perspective of the skilled person, with their common general knowledge, as at the application or priority date (also referred to as the relevant date) of the patent. This must be done by establishing what the invention adds to the state of the art, not by looking at the individual features of the claim, but by comparing the claim as a whole in context of the description and the drawings, thus also considering the inventive concept underlying the invention (the technical teaching), which must be based on the technical effect(s) that the skilled person on the basis of the patent understands is (are) achieved with the claimed invention.

200. In order to avoid hindsight, the objective problem should not contain pointers to the claimed solution.

201. The claimed solution is obvious when at the relevant date the skilled person, starting from a realistic starting point in the state of the art in the relevant field of technology, wishing to solve the objective problem, would (and not only: could) have arrived at the claimed solution.

202. The relevant field of technology is the field relevant to the objective problem to be solved as well as any field in which the same or similar problem arises and of which the person skilled in the art of the specific field must be expected to be aware.

203. A starting point is realistic if the teaching thereof would have been of interest to a skilled person who, at the relevant date, wishes to solve the objective problem. This may for instance be the case if the relevant piece of prior art already discloses several features similar to those relevant to the invention as claimed and/or addresses the same or a similar underlying problem as that of the claimed invention. There can be more than one realistic starting point and the claimed invention must be inventive starting from each of them.

204. The skilled person has no inventive skills and no imagination and requires a pointer or motivation that, starting from a realistic starting point, directs it to implement a next step in the direction of the claimed invention. As a general rule, a claimed solution must

be considered not inventive/obvious when the skilled person would take the next step prompted by the pointer or as a matter of routine, and arrive at the claimed invention.

205. A claimed solution is obvious if the skilled person would have taken the next step in expectation of finding an envisaged solution of his technical problem. This is generally the case when results of the next step were clearly predictable, or where there was a reasonable expectation of success.

206. The burden of proof that the results were clearly predictable or the skilled person would have reasonably expected success, i.e. that the solution he envisages by taking the next step would solve the objective problem, lies on the party asserting invalidity of the patent.

207. A reasonable expectation of success implies the ability of the skilled person to predict rationally, on the basis of scientific appraisal of the known facts before a research project was started, the successful conclusion of that project within acceptable time limits.

208. Whether there is a reasonable expectation of success depends on the circumstances of the case. The more unexplored a technical field of research, the more difficult it was to make predictions about its successful conclusion and the lower the expectation of success. Envisaged practical or technical difficulties as well as costs involved in testing whether the desired result will be obtained when taking a next step may also withhold the skilled person from taking that step. On the other hand, the stronger a pointer towards the claimed solution, the lower the threshold for a reasonable expectation of success.

Applying these principles to AR1

209. Document D1 is a realistic starting point for the assessment of inventive step as it relates to the same underlying problem (increasing protein expression efficiency) and shares many of the features with the claims of AR1 (see novelty discussion above). D1 would thus have been of interest to the skilled person.

210. The difference between what is directly and unambiguously disclosed in D1 and the subject matter of AR1 is – assuming for the benefit of the Counterdefendants that this feature is not already (implicitly) disclosed in D1 – that more than one secondary initiation codon is to be mutated.

211. As submitted by the Defendants in relation to granted claim 5 (and referred to in their attacks on AR1), D1 as a whole teaches the general concept of eliminating internal translation (see e.g. p.4, l.11-16). D1 also explicitly teaches the prevention of translation of a plurality of protein fragments, see D1, p. 5, l. 10-13: “The invention

improves yield of recombinant proteins and facilitates purification by preventing the production of non-functional truncated protein fragments beginning at internal initiation sites. (underline added by the Court)". The skilled person will therefore without inventive skill understand that if there are more than one secondary initiation sites, these should be mutated as well in order to (further) increase the expression of the protein of interest by preventing the production of unwanted protein fragments. In view of this, the next step of mutating at least one more secondary initiation codon would be a matter of routine for the skilled person who was seeking to increase protein expression efficiency.

212. That it would have been a matter of routine for the skilled person to mutate one or more secondary initiation codons is further supported by document D3. D3 is a PCT patent application and was published on 2 February 2006 and thus belongs to the state of the art. D3 discloses various therapeutic and cosmetic applications of Botulinum neurotoxins (BoNTs). D3 discloses modifying an open reading frame to increase the expression of the active BoNT in mammalian cells (e.g. claim 152). D3 is thus a prior art publication in the same field and directed at the same purposes as the Patent and will accordingly be consulted by the skilled person who is striving to increase the expression efficiency of a protein of interest, for instance starting from D1 as a realistic starting point.

213. D3 explicitly discloses the mutation of one or more internal translation start sites (whilst maintaining the same amino acid coded by the codon), see p.12, par. [034] of D3, snippet taken from the Defendants' submissions:

[034] In an aspect of this embodiment, a modified open reading frame is changed by altering the nucleotide sequence that alters an internal translational start site. An internal translational start site can be changed by substituting a nucleotide different from the one contained in the consensus sequence at the third position of a codon, reducing the nucleotide identity to the consensus sequence while still maintaining the same amino acid coded by the codon. As a non-limiting example, the typical translational start site in the insect *Drosophila melanogaster* is 5'-ACAACCAAAATG-3', and is present within an open reading frame would encode the peptide NH_2-threonine-threonine-lysine-methionine-COOH. This translational start site can be eliminated by changing the sequence to 5'-ACGACTAAGATG-3' and still encode the peptide NH_2-threonine-threonine-lysine-methionine-COOH. In another aspect of this embodiment, at least one nucleotide change may be made to a nucleic acid molecule altering the consensus sequence of an internal translational start site found in an open reading frame providing increased expression of the encoded active BoNT/E. In another aspect of this embodiment, a plurality of nucleotide changes are made to a nucleic acid molecule altering one or more internal translational start sites of an open reading frame providing increased expression of the encoded active BoNT/E. Therefore,

214. This teaching by D3 has not been contested by the Counterdefendants in the context of their application to amend. Even if the general defence by the Counterdefendants against the disclosure of D3 is considered, i.e. that D3 does not define "internal translation site" and in any event not only comprises the initiation codon "ATG", but also the nucleotides upstream thereof, this does not change the conclusions. After all,

it remains the case that D3 demonstrates that it was routine for the skilled person (starting from D1) to alter one <u>or more</u> internal translation sites. D3 therefore confirms that the skilled person would, as a matter of routine, mutate more than one secondary initiation codons.

215. In conclusion, the proposed amendment in AR1 cannot render the claimed subject matter inventive over the prior art, especially D1, considered alone or in combination with D3. As a consequence, AR1 has to be dismissed.

AR2

216. The amendment introduced in claim 1 of AR2 adds to feature 1.1.3 of claim 1 as granted that <u>the one or more secondary initiation codons comprise at least one of each of ACG, GUG, UUG, CUG, AUA, AUC, and AUU</u>, and adds to feature 1.4, <u>mutating the one or more secondary initiation codons comprises mutating at least one of each of ACG, GUG, UUG, CUG, AUA, AUC, and AUU</u>.

217. The Defendants say that this amendment introduces a lack of clarity.

218. It follows from, inter alia, Rule 30.1(b) RoP that the claims of an Auxiliary Request must satisfy the requirements of Art. 84 EPC, in particular that the claims shall be clear and concise and shall be supported by the description ("clarity"). In the case law of the UPC to date, it has been accepted that clarity shall only be examined to the extent the amendment gives rise to a violation of Art. 84 EPC (for the first time, i.e. as opposed to the claims as granted), see e.g. LD Munich (panel 1) decision dated 10 October 2025, UPC_CFI_114/2024 UPC_CFI_448/2024, Heraeus/Vibrantz, likewise CD Milan decision of 27 November 2025, UPC_CFI_613/2024, Pari Pharma v. Philips, with reference to LD Düsseldorf, Decision of 28 January 2025, UPC_CFI_355/2023, Fujifilm/Kodak. This corresponds to the practice of the EPO in opposition proceedings, see Enlarged Board of Appeal decision of 24 March 2014, G3/14.

219. In the present case, contrary to what the Counterdefendants have brought forward, the amendment itself introduces a potential non-compliance with Art. 84 EPC. However, the Court in this case does not have to conclusively decide whether the claim is unclear. Regardless thereof, assuming for the benefit of the Counterdefendants that the subject matter of claim 1 of AR2 is clear and the skilled person would, in accordance with the interpretation given by the Counterdefendants, interpret claim 1 according to AR2 such that it requires the mutation of at least seven secondary initiation codons (including each of the claimed codons), the basis for the claimed subject matter in the application as filed is lacking which results in added matter.

220. In accordance with Art. 138 (1)(c) EPC, a European patent may be revoked if its subject matter extends beyond the content of the application as filed. In accordance with Art. 123(2) EPC, a European patent may not be amended in such a way that it contains

subject-matter which extends beyond the content of the application as filed ("added matter"), also see R. 30(1)(b) RoP. In order to determine 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 (UPC_CoA_764/2024, UPC_CoA_774/2024, decision of 2 October 2025, expert e Commerce/Seoul Viosys; UPC_CoA_382/2024, order of 14 February 2025, Abbott/Sibio).

221. Applying these principles to the amendments introduced by AR2, the Court concludes that there is added matter. Whilst it is correct that the seven codons are mentioned in par. [0060] and [0070] and claim 7 of the application as filed as codons that can be mutated (see e.g. claim 7: "wherein the <u>one or more</u> secondary initiation codon is <u>selected from the group consisting of</u>…."), the combined mutation of (at least) all seven of these is not directly and unambiguously disclosed in the application. The requirement to mutate (at least) seven codons which in addition must include each of the seven different codons adds technical information compared to the original disclosure which is more generic in its disclosure. As correctly held by the LD Düsseldorf in its decision dated 28 January 2025, UPC_CFI_355/2023, Fujifilm/Kodak, III.2..a), for added matter, the correct question to be asked is not whether a skilled person would consider the subject-matter of an amended claim as falling within the scope of an originally disclosed broader teaching, but whether the skilled person would understand that the subject-matter of an amended claim is a specific, individualized embodiment which is also originally disclosed as such. As this is not the case here, the proposed claim therefore contains subject matter that extends beyond the application as filed.

222. In addition to, and regardless of, the extension of subject matter, still adopting the interpretation put forward by the Counterdefendants to their benefit, the features added to AR2 cannot render the subject matter claimed inventive over the prior art, starting from D1 as a realistic starting point for the reasons provided above for AR1. The Counterdefendants agree that secondary initiation codons comprising GUG, UUG and AUU are disclosed in D1 (p1, l. 24-33, see DtCC, 273). The selection of either one or more of those is thus disclosed and, in any event, not inventive over D1. The fact that these codons are disclosed preceded by a SD sequence in D1 does not change that. The four other non-canonical initiation codons (ACG, CUG, AUA, AUC) are not explicitly mentioned in D1, but it would be obvious to a person skilled in the art to mutate these as a next step when wanting to (further) increase protein expression as a matter of routine. As discussed above, D1 already suggests to remove a plurality of initiation codons. It is not in dispute that the non-canonical initiation codons ACG, CUG, AUA, AUC belonged to the common general knowledge as is presumed in the Patent

itself. The skilled person, in view of the problem of increasing protein expression, would therefore without inventive skill mutate away these secondary initiation codons in a given sequence of interest as well as a matter of routine.

AR3

223. AR3 requires that the claimed method improves full-length protein expression efficiency <u>in eukaryotic cells and bacteria</u>.

224. The only explanation provided by the Counterdefendants as to why this proposed claim is valid (Art. 30.1(b) RoP), was that the amendment further sets the claimed subject-matter in a novel and inventive manner apart from <u>D3 and D4</u>. As claim 1 of the Patent as granted was found to lack (novelty and/or) inventive step over D1 and/or D2, and no explanation has been provided by Counterdefendants as to why this amendment would restore novelty and/or inventive step over these prior art references, which were also relied upon by the Defendants in their defence to the application to amend in relation to AR3 (mn. 245), the subject matter of AR3 is deemed to lack novelty and/or inventive step for the same reasons as claim 1 of the Patent as granted.

225. The Court, moreover, fails to see how the requirement of improving expression efficiency in eukaryotic cells and bacteria would render the claimed subject matter inventive over the cited prior art. D2 discloses the mutation of a secondary initiation codon in eukaryotic cells and D1 in bacteria.

AR4

226. AR4 combines the subject matter of granted claims 1 and 10 (which claim referred back to claim 1).

227. In AR4, the following features are added to the features of granted claim 1 (following the feature breakdown numbering of granted claim 1, above):

> AR4 1.1.4 iv) one or more miRNA binding sites located within the coding sequence, and
>
> AR4 1.5 mutating the one or more miRNA binding sites, wherein
>
>> [1.5.1] the mutation results in a decrease in miRNA binding at the one or more miRNA binding sites
>>
>> [1.5.2] resulting in a reduction of miRNA-mediated down regulation of protein translation.

Original claim 10 is deleted in AR4.

228. AR4 requires, in addition to the features of claim 1 as granted that the DNA/RNA polynucleotide according to feature 1.1 comprises one or more miRNA binding sites within the coding sequence (feature 1.1.4). The one or more binding sites is/are mutated in such a way that there is a decrease in miRNA binding to it and thus a decrease in the suppression of the translation process (see also Patent [0081] et seq.).

229. The claim does not further specify how the additional features of AR4 are related to the remaining features of the claim, which correspond to the method claimed in claim 1 of the Patent as granted. The claim does not specify how and at which point in time the miRNA sequences must be mutated. In addition, the degree of decrease in miRNA binding nor the resulting reduction of miRNA-mediated down regulation of protein translation have been specified in claim 1 of AR4.

230. AR4 does require identifying and mutating one or more miRNA binding sites within the coding sequence so that the effects defined therein are achieved. Simply mutating known or predicted putative miRNA binding sites without achieving these effects is not sufficient to fall under the claimed subject matter. In a similar vein as discussed above for the mutation of the one or more secondary initiation codons, AR4 requires the mutation of an *actual* miRNA binding site and hence a causal relationship between the mutation and the effect of an increase in protein expression. The parties have also argued their case on the basis of this interpretation.

<u>Lack of inventive step AR4</u>

231. Notwithstanding the other validity attacks by the Defendants on the subject matter covered by AR4, the inventive step attack succeeds.

232. In their inventive step attack on AR4, the Defendants, in addition to the attacks on the subject matter covered by original claim 1, as discussed above, rely on documents D9 (“Forman”) and D10 (“Tay”) in support of their case that the additional features/method steps of dependent claim 10 as granted (now incorporated in AR4), which are not also in claim 1, are fully anticipated by D9 and D10 and therefore the subject matter of AR4 cannot be inventive.

233. The parties agree that D9 describes that the Dicer gene comprising three binding sites for the miRNA let-7, and a variant Dicer gene, wherein these three miRNA binding sites are mutated by silent mutations. The variant Dicer gene, with the miRNA binding sites mutated, is protected from downregulation by let-7; see Fig. legend 3 at page 14881 and page 14481, right column, first full paragraph to the paragraph spanning pages 14881 and 14882 of D9. Accordingly, D9 discloses that the mutation of let-7 binding site(s) in the coding region of the Dicer gene results in a decrease in miRNA-mediated down regulation of protein translation, is considered to be due to a decrease in let-7

miRNA binding to the Dicer coding sequence. D9 therefore discloses all the features added by AR4.

234. Similarly, there is no dispute between the parties that in D10 binding sites for the miRNAs 296, 470 and 134 were mutated in the Nanog, Oct4 and Sox2 genes, respectively, which repressed their miRNA-mediated down-regulation; see page 1125, left column, third paragraph and page 1126, right column, first paragraph of D10. Also D10 therefore discloses the features introduced in AR4.

235. More in general, the Counterdefendants have not contested the substantiated assertion by the Defendants that D9 and D10 disclose all the features of claim AR4, except for the features of granted claim 1 (i.e. all of the features added to granted claim 1 in AR4 are disclosed in D9 and D10). The Defendants, in turn, have not argued that the features of claim 1 as granted are disclosed in D9 or D10. The difference between D9 and D10 and claim 1 of AR4 is thus the features of claim 1 as granted (and *vice versa*, the difference between claim 1 of AR4 and the state of the art that was found to be detrimental for novelty and/or inventive step of granted claim 1 above, documents D1 and D2, are the additional features, which correspond to the feature of claim 10 as granted). The question is whether the combination of features as claimed in claim 1 of AR4 is inventive.

236. In this respect, the parties have discussed whether the so-called “partial problem approach” is to be applied by the UPC and, if so, whether this approach applies in the present case.

237. According to settled EPO case law: “partial problems exist if the features or sets of features of a claim are a mere aggregation of these features or sets of features (juxtaposition or collocation) which are not **functionally interdependent**, i.e. do not mutually influence each other to achieve a technical success over and above the sum of their respective individual effects, in contrast to what is assumed in the case of a combination of features. What must be established is whether each set of features is separately obvious in the light of the prior art” (see Case Law of the Boards of Appeal, I.D.9.3.2, first par.). The CD Munich has held in a similar vein that where the features of a patent claim, in an interdependent way, even if they are not synergetic in the sense of having a special combination effect, provide a solution to the objective problem, ignoring these interdependencies and dividing the objective problem up into separate problems amounts to hindsight reasoning which is to be avoided in the assessment of inventive step (decision of 24 February 2026, UPC_337/2025, TCL/Corning).

238. Regardless of whether the UPC should apply the “partial problems” approach in exactly the same way as the EPO, the UPC Court of Appeal has clarified in Amgen/Sanofi, see principles above, that the Court has to establish what the invention adds to the state of the art, not by looking at the individual features of the claim, but by comparing the claim as a whole in context of the description and the drawings, thus also

considering the inventive concept underlying the invention (the technical teaching), which must be based on the technical effect(s) that the skilled person on the basis of the patent understands is (are) achieved with the claimed invention.

239. The Court notes that in the present case the inventive concept that can be based on technical effects that the skilled person understands on the basis of the Patent is the mere aggregation (or "juxtaposition") of the features of granted claim 1 on the one hand and those of granted claim 10 on the other, with their respective effects, now claimed as a combination in claim 1 of AR4. Nowhere in the description it is disclosed, explicitly nor implicitly, that the miRNA mutation features are in any way functionally connected to or interdependent with the mutation of the one or more secondary initiation codon. Both methods are discussed in separate examples, whereby for the miRNA mutations (Example 2) the Patent contains no experimental results at all, let alone results that would support a contribution to the art by combining the two techniques (as opposed to using each method separately).

240. At most, the description of the Patent discloses in par. [0005] and [0009] (corresponding to paragraphs [0006] and [0016] of the application as filed) that both techniques can be used in combination (whether this is disclosed directly and unambiguously is even in debate between the parties in the context of added matter), but in any event it is disclosed that they can be used separately. That both methods increase protein expression efficiency does not imply that they function in an interdependent way. There is nothing in the Patent that points the skilled person in that direction. This seems to be acknowledged by the Counterdefendants in 185 DtCC: "miRNA-mediated increase of protein expression is independent of the increase of protein expression obtained upon removal of secondary start codons". To the extent that the Counterdefendants have argued that reducing ribosomal diversion away from the primary initiation codon increases the expression efficiency of the full-length protein initiated at the primary initiation codon and it is expected that this increased efficiency can be applied for a longer time to an mRNA with increased stability (186 DtCC and discussed at the oral hearing), this alleged effect does not find any basis in the Patent (or the application as filed, see below) nor has it been argued in a substantiated way that this would be derived therefrom by the skilled person.

241. In sum, both methods are presented as stand-alone, independent techniques and the skilled person will understand this accordingly. Put yet differently, the features of claim 1 of AR 4 (the two methods) each serve their own purpose; the skilled person does not understand them to functionally interact or have a combined effect (cf. UPC_CoA_71/2025, decision of 29 December 2025, VMR Products/NJOY, par. 81).

242. This is confirmed also by the fact that in the application as filed, (only) an independent claim (claim 15) was directed to the miRNA method. In line with this, during the prosecution of the application at the EPO, the Examiner noted a lack of unity within the

meaning of Art. 82 EPC between two separate inventions: 1) mutating one or more secondary initiation codons and 2) mutating one or more miRNA binding sites. The (then) applicant, now the patent proprietor, submitted to the EPO that the two methods can be used in conjunction with each other, not arguing that there was any functional interdependency, let alone synergy between the two methods (see the Defendants' Exhibits 30 and 31, respectively).

243. Against this background, the ("post-published") evidence submitted by the Counterdefendants dating from after the priority date (VB36) cannot change the separate assessment of the two concepts claimed in claim 1 and claim 10 (and 11). Insofar as the Claimant attempted at the oral hearing to demonstrate a synergistic effect by calculations based on the data submitted in Annex VB 36, this submission is late and cannot be admitted. Even if the data as such were not late filed, this does not apply to the calculations made and conclusions drawn therefrom for the first time during the oral hearing. Furthermore, the reliability of the data seems at least questionable in view of the Defendants' substantiated criticisms, see second report ███ █████ Defendants Exhibit 43. In addition, even if it were accepted for the benefit of the Counterdefendants that this evidence shows that there is in fact a synergistic effect instead of (merely) an additive effect, a patent proprietor may rely upon a technical effect for inventive step, provided that the skilled person understands on the basis of the patent that the effect is achieved with the claimed invention and provided that the skilled person having the common general knowledge in mind, and based on the application as originally filed, would consider said effect as being encompassed by the technical teaching and embodied by the same originally disclosed invention (cf. CoA Meril/Edwards, cited above, mn. 143, with reference to EPO Enlarged Board of Appeal decision G 2/21, mn 94). From the above it follows that these conditions are not met in the present case.

244. In conclusion, the combination of features of AR4 constitutes a mere aggregation of two independent methods, whereby the features of these methods do not interact functionally to produce an effect that goes beyond mere addition in solving the objective problem of increasing protein expression efficiency. In other words, the features are simply juxtaposed; no effect beyond the mere addition is apparent from the application/the Patent. As there is (rightfully so) no real discussion between the parties that the additional features of AR4 are clearly disclosed in D9 and D10, the combination of these two methods, both being not novel or at least non-inventive, cannot be held inventive. The skilled person would, as a matter of routine, combine these two methods and/or carry them out separately, one after the other, which is not excluded by claim 1 of AR4.

245. For the sake of completeness, the Court notes that the features of former claim 11, corresponding to the features of claim 10 of AR4, do not add anything inventive over the (obvious) subject matter of claim 1 of AR4. Avoiding the introduction of initiation

codons (one of the options of claim 10) already is obvious over the prior art references D2 and D1 that explicitly teach the removal of such codons.

246. Based on the above, the Court comes to the conclusion that the subject matter of AR4 lacks inventive step.

AR5

247. Claim 1 of AR5 requires that in the method having the features of claim 1 as granted, the mutated one or more secondary initiation codons is/are out-of-frame with the coding sequence.

248. This amendment cannot render the subject matter of this auxiliary request novel or inventive over the prior art. The Counterdefendants did not provide any explanation as to why AR5 would be novel or inventive over Matsuda (D2). In particular, the Counterdefendants have left undisputed that the secondary initiation codon in Matsuda is located downstream and out-of-frame compared to the p69 ORF. The subject matter of AR5 thus lacks novelty for the same reasons as the Patent as granted (see above). In addition, D1 discloses on p. 10, l. 3-4 that “the internal initiator codon” can be “out-of-frame with the desired full-length polypeptide”. In view of this disclosure, the subject matter of AR5 also lacks novelty vis-à-vis D1 for the same reasons as provided above for the subject matter of the Patent as granted.

AR6-25

249. ARs 6-25 are combinations and permutations of ARs 1-5. The Counterdefendants have not provided any additional reasons in support of the validity of these requests compared to the individual ARs 1-5. They have merely submitted that the explanations as to why the proposed amended claims of ARs 1 to 5 are valid apply *mutatis mutandis* to Auxiliary Requests 6 to 25 (at least this is how the Court understands the Counterdefendants’ submission). Indeed, no such reasons are apparent to the Court. Therefore, these ARs are invalid, at least for the same reasons as ARs 1-5, which apply to ARs 6-25 *mutatis mutandis*.

Conclusion

250. In conclusion, the Patent as granted is invalid. None of the Auxiliary Requests are valid. The application to amend must be dismissed. As a consequence, the Patent must be revoked in its entirety.

The infringement action

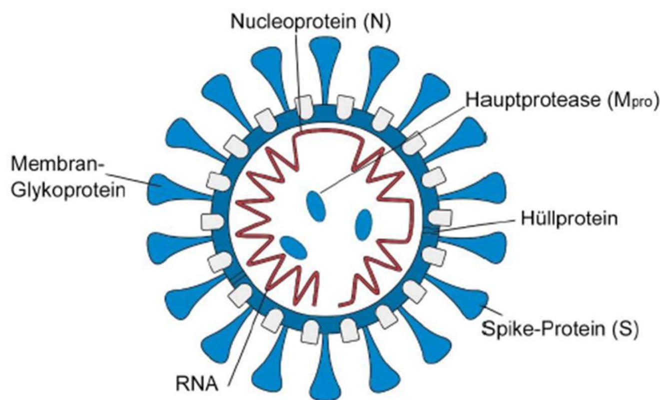
251. The infringement action is unfounded. The Infringement action is not successful, already for the reason that the Patent is not valid (see above).

252. In addition, the Claimant has not convincingly demonstrated that the attacked embodiments realise the features of the claims of the Patent. Infringement can therefore not be established.

VIII. Attacked embodiments

253. The attacked embodiments 2a-2e are so-called “mRNA vaccines” against the SARS-CoV-2 virus (“severe-acute-respiratory-syndrome-related coronavirus type 2”, also known as “corona virus”).

254. The parties agree that the attacked embodiments 2a-2e carry the blueprint (genetic code) in the form of mRNA for the spike protein of the SARS-CoV-2 virus, which the virus requires to bind to body cells. This protein is particularly suitable for immunization against SARS-CoV-2 because the spike protein is located on the surface of the SARS-CoV-2 virus particles, where it is particularly easily recognized by the body's immune system, and because mutations in this area, which is so important for the virus, are relatively rare. This is illustrated by the diagram below of a SARS-CoV-2 virus particle:



255. By encoding the spike protein, an mRNA vaccine can cause the human body to produce replica spike protein of the coronavirus, which will train the immune system to recognize and attack the coronavirus spike protein.

The parties’ core dispute on infringement

256. A core aspect of the dispute between the parties on infringement is whether in producing the attacked embodiments, the Defendants implemented step 1.2 of the claimed method (mutation of one or more secondary initiation codons) resulting in the

effects of feature group 1.3: a decrease of initiation of protein synthesis at the one or more secondary initiation codons (feature 1.3.1), resulting in ribosomal diversion away from the primary initiation codon (feature 1.3.2), thereby increasing the expression of the protein of interest (feature 1.3.2).

257. The Claimant has relied on evidence in the form of expert reports from ████ █████ (VB6 and VB35, with reference to experimental reports VB6a and VB34), in support of their assertions that in the attacked embodiments a plurality of secondary non-canonical and out-of-frame start codons are mutated downstream of the primary start codon within the coding sequence which does not change the amino acid sequence of the full-length protein. According to ████ █████ in VB6, the Defendants engineered the sequences of their Products to minimize the number of potential alternative translational start sites to maximise spike protein production (par. 33 of VB6).

258. The Defendants do not contest that they made mutations to the polynucleotide sequence encoding the spike protein of the virus RNA (also the "wild-type sequence"). There is the so-called "double proline mutation" (i.e., mutations K986P and V987P) which was made to stabilize the spike protein in the pre-fusion conformation preventing the conformational change that permits membrane fusion. Secondly, the Defendants submit that the DNA used for making Comirnaty® has been codon optimised. In relation to the latter codon optimisation, the Defendants also do not deny that these mutations result in an increased protein expression of the full-length (spike) protein. However, the Defendants do contest that they have mutated actual secondary initiation codons. Rather, they submit, the observed increase in protein expression is not the result of mutating (actual) secondary initiation codons, but is the result of the (ordinary) codon optimisation. As such, they expressly dispute that any actual secondary initiation codons in the mRNA encoding the SARS-CoV-2 spike protein with the double-proline mutation (hereinafter: "SARS-CoV-2 S 2P") were mutated for Comirnaty®, resulting in the claimed effects.

General remarks

259. Before assessing the available evidence, the Court notes that from the claim interpretation given above, it follows that the polynucleotide sequence that is to be provided at the start of the claimed method does not have to be a wild-type sequence, i.e. a sequence that occurs naturally (e.g. in a virus). The claims of the Patent do not preclude that the provided polynucleotide comprises mutations vis-à-vis the wild-type sequence, like stabilising mutations (for example the "double proline mutation") or is codon-optimised for expression in a particular host (e.g. humans).

260. To the extent the Defendants' case should be understood as that the claimed method requires a particular strict order of steps, in that the method of claim 1 may only be applied after any prior optimisations of the coding sequence, especially by way of

codon optimisation, and not before or simultaneously, and that already for this reason, infringement has not been shown, the Court disagrees. As follows from the claim interpretation provided above, the claimed method does not rule out that introducing "other" mutations (for example by codon optimisation) and mutating secondary start codons are carried out in one go: in particular, the steps of "providing" a polynucleotide and "mutating" one or more secondary initiation codons are broadly defined to cover this situation.

261. However, in order to demonstrate infringement, also according to the Claimant, a clear distinction has to be made between (a) host-adaptation routine codon optimisation and (b) mutating one or more secondary initiation codons to reduce ribosomal diversion and increase full-length protein expression (109 Reply to the Defence).

262. It is up to the Claimant, as the claimant in an infringement action, to substantiate and where necessary prove the infringement.

263. In this respect, the Court notes that it is not in dispute between the parties that not every mutation of a putative (i.e. potential) secondary downstream initiation codon results in an increase in protein expression. In fact, the Claimant has stated that functional internal start sites are indeed rare and difficult to detect (120 Reply to the Defence, first hyphen, also see ███ ████ Defendants´ Exhibit 9, par. 6 "in almost all cases, a putative secondary initiation codon will not in fact initiate translation", to which ███ █████ did not further respond). The contrary submissions made during the oral hearing by reference to D2 (Matsuda, p. 1339, lh col., l. 8 ff) are, apart from being late and disregarded already for that reason, not convincing as the referenced passage refers to the frequency of bi- or multicistronic mRNAs and not to the number of additional initiation sites within a single gene, let alone across all genes of different organisms. In addition, Matsuda also confirms that alternative ribosome behaviours that can expand the translation repertoire of an mRNA typically occur with low efficiency, such that the expression from secondary initiation codons is likely to be limited (p. 1339, lh col., last paragraph).

264. Against this background, in order to duly substantiate infringement in the present case, it does not suffice, for the Claimant to rely on the fact that a (large) number of putative secondary initiation codons have been mutated in combination with an observed overall increased translational efficiency of the protein of interest compared to the "wild-type" protein. An increase in protein expression efficiency is precisely the aim and expected result of (routine) codon optimisation techniques which the Defendants have said they have used (and which has not been disputed by the Claimant). It is therefore impossible, in the absence of further evidence, to distinguish between (non-infringing) codon optimisation and an infringement, for which the same "net" effect of an increase in protein expression efficiency has to be demonstrated. This does not put the Claimant under an undue burden as, according to the Claimant's own submission that where

mutations (meaning, mutations in accordance with the invention) change the codon usage bias, these effects can be simply evaluated (96 Reply to the Defence).

265. The fact that the Patent, in the examples, shows a comparison "before" and "after" mutation of multiple secondary initiation codons, without distinguishing between putative and actual secondary initiation codons, does not make this any different (also see claim interpretation above). In the Patent example, the sequences were first codon optimised and only then further mutated (par. [0075]). The increase in expression was subsequently determined compared to the already codon optimised sequence. In such an experimental setup, under the assumption that the mutations do not improve codon usage (codon optimisation), the increase in expression can reasonably be attributed to mutating the one or more secondary initiation codons since the only variable that was changed, is the mutation of the one or more secondary initiation codons.

266. In summary, in order to establish infringement, it has to be shown that one or more (actual) secondary initiation codons have been mutated resulting in a decrease of initiation of protein synthesis at the one or more secondary start codons, thereby increasing expression efficiency of the protein initiated at the primary initiation codon. Depending on the concrete facts and circumstances, it may be reasonable to assume that actual secondary initiation codons have been mutated leading to an increase in expression, but this is not the case here, where codon optimisation has been carried out on the same sequence.

267. That said, it must be noted that, once infringing mutations have been established, the Defendants cannot avoid being liable for patent infringement by arguing that they never intended to infringe the Patent. Unlike the provisions on indirect patent infringement, Art. 25(c) UPCA does not require a subjective element. In other words, if in the process of ordinary codon optimisation an actual secondary initiation codon is mutated resulting in an increase of protein expression, this would, in principle, be infringing.

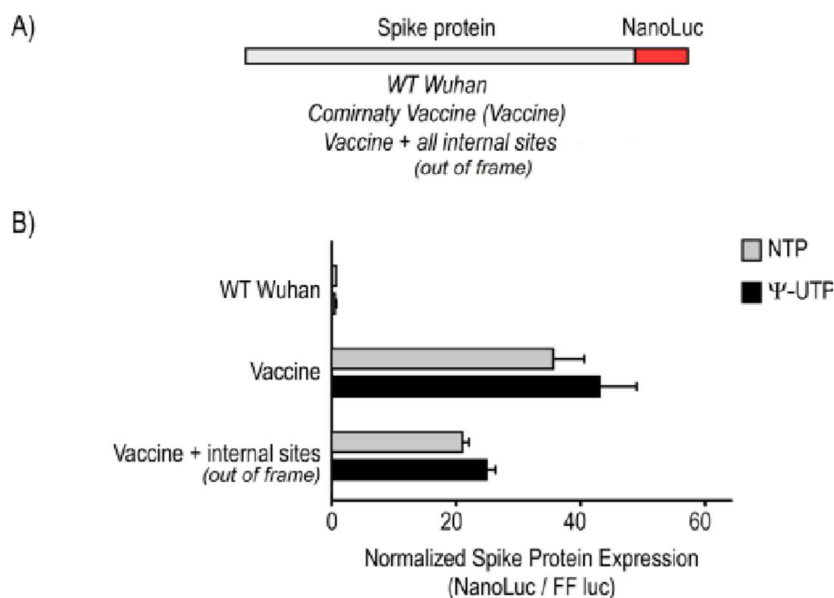
Assessment

268. The Claimant has not sufficiently substantiated the infringement. The Court cannot establish that the Defendants mutated any actual secondary initiation codons. In view of this, the Court cannot come to the finding that there is an infringement of the Patent.

269. It is indeed, as the Claimant argues, not in dispute that numerous potential secondary initiation codons present in the starting sequence (the wild-type sequence) have been changed (i.e. mutated) in the Comirnaty® mRNA sequence. As a consequence, the number of potential secondary initiation codons in the Comirnaty® mRNA sequence is lower compared to the wild-type sequence (also see the table below). However, the Defendants have expressly contested that any actual secondary initiation codons have

been changed. They essentially argue that any increased expression that is observed is due to routine codon optimisation.

270. The Claimant has not argued that any secondary initiation codons which were previously known as actual secondary initiation codons, have been mutated by the Defendants and resulted in an increased protein expression. Instead, the Claimant attempts to demonstrate, by comparing the protein expression of the attacked embodiment and various test constructs, that actual secondary initiation codons must have in fact been mutated in order to obtain the attacked embodiment. In support the Claimant relies primarily on two experimental reports Exhibits VB 06a and VB 34 which are discussed by ███ █████ in his expert reports (VB6 and VB35, respectively). In VB06a and VB34, leaving aside the criticisms made by the Defendants in relation to the experimental methods and analyses applied in the reports, the "original vaccine" sequence (the codon-optimised spike protein ORF as used in the attacked vaccine embodiments, including the double proline mutations) was compared to the same sequence in which all previously removed out-of-frame secondary initiation codons were systematically re-introduced. "Test A" is the wild-type sequence. "Test B" is the original attacked embodiment 2a (Comirnaty). "Test C" is the Comirnaty ORF sequence into which all putative out-of-frame secondary initiation codons present in the SARS-CoV-2 spike protein wild-type sequence were reintroduced. According to the Claimant, when comparing results for Test C with Test B, a decrease in initiation at secondary codons, a reduction of ribosomal diversion from the primary codon, and a significant increase in expression efficiency of the full-length spike protein is observed (143 Reply to the Defence), with reference to VB34, p. 17 (whereby only increased protein expression was actually measured, not the decrease in initiation at secondary codons or of ribosomal diversion):



Test A: WT Wuhan

Test B: Original BioNtech Comirnaty

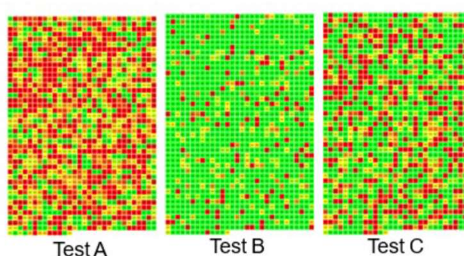
Test C: Engineer internal out of frame starts (incl. Alts) back into BioNtech

271. The Claimant has not submitted that it has provided any evidence that directly shows the mutation by the Defendants of one or more actual secondary initiation codons in the Comirnaty ORF sequence vis-à-vis the wild-type spike protein. Rather, according to the Claimant, Exhibits VB 06a and VB 34 show that the observed effect of increased protein expression in Test B (the vaccine sequence) does not simply track codon optimisation generally but correlates directly with the presence or absence of secondary initiation codons. According to the Claimant, they have made the decisive comparison: the only difference between the two sequences is the presence or absence of the secondary initiation codons.

272. However, as the Defendants have correctly argued, the experimental evidence provided by the Claimant is by its nature and setup not suitable to provide the necessary substantiation, let alone proof. First of all, the Defendants have credibly argued that the absence of the (putative) secondary initiation codons is <u>not</u> the only difference between the Test B and Test C constructs. As explained by the Defendants with reference to the table below, there is also a significant difference in the extent of codon optimisation between the two constructs (expressed in CAI-value, whereby a higher CAI represents a higher degree of codon optimisation, see technical background above):

Test	Total no. putative secondary start sites	No. putative out-of-frame secondary start sites	CAI	Relative expression compared to Test A – Wild-Type (unmodified)	Relative expression compared to unmodified Test A – Wild-Type (m1Ψ)
Test A – Wild-Type	669	508	0.71	1.00	0.80
Test B – Tozinameran	578	245	0.96	35.84	43.30
Test C – Deoptimized Tozinameran	805	510	0.85	21.19	25.06

273. The Defendants have visualised this by way of codon optimisation "heat maps", wherein "optimal" codons are marked green, "least optimal" codons are red and codons of "moderate" optimality are yellow or orange:

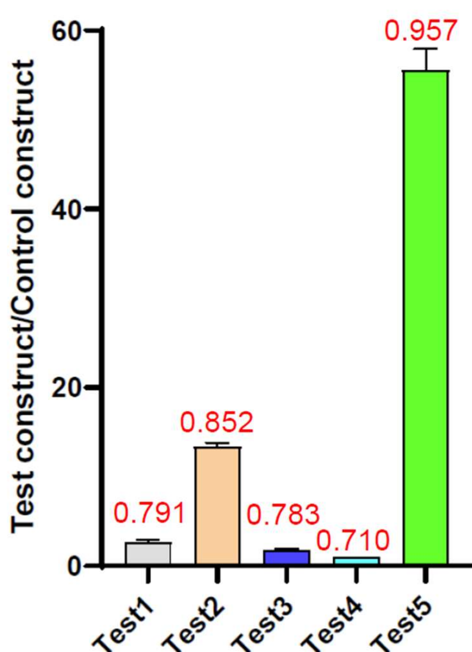


Colour key: Most optimal ■ ■ ■ ■ ■ Least optimal

274. As pointed out by the Defendants, the above data show that even though Test C ("Deoptimized Tozinameran", i.e. Comirnaty with all putative out-of- frame secondary initiation codons reintroduced) has both a higher number of total (in-frame and out-of-frame) putative secondary initiation codons, as well as a higher number of putative out-of-frame initiation codons alone compared to Test A – Wild-Type, it has a significantly higher expression than Test A – Wild-Type. Leaving aside whether this result can indeed only be explained by the difference in codon optimisation for the two constructs, as the Defendants have argued, this cannot in any event be ruled out. The Court does therefore accept that in the light of these observations it would have been up to the Claimant to provide further explanations in support of the existence of an infringement of the Patent. Such further explanations and evidence are lacking.

275. Nothing else follows from the data in the figure on p. 22 of VB6a which was referred to by the Claimant during the oral hearing. Apart from the fact that these experiments were flawed and were therefore redone (in VB34), also in the data of VB6a, the

difference between the constructs "Test 5" (the attacked embodiment, in which – according to the Claimant – secondary start codons were removed by the Defendants) and "Test 3" / "Test 1", both of which had secondary start codons "re-introduced" for purposes of the comparison made by the Claimant, is not only the number of (putative) start codons. "Test 4" is the wild-type. There is also a considerable difference in CAI, as pointed out by ███ █████ in his (as such undisputed) annotation of the Figure (Defendants' Exhibit 9, par. 20). The attacked embodiment has the highest expression, but also the highest CAI. The wild-type construct has the lowest expression level, but also the lowest CAI. In other words, the expression level correlates with the degree of codon optimisation (Defendants' Exhibit 9, par. 20, third sentence), although a strictly linear relationship between the number of optimised codons and the expression level cannot be assumed. Consequently, the Claimant cannot draw any reliable conclusion from the slight difference between the expression levels of "Test 1" / "Test 3" and "Test 4":



276. At the oral hearing, the Claimant questioned that the increase in expression of "Test 2" is due to codon optimisation, but still provided no concrete substantiation for the mutation of any actual secondary initiation codons. In essence, the Claimant makes its case on the basis of the factual premise that codon optimisation does not inevitably remove secondary start codons because codon usage bias is distinct from start codon identity. However, contrary to what the Claimant appears to be arguing, it does not logically follow from this premise that if a number of potential initiation codons have been removed and an increased expression is observed, these <u>must</u> have been (or at least, it is reasonable to assume) actual start codons. Rather, especially against the background that functional internal start codons are rare (see discussion above), taking into account the substantiated rebuttals by the Defendants, a mere mutation of

potential secondary initiation codons does not suffice to substantiate infringement in this case, where codon optimisation has been carried out at the same time. Precisely because the removal of the vast majority of potential secondary initiation codons, compared to the wild-type mRNA, can be explained by codon optimisation, the increased protein expression cannot be definitively attributed to a decrease in protein synthesis at these (now mutated) putative secondary initiation codons. It is therefore impossible to establish that any of these were actual secondary initiation codons (feature 1.3). Instead, it is at least plausible that the increased expression is due to the more favourable codon bias generated by codon optimisation. It is up to the Claimant to further substantiate that actual, functional start codons have been mutated causing the effects in feature group 1.3 to occur. The evidence relied on by the Claimant simply cannot show this.

277. In this respect, the reliance by the Claimant on a publication by one of the founders of the BioNTech Defendants, submitted as VB32, "Sahin et al.", does not provide the required substantiation. Apart from the fact that this publication (which was published in 2014) does not discuss the attacked embodiments (which did not even exist at the time), but is a general review article, it mentions that internal translation initiation *may* occur from actual secondary initiation codons and that these *may* be eliminated (automatically) by way of codon optimisation, see Exhibit VB32, p. 762, right column, section highlighted by the Claimant. As argued by the Defendants, these general statements (which are moreover not connected to the attacked embodiments) do not substantiate in a sufficiently concrete way that the disputed claim features are fulfilled in the attacked embodiments.

278. Similar considerations apply to the 2022 review article by Szábo et al., submitted by the Claimant as Exhibit VB33. The Claimant has highlighted the section on p. 1852, right-hand column, which confirms that the efficacy of a viral antigen-encoding mRNA vaccine is influenced by codon optimisation of the coding sequence, but not just in relation to stability and translatability (i.e. "ordinary" codon optimisation), but also refers to a recent study revealing that cryptic epitopes, originating from out-of-frame open reading frame translation during SARS-CoV-2 infection can be modified or lost during codon optimisation, leading to either enhanced or diminished immunogenic responses. Neither the article as a whole nor the passage highlighted by the Claimant refers to the attacked embodiments. The Court concurs with the Defendants, that the statements in Szábo et al. are too general to duly substantiate the alleged infringement, especially in light of the substantiated rebuttals provided by the Defendants (see discussion above).

Interim conclusion

279. In conclusion, the Claimant has not sufficiently substantiated that the Defendants have mutated one or more secondary initiation codons wherein the mutation results in a decrease in initiation of protein synthesis at the one or more secondary initiation codons, resulting in a reduction of ribosomal diversion away from the primary initiation

codon, thereby increasing expression efficiency of the full-length protein initiated at the primary initiation codon. Accordingly, the Court cannot find an infringement of claim 1 of the Patent as granted.

280. The Court notes that the same conclusion would apply to any of the Auxiliary Requests as they all contain the features of granted claim 1.

Comirnaty: codon optimisation method used

281. The Court furthermore notes that in coming to its conclusion, it has not relied on the information provided by the Defendants in the Rejoinder to the Reply to the Defence in relation to the codon optimisation method applied for Comirnaty. […].

Admissibility and Rule 36 RoP request

282. The admissibility of the pleadings and evidence of the Defendants on the codon optimisation method used to develop the attacked embodiments has been opposed to by the Claimant for the reason that it was newly submitted with the Rejoinder and there was no reason why this evidence could not have been produced with the SoD. Should the evidence and pleadings be admitted, the Claimant has asked for an opportunity to comment in writing under Rule 36 RoP and has done so in two submissions, to which the Defendant has, in turn, responded.

283. The Court considers the Defendants‘ pleadings in the Rejoinder in relation to codon optimisation admissible. Under the circumstances of the present case, the new facts and arguments are considered to be a *bona fide* and proportionate attempt to respond to the arguments and facts (including new experimental evidence) provided by the Claimant in the Reply to the Defence to revocation. The arguments are in-line with those already put forward in the statement of defence and do not unreasonably interfere with the Claimant's procedural position. They are not of such a nature or scope that the Claimant could not have reasonably responded to them adequately (particularly given the opportunity granted to do so under Rule 36, see below).

284. Against this background, the Claimant´s Rule 36 request succeeds in part. The Claimant is allowed to respond to the pleadings and evidence submitted by the Defendants in the Rejoinder related to their codon optimisation method by way of an exchange of further written pleadings. However, as allowing the exchange of further pleadings is exceptional (see e.g. UPC_CoA_579/2025, order of 24 July 2025, OTEC/STEROS) such further pleadings and evidence must be strictly limited to responding to the new arguments by the Defendant and must be proportionate to the aim of responding.

285. Concretely, this means that the submission made by the Claimant on 12 February 2026 is admissible, including the Exhibits VB39, VB40a and VB40b which all relate to and

respond directly to the codon optimisation method employed by the Defendants. The Defendants' comments thereto (submission of 2 March 2026) and the exhibit referred to (Defendants' exhibit 46) are also admitted.

Other evidence late: disregarded as late-filed (VB37 and VB38)

286. The Court disregards the remaining evidence and related pleadings filed by the parties in the infringement case after the Rejoinder. Specifically, this concerns exhibits VB37 and VB38, including the related explanatory pleadings. The response to those pleadings, submitted by the Defendants, including the new evidence provided with that response (Defendants' exhibits 47 and 48), and the reaction to that by the Claimant, and the further reaction by the Defendants are all disregarded because they are only relevant for the discussion relating to the, already deemed inadmissible exhibits VB37 and VB38.

287. VB37 and VB38 are two scientific articles which were submitted by the Claimant in an attempt to demonstrate that previously known actual secondary start codons were removed from the Defendants' vaccine, thereby increasing the expression of the full-length Spike protein. Even though these articles were submitted under the guise of a response to the Defendants' evidence on codon optimisation, they are not. These articles respond to the general point of whether or not actual secondary initiation codons have been mutated by the Defendants. This has been the central plank of the Defendants' defence from the beginning. In addition, no reason has been given by the Claimant why these articles, which are part of the public domain, were filed only after the Rejoinder. The late submission of these articles is also unduly burdensome for the Defendants and the Court. If anything, this is evidenced by the plethora of new submissions, including new experimental evidence and counter-evidence that was triggered by these submissions. As a consequence, Exhibits VB37 and VB38 are disregarded as being late-filed. They are unrelated to, and in any event extend beyond what is proportional to the further written pleadings that were allowed under Rule 36 RoP.

288. As VB37 and VB38 are disregarded, also the submissions responding to VB37 and VB38 are disregarded. As they have only been submitted in response to VB37 and VB38, there is no longer any reason to admit these documents which are even later filed.

On the substance of the new pleadings

289. The Court agrees with the Claimant that it cannot be deduced from the evidence provided in the Rejoinder that the Defendants did not mutate one or more secondary initiation codons, thereby achieving the results of the invention. The Court also agrees with the Claimant that, irrespective of whether this is done in isolation or as part of an applied codon optimisation method, if secondary initiation codons are mutated

according to the invention and the respective claimed effects are achieved claim 1 of the patent in suit is infringed. It is therefore of no relevance to the question of infringement whether the Defendants, as they say, indeed did not […]. What matters is whether any mutations of actual secondary initiation codons have taken place and result in the claimed effects. This, however, still needs to be substantiated by the Claimant who has, as follows from the above, in the opinion of the Court, not succeeded in doing so. In this respect, as already mentioned above, the new evidence and the response to that evidence by the Claimant ultimately do not affect the assessment nor the outcome of the case in any material way.

290. Regardless of their inadmissibility, documents VB37 and VB38 can in any event not convince the Court that there has been an infringement. Even if, for the benefit of the Claimant, it is assumed that VB37 and VB38 prove that in the wild-type gene encoding the SARS-CoV2 spike protein, overlapping ORFs are present, having their own (secondary) initiation codons, and that these secondary initiation codons have been mutated in the attacked embodiments, it still remains up to the Claimant to provide evidence that the claimed <u>effects</u> are present and are <u>caused</u> by the mutation of the secondary initiation codon. This evidence is lacking and within the context of these front-loaded UPC proceedings, there is no scope for the taking of any further evidence.

291. In conclusion, the Claimant has not sufficiently substantiated that the attacked embodiments make use of the claimed method. As a consequence, the Court cannot establish that the Defendants infringe the Patent.

IX. Legal Consequences

292. The legal consequences of the above are that the Patent must be revoked in its entirety with effect to the territory of Germany, France and Sweden. The application to amend is dismissed.

293. The infringement action is dismissed.

294. The Court shall decide on the obligation to bear legal costs based on Art. 69(1) UPCA in connection with Rule 118.5 RoP. The Claimant is regarded as the unsuccessful party in the infringement action and has to bear the costs of the Defendants. The Counterdefendants are regarded as the unsuccessful party in the counterclaim action and have to bear the costs of the Defendants.

Cost agreement

295. The parties agreed on flat fees covering the costs for the services of the respective representatives and cooperating attorneys and patent attorneys as well as the recoverable expenses (e.g. travel costs, expert costs, and experiments) and the court

fees which have been paid by the respective parties. The flat amount agreed for reimbursement for each party or rather group of parties shall be 750.000 EUR for the entire proceedings (i.e. infringement and counterclaim for revocation). This means that the maximum amount which is recoverable by the Defendants is 750.000 EUR per group of Defendants. This agreed amount of 750.000 EUR per group of Defendants, which (as confirmed during the oral hearing) is to be split equally between the infringement and counterclaim proceedings, is deemed reasonable and proportionate given the value of the case (more than 50 million euros) and the corresponding ceiling for recoverable costs of 2 million euros.

DECISION

1. The European patent EP 2 401 365 is revoked in its entirety with effect to the territory of Germany, France and Sweden.

2. The Application to amend the patent in suit is dismissed.

3. The Infringement action is dismissed.

4. The costs of the Counterclaim for revocation are to be borne by the Counterdefendants.

5. The costs of the Infringement action are to be borne by the Claimant.

Daniel Voß (Presiding Judge)	Daniel Voß Digital unterschrieben von Daniel Voß Datum: 2026.07.01 17:08:43 +02'00'
András Kupecz (Legally Qualified Judge)	András Ferenc Kupecz Digital unterschrieben von András Ferenc Kupecz Datum: 2026.07.01 12:12:50 +02'00'
Georg Werner (Legally Qualified Judge)	GEORG EDGAR WERNER Digital unterschrieben von GEORG EDGAR WERNER Datum: 2026.07.01 12:34:59 +02'00'
Martin Schmidt (Technically Qualified Judge)	Martin SCHMIDT Signature numérique de Martin SCHMIDT Date : 2026.07.01 13:04:10 +02'00'
For the Deputy-Registrar	Catrin Meyer Digital unterschrieben von Catrin Meyer Datum: 2026.07.02 08:09:44 +02'00'

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 7 July 2026.

Note

This document is a redacted version of the Decision, with confidential information removed.

ANNEX – SEQUENCES ATTACKED EMBODIMENTS

[in relation to attacked embodiment 2a – Comirnaty Original]

ATGTTCGTGTTCCTGGTGCTGCTGCCTCTGGTGTCCAGCCAGTGTGTGAACCTGACCACCAGAACACAGCTGCC
TCCAGCCTACACCAACAGCTTTACCAGAGGCGTGTACTACCCCGACAAGGTGTTCAGATCCAGCGTGCTGCACT
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TGCTCTGGAACCCCTGGTGGATCTGCCCATCGGCATCAACATCACCCGGTTTCAGACACTGCTGGCCCTGCACA
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CCTCTGAGCGAGACAAAGTGCACCCTGAAGTCCTTCACCGTGGAAAAGGGCATCTACCAGACCAGCAACTTCC
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TGGCAACTGCGACGTCGTGATCGGCATTGTGAACAATACCGTGTACGACCCTCTGCAGCCCGAGCTGGACAGC
TTCAAAGAGGAACTGGACAAGTACTTTAAGAACCACACAAGCCCCGACGTGGACCTGGGCGATATCAGCGGA

ATCAATGCCAGCGTCGTGAACATCCAGAAAGAGATCGACCGGCTGAACGAGGTGGCCAAGAATCTGAACGAG
AGCCTGATCGACCTGCAAGAACTGGGGAAGTACGAGCAGTACATCAAGTGGCCCTGGTACATCTGGCTGGGC
TTTATCGCCGGACTGATTGCCATCGTGATGGTCACAATCATGCTGTGTTGCATGACCAGCTGCTGTAGCTGCCT
GAAGGGCTGTTGTAGCTGTGGCAGCTGCTGCAAGTTCGACGAGGACGATTCTGAGCCCGTGCTGAAGGGCGT
GAAACTGCACTACACATGATGA

and

[in relation to attacked embodiment 2b -

ATGTTCGTGTTCCTGGTGCTGCTGCCTCTGGTGTCCAGCCAGTGTGTGAACCTGACCACCAGAACACAGCTGCC
TCCAGCCTACACCAACAGCTTTACCAGAGGCGTGTACTACCCCGACAAGGTGTTCAGATCCAGCGTGCTGCACT
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AAGATCTACAGCAAGCACACCCCTATCATCGTGAGAGAGCCCGAGGATCTGCCTCAGGGCTTCTCTGCTCTGG
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CTGGCCCCCTTCTTCACCTTCAAGTGCTACGGCGTGTCCCCTACCAAGCTGAACGACCTGTGCTTCACAAACGTG
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AAGTCAGCGGCAACTACAATTACCTGTACCGGCTGTTCCGGAAGTCCAATCTGAAGCCCTTCGAGCGGGACAT
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GCCGGGATATCGCCGATACCACAGACGCCGTTAGAGATCCCCAGACACTGGAAATCCTGGACATCACCCCTTG
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TGGCCAGCCAGAGCATCATTGCCTACACAATGTCTCTGGGCGCCGAGAACAGCGTGGCCTACTCCAACAACTC
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TGGACTGCACCATGTACATCTGCGGCGATTCCACCGAGTGCTCCAACCTGCTGCTGCAGTACGGCAGCTTCTGC
ACCCAGCTGAAAAGAGCCCTGACAGGGATCGCCGTGGAACAGGACAAGAACACCCAAGAGGTGTTCGCCCAA
GTGAAGCAGATCTACAAGACCCCTCCTATCAAGTACTTCGGCGGCTTCAATTTCAGCCAGATTCTGCCCGATCC
TAGCAAGCCCAGCAAGCGGAGCTTCATCGAGGACCTGCTGTTCAACAAAGTGACACTGGCCGACGCCGGCTTC
ATCAAGCAGTATGGCGATTGTCTGGGCGACATTGCCGCCAGGGATCTGATTTGCGCCCAGAAGTTTAAGGGAC
TGACAGTGCTGCCTCCTCTGCTGACCGATGAGATGATCGCCCAGTACACATCTGCCCTGCTGGCCGGCACAATC
ACAAGCGGCTGGACATTTGGAGCAGGCGCCGCTCTGCAGATCCCCTTTGCTATGCAGATGGCCTACCGGTTCA
ACGGCATCGGAGTGACCCAGAATGTGCTGTACGAGAACCAGAAGCTGATCGCCAACCAGTTCAACAGCGCCAT
CGGCAAGATCCAGGACAGCCTGAGCAGCACAGCAAGCGCCCTGGGAAAGCTGCAGGACGTGGTCAACCACAA
TGCCCAGGCACTGAACACCCTGGTCAAGCAGCTGTCCTCCAAGTTCGGCGCCATCAGCTCTGTGCTGAACGATA
TCTTCAGCAGACTGGACCCTCCTGAGGCCGAGGTGCAGATCGACAGACTGATCACAGGCAGACTGCAGAGCCT
CCAGACATACGTGACCCAGCAGCTGATCAGAGCCGCCGAGATTAGAGCCTCTGCCAATCTGGCCGCCACCAAG

ATGTCTGAGTGTGTGCTGGGCCAGAGCAAGAGAGTGGACTTTTGCGGCAAGGGCTACCACCTGATGAGCTTCC
CTCAGTCTGCCCCTCACGGCGTGGTGTTTCTGCACGTGACATATGTGCCCGCTCAAGAGAAGAATTTCACCACC
GCTCCAGCCATCTGCCACGACGGCAAAGCCCACTTTCCTAGAGAAGGCGTGTTCGTGTCCAACGGCACCCATT
GGTTCGTGACACAGCGGAACTTCTACGAGCCCCAGATCATCACCACCGACAACACCTTCGTGTCTGGCAACTGC
GACGTCGTGATCGGCATTGTGAACAATACCGTGTACGACCCTCTGCAGCCCGAGCTGGACAGCTTCAAAGAGG
AACTGGACAAGTACTTTAAGAACCACACAAGCCCCGACGTGGACCTGGGCGATATCAGCGGAATCAATGCCAG
CGTCGTGAACATCCAGAAAGAGATCGACCGGCTGAACGAGGTGGCCAAGAATCTGAACGAGAGCCTGATCGA
CCTGCAAGAACTGGGGAAGTACGAGCAGTACATCAAGTGGCCCTGGTACATCTGGCTGGGCTTTATCGCCGGA
CTGATTGCCATCGTGATGGTCACAATCATGCTGTGTTGCATGACCAGCTGCTGTAGCTGCCTGAAGGGCTGTTG
TAGCTGTGGCAGCTGCTGCAAGTTCGACGAGGACGATTCTGAGCCCGTGCTGAAGGGCGTGAAACTGCACTA
CACATGATGACTCGAGCTGGTACTGCATGCACGCAATGCTAGCTGCCCCTTTCCCGTCCTGGGTACCCCGAGTC
TCCCCCGACCTCGGGTCCCAGGTATGCTCCCACCTCCACCTGCCCCACTCACCACCTCTGCTAGTTCCAGACACC
TCCCAAGCACGCAGCAATGCAGCTCAAAACGCTTAGCCTAGCCACACCCCCACGGGAAACAGCAGTGATTAAC
CTTTAGCAATAAACGAAAGTTTAACTAAGCTATACTAACCCCAGGGTTGGTCAATTTCGTGCCAGCCACACCCT
GGAGCTAGCAAA

and

[in relation to attacked embodiment 2c - Comirnaty Original/Omicron BA.4-5]

ATGTTCGTGTTCCTGGTGCTGCTGCCTCTGGTGTCCAGCCAGTGTGTGAACCTGATCACCAGAACACAGTCATA
CACCAACAGCTTTACCAGAGGCGTGTACTACCCCGACAAGGTGTTCAGATCCAGCGTGCTGCACTCTACCCAG
GACCTGTTCCTGCCTTTCTTCAGCAACGTGACCTGGTTCCACGCCATCTCCGGCACCAATGGCACCAAGAGATT
CGACAACCCCGTGCTGCCCTTCAACGACGGGGTGTACTTTGCCAGCACCGAGAAGTCCAACATCATCAGAGGC
TGGATCTTCGGCACCACACTGGACAGCAAGACCCAGAGCCTGCTGATCGTGAACAACGCCACCAACGTGGTCA
TCAAAGTGTGCGAGTTCCAGTTCTGCAACGACCCCTTCCTGGACGTCTACTACCACAAGAACAACAAGAGCTGG
ATGGAAAGCGAGTTCCGGGTGTACAGCAGCGCCAACAACTGCACCTTCGAGTACGTGTCCCAGCCTTTCCTGA
TGGACCTGGAAGGCAAGCAGGGCAACTTCAAGAACCTGCGCGAGTTCGTGTTTAAGAACATCGACGGCTACTT
CAAGATCTACAGCAAGCACACCCCTATCAACCTCGGCCGGGATCTGCCTCAGGGCTTCTCTGCTCTGGAACCCC
TGGTGGATCTGCCCATCGGCATCAACATCACCCGGTTTCAGACACTGCTGGCCCTGCACAGAAGCTACCTGACA
CCTGGCGATAGCAGCAGCGGATGGACAGCTGGTGCCGCCGCTTACTATGTGGGCTACCTGCAGCCTAGAACCT
TCCTGCTGAAGTACAACGAGAACGGCACCATCACCGACGCCGTGGATTGTGCTCTGGATCCTCTGAGCGAGAC
AAAGTGCACCCTGAAGTCCTTCACCGTGGAAAAGGGCATCTACCAGACCAGCAACTTCCGGGTGCAGCCCACC
GAATCCATCGTGCGGTTCCCCAATATCACCAATCTGTGCCCCTTCGACGAGGTGTTCAATGCCACCAGATTCGC
CTCTGTGTACGCCTGGAACCGGAAGCGGATCAGCAATTGCGTGGCCGACTACTCCGTGCTGTACAACTTCGCC
CCCTTCTTCGCATTCAAGTGCTACGGCGTGTCCCCTACCAAGCTGAACGACCTGTGCTTCACAAACGTGTACGC
CGACAGCTTCGTGATCCGGGGAAACGAAGTGCGGCAGATTGCCCCTGGACAGACAGGCAACATCGCCGACTA
CAACTACAAGCTGCCCGACGACTTCACCGGCTGTGTGATTGCCTGGAACAGCAACAAGCTGGACTCCAAAGTC
GGCGGCAACTACAATTACAGGTACCGGCTGTTCCGGAAGTCCAATCTGAAGCCCTTCGAGCGGGACATCTCCA
CCGAGATCTATCAGGCCGGCAACAAGCCTTGTAACGGCGTGGCAGGCGTGAACTGCTACTTCCCACTGCAGTC
CTACGGCTTTAGGCCCACATACGGCGTGGGCCACCAGCCCTACAGAGTGGTGGTGCTGAGCTTCGAACTGCTG
CATGCCCCTGCCACAGTGTGCGGCCCTAAGAAAAGCACCAATCTCGTGAAGAACAAATGCGTGAACTTCAACT
TCAACGGCCTGACCGGCACCGGCGTGCTGACAGAGAGCAACAAGAAGTTCCTGCCATTCCAGCAGTTTGGCCG
GGATATCGCCGATACCACAGACGCCGTTAGAGATCCCCAGACACTGGAAATCCTGGACATCACCCCTTGCAGC
TTCGGCGGAGTGTCTGTGATCACCCCTGGCACCAACACCAGCAATCAGGTGGCAGTGCTGTACCAGGGCGTGA
ACTGTACCGAAGTGCCCGTGGCCATTCACGCCGATCAGCTGACACCTACATGGCGGGTGTACTCCACCGGCAG
CAATGTGTTTCAGACCAGAGCCGGCTGTCTGATCGGAGCCGAGTACGTGAACAATAGCTACGAGTGCGACATC
CCCATCGGCGCTGGAATCTGCGCCAGCTACCAGACACAGACAAAGAGCCACCGGAGAGCCAGAAGCGTGGCC
AGCCAGAGCATCATTGCCTACACAATGTCTCTGGGCGCCGAGAACAGCGTGGCCTACTCCAACAACTCTATCGC
TATCCCCACCAACTTCACCATCAGCGTGACCACAGAGATCCTGCCTGTGTCCATGACCAAGACCAGCGTGGACT
GCACCATGTACATCTGCGGCGATTCCACCGAGTGCTCCAACCTGCTGCTGCAGTACGGCAGCTTCTGCACCCAG
CTGAAAAGAGCCCTGACAGGGATCGCCGTGGAACAGGACAAGAACACCCAAGAGGTGTTCGCCCAAGTGAAG

CAGATCTACAAGACCCCTCCTATCAAGTACTTCGGCGGCTTCAATTTCAGCCAGATTCTGCCCGATCCTAGCAA
GCCCAGCAAGCGGAGCTTCATCGAGGACCTGCTGTTCAACAAAGTGACACTGGCCGACGCCGGCTTCATCAAG
CAGTATGGCGATTGTCTGGGCGACATTGCCGCCAGGGATCTGATTTGCGCCCAGAAGTTTAACGGACTGACAG
TGCTGCCTCCTCTGCTGACCGATGAGATGATCGCCCAGTACACATCTGCCCTGCTGGCCGGCACAATCACAAGC
GGCTGGACATTTGGAGCAGGCGCCGCTCTGCAGATCCCCTTTGCTATGCAGATGGCCTACCGGTTCAACGGCA
TCGGAGTGACCCAGAATGTGCTGTACGAGAACCAGAAGCTGATCGCCAACCAGTTCAACAGCGCCATCGGCAA
GATCCAGGACAGCCTGAGCAGCACAGCAAGCGCCCTGGGAAAGCTGCAGGACGTGGTCAACCACAATGCCCA
GGCACTGAACACCCTGGTCAAGCAGCTGTCCTCCAAGTTCGGCGCCATCAGCTCTGTGCTGAACGATATCCTGA
GCAGACTGGACCCTCCTGAGGCCGAGGTGCAGATCGACAGACTGATCACAGGCAGACTGCAGAGCCTCCAGA
CATACGTGACCCAGCAGCTGATCAGAGCCGCCGAGATTAGAGCCTCTGCCAATCTGGCCGCCACCAAGATGTC
TGAGTGTGTGCTGGGCCAGAGCAAGAGAGTGGACTTTTGCGGCAAGGGCTACCACCTGATGAGCTTCCCTCA
GTCTGCCCCTCACGGCGTGGTGTTTCTGCACGTGACATATGTGCCCGCTCAAGAGAAGAATTTCACCACCGCTC
CAGCCATCTGCCACGACGGCAAAGCCCACTTTCCTAGAGAAGGCGTGTTCGTGTCCAACGGCACCCATTGGTTC
GTGACACAGCGGAACTTCTACGAGCCCCAGATCATCACCACCGACAACACCTTCGTGTCTGGCAACTGCGACG
TCGTGATCGGCATTGTGAACAATACCGTGTACGACCCTCTGCAGCCCGAGCTGGACAGCTTCAAAGAGGAACT
GGACAAGTACTTTAAGAACCACACAAGCCCCGACGTGGACCTGGGCGATATCAGCGGAATCAATGCCAGCGTC
GTGAACATCCAGAAAGAGATCGACCGGCTGAACGAGGTGGCCAAGAATCTGAACGAGAGCCTGATCGACCTG
CAAGAACTGGGGAAGTACGAGCAGTACATCAAGTGGCCCTGGTACATCTGGCTGGGCTTTATCGCCGGACTG
ATTGCCATCGTGATGGTCACAATCATGCTGTGTTGCATGACCAGCTGCTGTAGCTGCCTGAAGGGCTGTTGTAG
CTGTGGCAGCTGCTGCAAGTTCGACGAGGACGATTCTGAGCCCGTGCTGAAGGGCGTGAAACTGCACTACAC
ATGA

and

[in relation to attacked embodiment 2d - [redacted]

ATGTTCGTGTTCCTGGTGCTGCTGCCTCTGGTGTCCAGCCAGTGTGTGAACCTGATCACCAGAACACAGTCATA
CACCAACAGCTTTACCAGAGGCGTGTACTACCCCGACAAGGTGTTCAGATCCAGCGTGCTGCACTCTACCCAG
GACCTGTTCCTGCCTTTCTTCAGCAACGTGACCTGGTTCCACGCCATCCACGTGTCCGGCACCAATGGCACCAA
GAGATTCGACAACCCCGCCCTGCCCTTCAACGACGGGGTGTACTTTGCCAGCACCGAGAAGTCCAACATCATC
AGAGGCTGGATCTTCGGCACCACACTGGACAGCAAGACCCAGAGCCTGCTGATCGTGAACAACGCCACCAAC
GTGGTCATCAAAGTGTGCGAGTTCCAGTTCTGCAACGACCCCTTCCTGGACGTCTACCAGAAGAACAACAAGA
GCTGGATGGAAAGCGAGTTCCGGGTGTACAGCAGCGCCAACAACTGCACCTTCGAGTACGTGTCCCAGCCTTT
CCTGATGGACCTGGAAGGCAAGGAGGGCAACTTCAAGAACCTGCGCGAGTTCGTGTTTAAGAACATCGACGG
CTACTTCAAGATCTACAGCAAGCACACCCCTATCAACCTCGAGCGGGATCTGCCTCAGGGCTTCTCTGCTCTGG
AACCCCTGGTGGATCTGCCCATCGGCATCAACATCACCCGGTTTCAGACACTGCTGGCCCTGCACAGAAGCTAC
CTGACACCTGTGGATAGCAGCAGCGGATGGACAGCTGGTGCCGCCGCTTACTATGTGGGCTACCTGCAGCCTA
GAACCTTCCTGCTGAAGTACAACGAGAACGGCACCATCACCGACGCCGTGGATTGTGCTCTGGATCCTCTGAG
CGAGACAAAGTGCACCCTGAAGTCCTTCACCGTGGAAAAGGGCATCTACCAGACCAGCAACTTCCGGGTGCAG
CCCACCGAATCCATCGTGCGGTTCCCCAATATCACCAATCTGTGCCCCTTCCACGAGGTGTTCAATGCCACCACC
TTCGCCTCTGTGTACGCCTGGAACCGGAAGCGGATCAGCAATTGCGTGGCCGACTACTCCGTGATCTACAACTT
CGCCCCCTTCTTCGCATTCAAGTGCTACGGCGTGTCCCCTACCAAGCTGAACGACCTGTGCTTCACAAACGTGT
ACGCCGACAGCTTCGTGATCCGGGGAAACGAAGTGTCACAGATTGCCCCTGGACAGACAGGCAACATCGCCG
ACTACAACTACAAGCTGCCCGACGACTTCACCGGCTGTGTGATTGCCTGGAACAGCAACAAGCTGGACTCCAA
ACCCAGCGGCAACTACAATTACCTGTACCGGCTGTTCCGGAAGTCCAAGCTGAAGCCCTTCGAGCGGGACATC
TCCACCGAGATCTATCAGGCCGGCAACAAGCCTTGTAACGGCGTGGCAGGCCCCAACTGCTACAGCCCACTGC
AGTCCTACGGCTTTAGGCCCACATACGGCGTGGGCCACCAGCCCTACAGAGTGGTGGTGCTGAGCTTCGAACT
GCTGCATGCCCCTGCCACAGTGTGCGGCCCTAAGAAAAGCACCAATCTCGTGAAGAACAAATGCGTGAACTTC
AACTTCAACGGCCTGACCGGCACCGGCGTGCTGACAGAGAGCAACAAGAAGTTCCTGCCATTCCAGCAGTTTG
GCCGGGATATCGCCGATACCACAGACGCCGTTAGAGATCCCCAGACACTGGAAATCCTGGACATCACCCCTTG
CAGCTTCGGCGGAGTGTCTGTGATCACCCCTGGCACCAACACCAGCAATCAGGTGGCAGTGCTGTACCAGGGC
GTGAACTGTACCGAAGTGCCCGTGGCCATTCACGCCGATCAGCTGACACCTACATGGCGGGTGTACTCCACCG

GCAGCAATGTGTTTCAGACCAGAGCCGGCTGTCTGATCGGAGCCGAGTACGTGAACAATAGCTACGAGTGCG
ACATCCCCATCGGCGCTGGAATCTGCGCCAGCTACCAGACACAGACAAAGAGCCACCGGAGAGCCAGAAGCG
TGGCCAGCCAGAGCATCATTGCCTACACAATGTCTCTGGGGCCGAGAACAGCGTGGCCTACTCCAACAACTCT
ATCGCTATCCCCACCAACTTCACCATCAGCGTGACCACAGAGATCCTGCCTGTGTCCATGACCAAGACCAGCGT
GGACTGCACCATGTACATCTGCGGCGATTCCACCGAGTGCTCCAACCTGCTGCTGCAGTACGGCAGCTTCTGCA
CCCAGCTGAAAAGAGCCCTGACAGGGATCGCCGTGGAACAGGACAAGAACACCCAAGAGGTGTTCGCCCAAG
TGAAGCAGATCTACAAGACCCCTCCTATCAAGTACTTCGGCGGCTTCAATTTCAGCCAGATTCTGCCCGATCCTA
GCAAGCCCAGCAAGCGGAGCTTCATCGAGGACCTGCTGTTCAACAAAGTGACACTGGCCGACGCCGGCTTCAT
CAAGCAGTATGGCGATTGTCTGGGCGACATTGCCGCCAGGGATCTGATTTGCGCCCAGAAGTTTAACGGACTG
ACAGTGCTGCCTCCTCTGCTGACCGATGAGATGATCGCCCAGTACACATCTGCCCTGCTGGCCGGCACAATCAC
AAGCGGCTGGACATTTGGAGCAGGCGCCGCTCTGCAGATCCCCTTTGCTATGCAGATGGCCTACCGGTTCAAC
GGCATCGGAGTGACCCAGAATGTGCTGTACGAGAACCAGAAGCTGATCGCCAACCAGTTCAACAGCGCCATC
GGCAAGATCCAGGACAGCCTGAGCAGCACAGCAAGCGCCCTGGGAAAGCTGCAGGACGTGGTCAACCACAAT
GCCCAGGCACTGAACACCCTGGTCAAGCAGCTGTCCTCCAAGTTCGGCGCCATCAGCTCTGTGCTGAACGATAT
CCTGAGCAGACTGGACCCTCCTGAGGCCGAGGTGCAGATCGACAGACTGATCACAGGCAGACTGCAGAGCCT
CCAGACATACGTGACCCAGCAGCTGATCAGAGCCGCCGAGATTAGAGCCTCTGCCAATCTGGCCGCCACCAAG
ATGTCTGAGTGTGTGCTGGGCCAGAGCAAGAGAGTGGACTTTTGCGGCAAGGGCTACCACCTGATGAGCTTCC
CTCAGTCTGCCCCTCACGGCGTGGTGTTTCTGCACGTGACATATGTGCCCGCTCAAGAGAAGAATTTCACCACC
GCTCCAGCCATCTGCCACGACGGCAAAGCCCACTTTCCTAGAGAAGGCGTGTTCGTGTCCAACGGCACCCATT
GGTTCGTGACACAGCGGAACTTCTACGAGCCCCAGATCATCACCACCGACAACACCTTCGTGTCTGGCAACTGC
GACGTCGTGATCGGCATTGTGAACAATACCGTGTACGACCCTCTGCAGCCCGAGCTGGACAGCTTCAAAGAGG
AACTGGACAAGTACTTTAAGAACCACACAAGCCCCGACGTGGACCTGGGCGATATCAGCGGAATCAATGCCAG
CGTCGTGAACATCCAGAAAGAGATCGACCGGCTGAACGAGGTGGCCAAGAATCTGAACGAGAGCCTGATCGA
CCTGCAAGAACTGGGGAAGTACGAGCAGTACATCAAGTGGCCCTGGTACATCTGGCTGGGCTTTATCGCCGGA
CTGATTGCCATCGTGATGGTCACAATCATGCTGTGTTGCATGACCAGCTGCTGTAGCTGCCTGAAGGGCTGTTG
TAGCTGTGGCAGCTGCTGCAAGTTCGACGAGGACGATTCTGAGCCCGTGCTGAAGGGCGTGAAACTGCACTA
CACATGATGACTCGAGCTGGTACTGCATGCACGCAATGCTAGCTGCCCCTTTCCCGTCCTGGGTACCCCGAGTC
TCCCCCGACCTCGGGTCCCAGGTATGCTCCCACCTCCACCTGCCCCACTCACCACCTCTGCTAGTTCCAGACACC
TCCCAAGCACGCAGCAATGCAGCTCAAAACGCTTAGCCTAGCCACACCCCCACGGGAAACAGCAGTGATTAAC
CTTTAGCAATAAACGAAAGTTTAACTAAGCTATACTAACCCCAGGGTTGGTCAATTTCGTGCCAGCCACACCCT
GGAGCTAGCAAAAAAAAAAAAAAAAAAA

and

[in relation to attacked embodiment 2e - [REDACTED]

ATGTTCGTGTTCCTGGTGCTGCTGCCTCTGGTGTCCAGCCAGTGTGTGATGCCCCTGTTCAACCTGATCACCACC
ACACAGTCATACACCAACAGCTTTACCAGAGGCGTGTACTACCCCGACAAGGTGTTCAGATCCAGCGTGCTGC
ACCTGACCCAGGACCTGTTCCTGCCTTTCTTCAGCAACGTGACCTGGTTCCACGCCATCTCCGGCACCAATGGC
ACCAAGAGATTCGACAACCCCGTGCTGCCCTTCAACGACGGGGTGTACTTTGCCAGCACCGAGAAGTCCAACA
TCATCAGAGGCTGGATCTTCGGCACCACACTGGACAGCAAGACCCAGAGCCTGCTGATCGTGAACAACGCCAC
CAACGTGTTCATCAAAGTGTGCGAGTTCCAGTTCTGCAACGACCCCTTCCTGGACGTCTACCACAAGAACAACA
AGAGCTGGATGGAAAGCGAGTCAGGCGTGTACAGCAGCGCCAACAACTGCACCTTCGAGTACGTGTCCCAGC
CTTTCCTGATGGACCTGGAAGGCAAGCAGGGCAACTTCAAGAACCTGCGCGAGTTCGTGTTTAAGAACATCGA
CGGCTACTTCAAGATCTACAGCAAGCACACCCCTATCATCGGCCGGGATTTCCCTCAGGGCTTCTCTGCTCTGG
AACCCCTGGTGGATCTGCCCATCGGCATCAACATCACCCGGTTTCAGACACTGCTGGCCCTGAACAGAAGCTAC
CTGACACCTGGCGATAGCAGCAGCGGATGGACAGCTGGTGCCGCCGACTACTATGTGGGCTACCTGCAGCCTA
GAACCTTCCTGCTGAAGTACAACGAGAACGGCACCATCACCGACGCCGTGGATTGTGCTCTGGATCCTCTGAG
CGAGACAAAGTGCACCCTGAAGTCCTTCACCGTGGAAAAGGGCATCTACCAGACCAGCAACTTCCGGGTGCAG
CCCACCGAATCCATCGTGCGGTTCCCCAATGTGACCAATCTGTGCCCCTTCCACGAGGTGTTCAATGCCACCAG
ATTCGCCTCTGTGTACGCCTGGAACCGGACCCGGATCAGCAATTGCGTGGCCGACTACTCCGTGCTGTACAACT
TCGCCCCCTTCTTCGCATTCAAGTGCTACGGCGTGTCCCCTACCAAGCTGAACGACCTGTGCTTCACAAACGTGT

ACGCCGACAGCTTCGTGATCAAGGGAAACGAAGTGTCACAGATTGCCCCTGGACAGACAGGCAACATCGCCG
ACTACAACTACAAGCTGCCCGACGACTTCACCGGCTGTGTGATTGCCTGGAACAGCAACAAGCTGGACTCCAA
ACACAGCGGCAACTACGACTACTGGTACCGGAGCTTCCGGAAGTCCAAGCTGAAGCCCTTCGAGCGGGACATC
TCCACCGAGATCTATCAGGCCGGCAACAAGCCTTGTAAGGGCAAGGGCCCCAACTGCTACTTCCCACTGCAGT
CCTACGGCTTTAGGCCCACATACGGCGTGGGCCACCAGCCCTACAGAGTGGTGGTGCTGAGCTTCGAACTGCT
GCATGCCCCTGCCACAGTGTGCGGCCCTAAGAAAAGCACCAATCTCGTGAAGAACAAATGCGTGAACTTCAAC
TTCAACGGCCTGACCGGCACCGGCGTGCTGACAAAGAGCAACAAGAAGTTCCTGCCATTCCAGCAGTTTGGCC
GGGATATCGTGGATACCACAGACGCCGTTAGAGATCCCCAGACACTGGAAATCCTGGACATCACCCCTTGCAG
CTTCGGCGGAGTGTCTGTGATCACCCCTGGCACCAACACCAGCAATCAGGTGGCAGTGCTGTACCAGGGCGTG
AACTGTACCGAAGTGAGCGTGGCCATTCACGCCGATCAGCTGACACCTACATGGCGGGTGTACTCCACCGGCA
GCAATGTGTTTCAGACCAGAGCCGGCTGTCTGATCGGAGCCGAGTACGTGAACAATAGCTACGAGTGCGACAT
CCCCATCGGCGCTGGAATCTGCGCCAGCTACCAGACACAGACAAAGAGCAGGCGGAGAGCCAGAAGCGTGGC
CAGCCAGAGCATCATTGCCTACACAATGTCTCTGGGCGCCGAGAACAGCGTGGCCTACTCCAACAACTCTATCG
CTATCCCCACCAACTTCACCATCAGCGTGACCACAGAGATCCTGCCTGTGTCCATGACCAAGACCAGCGTGGAC
TGCACCATGTACATCTGCGGCGATTCCACCGAGTGCTCCAACCTGCTGCTGCAGTACGGCAGCTTCTGCACCCA
GCTGAAAAGAGCCCTGACAGGGATCGCCGTGGAACAGGACAAGAACACCCAAGAGGTGTTCGCCCAAGTGAA
GCAGATCTACAAGACCCCTCCTATCAAGTACTTCGGCGGCTTCAATTTCAGCCAGATTCTGCCCGATCCTAGCA
AGCCCAGCAAGCGGAGCTTCATCGAGGACCTGCTGTTCAACAAAGTGACACTGGCCGACGCCGGCTTCATCAA
GCAGTATGGCGATTGTCTGGGCGACATTGCCGCCAGGGATCTGATTTGCGCCCAGAAGTTTAACGGACTGACA
GTGCTGCCTCCTCTGCTGACCGATGAGATGATCGCCCAGTACACATCTGCCCTGCTGGCCGGCACAATCACAAG
CGGCTGGACATTTGGAGCAGGCGCCGCTCTGCAGATCCCCTTTGCTATGCAGATGGCCTACCGGTTCAACGGC
ATCGGAGTGACCCAGAATGTGCTGTACGAGAACCAGAAGCTGATCGCCAACCAGTTCAACAGCGCCATCGGCA
AGATCCAGGACAGCCTGTTCAGCACAGCAAGCGCCCTGGGAAAGCTGCAGGACGTGGTCAACCACAATGCCC
AGGCACTGAACACCCTGGTCAAGCAGCTGTCCTCCAAGTTCGGCGCCATCAGCTCTGTGCTGAACGATATCCTG
AGCAGACTGGACCCTCCTGAGGCCGAGGTGCAGATCGACAGACTGATCACAGGCAGACTGCAGAGCCTCCAG
ACATACGTGACCCAGCAGCTGATCAGAGCCGCCGAGATTAGAGCCTCTGCCAATCTGGCCGCCACCAAGATGT
CTGAGTGTGTGCTGGGCCAGAGCAAGAGAGTGGACTTTTGCGGCAAGGGCTACCACCTGATGAGCTTCCCTCA
GTCTGCCCCTCACGGCGTGGTGTTTCTGCACGTGACATATGTGCCCGCTCAAGAGAAGAATTTCACCACCGCTC
CAGCCATCTGCCACGACGGCAAAGCCCACTTTCCTAGAGAAGGCGTGTTCGTGTCCAACGGCACCCATTGGTTC
GTGACACAGCGGAACTTCTACGAGCCCCAGATCATCACCACCGACAACACCTTCGTGTCTGGCAACTGCGACG
TCGTGATCGGCATTGTGAACAATACCGTGTACGACCCTCTGCAGCTGGAGCTGGACAGCTTCAAAGAGGAACT
GGACAAGTACTTTAAGAACCACACAAGCCCCGACGTGGACCTGGGCGATATCAGCGGAATCAATGCCAGCGTC
GTGAACATCCAGAAAGAGATCGACCGGCTGAACGAGGTGGCCAAGAATCTGAACGAGAGCCTGATCGACCTG
CAAGAACTGGGGAAGTACGAGCAGTACATCAAGTGGCCCTGGTACATCTGGCTGGGCTTTATCGCCGGACTG
ATTGCCATCGTGATGGTCACAATCATGCTGTGTTGCATGACCAGCTGCTGTAGCTGCCTGAAGGGCTGTTGTAG
CTGTGGCAGCTGCTGCAAGTTCGACGAGGACGATTCTGAGCCCGTGCTGAAGGGCGTGAAACTGCACTACAC
ATGATGACTCGAGCTGGTACTGCATGCACGCAATGCTAGCTGCCCCTTTCCCGTCCTGGGTACCCCGAGTCTCC
CCCGACCTCGGGTCCCAGGTATGCTCCCACCTCCACCTGCCCCACTCACCACCTCTGCTAGTTCCAGACACCTCC
CAAGCACGCAGCAATGCAGCTCAAAACGCTTAGCCTAGCCACACCCCCACGGGAAACAGCAGTGATTAACCTT
TAGCAATAAACGAAAGTTTAACTAAGCTATACTAACCCCAGGGTTGGTCAATTTCGTGCCAGCCACACCCTGGA
GCTAG

RNA *in-vitro* transcribed from the DNA sequences according to lit. a. having the following sequences

[in relation to attacked embodiment 2a – Comirnaty Original]

AUGUUCGUGUUCCUGGUGCUGCUGCCUCUGGUGUCCAGCCAGUGUGUGAACCUGACCACCAGAACACAG
CUGCCUCCAGCCUACACCAACAGCUUUACCAGAGGCGUGUACUACCCCGACAAGGUGUUCAGAUCCAGCG
UGCUGCACUCUACCCAGGACCUGUUCCUGCCUUUCUUCAGCAACGUGACCUGGUUCCACGCCAUCCACGU
GUCCGGCACCAAUGGCACCAAGAGAUUCGACAACCCCGUGCUGCCCUUCAACGACGGGGUGUACUUUGCC
AGCACCGAGAAGUCCAACAUCAUCAGAGGCUGGAUCUUCGGCACCACACUGGACAGCAAGACCCAGAGCC
UGCUGAUCGUGAACAACGCCACCAACGUGGUCAUCAAAGUGUGCGAGUUCCAGUUCUGCAACGACCCCU

UCCUGGGCGUCUACUACCACAAGAACAACAAGAGCUGGAUGGAAAGCGAGUUCCGGGUGUACAGCAGCG
CCAACAACUGCACCUUCGAGUACGUGUCCCAGCCUUUCCUGAUGGACCUGGAAGGCAAGCAGGGCAACUU
CAAGAACCUGCGCGAGUUCGUGUUUAAGAACAUCGACGGCUACUUCAAGAUCUACAGCAAGCACACCCCU
AUCAACCUCGUGCGGGAUCUGCCUCAGGGCUUCUCUGCUCUGGAACCCCUGGUGGAUCUGCCCAUCGGC
AUCAACAUCACCCGGUUUCAGACACUGCUGGCCCUGCACAGAAGCUACCUGACACCUGGCGAUAGCAGCA
GCGGAUGGACAGCUGGUGCCGCCGCUUACUAUGUGGGCUACCUGCAGCCUAGAACCUUCCUGCUGAAGU
ACAACGAGAACGGCACCAUCACCGACGCCGUGGAUUGUGCUCUGGAUCCUCUGAGCGAGACAAAGUGCAC
CCUGAAGUCCUUCACCGUGGAAAAGGGCAUCUACCAGACCAGCAACUUCCGGGUGCAGCCCACCGAAUCC
AUCGUGCGGUUCCCCAAUAUCACCAAUCUGUGCCCCUUCGGCGAGGUGUUCAAUGCCACCAGAUUCGCC
UCUGUGUACGCCUGGAACCGGAAGCGGAUCAGCAAUUGCGUGGCCGACUACUCCGUGCUGUACAACUCC
GCCAGCUUCAGCACCUUCAAGUGCUACGGCGUGUCCCCUACCAAGCUGAACGACCUGUGCUUCACAAACG
UGUACGCCGACAGCUUCGUGAUCCGGGGAGAUGAAGUGCGGCAGAUUGCCCCUGGACAGACAGGCAAGA
UCGCCGACUACAACUACAAGCUGCCCGACGACUUCACCGGCUGUGUGAUUGCCUGGAACAGCAACAACCU
GGACUCCAAAGUCGGCGGCAACUACAAUUACCUGUACCGGCUGUUCCGGAAGUCCAAUCUGAAGCCCUUC
GAGCGGGACAUCUCCACCGAGAUCUAUCAGGCCGGCAGCACCCCUUGUAACGGCGUGGAAGGCUUCAAC
UGCUACUUCCCACUGCAGUCCUACGGCUUUCAGCCCACAAAUGGCGUGGGCUAUCAGCCCUACAGAGUG
GUGGUGCUGAGCUUCGAACUGCUGCAUGCCCCUGCCACAGUGUGCGGCCCUAAGAAAAGCACCAAUCUC
GUGAAGAACAAAUGCGUGAACUUCAACUUCAACGGCCUGACCGGCACCGGCGUGCUGACAGAGAGCAACA
AGAAGUUCCUGCCAUUCCAGCAGUUUGGCCGGGAUAUCGCCGAUACCACAGACGCCGUUAGAGAUCCCCA
GACACUGGAAAUCCUGGACAUCACCCCUUGCAGCUUCGGCGGAGUGUCUGUGAUCACCCCUGGCACCAAC
ACCAGCAAUCAGGUGGCAGUGCUGUACCAGGACGUGAACUGUACCGAAGUGCCCGUGGCCAUUCACGCC
GAUCAGCUGACACCUACAUGGCGGGUGUACUCCACCGGCAGCAAUGUGUUUCAGACCAGAGCCGGCUGU
CUGAUCGGAGCCGAGCACGUGAACAAUAGCUACGAGUGCGACAUCCCCAUCGGCGCUGGAAUCUGCGCCA
GCUACCAGACACAGACAAACAGCCCUCGGAGAGCCAGAAGCGUGGCCAGCCAGAGCAUCAUUGCCUACAC
AAUGUCUCUGGGCGCCGAGAACAGCGUGGCCUACUCCAACAACUCUAUCGCUAUCCCCACCAACUUCACC
AUCAGCGUGACCACAGAGAUCCUGCCUGUGUCCAUGACCAAGACCAGCGUGGACUGCACCAUGUACAUCU
GCGGCGAUUCCACCGAGUGCUCCAACCUGCUGCUGCAGUACGGCAGCUUCUGCACCCAGCUGAAUAGAGC
CCUGACAGGGAUCGCCGUGGAACAGGACAAGAACACCCAAGAGGUGUUCGCCCAAGUGAAGCAGAUCUAC
AAGACCCCUCCUAUCAAGGACUUCGGCGGCUUCAAUUUCAGCCAGAUUCUGCCCGAUCCUAGCAAGCCCA
GCAAGCGGAGCUUCAUCGAGGACCUGCUGUUCAACAAAGUGACACUGGCCGACGCCGGCUUCAUCAAGC
AGUAUGGCGAUUGUCUGGGCGACAUUGCCGCCAGGGAUCUGAUUUGCGCCCAGAAGUUUAACGGACUG
ACAGUGCUGCCUCCUCUGCUGACCGAUGAGAUGAUCGCCCAGUACACAUCUGCCCUGCUGGCCGGCACAA
UCACAAGCGGCUGGACAUUUGGAGCAGGCGCCGCUCUGCAGAUCCCCUUUGCUAUGCAGAUGGCCUACC
GGUUCAACGGCAUCGGAGUGACCCAGAAUGUGCUGUACGAGAACCAGAAGCUGAUCGCCAACCAGUUCA
ACAGCGCCAUCGGCAAGAUCCAGGACAGCCUGAGCAGCACAGCAAGCGCCCUGGGAAAGCUGCAGGACGU
GGUCAACCAGAAUGCCCAGGCACUGAACACCCUGGUCAAGCAGCUGUCCUCCAACUUCGGCGCCAUCAGC
UCUGUGCUGAACGAUAUCCUGAGCAGACUGGACCCUCCUGAGGCCGAGGUGCAGAUCGACAGACUGAUC
ACAGGCAGACUGCAGAGCCUCCAGACAUACGUGACCCAGCAGCUGAUCAGAGCCGCCGAGAUUAGAGCCU
CUGCCAAUCUGGCCGCCACCAAGAUGUCUGAGUGUGUGCUGGGCCAGAGCAAGAGAGUGGACUUUUGC
GGCAAGGGCUACCACCUGAUGAGCUUCCCUCAGUCUGCCCCUCACGGCGUGGUGUUUCUGCACGUGACA
UAUGUGCCCGCUCAAGAGAAGAAUUUCACCACCGCUCCAGCCAUCUGCCACGACGGCAAAGCCCACUUUC
CUAGAGAAGGCGUGUUCGUGUCCAACGGCACCCAUUGGUUCGUGACACAGCGGAACUUCUACGAGCCCC
AGAUCAUCACCACCGACAACACCUUCGUGUCUGGCAACUGCGACGUCGUGAUCGGCAUUGUGAACAAUAC
CGUGUACGACCCUCUGCAGCCCGAGCUGGACAGCUUCAAAGAGGAACUGGACAAGUACUUUAAGAACCAC
ACAAGCCCCGACGUGGACCUGGGCGAUAUCAGCGGAAUCAAUGCCAGCGUCGUGAACAUCCAGAAAGAGA
UCGACCGGCUGAACGAGGUGGCCAAGAAUCUGAACGAGAGCCUGAUCGACCUGCAAGAACUGGGGAAGU
ACGAGCAGUACAUCAAGUGGCCCUGGUACAUCUGGCUGGGCUUUAUCGCCGGACUGAUUGCCAUCGUGA
UGGUCACAAUCAUGCUGUGUUGCAUGACCAGCUGCUGUAGCUGCCUGAAGGGCUGUUGUAGCUGUGGC
AGCUGCUGCAAGUUCGACGAGGACGAUUCUGAGCCCGUGCUGAAGGGCGUGAAACUGCACUACACAUGA
UGA

and

[in relation to attacked embodiment 2b - [redacted]

AUGUUCGUGUUCCUGGUGCUGCUGCCUCUGGUGUCCAGCCAGUGUGUGAACCUGACCACCAGAACACAG
CUGCCUCCAGCCUACACCAACAGCUUUACCAGAGGCGUGUACUACCCCGACAAGGUGUUCAGAUCCAGCG
UGCUGCACUCUACCCAGGACCUGUUCCUGCCUUUCUUCAGCAACGUGACCUGGUUCCACGUGAUCUCCG
GCACCAAUGGCACCAAGAGAUUCGACAACCCCGUGCUGCCCUUCAACGACGGGGUGUACUUUGCCAGCAU
CGAGAAGUCCAACAUCAUCAGAGGCUGGAUCUUCGGCACCACACUGGACAGCAAGACCCAGAGCCUGCUG
AUCGUGAACAACGCCACCAACGUGGUCAUCAAAGUGUGCGAGUUCCAGUUCUGCAACGACCCCUUCCUGG
ACCACAAGAACAACAAGAGCUGGAUGGAAAGCGAGUUCCGGGUGUACAGCAGCGCCAACAACUGCACCUU
CGAGUACGUGUCCCAGCCUUUCCUGAUGGACCUGGAAGGCAAGCAGGGCAACUUCAAGAACCUGCGCGA
GUUCGUGUUUAAGAACAUCGACGGCUACUUCAAGAUCUACAGCAAGCACACCCCUAUCAUCGUGAGAGA
GCCCGAGGAUCUGCCUCAGGGCUUCUCUGCUCUGGAACCCCUGGUGGAUCUGCCCAUCGGCAUCAACAU
CACCCGGUUUCAGACACUGCUGGCCCUGCACAGAAGCUACCUGACACCUGGCGAUAGCAGCAGCGGAUGG
ACAGCUGGUGCCGCCGCUUACUAUGUGGGCUACCUGCAGCCUAGAACCUUCCUGCUGAAGUACAACGAG
AACGGCACCAUCACCGACGCCGUGGAUUGUGCUCUGGAUCCUCUGAGCGAGACAAAGUGCACCCUGAAG
UCCUUCACCGUGGAAAAGGGCAUCUACCAGACCAGCAACUUCCGGGUGCAGCCCACCGAAUCCAUCGUGC
GGUUCCCCAAUAUCACCAAUCUGUGCCCCUUCGACGAGGUGUUCAAUGCCACCAGAUUCGCCUCUGUGU
ACGCCUGGAACCGGAAGCGGAUCAGCAAUUGCGUGGCCGACUACUCCGUGCUGUACAACCUGGCCCCCUU
CUUCACCUUCAAGUGCUACGGCGUGUCCCCUACCAAGCUGAACGACCUGUGCUUCACAAACGUGUACGCC
GACAGCUUCGUGAUCCGGGGAGAUGAAGUGCGGCAGAUUGCCCCUGGACAGACAGGCAACAUCGCCGAC
UACAACUACAAGCUGCCCGACGACUUCACCGGCUGUGUGAUUGCCUGGAACAGCAACAAGCUGGACUCCA
AAGUCAGCGGCAACUACAAUUACCUGUACCGGCUGUUCCGGAAGUCCAAUCUGAAGCCCUUCGAGCGGG
ACAUCUCCACCGAGAUCUAUCAGGCCGGCAACAAGCCUUGUAACGGCGUGGCCGGCUUCAACUGCUACUU
CCCACUGCGGUCCUACAGCUUUAGGCCCACAUACGGCGUGGGCCACCAGCCCUACAGAGUGGUGGUGCU
GAGCUUCGAACUGCUGCAUGCCCCUGCCACAGUGUGCGGCCCUAAGAAAAGCACCAAUCUCGUGAAGAAC
AAAUGCGUGAACUUCAACUUCAACGGCCUGAAGGGCACCGGCGUGCUGACAGAGAGCAACAAGAAGUUC
CUGCCAUUCCAGCAGUUUGGCCGGGAUAUCGCCGAUACCACAGACGCCGUUAGAGAUCCCCAGACACUGG
AAAUCCUGGACAUCACCCCUUGCAGCUUCGGCGGAGUGUCUGUGAUCACCCCUGGCACCAACACCAGCAA
UCAGGUGGCAGUGCUGUACCAGGGCGUGAACUGUACCGAAGUGCCCGUGGCCAUUCACGCCGAUCAGCU
GACACCUACAUGGCGGGUGUACUCCACCGGCAGCAAUGUGUUUCAGACCAGAGCCGGCUGUCUGAUCGG
AGCCGAGUACGUGAACAAUAGCUACGAGUGCGACAUCCCCAUCGGCGCUGGAAUCUGCGCCAGCUACCAG
ACACAGACAAAGAGCCACCGGAGAGCCAGAAGCGUGGCCAGCCAGAGCAUCAUUGCCUACACAAUGUCUC
UGGGCGCCGAGAACAGCGUGGCCUACUCCAACAACUCUAUCGCUAUCCCCACCAACUUCACCAUCAGCGU
GACCACAGAGAUCCUGCCUGUGUCCAUGACCAAGACCAGCGUGGACUGCACCAUGUACAUCUGCGGCGAU
UCCACCGAGUGCUCCAACCUGCUGCUGCAGUACGGCAGCUUCUGCACCCAGCUGAAAAGAGCCCUGACAG
GGAUCGCCGUGGAACAGGACAAGAACACCCAAGAGGUGUUCGCCCAAGUGAAGCAGAUCUACAAGACCCC
UCCUAUCAAGUACUUCGGCGGCUUCAAUUUCAGCCAGAUUCUGCCCGAUCCUAGCAAGCCCAGCAAGCGG
AGCUUCAUCGAGGACCUGCUGUUCAACAAAGUGACACUGGCCGACGCCGGCUUCAUCAAGCAGUAUGGC
GAUUGUCUGGGCGACAUUGCCGCCAGGGAUCUGAUUUGCGCCCAGAAGUUUAAGGGACUGACAGUGCU
GCCUCCUCUGCUGACCGAUGAGAUGAUCGCCCAGUACACAUCUGCCCUGCUGGCCGGCACAAUCACAAGC
GGCUGGACAUUUGGAGCAGGCGCCGCUCUGCAGAUCCCCUUUGCUAUGCAGAUGGCCUACCGGUUCAAC
GGCAUCGGAGUGACCCAGAAUGUGCUGUACGAGAACCAGAAGCUGAUCGCCAACCAGUUCAACAGCGCCA
UCGGCAAGAUCCAGGACAGCCUGAGCAGCACAGCAAGCGCCCUGGGAAAGCUGCAGGACGUGGUCAACCA
CAAUGCCCAGGCACUGAACACCCUGGUCAAGCAGCUGUCCUCCAAGUUCGGCGCCAUCAGCUCUGUGCUG
AACGAUAUCUUCAGCAGACUGGACCCUCCUGAGGCCGAGGUGCAGAUCGACAGACUGAUCACAGGCAGAC
UGCAGAGCCUCCAGACAUACGUGACCCAGCAGCUGAUCAGAGCCGCCGAGAUUAGAGCCUCUGCCAAUCU
GGCCGCCACCAAGAUGUCUGAGUGUGUGCUGGGCCAGAGCAAGAGAGUGGACUUUUGCGGCAAGGGCU
ACCACCUGAUGAGCUUCCCUCAGUCUGCCCCUCACGGCGUGGUGUUUCUGCACGUGACAUAUGUGCCCG
CUCAAGAGAAGAAUUUCACCACCGCUCCAGCCAUCUGCCACGACGGCAAAGCCCACUUUCCUAGAGAAGG
CGUGUUCGUGUCCAACGGCACCCAUUGGUUCGUGACACAGCGGAACUUCUACGAGCCCCAGAUCAUCACC
ACCGACAACACCUUCGUGUCUGGCAACUGCGACGUCGUGAUCGGCAUUGUGAACAAUACCGUGUACGAC
CCUCUGCAGCCCGAGCUGGACAGCUUCAAAGAGGAACUGGACAAGUACUUUAAGAACCACACAAGCCCCG
ACGUGGACCUGGGCGAUAUCAGCGGAAUCAAUGCCAGCGUCGUGAACAUCCAGAAAGAGAUCGACCGGC

UGAACGAGGUGGCCAAGAAUCUGAACGAGAGCCUGAUCGACCUGCAAGAACUGGGGAAGUACGAGCAGU
ACAUCAAGUGGCCCUGGUACAUCUGGCUGGGCUUUAUCGCCGGACUGAUUGCCAUCGUGAUGGUCACAA
UCAUGCUGUGUUGCAUGACCAGCUGCUGUAGCUGCCUGAAGGGCUGUUGUAGCUGUGGCAGCUGCUGC
AAGUUCGACGAGGACGAUUCUGAGCCCGUGCUGAAGGGCGUGAAACUGCACUACACAUGAUGACUCGAG
CUGGUACUGCAUGCACGCAAUGCUAGCUGCCCCUUUCCCGUCCUGGGUACCCCGAGUCUCCCCCGACCUC
GGGUCCCAGGUAUGCUCCCACCUCCACCUGCCCCACUCACCACCUCUGCUAGUUCCAGACACCUCCCAAGC
ACGCAGCAAUGCAGCUCAAAACGCUUAGCCUAGCCACACCCCCACGGGAAACAGCAGUGAUUAACCUUUA
GCAAUAAACGAAAGUUUAACUAAGCUAUACUAACCCCAGGGUUGGUCAAUUUCGUGCCAGCCACACCCU
GGAGCUAGCAAA

and

[in relation to attacked embodiment 2c - Comirnaty Original/Omicron BA.4-5]

AUGUUCGUGUUCCUGGUGCUGCUGCCUCUGGUGUCCAGCCAGUGUGUGAACCUGAUCACCAGAACACAG
UCAUACACCAACAGCUUUACCAGAGGCGUGUACUACCCCGACAAGGUGUUCAGAUCCAGCGUGCUGCACU
CUACCCAGGACCUGUUCCUGCCUUUCUUCAGCAACGUGACCUGGUUCCACGCCAUCUCCGGCACCAAUGG
CACCAAGAGAUUCGACAACCCCGUGCUGCCCUUCAACGACGGGGUGUACUUUGCCAGCACCGAGAAGUCC
AACAUCAUCAGAGGCUGGAUCUUCGGCACCACACUGGACAGCAAGACCCAGAGCCUGCUGAUCGUGAACA
ACGCCACCAACGUGGUCAUCAAAGUGUGCGAGUUCCAGUUCUGCAACGACCCCUUCCUGGACGUCUACUA
CCACAAGAACAACAAGAGCUGGAUGGAAAGCGAGUUCCGGGUGUACAGCAGCGCCAACAACUGCACCUUC
GAGUACGUGUCCCAGCCUUUCCUGAUGGACCUGGAAGGCAAGCAGGGCAACUUCAAGAACCUGCGCGAG
UUCGUGUUUAAGAACAUCGACGGCUACUUCAAGAUCUACAGCAAGCACACCCCUAUCAACCUCGGCCGGG
AUCUGCCUCAGGGCUUCUCUGCUCUGGAACCCCUGGUGGAUCUGCCCAUCGGCAUCAACAUCACCCGGU
UUCAGACACUGCUGGCCCUGCACAGAAGCUACCUGACACCUGGCGAUAGCAGCAGCGGAUGGACAGCUG
GUGCCGCCGCUUACUAUGUGGGCUACCUGCAGCCUAGAACCUUCCUGCUGAAGUACAACGAGAACGGCA
CCAUCACCGACGCCGUGGAUUGUGCUCUGGAUCCUCUGAGCGAGACAAAGUGCACCCUGAAGUCCUUCA
CCGUGGAAAAGGGCAUCUACCAGACCAGCAACUUCCGGGUGCAGCCCACCGAAUCCAUCGUGCGGUUCCC
CAAUAUCACCAAUCUGUGCCCCUUCGACGAGGUGUUCAAUGCCACCAGAUUCGCCUCUGUGUACGCCUG
GAACCGGAAGCGGAUCAGCAAUUGCGUGGCCGACUACUCCGUGCUGUACAACUUCGCCCCCUUCUUCGCA
UUCAAGUGCUACGGCGUGUCCCCUACCAAGCUGAACGACCUGUGCUUCACAAACGUGUACGCCGACAGCU
UCGUGAUCCGGGGAAACGAAGUGCGGCAGAUUGCCCCUGGACAGACAGGCAACAUCGCCGACUACAACUA
CAAGCUGCCCGACGACUUCACCGGCUGUGUGAUUGCCUGGAACAGCAACAAGCUGGACUCCAAAGUCGGC
GGCAACUACAAUUACAGGUACCGGCUGUUCCGGAAGUCCAAUCUGAAGCCCUUCGAGCGGGACAUCUCC
ACCGAGAUCUAUCAGGCCGGCAACAAGCCUUGUAACGGCGUGGCAGGCGUGAACUGCUACUUCCCACUG
CAGUCCUACGGCUUUAGGCCCACAUACGGCGUGGGCCACCAGCCCUACAGAGUGGUGGUGCUGAGCUUC
GAACUGCUGCAUGCCCCUGCCACAGUGUGCGGCCCUAAGAAAAGCACCAAUCUCGUGAAGAACAAAUGCG
UGAACUUCAACUUCAACGGCCUGACCGGCACCGGCGUGCUGACAGAGAGCAACAAGAAGUUCCUGCCAUU
CCAGCAGUUUGGCCGGGAUAUCGCCGAUACCACAGACGCCGUUAGAGAUCCCCAGACACUGGAAAUCCUG
GACAUCACCCCUUGCAGCUUCGGCGGAGUGUCUGUGAUCACCCCUGGCACCAACACCAGCAAUCAGGUGG
CAGUGCUGUACCAGGGCGUGAACUGUACCGAAGUGCCCGUGGCCAUUCACGCCGAUCAGCUGACACCUAC
AUGGCGGGUGUACUCCACCGGCAGCAAUGUGUUUCAGACCAGAGCCGGCUGUCUGAUCGGAGCCGAGUA
CGUGAACAAUAGCUACGAGUGCGACAUCCCCAUCGGCGCUGGAAUCUGCGCCAGCUACCAGACACAGACA
AAGAGCCACCGGAGAGCCAGAAGCGUGGCCAGCCAGAGCAUCAUUGCCUACACAAUGUCUCUGGGCGCCG
AGAACAGCGUGGCCUACUCCAACAACUCUAUCGCUAUCCCCACCAACUUCACCAUCAGCGUGACCACAGAG
AUCCUGCCUGUGUCCAUGACCAAGACCAGCGUGGACUGCACCAUGUACAUCUGCGGCGAUUCCACCGAG
UGCUCCAACCUGCUGCUGCAGUACGGCAGCUUCUGCACCCAGCUGAAAAGAGCCCUGACAGGGAUCGCCG
UGGAACAGGACAAGAACACCCAAGAGGUGUUCGCCCAAGUGAAGCAGAUCUACAAGACCCCUCCUAUCAA
GUACUUCGGCGGCUUCAAUUUCAGCCAGAUUCUGCCCGAUCCUAGCAAGCCCAGCAAGCGGAGCUUCAU
CGAGGACCUGCUGUUCAACAAAGUGACACUGGCCGACGCCGGCUUCAUCAAGCAGUAUGGCGAUUGUCU
GGGCGACAUUGCCGCCAGGGAUCUGAUUUGCGCCCAGAAGUUUAACGGACUGACAGUGCUGCCUCCUCU
GCUGACCGAUGAGAUGAUCGCCCAGUACACAUCUGCCCUGCUGGCCGGCACAAUCACAAGCGGCUGGACA

UUUGGAGCAGGCGCCGCUCUGCAGAUCCCCUUUGCUAUGCAGAUGGCCUACCGGUUCAACGGCAUCGGA
GUGACCCAGAAUGUGCUGUACGAGAACCAGAAGCUGAUCGCCAACCAGUUCAACAGCGCCAUCGGCAAGA
UCCAGGACAGCCUGAGCAGCACAGCAAGCGCCCUGGGAAAGCUGCAGGACGUGGUCAACCACAAUGCCCA
GGCACUGAACACCCUGGUCAAGCAGCUGUCCUCCAAGUUCGGCGCCAUCAGCUCUGUGCUGAACGAUAU
CCUGAGCAGACUGGACCCUCCUGAGGCCGAGGUGCAGAUCGACAGACUGAUCACAGGCAGACUGCAGAGC
CUCCAGACAUACGUGACCCAGCAGCUGAUCAGAGCCGCCGAGAUUAGAGCCUCUGCCAAUCUGGCCGCCA
CCAAGAUGUCUGAGUGUGUGCUGGGCCAGAGCAAGAGAGUGGACUUUUGCGGCAAGGGCUACCACCUG
AUGAGCUUCCCUCAGUCUGCCCCUCACGGCGUGGUGUUUCUGCACGUGACAUAUGUGCCCGCUCAAGAG
AAGAAUUUCACCACCGCUCCAGCCAUCUGCCACGACGGCAAAGCCCACUUUCCUAGAGAAGGCGUGUUCG
UGUCCAACGGCACCCAUUGGUUCGUGACACAGCGGAACUUCUACGAGCCCCAGAUCAUCACCACCGACAA
CACCUUCGUGUCUGGCAACUGCGACGUCGUGAUCGGCAUUGUGAACAAUACCGUGUACGACCCUCUGCA
GCCCGAGCUGGACAGCUUCAAAGAGGAACUGGACAAGUACUUUAAGAACCACACAAGCCCCGACGUGGAC
CUGGGCGAUAUCAGCGGAAUCAAUGCCAGCGUCGUGAACAUCCAGAAAGAGAUCGACCGGCUGAACGAG
GUGGCCAAGAAUCUGAACGAGAGCCUGAUCGACCUGCAAGAACUGGGGAAGUACGAGCAGUACAUCAAG
UGGCCCUGGUACAUCUGGCUGGGCUUUAUCGCCGGACUGAUUGCCAUCGUGAUGGUCACAAUCAUGCU
GUGUUGCAUGACCAGCUGCUGUAGCUGCCUGAAGGGCUGUUGUAGCUGUGGCAGCUGCUGCAAGUUCG
ACGAGGACGAUUCUGAGCCCGUGCUGAAGGGCGUGAAACUGCACUACACAUGA

and

[in relation to attacked embodiment 2d - [redacted]

AUGUUCGUGUUCCUGGUGCUGCUGCCUCUGGUGUCCAGCCAGUGUGUGAACCUGAUCACCAGAACACAG
UCAUACACCAACAGCUUUACCAGAGGCGUGUACUACCCCGACAAGGUGUUCAGAUCCAGCGUGCUGCACU
CUACCCAGGACCUGUUCCUGCCUUUCUUCAGCAACGUGACCUGGUUCCACGCCAUCCACGUGUCCGGCAC
CAAUGGCACCAAGAGAUUCGACAACCCCGCCCUGCCCUUCAACGACGGGGUGUACUUUGCCAGCACCGAG
AAGUCCAACAUCAUCAGAGGCUGGAUCUUCGGCACCACACUGGACAGCAAGACCCAGAGCCUGCUGAUCG
UGAACAACGCCACCAACGUGGUCAUCAAAGUGUGCGAGUUCCAGUUCUGCAACGACCCCUUCCUGGACGU
CUACCAGAAGAACAACAAGAGCUGGAUGGAAAGCGAGUUCCGGGUGUACAGCAGCGCCAACAACUGCACC
UUCGAGUACGUGUCCCAGCCUUUCCUGAUGGACCUGGAAGGCAAGGAGGGCAACUUCAAGAACCUGCGC
GAGUUCGUGUUUAAGAACAUCGACGGCUACUUCAAGAUCUACAGCAAGCACACCCCUAUCAACCUCGAGC
GGGAUCUGCCUCAGGGCUUCUCUGCUCUGGAACCCCUGGUGGAUCUGCCCAUCGGCAUCAACAUCACCC
GGUUUCAGACACUGCUGGCCCUGCACAGAAGCUACCUGACACCUGUGGAUAGCAGCAGCGGAUGGACAG
CUGGUGCCGCCGCUUACUAUGUGGGCUACCUGCAGCCUAGAACCUUCCUGCUGAAGUACAACGAGAACG
GCACCAUCACCGACGCCGUGGAUUGUGCUCUGGAUCCUCUGAGCGAGACAAAGUGCACCCUGAAGUCCU
UCACCGUGGAAAAGGGCAUCUACCAGACCAGCAACUUCCGGGUGCAGCCCACCGAAUCCAUCGUGCGGUU
CCCCAAUAUCACCAAUCUGUGCCCCUUCCACGAGGUGUUCAAUGCCACCACCUUCGCCUCUGUGUACGCC
UGGAACCGGAAGCGGAUCAGCAAUUGCGUGGCCGACUACUCCGUGAUCUACAACUUCGCCCCCUUCUUC
GCAUUCAAGUGCUACGGCGUGUCCCCUACCAAGCUGAACGACCUGUGCUUCACAAACGUGUACGCCGACA
GCUUCGUGAUCCGGGGAAACGAAGUGUCACAGAUUGCCCCUGGACAGACAGGCAACAUCGCCGACUACAA
CUACAAGCUGCCCGACGACUUCACCGGCUGUGUGAUUGCCUGGAACAGCAACAAGCUGGACUCCAAACCC
AGCGGCAACUACAAUUACCUGUACCGGCUGUUCCGGAAGUCCAAGCUGAAGCCCUUCGAGCGGGACAUC
UCCACCGAGAUCUAUCAGGCCGGCAACAAGCCUUGUAACGGCGUGGCAGGCCCCAACUGCUACAGCCCAC
UGCAGUCCUACGGCUUUAGGCCCACAUACGGCGUGGGCCACCAGCCCUACAGAGUGGUGGUGCUGAGCU
UCGAACUGCUGCAUGCCCCUGCCACAGUGUGCGGCCCUAAGAAAAGCACCAAUCUCGUGAAGAACAAAUG
CGUGAACUUCAACUUCAACGGCCUGACCGGCACCGGCGUGCUGACAGAGAGCAACAAGAAGUUCCUGCCA
UUCCAGCAGUUUGGCCGGGAUAUCGCCGAUACCACAGACGCCGUUAGAGAUCCCCAGACACUGGAAAUCC
UGGACAUCACCCCUUGCAGCUUCGGCGGAGUGUCUGUGAUCACCCCUGGCACCAACACCAGCAAUCAGGU
GGCAGUGCUGUACCAGGGCGUGAACUGUACCGAAGUGCCCGUGGCCAUUCACGCCGAUCAGCUGACACC
UACAUGGCGGGUGUACUCCACCGGCAGCAAUGUGUUUCAGACCAGAGCCGGCUGUCUGAUCGGAGCCGA
GUACGUGAACAAUAGCUACGAGUGCGACAUCCCCAUCGGCGCUGGAAUCUGCGCCAGCUACCAGACACAG
ACAAAGAGCCACCGGAGAGCCAGAAGCGUGGCCAGCCAGAGCAUCAUUGCCUACACAAUGUCUCUGGGGC

CGAGAACAGCGUGGCCUACUCCAACAACUCUAUCGCUAUCCCCACCAACUUCACCAUCAGCGUGACCACAG
AGAUCCUGCCUGUGUCCAUGACCAAGACCAGCGUGGACUGCACCAUGUACAUCUGCGGCGAUUCCACCGA
GUGCUCCAACCUGCUGCUGCAGUACGGCAGCUUCUGCACCCAGCUGAAAAGAGCCCUGACAGGGAUCGCC
GUGGAACAGGACAAGAACACCCAAGAGGUGUUCGCCCAAGUGAAGCAGAUCUACAAGACCCCUCCUAUCA
AGUACUUCGGCGGCUUCAAUUUCAGCCAGAUUCUGCCCGAUCCUAGCAAGCCCAGCAAGCGGAGCUUCA
UCGAGGACCUGCUGUUCAACAAAGUGACACUGGCCGACGCCGGCUUCAUCAAGCAGUAUGGCGAUUGUC
UGGGCGACAUUGCCGCCAGGGAUCUGAUUUGCGCCCAGAAGUUUAACGGACUGACAGUGCUGCCUCCUC
UGCUGACCGAUGAGAUGAUCGCCCAGUACACAUCUGCCCUGCUGGCCGGCACAAUCACAAGCGGCUGGAC
AUUUGGAGCAGGCGCCGCUCUGCAGAUCCCCUUUGCUAUGCAGAUGGCCUACCGGUUCAACGGCAUCGG
AGUGACCCAGAAUGUGCUGUACGAGAACCAGAAGCUGAUCGCCAACCAGUUCAACAGCGCCAUCGGCAAG
AUCCAGGACAGCCUGAGCAGCACAGCAAGCGCCCUGGGAAAGCUGCAGGACGUGGUCAACCACAAUGCCC
AGGCACUGAACACCCUGGUCAAGCAGCUGUCCUCCAAGUUCGGCGCCAUCAGCUCUGUGCUGAACGAUA
UCCUGAGCAGACUGGACCCUCCUGAGGCCGAGGUGCAGAUCGACAGACUGAUCACAGGCAGACUGCAGA
GCCUCCAGACAUACGUGACCCAGCAGCUGAUCAGAGCCGCCGAGAUUAGAGCCUCUGCCAAUCUGGCCGC
CACCAAGAUGUCUGAGUGUGUGCUGGGCCAGAGCAAGAGAGUGGACUUUUGCGGCAAGGGCUACCACCU
GAUGAGCUUCCCUCAGUCUGCCCCUCACGGCGUGGUGUUUCUGCACGUGACAUAUGUGCCCGCUCAAGA
GAAGAAUUUCACCACCGCUCCAGCCAUCUGCCACGACGGCAAAGCCCACUUUCCUAGAGAAGGCGUGUUC
GUGUCCAACGGCACCCAUUGGUUCGUGACACAGCGGAACUUCUACGAGCCCCAGAUCAUCACCACCGACA
ACACCUUCGUGUCUGGCAACUGCGACGUCGUGAUCGGCAUUGUGAACAAUACCGUGUACGACCCUCUGC
AGCCCGAGCUGGACAGCUUCAAAGAGGAACUGGACAAGUACUUUAAGAACCACACAAGCCCCGACGUGGA
CCUGGGCGAUAUCAGCGGAAUCAAUGCCAGCGUCGUGAACAUCCAGAAAGAGAUCGACCGGCUGAACGA
GGUGGCCAAGAAUCUGAACGAGAGCCUGAUCGACCUGCAAGAACUGGGGAAGUACGAGCAGUACAUCAA
GUGGCCCUGGUACAUCUGGCUGGGCUUUAUCGCCGGACUGAUUGCCAUCGUGAUGGUCACAAUCAUGC
UGUGUUGCAUGACCAGCUGCUGUAGCUGCCUGAAGGGCUGUUGUAGCUGUGGCAGCUGCUGCAAGUUC
GACGAGGACGAUUCUGAGCCCGUGCUGAAGGGCGUGAAACUGCACUACACAUGAUGACUCGAGCUGGUA
CUGCAUGCACGCAAUGCUAGCUGCCCCUUUCCCGUCCUGGGUACCCCGAGUCUCCCCCGACCUCGGGUCC
CAGGUAUGCUCCCACCUCCACCUGCCCCACUCACCACCUCUGCUAGUUCCAGACACCUCCCAAGCACGCAG
CAAUGCAGCUCAAAACGCUUAGCCUAGCCACACCCCCACGGGAAACAGCAGUGAUUAACCUUUAGCAAUA
AACGAAAGUUUAACUAAGCUAUACUAACCCCAGGGUUGGUCAAUUUCGUGCCAGCCACACCCUGGAGCU
AGCAAAAAAAAAAAAAAAAAAAA

and

[in relation to attacked embodiment 2e -

AUGUUCGUGUUCCUGGUGCUGCUGCCUCUGGUGUCCAGCCAGUGUGUGAUGCCCCUGUUCAACCUGAU
CACCACCACACAGUCAUACACCAACAGCUUUACCAGAGGCGUGUACUACCCCGACAAGGUGUUCAGAUCC
AGCGUGCUGCACCUGACCCAGGACCUGUUCCUGCCUUUCUUCAGCAACGUGACCUGGUUCCACGCCAUCU
CCGGCACCAAUGGCACCAAGAGAUUCGACAACCCCGUGCUGCCCUUCAACGACGGGGUGUACUUUGCCAG
CACCGAGAAGUCCAACAUCAUCAGAGGCUGGAUCUUCGGCACCACACUGGACAGCAAGACCCAGAGCCUG
CUGAUCGUGAACAACGCCACCAACGUGUUCAUCAAAGUGUGCGAGUUCCAGUUCUGCAACGACCCCUUCC
UGGACGUCUACCACAAGAACAACAAGAGCUGGAUGGAAAGCGAGUCAGGCGUGUACAGCAGCGCCAACAA
CUGCACCUUCGAGUACGUGUCCCAGCCUUUCCUGAUGGACCUGGAAGGCAAGCAGGGCAACUUCAAGAA
CCUGCGCGAGUUCGUGUUUAAGAACAUCGACGGCUACUUCAAGAUCUACAGCAAGCACACCCCUAUCAUC
GGCCGGGAUUUCCCUCAGGGCUUCUCUGCUCUGGAACCCCUGGUGGAUCUGCCCAUCGGCAUCAACAUC
ACCCGGUUUCAGACACUGCUGGCCCUGAACAGAAGCUACCUGACACCUGGCGAUAGCAGCAGCGGAUGG
ACAGCUGGUGCCGCCGACUACUAUGUGGGCUACCUGCAGCCUAGAACCUUCCUGCUGAAGUACAACGAG
AACGGCACCAUCACCGACGCCGUGGAUUGUGCUCUGGAUCCUCUGAGCGAGACAAAGUGCACCCUGAAG
UCCUUCACCGUGGAAAAGGGCAUCUACCAGACCAGCAACUUCCGGGUGCAGCCCACCGAAUCCAUCGUGC
GGUUCCCCAAUGUGACCAAUCUGUGCCCCUUCCACGAGGUGUUCAAUGCCACCAGAUUCGCCUCUGUGU
ACGCCUGGAACCGGACCCGGAUCAGCAAUUGCGUGGCCGACUACUCCGUGCUGUACAACUUCGCCCCCUU
CUUCGCAUUCAAGUGCUACGGCGUGUCCCCUACCAAGCUGAACGACCUGUGCUUCACAAACGUGUACGCC

GACAGCUUCGUGAUCAAGGGAAACGAAGUGUCACAGAUUGCCCCUGGACAGACAGGCAACAUCGCCGAC
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