Unified Patent Court
Einheitliches Patentgericht
Juridiction unifiée du brevet

Local Division Munich
UPC_CFI_146/2024 - UPC_CFI_496/2024
UPC_CFI_147/2024 - UPC_CFI_374/2024
UPC_CFI_148/2024 - UPC_CFI_503/2024

Decision

of the Court of First Instance of the Unified Patent Court
Local Division Munich
issued on 12 December 2025
concerning European Patent 2 493 466

CLAIMANTS

1) Sanofi SA as successor of Sanofi Mature IP
2) Sanofi Winthrop Industrie
3) Sanofi Aventis France
4) Sanofi-Aventis GmbH
5) Sanofi Belgium
6) Sanofi-Aventis Deutschland GmbH
7) Sanofi S.r.l.
8) Sanofi B.V.
9) Sanofi - Produtos Farmaceuticos Lda
10) Sanofi AB
11) Sanofi A/S

represented by: Frédéric Chevallier (McDermott Will & Schulte).

DEFENDANTS – UPC_CFI_146/2024 - UPC_CFI_496/2024

1) STADAPHARM GmbH
2) STADA Arzneimittel AG
3) STADA Nordic ApS

represented by: Daniel Hoppe (Bonabry).

DEFENDANTS – UPC_CFI_147/2024 - UPC_CFI_374/2024

1) Reddy Pharma SAS
2) betapharm Arzneimittel GmbH
3) Dr Reddy's Srl

represented by: Dr. Christian Meyer (Maiwald Intellectual Property).

DEFENDANTS – UPC_CFI_148/2024 - UPC_CFI_503/2024

1) Zentiva France
2) Zentiva Pharma GmbH
3) Zentiva, k.s.

represented by: Dr. Anja Lunze (PENTARC Rechtsanwälte).

PATENT AT ISSUE

European patent n° 2 493 466

PANEL/DIVISION

Panel 1 of the Local Division Munich

DECIDING JUDGES

This decision has been issued by Presiding Judge Dr. Matthias Zigann acting as judge-rapporteur, the legally qualified judges Alima Zana and Tobias Pichlmaier and the technically qualified judge Carola Wagner.

LANGUAGE OF THE PROCEEDINGS

English.

SUBJECT-MATTER OF THE PROCEEDINGS

Patent infringement with counterclaims for revocation.

DATES OF THE ORAL HEARING

14 and 15 October 2025.

ANNOUNCEMENT DATE

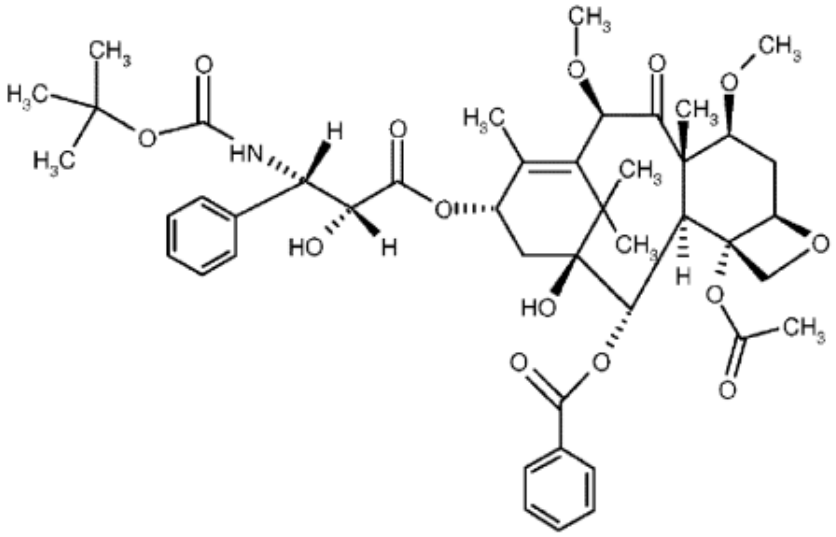
12 December 2025.

SUMMARY OF FACTS

Sanofi SA is the legal successor of Sanofi Mature IP and the registered proprietor of European Patent 2,493,466 (the 'patent at issue'). This patent relates to a novel anti-tumoral use of cabazitaxel and was filed on 27 October 2010, claiming seven priority dates, with the earliest being 29 October 2009 (US 256160 P). The publication and grant date is 10 March 2021. The patent is currently valid in several states, including Austria, Belgium, Germany, Denmark, France, Italy, the Netherlands, Portugal and Sweden.

The patent at issue comprises one independent and 8 dependant claims:

1. Compound of formula



which may be in base form or in the form of a hydrate or a solvate,
in combination with prednisone or prednisolone,
for use in treating prostate cancer,
in patients with castration resistant metastatic prostate cancer who have been previously treated with docetaxel based regimen and have prostate cancer that progressed during or after said treatment.

2. Compound for use according to claim 1, where the prostate cancer is an advanced metastatic disease.

3. Compound for use according to any one of claims 1 to 2, in the form of an acetone solvate.

4. Compound for use according to claim 3, in which the acetone solvate contains between 5% and 8% and preferably between 5% and 7% by weight of acetone.

5. Compound for use according to any one of claims 1 to 4, administered at a dose of between 15 and 25 mg/m^2, the prednisone or prednisolone being administered at a dose of 10 mg/day.

6. Compound for use according to claim 5, administered at a dose of 25 mg/m^2.

7. Compound for use according to any one of claims 1 to 6, comprising repeating the administration of such compound as a new cycle every 3 weeks.

8. Compound for use according to any one of claims 1 to 7, in combination with prednisone.

9. Compound for use according to any one of claims 1 to 8, wherein said patients have been previously treated with at least 225 mg/m^2 cumulative dose of docetaxel.

The claimants are entities belonging to the Sanofi Group, a French company that is one of the world's leading pharmaceutical companies.

Sanofi manufactures and sells the pharmaceutical product JEVTANA as a second-line treatment for prostate cancer patients.

JEVTANA was authorised by the European Medicines Agency (EMA) on 17 March 2011 under the name 'JEVTANA 60 mg concentrate and solvent for solution for infusion' (see Exhibits No. C1, page 5, and C.1.2, page 2, first paragraph). The medicinal product is marketed as a cabazitaxel concentrate in 1.5 ml vials containing 60 mg of cabazitaxel. Therefore, 1 ml of the concentrate contains 40 mg of cabazitaxel (see Exhibit C.1.2, second paragraph). The recommended cabazitaxel dose is 25 mg/m², administered via intravenous infusion every three weeks in combination with 10 mg of prednisone or prednisolone administered orally daily throughout treatment (Exhibit No. C.1.2, page 3, first paragraph).

The Stada, Dr. Reddy and Zentiva defendants are entities of pharmaceutical companies who produce and sell generic versions of JEVTANA, namely CABAZITAXEL STADA, CABAZITAXEL REDDY PHARMA, CABAZITAXEL BETA, and CABAZITAXEL DR. REDDY and CABAZITAXEL ZENTIVA, respectively:

STADAPHARMA GmbH and STADA Arzneimittel AG hold the marketing authorisation for the generic product Cabazitaxel STADA 20 mg/ml concentrate for solution for infusion. The authorisation applications were filed under decentralised procedures in Germany, Sweden and Denmark. Marketing authorisations were granted in Germany on 10 November 2020 and in Denmark on 9 March 2021 (see Exhibit No. D1.1, pages 1 and 3; D1.2, page 1). CABZITAXEL STADA contains the active substance cabazitaxel. It is sold as a 20 mg/ml concentrate for solution for infusion. The concentrate is supplied in a 3 ml vial containing 60 mg of cabazitaxel (see Exhibit No. D1.2, section 'Summary of Product Characteristics', pages 1–2, items 1 and 2).

Betapharm Arzneimittel GmbH is the marketing authorisation holder for the generic marketing authorisation filed under the decentralised procedure DE/H6219/001 (D.1.1 page 1, first entry), and the other Dr Reddy defendants are the marketing authorisation holders and local representatives respectively in France and Italy. Since the present action was launched, the defendants have ceased marketing the infringing product in France as of 31 December 2023. Sales have continued in Italy and Germany. All of these entities belong to the same group of companies headquartered in India as Dr Reddy's Laboratories Ltd. They market the medicinal products “Cabazitaxel beta 60 mg Konzentrat und Lösungsmittel zur Herstellung einer Infusionslösung” (DE), “CABAZITAXEL REDDY PHARMA 60 mg, solution for dilution and solvent for solution for

infusion" (FR), and "CABAZITAXEL DR. REDDY´S 40 mg/ml SOLUZIONE PER INFUSIONE ENDOVENOSA" (IT) (D.1.1–D.1.5, page 1, entry 'product name'). Marketing authorisations were granted in Germany on 20 July 2020, in France on 18 June 2020, and in Italy on 13 May 2021 (see Exhibits D1.1 to D1.5, page 1). Each product contains the active substance cabazitaxel. The products are sold as a 60 mg/ml concentrate for solution for infusion. The concentrate is in a 1.5 ml vial containing 60 mg of cabazitaxel (Exhibit No. D1.2 to D1.5, Section 'Summary of Product Characteristics', Page 1, Items 1 and 2).

Zentiva Pharma GmbH and Zentiva k.s. hold the marketing authorisations for the generic products filed under decentralised procedures DE/H/6784/001 and DK/H/3187/001, for Germany and France, among others (see D.1.1, page 1 and page 3, first entries). According to Zentiva, no products are sold in Italy or Denmark. Zentiva Pharma GmbH and Zentiva France market the medicinal products 'Cabazitaxel Zentiva 20 mg/ml concentrate for solution for infusion' (DE) and 'Cabazitaxel Zentiva solution for dilution for infusion' (FR) (D.1.1, page 1 , entry 'product name', D.1.4, page 1, entry 'product name'). Marketing authorisations were granted in Germany on 12 February 2021 and in France on 6 July 2021 (see Exhibits D1.3 and D1.4, page 1; and D4, page 2). According to D1.2, the marketing authorisation was granted for Germany on 9 February 2021 (D1.3, page 55, no. 9). Each product contains the active substance cabazitaxel. The products are sold as a 20 mg/ml concentrate for a solution for infusion. The concentrate is supplied in a 3 ml vial containing 60 mg of cabazitaxel (see Exhibits D1.3 and D1.4, page 2, section 2. Qualitative and quantitative composition). The infringing products in question were first placed on the market in 2021.

On 6 September 2024, the Tribunal Judiciaire de Paris invalidated the French designation of the patent in question in proceedings involving Sanofi and Accord. Sanofi appealed (RG No. 21/06416, Portalis No. 352J-W-B7F-CUMKO). The court held that the patent in question was obvious in light of documents describing a Phase III clinical trial with cabazitaxel. A skilled person at the priority date would have had a reasonable expectation of success. On 25 October 2025, Accord Healthcare and Sanofi submitted appeal briefs to the Paris Court of Appeal, requesting the reversal of the French first-instance decision of 6 September 2024, in accordance with the Confidential Patent Settlement and Licence Agreement executed by these entities.

On 15 December 2023, the Opposition Division of the European Patent Office rejected the oppositions filed against the patent in suit by Accord, Zentiva, Dr

Reddy, Stada and others. On 3 June 2025, the Boards of Appeal dismissed the appeals (T 0136/2024 – 3.3.04). Both the OD and the BoA held that the patent in question was not obvious based on documents describing a clinical Phase III trial with cabazitaxel. The skilled person at the priority date would not have had a reasonable expectation of success.

On 13 May 2024, several Sanofi entities filed infringement actions against several Accord entities (UPC_CFI_145/2024), as well as against Stada (UPC_CFI_146/2024), Dr. Reddy (UPC_CFI_147/2024) and Zentiva (UPC_CFI_148/2024) with the Local Division Munich. Each of the defendant groups filed counterclaims for revocation (Accord: UPC_CFI_463/2024; Stada: UPC_CFI_496/2024; Dr. Reddy: UPC_CFI_374/2024; Zentiva: UPC_CFI_503/2024).

Following the Confidential Patent Settlement and Licence Agreement executed between Sanofi and Accord, the infringement action (UPC_CFI_145/2024) and the revocation counterclaim (UPC_CFI_463/2024) were withdrawn prior to the oral hearing.

The Local Division of Munich decided to hear the remaining three counterclaims for revocation together, and the three infringement actions separately, following the joint hearing on validity. On the afternoon of the first day of the oral hearing, scheduled for 14–17 October 2025, the expert witnesses from Stada (Dr Denmeade), Dr Reddy's and Zentiva (Dr Nelson) were questioned on the following: 'What information would a person working in the industry at the priority date have derived from the Phase III TROPIC study and the time that has passed since it started? Was there a reasonable expectation of a positive outcome?' The panel asked the expert witnesses ten more detailed questions on this topic, which had been communicated in advance (see order dated 15 September 2025). Several ad hoc questions from the panel and the UPC representatives of the parties followed. Both experts confirmed their written expert reports: Dr Nelson (Exhibit B26 (Sanofi)), Dr Denmeade (Exhibits D54 and PBP1 (Stada), DFMP D116 (Zentiva) and MWCC 22 (Dr Reddy's)).

On the second day, the panel announced that they were inclined to declare the patent in question invalid. The presiding judge then closed the hearing, announcing 12 December 2025 as the date on which the decision would be announced.

The values of the infringement actions and the counterclaims were set by the judge-rapporteur in an order dated 22 January 2025.

In view of the outcome of the counterclaims, the Local Division Munich decided to issue a joint decision on the three infringement actions. Any confidential information forming part of the infringement proceedings has been omitted. Instead, reference is made to the respective briefs.

Further reference is made to the recordings of the oral hearing and the two interim conferences, as well as to the parties' submissions and the court's orders, respectively.

REQUESTS OF THE PARTIES

Counterclaims for revocation:

Stada, Dr Reddy's and Zentiva request the revocation of EP 2 493 466 B1 in its entirety (claims 1–9) in all Contracting Member States in which it is in force: Austria, Belgium, Germany, Denmark, France, Italy, the Netherlands, Portugal and Sweden. They also request that Sanofi bear the costs of the counterclaims for revocation.

Sanofi requests that the revocation counterclaim lodged by the defendants be dismissed, that European patent No. 2 493 466 be ruled valid in all UPC Contracting Member States in which the patent is in force, and that the defendants be ordered to bear the costs of the counterclaims for revocation.

Infringement actions:

Sanofi requests that it be declared that at least claims 1, 2, 5, 6, 7, 8 and 9 of European patent No. 2 493 466 have been directly infringed by the defendants (Stada in Denmark, Germany and Sweden; Dr. Reddy in France, Germany and Italy; and Zentiva in France and Germany), and that an injunction be ordered, as well as the payment of damages subject to further assessment, the publication on websites, the recall and removal of products from the channel of commerce, the destruction of products, the provision of information for the final calculation of damages, and the payment of the costs of the infringement proceedings.

The defendants request that the action be dismissed and that the claimants pay the costs of the proceedings.

At the request of the defendants, the judge rapporteur urged Sanofi to provide more detail on who is asking what from whom in which territory during the written procedure.

Sanofi subsequently filed amended requests to specify more clearly which claimant is asking for what, from whom, and in which territory. Some of the claimants no longer formally request any kind of relief. Furthermore, the request for damages has changed to one for provisional damages and a declaration of liability for damages. Additionally, a claim for indirect infringement has been introduced. Finally, a request for an interim award of costs has been introduced.

The parties are arguing about the admissibility of these amendments and their consequences.

Furthermore, the defendants filed preliminary objections. The judge-rapporteur informed the parties that these preliminary objections would be dealt with in the main proceedings (Rule 20.2 of the Rules of Procedure).

POINTS AT ISSUE

Preliminary objections:

Stada, Dr. Reddy and Zentiva argue that the Unified Patent Court lacked jurisdiction for countries which are not yet Contracting Member States to the Agreement on a Unified Patent Court (Ireland, Poland, Czech Republic, Slovakia, Hungary, Romania, Spain, Croatia, Greece and Cyprus). Further, they argued that the Unified Patent Court lacked jurisdiction over claims arising before the entry into force of the Agreement on a Unified Patent Court. Zentiva additionally argues that it is inadmissible to offer evidence in support of Claimants' standing to sue in French, a language other than the language of the proceedings (English).

Counterclaims for revocation:

In the respective counterclaims all defendants request that the patent in question be revoked. All three argue – already in the counterclaim - a lack of novelty and inventive step. Stada and Dr Reddy addition argue – already in the

counterclaim - added matter. Zentiva additionally argues – already in the counterclaim - a lack of sufficient disclosure (Art. 65(2) UPCA in connection with Art. 138(1)(b) and 83 EPC). Later amendments to the counterclaims do not play a role with view to the outcome of the decision. Reference is made to the respective briefs.

All three counterclaimants argue from the very beginning that the patent lacks an inventive step in relation to documents describing a Phase III clinical trial with cabazitaxel. They endorse the reasoning of the Tribunal Judiciaire de Paris in this regard. Based on the available information and the fact that the trial was shortly to conclude and had not been stopped prematurely, the counterclaimants argue that a skilled person at the priority date would have had a reasonable expectation of success.

Sanofi, who did not file a request to amend the patent, argues that the counterclaims for revocation should be dismissed. They claim that the Tribunal Judiciaire de Paris erred in revoking the French designation of the patent in question due to obviousness considering documents describing a clinical Phase III trial with cabazitaxel. Sanofi endorses the views of the Boards of Appeal, which upheld the patent despite those documents. In particular, Sanofi argues that a skilled person would not have had a reasonable expectation of success, but rather a mere hope that it could work.

Infringement actions:

The defendants argue that not all claimants have standing to sue, as the sub-conditions of Art. 47(2-3) UPCA have not been met.

According to Sanofi all claimants have standing to sue, because Articles 47(2) and (3) UPCA are not applicable when a patent proprietor brings an infringement action along with its own subsidiaries acting as licensees. The clause 5.1 of the licence agreement of 1st December 2018 was amended on 18th March 2025 in view that the “LICENCEE thus has the express right to institute, bring or join any infringement action instituted, brought or joined by LICENSOR as from the date on which the Agreement has been effective, in order to seek relief for the infringement of the Patents” (B1.1.b). Similarly, the sublicense agreement has been amended on 18th March 2025 (B1.1.2.b). The amendment is drawn up to retroactively establish the licensees’ rights to sue.

Defendants further argue that they do not directly infringe the patent in suit as their respective products do not contain prednisone or prednisolone. The later introduction of claims relating to indirect infringement is too late and should not be permitted.

In any case, the infringement actions must be dismissed as the patent is invalid.

GROUNDS FOR THE DECISION

The preliminary objections are dismissed. The patent in question is invalid and shall be revoked in its entirety. Therefore, the infringement actions shall be dismissed. Any other outstanding applications and requests relating to the infringement actions shall be dismissed, as there is no longer any need to adjudicate them.

A. Preliminary objections:

Sanofi has limited the infringement actions to the aforementioned territories. Therefore, preliminary objections relating to other territories can be dismissed (Rule 334 of the Rules of Procedure).

The same applies to the preliminary objections relating to the Unified Patent Court's competence to deal with infringing acts committed prior to the entry into force of the Agreement on a Unified Patent Court. However, it should be noted that the Unified Patent Court does have jurisdiction in this regard, as detailed in the Court of Appeal's decision on 2 June 2025 (UPC_CoA_156/2025, APL_8790/2025 – XSYS v. ESKO).

Finally, Zentiva's preliminary objection regarding the language of the evidence presented to support standing to sue is no longer relevant.

B. Counterclaims for revocation:

I. The Patent in suit EP 2 493 466

The patent describes the use of cabazitaxel in the treatment of prostate cancer, and in particular, castration resistant metastatic prostate cancer in patients who have already received docetaxel treatment, which it states is a previously unmet need.

Prostate cancer affects a large proportion of the male population worldwide. It is treated at the start by depriving the androgenic hormones, through excision of the testicles, or by radiotherapy treatment, while chemotherapy, despite its effect on the relief of symptoms, is not a routine treatment, due to its toxicity, especially in elderly patients, and until recently had only mediocre effects. In particular, mitoxantrone, in combination with prednisone or hydrocortisone, was used with palliative effects. More recently, treatments with docetaxel, part of the taxane family, in combination with estramustine or prednisone have increased patient survival by 2.4 months.

However, it points out that cancer can become resistant to medicines and in particular to taxanes, as several resistance mechanisms have been described, such as the expression of P-glycoprotein (or P-gp), the mdr-1 gene, the modification of the metabolism of taxane and the mutation of the tubulin gene.

The patent states that responses to treatments in this cancer are difficult to evaluate due to the heterogeneity of the disease and the lack of consensus regarding the treatment response criteria, but specifies that the level of prostate-specific antigen (PSA) has proven to be a means for evaluating novel candidates, with measurement of tumour and bone metastases (where possible), quality of life and pain.

In order to provide the missing treatment to the patients concerned, the invention discloses the use of cabazitaxel, a taxane, in combination with prednisone or prednisolone.

It indicates that one aspect of the invention includes increasing patient survival, describes the methods of administration, consideration, and prevention of the risk of various adverse effects, and contraindications to the administration of cabazitaxel, then describes, through several examples, the results of a clinical trial, otherwise known as the ‘Tropic study’, which concerned 755 patients and the purpose of which was to compare cabazitaxel (with prednisone) with mitoxantrone (with prednisone).

These results indicate in particular that the median overall survival of patients receiving cabazitaxel was improved by 2.4 months compared to patients receiving mitoxantrone (15.1 months versus 12.7 months).

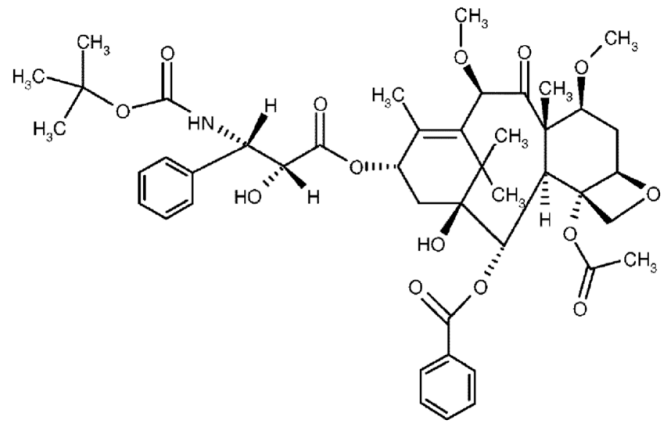
The patent states that this prolongation of survival had been observed even in the third of patients not responding to docetaxel, in whom the disease had progressed during docetaxel treatment.

It also mentions the other criteria cited above, such as the PSA response rate, the tumour response rate, the pain response rate, as well as the duration without progression of the tumour, without progression of the PSA and without progression of the pain, all of which are favourable for cabazitaxel (Table 1).

The technical problem that the patent in suit intends to solve, is therefore to provide a therapeutic option for treating patients suffering of castration resistant metastatic prostate cancer who have been previously treated with docetaxel-based regimen and have prostate cancer that progressed during or after that treatment (EP 466 [0008]). This includes both, increased overall survival and palliative treatment only.

The proposed solution introduces an antitumoral pharmaceutical therapeutic use comprising cabazitaxel according to claim 1 (feature breakdown):

A1 Compound of formula



which may be in base form or in the form of a hydrate or a solvate,

A2 in combination with prednisone or prednisolone,

B for use in treating prostate cancer,

B1 in patients with castration resistant metastatic prostate cancer

B2 who have been previously treated with docetaxel-based regimen and

B3 have prostate cancer that progressed during or after said treatment.

The patent in suit contains further eight dependent claims (claims 2 to 9):

2. Compound for use according to claim 1, where the prostate cancer is an advanced metastatic disease.

3. Compound for use according to any one of claims 1 to 2, in the form of an acetone solvate.

4. Compound for use according to claim 3, in which the acetone solvate contains between 5% and 8% and preferably between 5% and 7% by weight of acetone.

5. Compound for use according to any one of claims 1 to 4, administered at a dose of between 15 and 25 mg/m², with prednisone or prednisolone administered at a dose of 10 mg/day.

6. Compound for use according to claim 5, administered at a dose of 25 mg/m².

7. Compound for use according to any one of claims 1 to 6, comprising repeating the administration of such compound as a new cycle every 3 weeks.

8. Compound for use according to any one of claims 1 to 7, in combination with prednisone.

9. Compound for use according to any one of claims 1 to 8, wherein said patients have been previously treated with at least 225 mg/m² cumulative dose of docetaxel.

2. On Interpretation

According to Art. 69 EPC in conjunction with the Protocol on its interpretation, the patent claim is not only the starting point but also the decisive basis for determining the scope of protection of a European patent. The interpretation of a patent claim does not depend solely on its literal wording. Rather, the description and the drawings must always be consulted as aid to the interpretation of the claim and not only to clarify any ambiguities in the claim.

This does not mean, however, that the patent claim only serves as a guideline and that its subject matter also extends to what is presented as the applicant's claim after examination of the description and drawings (UPC_CoA_335/2023, decision of 26 February 2023 in conjunction with decision of 11 March 2024, GRUR-RS 2024, 2829, headnote 2 and margin no. 73 - 77 - Nachweisverfahren; UPC_CFI_452/2023 (LD Düsseldorf), Order of 9 April 2024, p. 13, GRUR-RS 2024, 7207, margin no. 49).

a) Claim 1 as granted is directed to a further medical use and has been drafted as a purpose-limited product claim in the format according to Article 54(5) EPC. In accordance with the established practice, for claims directed to a further medical use, attaining the claimed therapeutic effect is regarded as a functional technical feature of the claim (see e.g. T 609/02, Reasons 9). While the pertinent comments in T 609/02 relate to claims drafted in the so-called Swiss-type format established by the Enlarged Board in G 5/83, they apply equally to claims drafted in the newer format according to Article 54(5) EPC).

In the present case, this therapeutic effect is the treatment of prostate cancer in the specified patient group. Claim 1 as granted specifies in this regard "for use in treating prostate cancer, in patients with castration resistant metastatic prostate cancer who have been previously treated with docetaxel-based regimen and have prostate cancer that progressed during or after said treatment."

b) Feature A1

The compound cabazitaxel belongs to the taxoid family and has the formula indicated in feature A1. The chemical name of cabazitaxel is 4α-acetoxy-2α-benzoyl oxy-5β, 20-epoxy-1β-hydroxy-7β,10β-dimethoxy-9-oxo-11-taxen-13α-yl(2R,3S)-3-*tert*-butoxycarbonylamino-2-hydroxy-3-phenylpropionate.
Cabazitaxel is synonymously known as (2α, 5β, 7β, 10β, 13α)- 4-acetoxy- 13-({(2R, 3S)- 3-[(*tert*-butoxycarbonyl)amino]-2-hydroxy-3-phenylpropanoyl}oxy)-1-hydroxy-7,10-dimethoxy-9-oxo-5, 20-epoxytax-11-en-2-yl benzoate (EP 466 para [0023]). It is also known by its study name XRP6258 (RPR 116258A) (EP 466 para [0010]).
Cabazitaxel may be in form of an anhydrous base (cf. formula above), a hydrate or a solvate, in particular an acetone solvate (EP 466, claim 3, para. [0014], [0024]).

c) Feature A2

According to feature A2 cabazitaxel is administered in combination with prednisone or prednisolone. As to claim 8 and paragraph [0026] prednisone and prednisolone are alternative corticoids. In the dependent claim 8 the combination is restricted to cabazitaxel and prednisone. Thus, feature A2 is not directed to a triple combination of cabazitaxel with both prednisone and prednisolone.

As per the description of EP 466 cabazitaxel and the corticoid are administered as two distinct pharmaceutical preparations (EP 466 para. [0026]). The combination is administered repeatedly according to a protocol that depends on the patient to be treated. Cabazitaxel is administered by perfusion to the patient according to an intermittent program with an interval between each administration of 3 weeks. Prednisone or prednisolone may be administered daily, for example in the form of one dosage intake per day, throughout the duration of the treatment. According to claim 5 cabazitaxel is administered at a dose of between 15 to 25 mg/m^2 and prednisone or prednisolone being administered at a dose of 10 mg/day. The recommended dose of 25 mg/m^2 for cabazitaxel is administered as one-hour infusion, while prednisone or prednisolone is administered orally in a dose of 10 mg per day (EP 466 claim 5 to 7, para. [0027]).

c) Feature group B

aa) The treatment according to feature B must be understood as a non-curative therapy, because metastatic castration resistant prostate cancer is an incurable condition. A therapeutic effect according to the patent is the absence of progression or death when the progression is either an increase of the PSA, or of the tumour, or of the pain (EP 466, para. [0074]). Therefore, the treatment is a life extending therapy, delaying tumour recurrence and progression, or a palliative therapy focused on maintaining the quality of life (EP 466, para [0017]; B0.7.1, para 35, 87).

bb) According to features B1 to B3 the patients to be treated are men who suffer from castration resistant metastatic prostate cancer who have been previously treated with docetaxel-based regimen and who have prostate cancer that progressed during or after said treatment (EP 466 claim 1, para. [0013]).

Cancer which has spread beyond the prostate is called metastatic. At the start prostate cancer is treated with hormone-based therapy to lower or block the hormones that promote prostate cancer growth. Typically, the hormonal therapy is surgical or medical castration to drastically reduce the levels of testosterone. When the patient's cancer worsens despite castrate levels of testosterone, the cancer is referred to as castration resistant prostate cancer (CRPC) or hormone-refractory prostate cancer (EP 466 para. [0003], [0021], third bullet point; Dr. [redacted] B0.7.1, para 32 to 34). Metastatic prostate cancer which has progressed to castration resistant prostate cancer, is commonly referred to as "mCRPC" (Dr. [redacted] B.07.1, page 10, para 0035).

According to features B2 und B3 the prostate cancer of these patients has progressed during or after a previous docetaxel treatment. These features therefore include both patients who responded to a docetaxel therapy but progressed afterwards and patients who developed resistance to docetaxel (EP 466 para. [0028]; expert witness statements).

3. On inventive step of Claim 1

The following documents will be discussed:

D-Number	Catchword	Full data	Sanofi exhibit number
D1	TROPIC 2009	Tropic 2009, idem, ibidem, as at 11 September 2009	B.17
D2	NHSC 2009	NHSC, Cabazitaxel (XRP-6258) for hormone refractory, metastatic prostate cancer - second line after docetaxel, National Horizon Scanning Centre, April 2009	B.20
D4	[redacted]	[redacted] 'Phase I and Pharmacokinetic Study of XRP6258 (RPR 116258A), a Novel Taxane, Administered as a 1-Hour Infusion Every 3 Weeks in Patients with Advanced Solid Tumours, Clinical Cancer Research, 15(2), 723-730, 15 January 2009	B.18
D6	TROPIC 2008	Tropic 2008, XRP6258 Plus Prednisone Compared to Mitoxantrone Plus Prednisone in Hormone Refractory Metastatic Prostate Cancer (Tropic), taken from the website ClinicalTrials.gov, saved at archive.org, on 23 October 2008	B.17.1
D7	[redacted]	[redacted] and [redacted] Systemic therapy after first-line	B.6

		docetaxel in metastatic castration – resistant prostate cancer, Current Opinion in Supportive and Palliative Care, 2:161-166, 2008	
D9	[redacted]	[redacted] and others, Paclitaxel And Docetaxel Resistance: Molecular Mechanisms and Development of New Generation Taxanes, ChemMedChem, 2007, 2, 920-242, 2007	B.13
D12	Dr. [redacted]	Declaration by Dr. [redacted] of 23 December 2020	B.7.6
D13	Pivot	X. Pivot, and others, A multicenter phase II study of XRP6258 administered as a 1-h i.v. infusion every 3 weeks in taxane-resistant metastatic breast cancer patients, Annals of Oncology 19: 1547-1552, [redacted]	B.19
D18	Guideline on the Evaluation of Anti-Cancer Medicinal Products in Man	EMA Guidelines on the Evaluation of Anticancer Medicinal Products in Man (June 2006)	B.33
D20	Annual Report 2008	Sanofi 2008 (Annual Report), Accord Exhibit No. 5.12	B.22.2
D21	EMA Assessment Report for Jevtana (cabazitaxel), January 20, 2011	EMA/CHMP/66633/2011 Assessment Report for Jevtana (cabazitaxel), procedure no.: EMEA/H/C/002018, footnote on 2-66: EMA/CHMP/782336/2010	- (Stada D21; Zentiva DFMP D21)
D26	[redacted]	[redacted] and others, Update on tubulin-binding agents, Pathology Biology, 54:72-8 4, 2006	B12
D35	Leaflet	Leaflet "XRP6258 and XRP9881 Novel Taxoids" by Aventis Pharmaceuticals Inc., 2003	B.37
D58	[redacted]	Declaration by [redacted] (23 April 2022)	B.25
D59	[redacted]	[redacted] and [redacted] New drugs in prostate cancer, Current Opinion in Urology, 6:138-145, 2006	B.9
D91	[redacted]	[redacted] et al. 2000	B.36
-	[redacted]	Expert report of Dr. [redacted] of 22 December 2016	B.07.1
-	[redacted]	[redacted] and [redacted] Can the pharmaceutical industry reduce attrition rates?, Nature Reviews Drug Discovery, Vol. 3, p. 711, August 2004	B.14
-	[redacted] and [redacted]	[redacted] and [redacted] Estimation of clinical trial success rates and related parameters, Biostatistics, 20, 2, pp. 273-286, 2019	B.16

a. The defendants‘ position

The defendants maintain that, according to settled case-law in France, Germany and at the European Patent Office, the disclosure of phase III clinical trials relating to the claimed application gives rise to a reasonable expectation of success for the person skilled in the art, unless there is evidence to the contrary since these trials, which constitute routine tests for the person skilled in the art, are selected on the basis of experimental data suggesting their success, and that this is particularly true when they are supported by previous studies.

In this particular case, in order to demonstrate the obvious use of cabazitaxel to treat castration-resistant metastatic prostate cancer which progressed during or after a previous treatment with docetaxel, they argue that the disclosure of the Tropic study (Tropic documents or NHSC), a Phase III clinical trial specifically relating to that therapeutic application, corroborated by various pre-clinical and clinical data, created a reasonable expectation in the person skilled in the art that that application would be successful.

They consider that the closest prior art document is the NHSC document, in that it discloses, in addition to the protocol of the Tropic study, the existence of promising results and the dosage of 25 mg/m² every 3 weeks claimed in the patent, whereas the Tropic documents do not disclose the existence of a technical effect or this dosage; that the objective technical problem is the provision of alternative treatment for castration-resistant metastatic prostate cancer in patients previously treated with a docetaxel-based regime and whose cancer has progressed during or after such treatment. They state that this problem should not be limited to improving overall survival but includes several other criteria that were also evaluated in the Tropic study (progression-free survival, percentage of objective or biological responses, progression of PSA level, progression of pain and so on), adding that in practice, it is not possible to confine oneself to survival because one cannot wait for the patient's death to evaluate the treatment given to him. In any case, they believe, even if limited to overall survival, the technical problem is an improvement that only needs to be compared with patients treated with mitoxantrone, because this is the only comparative effect that the study (and the patent that includes the results) demonstrates.

According to them, the person skilled in the art is a team of scientists composed in particular of a pharmacologist with experience in the treatment of cancer by means of taxanes, a person with experience in the regulation of oncological

medicinal products and the approval of clinical studies by the regulatory authorities.

In this context, they claim that pre-clinical data showed that cabazitaxel was effective on taxane-resistant cancer cell lines, in particular docetaxel, and indicated that it had a lower affinity than docetaxel with the P-glycoprotein efflux pump or P-gp, which is responsible for docetaxel resistance [redacted] documents); whereas a Phase I study of different types of cancer, including castration-resistant metastatic prostate cancer, showed a promising safety profile of cabazitaxel and an effectiveness in PSA levels in two patients with this cancer (Mita document); lastly, a Phase II study, conducted on breast cancer and not prostate cancer, showed an encouraging response to cabazitaxel in patients previously treated with docetaxel and having developed resistance to this molecule (Pivot, Beardsley documents). The difference in cancer at issue is not decisive, in their view, because they are tumours with common properties, for which the same molecule, docetaxel, is an approved standard treatment, a molecule which, moreover, had itself initially been studied for the prostate cancer because it had been shown to be effective on the breast cancer, and the lesson from this trial is also the promising activity of cabazitaxel against a tumour which has become resistant to docetaxel, as in the indication which is the subject of the patent.

They add that the prior art also suggested further treatment with docetaxel itself, despite the resistance acquired by the tumour, after an interruption of a few months, in patients who initially responded well to the first-line treatment (Beardsley document), which is also confirmed by a subsequent opinion of the French National Authority for Health (after the priority date). They conclude that cabazitaxel, which is of the same taxane class but has less affinity with one of the resistance factors to docetaxel, was even more likely to be effective. They point out in that regard that the Tropic study concerned only patients with an 'ECOG PS' of 0 to 2 (NHSC document), that is to say, patients who were either asymptomatic, completely ambulatory or bedridden for less than half a day, and therefore patients in a good situation, which implies, they consider, that they have tolerated the first docetaxel treatment, and therefore that further treatment with docetaxel could be envisaged for them.

They also rely on Sanofi's financial report for 2008 (Sanofi 2008 document), in which the company states that it has refocused its research efforts on the 'most promising projects' and that, as a result, while research on cabazitaxel in breast cancer, which is the subject of the abovementioned Phase II study, has been

abandoned, the development of cabazitaxel continues. They infer from this that the person skilled in the art was aware of the significant potential of cabazitaxel in the treatment of metastatic prostate cancer and that this development was maintained in the light of intermediate results showing that the chances of success were great.

As regards the toxicity of cabazitaxel, the defendants state that the abovementioned phase I and II tests showed relatively encouraging toxicity data, taking into account the fact that the serious adverse effects encountered (in particular neutropenia) were known and considered acceptable, the patent itself indicating a high toxicity which did not prevent the approval of the medicinal product, so that these data would not have deterred the person skilled in the art.

They consider that the chances of success of the Tropic trial were all the greater because its ambition was low, comparing cabazitaxel with mitoxantrone, which is known to be ineffective while being toxic (and which itself had never been authorised for second-line treatment as in this particular case), to the extent that no clinical trial comparing mitoxantrone with another molecule had ever shown greater efficacy of that molecule, whereas the Tropic trial, representing a very high cost, probably greater than 100 million dollars, had, by definition, required prior convergent analyses in order to justify it, and having been in progress for 3 years at the priority date, without having been interrupted (which would have been the case if the patients were put in danger), finally close to its originally announced end date, gave in itself reasonable expectation of success as regards its object, without any element of the prior art contradicting this expectation. In this respect, they also dispute the relevance of the statistics invoked by the Sanofi companies on the failure rate of the phase III trials, due to the parameters specific to each study and argue that the same statistics show a success rate of more than 50% when the study relates to the main indication of the medicinal product, as in this particular case.

Lastly, they argue that the decisions of the United States are irrelevant because the claims of the patent have been substantially modified in comparison with those of this patent.

In the alternative, the defendants rely on what is known as a ‘test to see’ approach, according to which, when the implementation or testing of an approach suggested by the prior art does not present any particular technical

difficulty, the person skilled in the art would have been required to test it, even if there was no reasonable prospect of success.

b. Sanofi`s position

In response, Sanofi argues that the effect of the disclosure of a Phase III clinical trial on the inventive step must be analysed according to the specifics of each case, that the European Patent Office's decision T0239/16 opens the possibility that the prior art deters the person skilled in the art, that the previous decisions which rejected the inventive step because of the disclosure of a clinical trial concerned very different situations, in particular dosage patents. They point out that drug patents are often revoked on the grounds that they are filed too early, before possession of the invention (in the case of finasteride, raloxifene), and that this would have been the case here before the results of the Tropic trial were obtained. They rely on the decisions of the Opposition Division of the European Patent Office in the patent at issue and of the US courts in the parent patent (whose claims differ little according to them) which had concluded that the patent was valid.

They explain that the closest prior art consists of the Tropic 2009 document, because it is more recent than the NHSC document, which is moreover speculative and removes the person skilled in the art from the invention by confirming the unsatisfied need for the treatment which is the subject of the invention. According to them, this Tropic document differs from the invention in that it is merely a description of a clinical trial which does not disclose any effect of the treatment, whereas the invention consists in providing a treatment which prolongs the life of patients, constituting the first effective second-line treatment in the indication in question. They infer from this that the objective technical problem is to increase the survival of the patient concerned, and not only to provide an alternative treatment, which would only be the case if the invention did not provide a therapeutic advantage (and in particular, here, a prolongation of survival). Nor, in their view, is it a question of confirming effective treatment in the broad sense, but of overall survival alone, which is the reference for evaluating new treatments, and moreover the condition without which the treatment would not have been authorised.

The person skilled in the art is, according to Sanofi, a team comprising a medical oncologist with clinical experience in the treatment of castration-resistant metastatic prostate cancer and chemical and biochemical researchers working in the field of research and development of such treatments, and therefore

familiar with the mechanisms of action of the taxanes and of resistance to this agent.

In this context, they argue that castration-resistant metastatic prostate cancer is a disease that is particularly difficult to treat, especially in the second line after the reference treatment with docetaxel, which is heterogeneous (results vary greatly between patients), and with treatment that is difficult to measure (the measurement of overall survival involves controlled trials with a large number of patients), for which finally, more than 200 candidate medicines [redacted] document) have proved to be failures, only cabazitaxel having finally proved to be effective; cabazitaxel is still the only successful new taxane, out of 9 molecules studied [redacted] document), including larotaxel, which has been the subject of three phase III trials (including one on breast cancer), all of which were failures. They point out that, more generally, the success rate of candidate medicines in oncology is 3.4% (and only 1.6% when, as here, they are not associated with biomarkers, as indicated in the 2019 [redacted] document), that this is 70% in phase II and still 59% in phase III [redacted] document), that is to say, 12.3% when combining phases II and III; this makes the pre-clinical data even less relevant, especially for metastatic prostate cancer, for which there is no relevant preclinical model.

They claim, in particular that the other parameters, in particular the PSA level, are unreliable, as they may be influenced by causes other than the course of the disease, in addition to the fact that the PSA response in itself has no benefit for the patient; whereas resistance to taxanes involves several mechanisms and not only affinity with P-gp, so that efficacy could not be expected on that basis alone; that the response rate (of only 14%) obtained in phase II in another indication (breast cancer) is also not predictive of a future outcome and in any event not relevant for prostate cancer.

They explain that the indication subject of the patent had been directly tested in a Phase III clinical trial, without a Phase II trial, which is rare but justified here, they continue, because of the ‘compelling need’ for treatment to extend the life of patients who previously died of their disease (they do not claim, however, that the patent treatment cures patients but only show a median survival of 2.4 months longer than the mitoxantrone treatment), and was made possible by the acceptable toxicity of cabazitaxel, studied in the Phase I trial which was only intended to do so (not the evaluation of effectiveness), so the expectation of success of the Tropic trial was ‘dreadful’ and a reluctance to launch the study had been encountered.

Against the [redacted] document, they claim that this involves old data (2001 trial), already criticised [redacted] document), showing an effect on a single patient concerned by the indication in question (patient already treated with docetaxel), measured only by the PSA level (moreover in a single measurement) without any effect being inferred on his lifetime, and after administration of a dose of 25 mg/m², to which the other patients have shown serious adverse effects, in particular neutropenia, to the extent that the document subsequently recommends a dose of only 20 mg/m², from which the person skilled in the art would have deduced that the dose likely to be effective might well be too high to be tolerable, with potentially counterproductive effects (myelosuppression which may limit the extent of tumour destruction). For example, the [redacted] document argues that it is unlikely that the new taxanes, including cabazitaxel, will 'have a significant impact on patients' or that 'major improvements to currently approved drugs will be achieved.'

They add that these toxicity data, which gave rise to the fear of failure at the dose covered by the patent (25 mg/m²), could not be attenuated by the lesson learnt from the Phase II trial on breast cancer (the Pivot document) since patients with two different cancers may react differently, especially here, since they are women in one case and men in the other, since men with prostate cancer often undergo radiation therapy on the pelvis which weakens a significant part of the bone marrow where blood cells are produced, which would have led to the fear of greater sensitivity to cabazitaxel toxicity, and that in any case, the same doubts result (only 28% of the patients were able to increase the dose up to 25 mg/m²).

Against the [redacted] document, Sanofi companies argue that it only refers to the Phase II trial described in the Pivot document and the Tropic trial by offering an explanation for the initiation of this trial (the activity of cabazitaxel in the docetaxel refractory framework) without allowing a positive outcome to be predicted. Against the NHSC document, they argue that this is not a scientific publication but a prospective and speculative document from a public health centre, that the person skilled in the art did not consult it and did not attach importance to it, and that it merely describes the objective of the Tropic trial by indicating the speculative aspect of the situation and confirming that the lifetime is the objective of the treatment. The Sanofi 2008 document does not create any expectation of success, according to them, despite the heading 'the most promising projects', in that it indicates that the development of larotaxel has been stopped for breast cancer and that the Tropic trial is continuing while

cabazitaxel has also been stopped for breast cancer. Moreover, they consider that what this document reveals is only the opinion of the inventor, which is not the opinion of the person skilled in the art.

As for the 'test to see' approach, the Sanofi companies, who consider this approach inapplicable here, argue that its underlying idea is to test whether a potential solution would work with routine testing when the reasonable expectation of success test cannot be applied; whereas the Boards of Appeal of the European Patent Office have already considered that tests on humans were not known routine tests; that exceptions are only allowed on a case-by-case basis, e.g., for tests concerning the maximum duration of application of a device already in use with known properties (T 293/07).

c. Findings of the Court

The panel finds that the invention of the patent in suit is obvious over the Phase III TROPIC trial (NHSC) document. All other invalidity attacks therefore do not need to be considered.

aa. Test on inventive step

Among the conditions for patentability referred to in Article 138(1)(a) EPC, Articles 52 and 56 require that an invention must involve an inventive step, that is to say, if, having regard to the state of the art, it is not obvious to a person skilled in the art. The elements of the prior art are destructive of an inventive step only if, taken in isolation or placed together in a combination reasonably accessible to the person skilled in the art, they clearly enabled the latter to provide the same solution to the problem solved by the invention as the latter.

In order to assess inventive step, the European Patent Office and some national courts usually proceed according to what is known as the problem-solution approach, which consists in determining the closest prior art, establishing, by comparison with the claimed invention, the objective technical problem to be solved, and then considering whether the solution proposed by the invention to this problem would have been obvious to the person skilled in the art. In particular, the Office defines the objective technical problem as 'the aim and task of modifying or adapting the closest prior art to provide the technical effects that the invention provides over the closest prior art' (EPO Guidelines for Examination, G, VII, 5.2).

The Court of Appeal of the Unified Patent Court has in its decision dated 25 November 2025 (UPC_CoA_528-2024, 529/2024 – Amgen v. Sanofi-Aventis): applied the following test to determine inventive step of a second medical use claim:

> "123. 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).
>
> 124. National courts of the various EPC countries have different approaches and use different guidelines when assessing whether an invention involves an inventive step. One of those approaches is the so-called 'problem-solution-approach' used by the European Patent Office (EPO) and the Technical Boards of Appeal (TBA) of the EPO. In some jurisdictions, such as France, Italy, The Netherlands and Sweden, this approach is applied as well, but not necessarily as the only possible approach. In other jurisdictions, such as Germany and the UK, other approaches – sometimes referred to as more 'holistic' – are used. Despite the differences in approach, all of these are just guidelines to assist in the establishment of inventive step as required by Art. 56 EPC, that, when properly applied, should and generally do lead to the same conclusion. 21
>
> 125. The burden and presentation of proof with regard to the facts from which the lack of validity of the patent is derived and other circumstances favourable to the invalidity or revocation lies with the claimant in a revocation action (Art. 54 and 65(1) UPCA, R. 44(e)-(g), 25.1(b)-(d) RoP). Even though proof of certain facts, if contested, may be required, the assessment of whether the legal consequence for which the facts and circumstances have been submitted is justified, is a question of law.
>
> 126. The approach taken by the Unified Patent Court when establishing inventive step, which can already be derived from the Order of the Court of Appeal in Nanostring/10X Genomics (supra), is as follows.
>
> 127. 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 (m/f – hereinafter referred to as 'it'), with its 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 application understands is (are) achieved with the claimed invention.

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

129. 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.

130. 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.

131. 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.

132. 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.

133. 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.

134. 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.

135. 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.

136. 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.

137. When the patentee brings forward and sufficiently substantiates uncertainties and / or practical or technical difficulties, the burden of proof that these would not prevent a skilled person from having a reasonable expectation of success, falls on the party alleging obviousness.

138. The fact that other persons or teams were working contemporaneously on the same project does not necessarily imply that there was a reasonable expectation of success. It may also indicate that it was an interesting area to explore with a mere hope to succeed."

The second decision from the same date (UPC_CoA_464/2024, 457/2024, 458/2024, 530/2024, 532/2024, 533/2024, 21/2025, 27/2025 – Meril v. Edwards) applies the same test on inventive step.

Both decisions were delivered after the oral hearing had closed. The approach adopted by the Court of Appeal is similar to that taken by the Tribunal Judiciaire de Paris when deciding the revocation action against the French part of the patent in suit. The parties presented extensive arguments. These included arguments both for and against this approach. Neither the oral hearing nor the hearing of the two experts focused on a specific legal test to be applied. In fact, the legal test to be applied was also discussed at the oral hearing. Therefore, this panel holds that it is not necessary to reopen the oral hearing. The case can be decided on the basis of the arguments and facts provided to date.

Therefore, the test set out by the Court of Appeal will be used.

bb. Skilled person

The person skilled in the art is the person in the technical field in which there emerges the problem which the invention, which is the subject of the patent, is intended to solve. In this particular case, while the parties define this differently, they do not explicitly draw any conclusion from it on the inventive step.

Since the patent concerns a medicinal product for treating a castration-resistant metastatic prostate cancer after first-line treatment with docetaxel, which is a taxane, the person skilled in the art is a team comprising an oncologist who is familiar with the treatment of this type of cancer, and a chemist plus a pharmacologist, who are familiar with pharmacokinetic and the formulation of chemotherapeutic drugs including taxanes.

cc. Objective technical problem

Adopting the problem-solution approach, the EPO BoA in T 0136/24-3.3.04 defined the technical problem in face of the NHSC document in “to put into practice the effective treatment of prostate cancer with cabazitaxel in co-administration with prednisone in patients with mCRPC who have previously been treated with a docetaxel-based regimen and who have prostate cancer that progressed during or after that treatment” (EPO BoA paragraph 7.8).

This deviates from the approach formulated by the Court of Appeal as the formulation of the objective technical problem contains parts of the solution and thus does not avoid hindsight.

The objective technical problem to be solved by the invention is therefore to provide a therapeutic option for treating patients suffering of castration resistant metastatic prostate cancer who have been previously treated with docetaxel-based regimen and have prostate cancer that progressed during or after that treatment. This includes both, increased overall survival and palliative treatment only.

dd. NHSC (D2) as starting point

D2 discloses the protocol of the clinical phase III trial with Cabazitaxel (XRP-6258) in combination with prednisone (features A1 and A2) for hormone refractory, metastatic prostate cancer, a second line treatment after a docetaxel treatment (features B, B1, B2 and B3) (D2, page 2, title, first to third and fifth para., page 3, table, sixth entry, page 4, second para.). D2, like the Tropic 2009 document (D1) proposed by the Sanofi, therefore discloses all features of claim 1, but feature group B), comprising features B-B3, is only disclosed in the form of a hypothesis that is currently being verified.

(1) Background information

By way of background information, the party experts, Dr Nelson and Dr Denmeade, have unanimously testified that new pharmaceuticals are generally discovered and approved through pre-clinical and clinical trials. Clinical trials have three phases. In the pre-clinical phase, a molecule is tested in vitro for activity related to the disease to be cured. Clinical Phase I involves testing on a relatively small number of healthy volunteers to obtain information on dosage and tolerance. Clinical Phase II is dedicated to obtaining information on symptoms from tests with a small number of patients. Phase III involves testing the new drug on a larger number of patients to determine its performance compared to a placebo or standard treatment.

However, in the field of oncology, Dr Nelson and Dr Denmeade both agreed that all phases are conducted with patients who have the disease under investigation, as the drugs to be tested are essentially poisonous and it would be unethical to administer them to healthy volunteers. Further phase I is basically dedicated to initially understand whether and to what extend the drug shows some anti-tumour activity in humans and which dose is safe and tolerated. In phase II the focus lies in further defining the anti-tumoral activity with the dose tested in phase I. In phase III the anti-tumoral drug is tested against the standard of care.

Both experts explained that to get a phase III trial started an expert review of the data on safety, toxicity management, dosing schedule and anti-tumoral activity derived from phases I and II must be passed. To this end an expectation that the trial will meet the defined endpoint, or in other words, will be successful, must be established. Further a monitoring plan and a statistical plan must be developed and approved.

According to Dr Denmeade, in oncology, it is not mandatory for a phase III trial to receive DSMB (Data Safety Monitoring Board) approval based on patients with the same tumour type as in phase II. Information on the safety, toxicity and management of the drug derived from a phase II trial involving patients with a different tumour can be transferred if the tumours are comparable. This happens in about 1/3 of the oncological phase III trials. Nowadays, it is even possible to skip phase II completely. Dr Nelson agreed, but pointed out that such an approach carries more risks, and that the tumours discussed (breast and prostate cancer) are, in his view, not comparable, which renders the results of the phase II trial irrelevant to the approval of the phase III trial. He explained that, in his view, younger women tolerate taxanes better than older men.

The DSMB will closely monitor the data on toxicity, chances of success, evidence of superiority compared to the control arm and data integrity. The results of these activities will be reported to the sponsor. A phase III trial will not be stopped but will continue in the absence of relevant negative or positive triggers. A negative trigger might be higher toxicity than previously anticipated. A positive trigger might be clear superiority of the tested drug over the control arm, in which case it would be unethical to withhold the superior treatment from patients in the control arm. An early intervention is an unusual event.

Both experts explained that the failure rate of phase III trial in general is between 40 to 50 percent. Dr. Denmeade additionally pointed out that the percentage goes down with the progress of the trial. Dr. Nelson did not object.

Dr Denmeade explained that the combination of mitoxantrone and prednisone is the standard comparator used in phase III oncology trials, as this is the standard treatment available. However, as this standard treatment has no anti-tumoral effect, but only a palliative effect, any promising anti-tumoral drug will show a 100 percent success rate. Dr Nelson added that the same drug might fail with other comparators.

Cabazitaxel (XRP-6258) is a taxane anti-neoplastic agent. It works by disrupting the microtubular network that is essential for mitotic and interphase cellular functions and causes inhibition of cell division and cell death. Cabazitaxel in combination with prednisone is intended to provide a further treatment option for patients with progressive disease following or during docetaxel-based treatment (feature B3). Cabazitaxel is administered by intravenous (IV) infusion at 25 mg/m^2 every 3 weeks (D2 page 2, second para.).

(2) Details of the disclosure of D2

At the publication date of D2, April 2009, the TROPIC study was still ongoing (D2 page 3, table, line 3). The expected reporting date (ending) of the study was May 2010 (D2, page 3, table, last entry). D2 mentions also, that cabazitaxel has shown a promising safety profile and activity in patients progressing after docetaxel therapy (D2 page 1, third para.). This is in accordance with the Guideline on the Evaluation of Anti-Cancer Medicinal Products in Men (D18), which demands that a clinical phase III trial must be based on results that had been obtained in earlier studies, which prove the anti-tumour efficacy and safety of the active ingredient (D18, page 16, para. 3). These earlier studies are documented in D9-Galetti 2007, D4-Mita 2009, D13-Pivot 2008 and D7-Beardsley.

However, D2, like the Tropic 2009 document (D1) proposed by the Sanofi, only discloses feature group B), comprising features B-B3, in the form of a hypothesis that is currently being verified.

D6 is an earlier publication (14.11.2008) of the TROPIC trial than D2. The information in D6 is the same as in D2.

The Tropic trial (D2) is thus not novelty destroying but constitutes a relevant starting point for the thought processes of the person skilled in the art and obviousness can be assessed with regard to it.

(3) Reasonable expectation of success based on the disclosure of D2

The invention is obvious if the hypothesis on which it is based — which is fully disclosed by the TROPIC trial — was followed by the person skilled in the art, checking this, if necessary, by routine operations, with a reasonable expectation of success.

However, it is important to note that the question of reasonable expectation of success of the approach disclosed in the TROPIC trial documents, in terms of assessing an inventive step, is not the same as the question of whether the TROPIC trial will meet its primary endpoint. This is because the technical problem that the patent in suit intends to solve is to provide a therapeutic option for treating patients with castration-resistant metastatic prostate cancer who have previously been treated with a docetaxel-based regimen and whose cancer has progressed during or after that treatment. This includes both increased overall survival and palliative treatment. The primary endpoint of the TROPIC trial, however, is defined as overall survival in patients in the cabazitaxel group compared to the control group.

The Panel notes that the EPO BoA adopted a similar approach in paragraph 7.10, stating that the invention would be obvious if the person skilled in the art had had a reasonable expectation of success with regard to the experimental arm of the TROPIC trial.

(4) Positive and negative pointers as indicators

Thus, faced with the disclosure of a therapeutic avenue which has been considered sufficiently promising to initiate a phase III clinical trial (the Tropic trial), the person skilled in the art is encouraged to seek in the prior art what is likely to support or refute this hypothesis.

In the words of the Technical Board 3.3.04 positive and negative pointers must be evaluated and weighed against each other.

In more neutral terms, this panel must evaluate various indicators in the prior art and provide an overall assessment.

ee. Indicators

(1) [redacted] (D7)

The [redacted] (D7) document is meant to review ongoing developments in the search for a treatment for castration-resistant prostate cancer that has progressed after docetaxel-based first-line chemotherapy. This is the therapeutic indication for the Tropic trial and the patent.

Beardsley talks about several options, including cabazitaxel. She says that this has been tested in a trial on patients with metastatic breast cancer who don't respond to docetaxel. The trial found that 14 percent of patients had a positive response (p.163, right column, fourth para.). She says that cabazitaxel could be tested in a Phase III trial for prostate cancer (the Tropic phase III trial) without first being tested in a Phase II trial for this type of cancer because of how well it worked in a trial for breast cancer that did not respond to docetaxel:

“A phase II trial with XRP6258 has not been performed in patients with CRPC; however, given its activity in the docetaxel refractory setting described above, this agent in currently being investigated on a phase III multi-center, randomized superiority trial comparing 3-weekly XRP6258 with prednisone to mitoxantrone with prednisone in patients with castrate resistant metastatic prostate cancer previously treated with docetaxel-containing treatment." (p.163, right column, fifth para.)

It is important to remember that the survival of a patient depends on the type of cancer and how far the disease has spread. Because of this, the skilled person generally must have more information before he can use the results of a phase II clinical study on breast cancer to predict how it might work with prostate cancer. But this document makes it clear how the treatments of these two illnesses (breast cancer and prostate cancer) are connected, which would have been hard to predict otherwise: “given its activity in the docetaxel refractory setting described above". The document explains that, in both types of cancer, the problem of resistance to taxanes in general, and to docetaxel in particular, can be overcome by administering cabazitaxel along with prednisone.

In this context, the fact that cabazitaxel is in the same class as docetaxel — which would generally dissuade the skilled person from expecting an alternative treatment for patients who have progressed during or after docetaxel treatment — and the fact that both experts testified that the mechanism of resistance to a particular taxane in humans is still to be fully understood and requires further research, are not particularly relevant, as this document suggests otherwise.

This is supported by the fact that the skilled person will appreciate that cabazitaxel was specifically developed to treat tumour diseases such as prostate cancer, and to overcome docetaxel resistance in these treatments (D4, page 727, left column, paragraph 2; page 729, right column, paragraph 2; D9, page 922, right column, paragraph 1; page 933, right column, final paragraph; page 938, left column, paragraph 1; D26, page 75, left column, paragraph 2, table 3).

Further its efficacy in cases of docetaxel resistance has already been described in Pivot (D13, page 1551, left column, paragraph 3).

(2) Pivot (D13)

In 2008, the pivot (D13) study revealed favourable outcomes for cabazitaxel in patients with taxane-resistant metastatic breast cancer. Cabazitaxel was described as active and tolerable in selected patients at doses of up to 25 mg/m². Despite neutropenia being an adverse effect, Pivot concluded that the results supported further clinical trials (D13, page 1547, title and abstract). The two experts explained that, given cabazitaxel's similar chemical structure to docetaxel, it was expected to have some anti-tumour activity, but also to be more toxic to the bone marrow. Given the positive conclusion in the Pivot document, this side effect would not have prevented the skilled person from continuing the trials.

The Pivot (D13) document also explains that the breast cancer patients in this Phase II trial had all previously been treated with a taxane, with most having received docetaxel (65 per cent received docetaxel alone and 10 per cent received more than one taxane), as specified in the patent. Although breast cancer is a different type of cancer, and the patient groups differ in terms of sex and age, as Dr Nelson testified, this study sheds light on an interesting property of cabazitaxel with regard to the problem addressed by the patent (the treatment of patients who are resistant to a first taxane, namely docetaxel). While the results of this study are limited, they are also encouraging. According to the Pivot document, the results justified the continuation of the clinical development of this agent and demonstrated activity even when the strictest resistance criterion was used.

(3) [redacted] (D9)

[redacted] (D9) shows as does Pivot (D13) that this potential property is supported metabolically by the lower affinity of cabazitaxel to the P-glycoprotein (or P-gp), which is a known cause of tumour resistance to taxanes, as well as by preclinical studies showing a cytotoxic effect of cabazitaxel on cell lines having acquired resistance, in particular, to docetaxel.

Sanofi's assertion that resistance to taxanes involves several factors confirms that this approach is uncertain by definition and that the mechanisms involved are complex.

(4) [redacted] (D4)

The [redacted] (D4) document refers to a Phase I study on cabazitaxel, conducted in 25 patients with different tumours, eight of which were prostate cancer, two of whom showed a more than half reduction in the prostate specific antigen (PSA), or PSA-50, as well as a decrease in the size of measurable tumours and, for one of them, a reduction in pain. One of these two patients had previously been treated with docetaxel:

"An 80-year-old male with prostate cancer metastatic to liver and bones whose disease had progressed through surgical castration, bicalutamide, diethyl stilbestrol, and mitoxantrone and prednisone experienced a reduction in prostate-specific antigen from 62 to 21 ng/mL, decreased disease-related bone pain, and reduction in his target lesion, a lymph node metastasis, which qualified as confirmed partial response after four courses at the 15 mg/m2 dose level. The patient declined further treatment after his sixth course, at which time his response persisted. A 50-year-old male with hormone- and docetaxel-refractory prostate cancer metastatic to bone and iliac lymph nodes also experienced a partial response after treatment with XRP6258 at the 25 mg/m2 dose level of XRP6258. His prostate-specific antigen decreased from 415 to 44 ng/mL, and his measurable disease showed a confirmed partial response. Progressive disease was noted after eight courses (D4, page 727 left col. second para.)."

Further Cabazitaxel is characterised by convenient administration with less premedication, linear PKs, and a favourable safety profile for hematologic toxicity and hypersensitivity reaction. Cabazitaxel is described in D4 as promising candidate for the treatment of patients with taxane resistance (D4 page 729, right col., last para.).

Further D4 indicated that 82 percent of patients treated with 25 mg/m^2 cabazitaxel experienced as side effect grade 3 or 4 neutropenia. [redacted] describes the duration of severe neutropenia as typically brief and rarely associated with fever, which means to skilled person that it is manageable (D4 page 728 left col., second para., first sentence).

This document concludes that there is encouraging antitumor activity in patients resistant to taxanes and considers that cabazitaxel is recommended for Phase II.

The person skilled in the art will appreciate that in vitro testing with prostate cancer cells (D4 Page 724, left col., second para.; D26 page 74, right col., last para. to page 75 first para, Table 3, first entry), but not with docetaxel-resistant cancer cells, had been completed as the phase I study started. Further cabazitaxel was tested on cell lines with docetaxel resistance (D91). An overview is provided in D35.

Despite the limitations of this data from the preclinical phase the Phase I study demonstrated a response to treatment with docetaxel alone. This finding suggests the efficacy of docetaxel in treating this specific tumour type in patients who had been previously treated with docetaxel. Whilst this assertion is indeed accurate, it should be noted that the nature of the data did not permit any observations to be made with regard to a potential increase in overall survival. This question was left for further trials.

Doubts that cabazitaxel will work in every case of docetaxel-resistance, e.g., in cases where the resistance is not caused by P-gp-upregulation, like a docetaxel-resistance based on tubulin-alterations, are overcome by the positive results of the phase I and II clinical studies.

As laid out in D4 cabazitaxel is characterised by convenient administration with less premedication, linear PKs and a favourable safety profile for hepatologic toxicity and hypersensitivity reaction. It is a weak P-gp substrate in preclinical models (D4 page 729, right col).

Sanofi argues that the skilled clinician would not have viewed the partial response in this single patient in [redacted] as sufficient to reasonably expect that cabazitaxel would provide an improved treatment to patients having progressed during or after the treatment with docetaxel. This might be true, if there was no phase III trial. However, in the present case the phase III trial TROPIC was almost complete, without interruption or discontinuation. This implied for the skilled person that this was effective in the treatment of patients with mCRPC previously treated with docetaxel.

In contrary to Sanofis' view it is not unusual in the field of oncology that a clinical phase III trial is based on a phase I trial including patients having different types of cancer besides the cancer type selected for the phase III trial and a phase II

trial concerning a different type cancer as such of the phase III trial (e.g. “Larotaxol”, B07.1 para. 59-64).

In conclusion, there was no evidence against cabazitaxel’s efficacy in the treatment of mCRPC as a second-line treatment after a docetaxel regimen has been discontinued.

(5) Elements considered collectively

When considered collectively, these elements substantiate the chances of success of cabazitaxel in cases of docetaxel-resistant prostate cancer, as envisaged by the launch of the TROPIC trial. Even more so, this is true of the prospect of success of the patented treatment for patients who have previously been treated with docetaxel, but that treatment was discontinued. As mentioned above, the patient group referred to in the patent claim is not limited to patients who have developed a resistance to docetaxel or do not respond to docetaxel. The patient group is simply defined as those who have previously received a docetaxel treatment. As Dr Denmeade explained, it is not uncommon for patients receiving a docetaxel-based treatment to stop treatment temporarily, referred to as “treatment holiday”, and then resume it.

When discussing whether the skilled person in the view of the indicators at hand would have taken the claimed steps to solve the objective technical problem the probability of success needs to be balanced against the therapeutic options available for this patient group at the priority date. In this regard it must be noted that no accepted standard systemic treatment existed for those patients (D7, page 161, Abstract, Summary, D12 page 5, sect. 26-27). In many cases only a palliative treatment was possible (D12, page 2, sect. 16). Since cabazitaxel was determined to be safe and tolerable (results of the phase I and II studies on prostate cancer and breast cancer), the risks of verifying the actual efficacy of cabazitaxel were rather low, but the possible results were extremely valuable.

The observation that one of the two patients in the Phase I study exhibited a response to treatment with docetaxel alone suggests the efficacy of docetaxel in treating this particular tumour type. This finding is a valuable lesson in itself. The efficacy of the treatment in combating docetaxel resistance is indicated by two main factors. Firstly, the results observed in the other patient enrolled in the Phase I study are indicative of the treatment's effectiveness. Secondly, the combination of all the data discussed above provides further evidence for the treatment's efficacy.

It has been asserted that, in the case under consideration, the conventional pathway of drug development, which encompasses a phase I study, followed by a phase II study to evaluate dosage and efficacy, and subsequently a "confirmatory" phase III study in a substantial population to substantiate the efficacy (see D18), is only inadequately reflected. No phase II study in mCRPC was carried out. The phase II study in breast cancer (see D13) was not followed by a phase III study in breast cancer, as this line of development was discontinued (see D20). Consequently, the TROPIC study on prostate cancer cannot be regarded as a standard confirmatory study, as earlier data are lacking and only a single patient in the population to be treated had been reported in phase I (see D4). However, it is imperative to emphasise that the evaluation of each case must be conducted with a meticulous consideration for its unique set of circumstances. Automatic inference is not possible in this case. As outlined above, the absence of a phase II trial for prostate cancer in the conduct of a phase III clinical trial on prostate cancer does not preclude the successful development of a new drug or drug application, despite deviating from the conventional approach. As testified by both experts this happens in about a third of all oncological phase III studies. Anecdotally, D21, which was published after the priority date, reveals that Sanofi relied on the breast cancer Phase II trial to support its application to have the Phase III prostate cancer trial approved (see D21, p. 27, 30, 33-34,52 and 60).

(6) PSA level as indicator

Admittedly, indirect indicators such as the PSA level are not in themselves evidence of an effect on the patient's survival time; however, as the patent itself states both in its introduction and in the data it discloses to support its therapeutic effect, this PSA level, as well as the measurement of tumour, pain and the duration without progression of the disease, were accepted criteria as indicators of the potential effectiveness of the treatment, which includes the prospect of prolongation of survival. It is therefore irrelevant whether or not the patent is limited to survival alone (certainly its therapeutic effect, in fact, is not limited to survival alone) because, as the judges in interim proceedings have pointed out, these different indicators are indissociable and it is not possible artificially to isolate different aspects of the therapeutic effect. Otherwise formulated, the technical effect of the invention is a favourable response of the disease with a prolongation of survival (which is an inseparable whole) but this effect could reasonably be expected on the basis of the usual criteria such as the

PSA rate notwithstanding their imperfection. Again, reasonable expectation of success is not the certainty or even the near certainty of success.

As a result, for the person skilled in the art, the encouraging results of cabazitaxel on prostate cancer on the one hand, and on resistance to docetaxel on the other hand, could give him expectation of a favourable effect on survival, even though these results related only to indicators other than survival alone.

(7) Dosage

More specifically, as regards the dose likely to have a favourable effect, the Tropic trial was carried out at a dose of 25 mg/m² (although the patent covers a range of 15 to 25), whereas the [redacted] document deduces from the Phase I test that the recommended dose for the Phase II tests should be only 20 mg/m², whereas the patient resistant to docetaxel on which cabazitaxel had an effect in the Phase I test had received a dose greater than 25 mg/m², which the Sanofi companies infer from the fact that the Tropic trial would have been considered doomed to failure due to the risk of excessive toxicity.

In D26 [redacted] the adverse effect of myelosuppression was only mentioned in relation to maximum tolerated dose up to 30 mg/m2, which would be limited to some extend by this side effect (D26 page 75, right col. first para.). Due to the safety results of the Pivot study (D13) this side effect was not a major concern, when the regulatory authorities approved the clinical trial TROPIC with 25 mg/m^2.

However, the [redacted] document more generally found that the toxicity data for cabazitaxel were encouraging compared to other taxanes, while the Pivot document showed that the Phase II breast cancer study increased the dose to 25 mg/m² in 28 percent of patients. Therefore, the person skilled in the art, noting that the dose of 25 mg/m² was approved for the conduct of a phase III trial involving 750 patients, would not have seen it as an indication of probable failure but as a rational choice of experimentation. Moreover, the patent itself does not provide any surprising information on the toxicity of cabazitaxel in the indication at issue, which remains high, concerns a large number of patients and requires special consideration, which it describes. This is therefore a foreseeable disadvantage consistent with the reasonable expectation of the person skilled in the art in the light of the protocol of the Tropic trial.

(8) [redacted] (D26)

As for the opinion expressed by the [redacted] (D26) document and relied on by Sanofi, according to which it was unlikely that taxanes would have a ‘major impact on the fate of the patients’, it must be noted that this is not called into question by the patent, the moderate effect of which on the increase in overall survival cannot reasonably be described as a ‘major’ impact on the ‘fate’ of the patients. The fact that the person skilled in the art would not have expected such an impact is therefore irrelevant.

(9) Study was nearing completion

It is true, as the Technical Board 3.3.04 noted (EPO BoA paragraph 7.15.5), that the fact that a study is nearing completion per se, is in the absence of knowledge of the parameters selected for monitoring, neither a positive nor a negative pointer when assessing expectation of success. Further in this case no information is on file regarding the work of the Data Safety Monitoring Board (DSMB), the timing of interim reviews and the predetermined criteria on which such interim reviews would have been based. Further it is true that no specific information was available at the priority date on why the regulatory authorities have approved the phase III TROPIC study. While D21 indicates that "non-clinical and clinical data based on applicants’ own tests and studies" were submitted, the nature and content of these data are not mentioned (see D21: page 4).

But what can however be derived from the fact that the Tropic trial had been approved and had been in progress for three years at the priority date without having been stopped, is that at least the sponsor of this trial had not considered it disappointing at the start and at no time until the priority date.

This supports the expectation of success, because the Phase III study “TROPIC” was based on successful previous preclinical and clinical data and was expected to end very soon in May 2010 after 4 years. Six months before the ending of the trial the skilled person knowing that in a clinical trial interim results must be evaluated in view of benefits and risks according to the clinical trial plan periodically, and noticing that no negative events had occurred or were published, had a reasonable expectation for success for the use of the combination of cabazitaxel and prednisone in the treatment of the patient group in question.

This view is supported by Dr. Nelson`s and Dr. Denmeade`s testimony who both said that an untimely termination of the TROPIC trial would have been made public, and by Dr. [redacted] testimony (B.25, para. 58: “The fact that a trial had been ongoing for some time would mean only that there has not been a very severe adverse safety signal and that in a very stringent statistical analysis, the trials was not destined to fail unequivocally.”) Contrary to the argument of Sanofi, that many trails proceed for years and eventually fail, thus a guarantee for a positive outcome does not exist, the skilled person gains an expectation of success, because of the late stage of the ongoing clinic trial phase III.

The sponsor of the TROPIC study may have considered the poor prognosis for patients with metastatic castration-resistant prostate cancer (mCRPC), particularly those with docetaxel-refractory mCRPC, as a key factor in allowing the study to proceed, given that the risk/benefit assessment would have favoured moving forward. The patients had a terminal disease and there were no approved treatment options available. The de facto standard treatment was highly toxic chemotherapy with no clear data on a palliative effect. In contrast, the potential benefits to patients of a positive finding in the study were significant. Phase I toxicity studies had been completed, suggesting that the risks were manageable. Even the slightest hope of success would have been sufficient to tip the balance in favour of proceeding with the study. However, as no details on these considerations have been made available to the skilled person on the priority date, these considerations cannot be taken into account when assessing inventive step.

This assessment is also supported by the differing answers of the two experts to the question of whether the skilled person would have had reason to expect the TROPIC study to be successful, given that they knew the study had been approved and had been ongoing for three years without premature interruption. Dr Denmeade refuted the notion put forward by Dr Nelson that the DSMB might have lowered the bar to give the go-ahead for the phase III study, given that the patients had a lethal disease and no further treatment was available, only palliative care. In his view, the DSMB would always insist that safety and some degree of efficiency be demonstrated so that the benefits outweigh the risks, as there was nothing special about the urgent need in this case. Treatment for all kinds of cancer is needed. Ultimately, this discussion does not provide any additional guidance on the question of inventive step, as the DSMB's considerations were unavailable to the skilled person at the priority date.

(10) Other Phase III taxane trials discontinued

The fact that other Phase III taxane trials, in particular the one on cabazitaxel in breast cancer, had been discontinued (Sanofi 2008 document) cannot generally call into question the promising elements described above. These discontinuations could be interpreted in different ways (i.e., by comparison, the continuation of cabazitaxel research for the prostate revealed that it was more promising, or conversely, that taxanes were beginning, as a class, to prove a dead end, with this second interpretation not explaining why, then, the cabazitaxel trial should be continued if such a general conclusion on taxanes were to be drawn), without leading the person skilled in the art to unfavourably modify the teaching of the previous data corroborated by the launch and then the continuation of the Tropic trial.

In this respect, the statistical data cited by the Sanofi companies and available at the priority date [redacted] and [redacted] UPC Sanofi Exhibit No. B.14 document), according to which phase III trials are successful in 41 percent of cases in oncology, only confirm the fact that any trial is uncertain, while indicating that at this advanced stage of development, the average chances of success are close to half. In fact, the same document states that the chances of success vary greatly depending on the case and states in particular that success is more likely for compounds whose mechanism of action is already implemented by another compound [redacted] and [redacted] document, p. 713, nd column, l. 4-11), which is the case for the cabazitaxel selected because it belongs to the same taxane class as docetaxel, with the known effect, while having promising characteristics in the face of the resistance encountered by taxanes.

Also, the argument that all the mentioned failed Phase III trials show that authorisation to carry out a Phase III trial does not mean that the trail is successful, is not sustainable. As mentioned before, the crucial point in the present case is not the authorisation of the trial, it is the course of the trial without incident and the near ending of the trial, which leads to an expectation of success.

ff. Overall assessment

Thus, in the light of these prior art data, the person skilled in the art would have considered that, compared to mitoxantrone plus prednisone, which he knew had only a first-line palliative effect and was not even approved for second-line use, the second-line cabazitaxel plus prednisone experiment in progress in a

phase III trial for more than three years, had a reasonable chance of showing a favourable effect including the (moderate) increase in survival.

As a matter of fact, the skilled person does not need to have been certain of success by any means; for rendering a solution obvious, it is sufficient if the skilled person would have followed the teaching available in the prior art with a reasonable expectation of success (case law of the Boards of Appeal, I.D.7.1: https://www.epo.org/en/legal/case-law/2022/clr_i_d_7_1.html; EPO Board of Appeal T 2506/12, para. 3.12.2; T 0096/20, para. 8 and 9), which is the case here.

gg. No binding effect of decisions by the EPO or national courts

In light of the differing findings of the Opposition Division and the Boards of Appeal regarding the opposition to the patent in question, the Unified Patent Court may, in principle, consider decisions and opinions issued by national courts and the EPO when interpreting the EPC. However, this does not relieve a UPC panel of its duty as an independent judicial body to interpret and apply the EPC, nor does it relieve them of their duty to decide on the counterclaims. Thus, national decisions and EPO decisions are elements to be considered by UPC panels, but are not binding on them. In this sense, they may have a persuasive effect. Within this framework, this panel has carefully considered the findings of the Opposition Division and the Boards of Appeal. However, in view of the reasoning set out above, the panel follows the Tribunal Judiciaire de Paris and cannot agree with the conclusions reached by the Opposition Division and the Boards of Appeal regarding inventive step.

Therefore, claim 1 does not involve an inventive step.

3. On inventive step of Claims 2-8

Sanofi did not argue that dependent claims 2 to 8 contain subject matter that is inventive in relation to the prior art, independently of claim 1. The following discussion is therefore included for the sake of completeness.

As the defendant companies point out, claim 2, by specifying that the use of the drug is for an advanced metastatic disease, does not bring anything inventive, the metastatic prostate cancer considered in claim 1 already being an advanced metastatic disease.

The features of dependent claims 3 and 4, which relate to cabazitaxel being in the form of an acetone solvate, are not linked to any technical effect. Furthermore, it is within the skilled person's common general knowledge to provide a specific solvate, such as the acetone solvate, of an active agent such that these features are not suited to establish an inventive step.

The doses of cabazitaxel and prednisone and the 3-week dosing interval, which are the subject of claims 5, 6 and 7, are disclosed in the NHSC document and the evidence of their effect follows from the foregoing considerations on claim 1. A fortiori, the combination with prednisone per se, which is the subject of claim 8.

Nor is it disputed lastly, that the limitation to patients who have previously received a minimum dose of 225 mg/m² of docetaxel, which is the subject of claim 9, does not provide any distinct technical effect, so that, responding to the same problem or merely providing an arbitrary characteristic, it is not inventive either.

Consequently, the European Patent 2 493 466 is revoked in its entirety (claims 1 to 9) with effect for the following UPC Contracting Member States:

Austria, Belgium, Germany, Denmark, France, Italy, the Netherlands, Portugal and Sweden.

4. No auxiliary requests

Sanofi did not file an application pursuant to Rule 30 of the Rules of procedure. Therefore, no auxiliary requests must be considered.

C. Infringement actions:

As the patent in question is invalid and is revoked in its entirety the infringement actions shall be dismissed.

D. Any other outstanding applications and requests:

As the infringement actions are dismissed, any other outstanding applications and requests relating to them no longer need to be adjudicated (R. 334 RoP). These requests shall be set aside.

E. Costs

As losing party Sanofi SA must bear the costs of the counterclaims. All Sanofi claimants must bear the costs of the infringement actions as they have either withdrawn the infringement claims or lost them, due to the invalidity of the patent.

DECISION

1. The European Patent 2 493 466 is revoked in its entirety (claims 1 to 9) with effect for the following UPC Contracting Member States: Austria, Belgium, Germany, Denmark, France, Italy, the Netherlands, Portugal and Sweden.

2. The infringement actions are dismissed.

3. The costs of the counterclaims for revocation shall be borne by Sanofi SA.

4. The costs of the infringement actions shall be borne by all Sanofi claimants.

5. All other outstanding applications and requests, including the preliminary objections, do not need consideration and are set aside.

INFORMATION ON APPEAL

An appeal against the present Decision may be lodged at the Court of Appeal, by any party which has been unsuccessful, in whole or in part, in its submissions, within two months of the date of its notification (Art. 73(1) UPCA, R. 220.1(a), 224.1(a) RoP).

INFORMATION ABOUT ENFORCEMENT

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

INSTRUCTIONS TO THE REGISTRY

A copy of this decision, once it has become final, is to be sent to the European Patent Office and the

- Österreichisches Patentamt
- Belgian Office for Intellectual Property
- Deutsches Patent- und Markenamt
- Danish Patent and Trademark Office
- Institut National de la Propriété Industrielle
- Italian Patent and Trademark Office
- Netherlands Patent Office
- Portuguese Institute of Industrial Property
- Swedish Intellectual Property Office.

This decision was issued on 12 December 2025.

Dr. Zigann Presiding Judge	Matthias ZIGANN Digital unterschrieben von Matthias ZIGANN Datum: 2025.12.09 10:43:47 +01'00'
Zana Legally Qualified Judge	Alima ZANA Firmato digitalmente da Alima ZANA Data: 2025.12.10 08:03:03 +01'00'
Pichlmaier Legally Qualified Judge	Tobias Günther Pichlmaier Digital unterschrieben von Tobias Günther Pichlmaier Datum: 2025.12.09 11:41:58 +01'00'
Wagner Technically Qualified Judge	Carola Wagner Digital signiert von Carola Wagner DN: cn=Carola Wagner, c=DE Datum: 2025.12.10 07:45:38 +01'00'
For the Deputy-Registrar	Anja Mittermeier Digital unterschrieben von Anja Mittermeier Datum: 2025.12.10 10:16:07 +01'00'