

UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE PATENT TRIAL AND APPEAL BOARD

CSPC PHARMACEUTICAL GROUP LIMITED,
CSPC OUYI PHARMACEUTICAL CO., LTD., AND
CONJUPRO BIOTHERAPEUTICS, INC.,
Petitioners,

v.

IPSEN BIOPHARM LTD.,
Patent Owner.

Case No. IPR2025-00505
Patent No. 11,344,552

PETITIONERS' SUPPLEMENTAL BRIEF

TABLE OF AUTHORITIES

	Page(s)
Cases	
<i>In re Crish</i> , 393 F.3d 1253 (Fed. Cir. 2004).....	5
<i>Multilayer Stretch Cling Film Holdings, Inc. v. Berry Plastics Corp.</i> , 831 F.3d 1350 (Fed. Cir. 2016).....	5
<i>Wasica Finance GmbH v. Continental Automotive Sys., Inc.</i> , 853 F.3d 1272 (Fed. Cir. 2017).....	2
Other Authorities	
MPEP 2111.03	5

The phrase in claim 1 “in a human patient who has not previously received an antineoplastic agent to treat the metastatic adenocarcinoma of the pancreas” refers to first-line therapy, which was undisputed at oral argument and is supported by the record. *See* EX1001, 1:20-25 (“This disclosure relates to...(first line) treatment of patients diagnosed with previously untreated pancreatic cancer.”). This means that the patient has not received a previous anti-cancer drug *other than the claimed regimen that that patient has already started*. A “first-line therapy” is the first regimen used to treat a patient. For example, for a patient receiving the first-line regimen of claim 1 for several months and then a different regimen subsequently, claim 1 is the first-line treatment and the different regimen the second-line treatment. PO conflates first-line therapy with a starting dose, but a “starting dose” is just the first dose a patient receives as part of any regimen. Here, claim 1 requires that the method of treatment is a first-line therapy, but does not require that the claimed doses be used as a starting dose. Support for this comes from the claims and the specification. Claim 1 states that the method comprises administering the claimed anti-cancer therapy to the patient “once ***every two weeks***,” and claim 5 states that the claimed regimen is administered “on days 1 and 15 of a 28-day treatment cycle,” but these claims are silent as to any starting dose. *See also* EX1001, Abstract (“the administration of liposomal irinotecan, oxaliplatin, leucovorin and 5-fluorouracil once every two weeks); 2:28-29 (“once every two weeks”); 2:64-65 (same); 2:67-

3:2 (same); 24:39-42 (same). If claim 1 is construed such that the patient cannot have “previously received” an “antineoplastic agent,” then any treatment after the starting dose could not practice the claim since the patient has already received an “antineoplastic agent” of the claimed regimen at the beginning of week 1.¹ This would render the claims internally inconsistent and the “every two weeks” limitation superfluous. See *Wasica Finance GmbH v. Continental Automotive Sys., Inc.*, 853 F.3d 1272, 1288 n.10 (Fed. Cir. 2017) (“It is highly disfavored to construe terms in a way that renders them void, meaningless, or superfluous.”).

Because claim 1 is not limited to just a starting dose, it encompasses a regimen where for example, the patient was first given a starting dose of 85 mg/m² of oxaliplatin (outside the claims) and then two weeks later, the same patient was given a reduced dose of 60 mg/m² (inside the claims) and two weeks later the patient commences a second cycle (inside the claims) where the patient is again given the reduced dose of 60 mg/m² oxaliplatin every two weeks (inside the claims). The plain language of claim 1 only limits the timing of the administration to once every two

¹ Claim 12 further supports Petitioner’s position. Claim 12 is identical to claim 1 except that instead of any antineoplastic agent, claim 12 requires that the patient was not previously treated with gemcitabine, a then known available first-line option for metastatic pancreatic cancer patients. See EX1001 at 2:8-14. Thus, while claim 12 has a narrower scope than claim 1, they both limit the claims to first-line therapy.

weeks. This addresses the Board’s first (1) inquiry.² Support for this comes from the claim language, the specification, and the file history. As stated above, there is nothing in the claims that limits the claimed methods to just a starting dose, or even just one treatment cycle of 28 days. The specification repeatedly describes the claimed method as covering multiple 28-day cycles, which is not surprising since this is how chemotherapy works, where patients go through multiple cycles until they can no longer tolerate the treatment. *See* EX1001 at 18:62-63 (“The method of any one of embodiments 1-7, wherein **multiple cycles** are administered.”) (emphasis added); 19:35-36 (“wherein the human patient is treated with one or **multiple cycles**.”) (emphasis added); 25:25-27 (“Actual dose of oxaliplatin to be administered is determined by calculating the patient’s body surface area prior to each cycle.”); Table 16, 43:59 – 44:12 (clinical trial design where patient is provided a “R” dose [reduced dose of 60 mg/m² oxaliplatin] at cycle 2 day 1, cycle 2 day 15, cycle 3 day 1, and cycle 3 day 15).

² Even if the Board were to rule that claim 1 is limited to a starting dose of 60 mg/m² of oxaliplatin or a claimed regimen which requires a starting dose of 60 mg/m² of oxaliplatin, the record fully supports obviousness of this construction based on the POSA’s understanding that given FOLFIRINOX’s known toxicities regarding oxaliplatin, the POSA would be able to provide a starting dose of 60 mg/m² of oxaliplatin. *See* Ratain Declaration (Ex. 1002) at ¶¶ 77-82, 241-242, Conroy article (Ex. 1003), Conroy Protocol (Ex. 1004 at 16-18), Conroy Appendix (Ex. 1017) at 3-7, Cantore (Ex. 1009) at 1-5.

Moreover, while Petitioner ***maintains*** that PO has not proven the required nexus to establish unexpected results, PO argued during prosecution that the claimed methods showed unexpected results based on the NALIRIFOX results (as described in the Wainberg references). *See* EX1119 at 151-152. However, Wainberg reveals that the mean durations of treatment of NALIRIFOX for all of the claimed regimens were all more than 200 days (approximately seven 28-day cycles) and that the median duration of response was 9.4 months (approximately nine 28-day cycles). *See* EX1018 at 2, 6.

Regarding the Board's second (2) inquiry, ***any deviation*** from the recited doses of the claimed drugs means that one is no longer practicing the claims. Thus, under the scenario presented by the Board, where "in the second administration two weeks later, the patient is treated with the same four drugs, but with at least one drug as a different dose" from what is recited in claim 1, the claimed method is no longer being practiced. PO's argument, ***raised for the first time at oral argument***, that the "comprising" language in claim 1 somehow allows for the claim to cover any conceivable dose of the drugs, including lower doses, is wrong. As the Board pointed out during oral argument, when defining the claimed antineoplastic therapy, claim 1 uses the transitional phrase "consisting of." EX1001, claim 1 ("the antineoplastic therapy consisting of: [the recited doses of drugs]"). As a strictly closed transitional phrase, it limits the scope of the claimed antineoplastic therapy to ***only*** the doses

specifically listed, and ***excludes*** any other dose not specified in the claims. *See* MPEP 2111.03; *Multilayer Stretch Cling Film Holdings, Inc. v. Berry Plastics Corp.*, 831 F.3d 1350, 1358 (Fed. Cir. 2016). The “comprising” term preceding this closed antineoplastic therapy does not change this. That part of the claim describes the broader method of treatment, which includes the closed antineoplastic therapy, but can also include other non-antineoplastic therapies, which can still treat metastatic pancreatic cancer. EX1001, claim 1 (“the method comprising administering an antineoplastic therapy”). The ’522 patent describes these non-antineoplastic therapies as including corticosteroids, such as dexamethasone, or anti-emetics, such as a 5-HT3 antagonist, which prevent and treat nausea and vomiting. *See* EX1001 at 18:13-17 (“In various embodiments, the human patient with metastatic pancreatic cancer is pre-medicated with dexamethasone and a 5-HT3 antagonist or other anti-emetic prior to administering the MM-398 liposomal irinotecan, and other active agents.”); 24:14-17. Claim 15 confirms this point since it states that “the method further comprises administering a corticosteroid and an anti-emetic to the patient prior to the antineoplastic therapy.” *See In re Crish*, 393 F.3d 1253, 1256, 1257 (Fed. Cir. 2004) (“The reasonable interpretation of the claims containing both of the terms ‘comprising’ and ‘consists’ is that the term ‘consists’ limits the ‘said portion’ language to the subsequently recited numbered nucleotides, but the earlier term ‘comprising’ means that the claim can include that portion plus other nucleotides.”).

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CERTIFICATE OF COMPLIANCE

The undersigned certifies that the foregoing Petitioners' Supplemental Brief contains no more than 5 pages pursuant to the Order dated May 21, 2026.

Dated: May 29, 2026

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CERTIFICATE OF SERVICE

Pursuant to 37 CFR § 42.6(e), the undersigned hereby certifies that on May 29, 2026, the foregoing Petitioners' Supplemental Brief was served via electronic mail, as authorized by Patent Owner, at the following email addresses:

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