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Datasheet for the decision of 25 January 2022

Case Number:	T 2627/17 - 3.3.02
Application Number:	14155086.3
Publication Number:	2735562
IPC:	C07D231/56, C07D249/18, C07D409/06, C07D401/06, C07D401/12, C07D403/10, C07D413/10, C07D417/10, A61K31/4192, A61K31/416, A61P35/00
Language of the proceedings:	EN

Title of invention:
Estrogen receptor modulators and uses thereof

Patent Proprietor:
Seragon Pharmaceuticals, Inc.

Opponent:
Furo Ventures B.V.

Headword:

Relevant legal provisions:
EPC Art. 83, 56

Keyword:
Sufficiency of disclosure
Inventive step

Decisions cited:
T 0609/02, T 1329/04, T 1592/12, T 2059/13, T 0488/16, T 0116/18

Catchword:

Europäisches Patentamt
European Patent Office
Office européen des brevets

Beschwerdekammern

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Case Number: T 2627/17 - 3.3.02

D E C I S I O N
of Technical Board of Appeal 3.3.02
of 25 January 2022

Appellant: (Opponent)	Furo Ventures B.V. Willemsplein 2 5211 AK s'Hertogenbosch (NL)
Respondent: (Patent Proprietor)	Seragon Pharmaceuticals, Inc. 12780 El Camino Real, Suite No. 301 San Diego, CA 92130 (US)
Representative:	Carpmaels & Ransford LLP One Southampton Row London WC1B 5HA (GB)
Decision under appeal:	**Decision of the Opposition Division of the European Patent Office posted on 15 November 2017 rejecting the opposition filed against European patent No. 2735562 pursuant to Article 101(2) EPC.**

Composition of the Board:

Chairman	M. O. Müller
Members:	P. O'Sullivan
	R. Romandini

Summary of Facts and Submissions

I. The appeal of the opponent (hereinafter appellant) lies from the decision of the opposition division according to which European patent 2 735 562 in amended form met the requirements of the EPC.

II. Among the evidence cited in opposition proceedings, the following documents were invoked by the parties during appeal proceedings:

D1: Weatherman *et al.*, Chemistry and Biology 8 (2001), 427-436
D2: Pages 211-223 of the contested patent, including an annotated table 11
D3: Keseru *et al.*, Drug Discovery Today, 2006, 11, 741-748
D4: Fan *et al.*, Breast Cancer Res Treat, 2007, 103, 37-44.

III. According to the contested decision, the invention defined in the claims of the patent as granted was sufficiently disclosed and involved an inventive step.

IV. With a communication pursuant to Article 15(1) RPBA, the board set out its preliminary opinion, including in particular that the subject-matter of granted claims 1-14 involved an inventive step and that the invention disclosed in *inter alia* second medical use claim 18 was not defined in a manner sufficiently clear and complete for it to be carried out by a person skilled in the art.

V. With the letter dated 19 November 2021 the patent proprietor (hereinafter respondent) submitted the following documents:

D9: Welborn et al., Endocrine-Related Cancer, 2009, vol. 16, 1073-1089
D10: Klinge, Steroid, 200, vol. 65, 227-251

VI. With the letter dated 15 January 2022, the appellant announced that it would not attend the oral proceedings scheduled for 25 January 2022.

VII. With the letter dated 20 January 2022, the respondent stated that in view of the non-attendance of the appellant at oral proceedings, and the preliminary opinion of the board set out in its communication pursuant to Article 15(1) RPBA, the respondent would "*consent to dispensing with the oral proceedings if the Board would agree to maintain the patent on the basis of the auxiliary request 5 and continue the procedure in writing.*"

VIII. Since the board found auxiliary request 5 allowable, there was no need to hold oral proceedings, and the proceedings were continued in writing. The scheduled oral proceedings were cancelled.

Requests

The appellant requested that the contested decision be set aside and that the patent be revoked in its entirety.

The respondent requested that the appeal be dismissed, implying maintenance of the patent on the basis of the main request held allowable by the opposition division

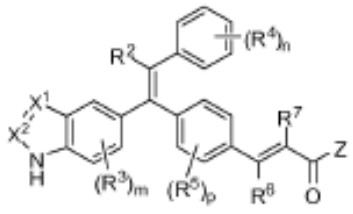
(which consisted of the granted claims and included page 123 of the granted patent in amended form as filed with the letter dated 15 September 2017).

Alternatively, maintenance of the patent was requested on the basis of:

- one of the sets of claims of auxiliary requests 1 to 3 submitted during opposition proceedings with the letter of 16 August 2017, all claim requests in combination with amended page 123 of the granted patent filed with the letter dated 15 September 2017, or
- the set of claims of auxiliary request 4, submitted with the reply to the statement of grounds of appeal, in combination with amended page 123 of the granted patent filed with the letter dated 15 September 2017, or
- the sets of claims of auxiliary requests 5-9 submitted with the letter dated 19 November 2021, all claim requests in combination with amended page 123 of the granted patent filed with the letter dated 15 September 2017.

IX. Independent compound claim 1 of the main request (claims as granted) reads as follows:

"*1. A compound that has the structure of Formula (XII):*



Formula (XII)

wherein,

X^1 is CH, CR^3 or N;
X^2 is N, CH, or CR^3;
Z is -OH or $-OR^{10}$;
R^2 is C_1-C_4alkyl, C_1-C_4fluoroalkyl, C_1-C_4deuteroalkyl, C_3-C_6cycloalkyl, or C_1-C_4alkylene-W;
W is hydroxy, halogen, CN, C_1-C_4alkyl, C_1-C_4haloalkyl, C_1-C_4alkoxy, C_1-C_4haloalkoxy, and C_3-C_6cycloalkyl;
each R^3 is independently halogen, C_1-C_4alkyl, or C_1-C_4fluoroalkyl;
each R^4 is independently halogen, -CN, OR^9, $-S(=O)_2R^{10}$, C_1-C_4alkyl, C_1-C_4fluoroalkyl, or C_1-C_4heteroalkyl;
each R^5 is independently halogen, -CN, OR^9, $-S(=O)_2R^{10}$, C_1-C_4alkyl, C_1-C_4fluoroalkyl, or C_1-C_4heteroalkyl;
R^6 is H, C_1-C_4alkyl, or halogen;
R^7 is H, C_1-C_4alkyl, or halogen;
R^9 is H, C_1-C_6alkyl, C_1-C_6fluoroalkyl, or C_3-C_6cycloalkyl;
R^{10} is C_1-C_6alkyl;
m is 0, 1, or 2;
n is 0, 1, 2, 3, or 4; and
p is 0, 1, or 2;

or a pharmaceutically acceptable salt, or N-oxide thereof"

Independent claim 12 reads as follows:

"*12. A pharmaceutical composition comprising a compound as claimed in any one of claims 1 to 10, or a pharmaceutically acceptable salt, or N-oxide thereof and at least one pharmaceutically acceptable inactive ingredient.*"

Further claims of the patent as granted read as follows:

"*15. A compound of any one of claims 1 to 10, or a pharmaceutically acceptable salt, or N-oxide thereof, for use in medicine.*

18. A compound of any one of claims 1 to 10, or a pharmaceutically acceptable salt, or N-oxide thereof, for use in the treatment of bone cancer, breast cancer, colorectal cancer, endometrial cancer, prostate cancer, ovarian cancer, uterine cancer, cervical cancer, lung cancer, leiomyoma, uterine leiomyoma, alcoholism, migraine, aortic aneurysm, susceptibility to myocardial infarction, aortic valve sclerosis, cardiovascular disease, coronary artery disease, hypertension, deep vein thrombosis, Graves' Disease, arthritis, multiple sclerosis, cirrhosis, hepatitis B, chronic liver disease, bone density, cholestasis, hypospadias, obesity, osteoarthritis, osteopenia, osteoporosis, Alzheimer's disease, Parkinson's disease, migraine, vertigo, anorexia nervosa, attention deficit hyperactivity disorder (ADHD), dementia, major depressive disorder, psychosis, age of menarche, endometriosis, or infertility in a mammal."

X. The arguments of the appellant insofar as relevant to the present decision, may be summarised as follows:

Main request

Sufficiency of disclosure

The invention defined in claims 15-18 was not disclosed in a manner sufficiently clear and complete for it to be carried out by a person skilled in the art.

Inventive step - Article 56 EPC

The subject-matter of claims 1-14 did not involve an inventive step. There was no justified expectation that the compounds and compositions claimed actually solved a technical problem. Even if a technical problem were to be acknowledged, the solution was obvious in view of the compounds disclosed in D1 or D4.

XI. The arguments of the respondent insofar as relevant to the present decision, may be summarised as follows:

Main request

Sufficiency of disclosure

The invention defined in the claims was disclosed in a manner sufficiently clear and complete for it to be carried out by a person skilled in the art. In particular in relation to the claims directed to a second medical use, the information in the patent, in combination with that provided in D9 and D10, demonstrated the link between ER-activity and the diseases and conditions listed in claim 18.

Inventive step - Article 56 EPC

The subject-matter of claims 1-14 involved an inventive step in view of D1 or D4 as closest prior art.

Reasons for the Decision

1. Priority

The appellant argued that the priority claims of the contested patent were to be considered invalid. Validity of priority is however not a ground for opposition. Rather, in opposition proceedings it may be of importance when the effective date of the patent is to be determined, for example with regard to the question whether certain evidence is to be considered as part of the state of the art, and thus relevant to the grounds for opposition under Article 100(a) EPC (novelty and inventive step). Since no such issues arise with the relevant state of the art cited in the present case, the validity of the claimed priorities does not need to be examined.

Main request

2. Sufficiency of disclosure - claims 15-18

The patent is concerned with compounds to treat, prevent or diagnose diseases or conditions that are estrogen sensitive, estrogen receptor dependent, or estrogen receptor mediated (patent, paragraph [0002]).

The appellant's objections in relation to sufficiency of disclosure solely concerned the invention defined in medical use claims 15-18.

2.1 First medical use claim 15

Claim 15 is directed to a compound of any one of claims 1 to 10, or a pharmaceutically acceptable salt, or N-oxide thereof, for use in medicine.

2.1.1 The appellant argued in respect of claim 15 that the alleged biological effects had not been supported across the full range of compounds claimed, and that even for the tested compounds, the data of table 11 did not allow the skilled person to identify which compounds actually provided a suitable effect in the tests employed, i.e. whether a sufficient biological effect had been achieved. According to the appellant, the conclusion of the opposition division that the requirements of sufficiency of disclosure were met in this regard was incorrect, since the relevant case law had not been correctly applied.

2.1.2 More specifically, the appellant submitted that the "relevant test" in view of decision T 609/02 and decisions citing it such as T 1592/12 and T 2059/13, was whether the patent application as filed disclosed the suitability of the product (in the present case, the claimed compounds) for the claimed therapeutic applications to the skilled person using common general knowledge. The conclusion of the opposition division was incorrect since, in the case underlying T 609/02, the fact that no data was presented in the application as filed demonstrating an impact of the relevant hormone on the listed diseases, did not automatically mean that the issues addressed therein could not be applied to the present case. Specifically, as pointed out in both T 1592/12 (reasons 15-17) and T 2059/13 (reasons 4.2.1-4.2.4), the points of law presented in T 609/02 applied to the therapeutic use of chemical compounds in general, and thus also to the facts of the present case.

Similarly, the appellant submitted that the conclusion of the opposition division regarding the applicability

of the facts underlying T 488/16 was also incorrect. This view was supported by *inter alia* the statement in T 2059/13 (reasons 4.2.3) that "*differences are normal and the usefulness of case law is not confined to similar or identical facts, but lies in the principles or guidance which can be extracted from earlier cases*". Thus, the appellant argued, in view of T 488/16 (reasons 4.10), when opponents had provided technically sound and persuasive arguments as to why an alleged effect had not been made plausible, which raised doubts as to whether the technical problem had been solved at the filing date, they had discharged their burden of proof.

2.1.3 The board's view is as follows.

The relevant biological activity ascribed to the claimed compounds in the patent is the treatment or prevention of diseases or conditions which are estrogen sensitive, estrogen receptor dependent, or estrogen receptor mediated (paragraph [0002]), i.e. involve activity at the estrogen receptor. Such activity is described differently in the various submissions of the parties, as well as in the cited prior art. Since the exact nature of the activity at the estrogen receptor was not a matter of discussion nor dispute in the present proceedings, for ease of reference the board in the following employs "estrogen receptor activity", abbreviated as "ER activity", as representative of all terminology employed in relation to the alleged effect of the claimed compounds.

In table 1 of the patent (pages 24-115), 453 specific compounds, many of which fall within the scope of claim 1, are disclosed. In table 11 (page 211), biological data is provided for said compounds based on IC_{50}

activity in an "MCF7 Viability Assay" (described in examples 84 and 85; paragraphs [0810] and [0811]) and an "ER-α In Cell Western Assay (ski)" (described in example 86; paragraph [0813]), both assays concerning breast cancer cell lines.

Thus, the patent comprises biological data in relation to specific breast cancer cell lines for a wide range of compounds falling within the scope of claim 1.

The situation in the decisions cited by the appellant was however different, as set out in the following.

In T 609/02, not only was no evidence presented in the patent that the alleged effect took place, but the patent was also silent with regard to the identification of a specific steroid hormone allegedly providing said effect (reasons, 5). Thus, in view of the lack of information provided in the patent, sufficiency of disclosure was denied.

In T 1592/12, the relevant claims concerned a specific dosage regimen. Since the patent provided no data, and the half-life of the active compound in question (a specific antibody) would have provided the skilled person with serious doubt that the claimed administration would suffice (reasons, 28), the suitability of the claimed dosage regimen to obtain the required therapeutic effect was deemed not to be sufficiently disclosed in the patent (reasons, 41).

Similarly, in T 0488/16, no data was provided in the application as filed to support the allegation that the sole claimed compound provided a particular therapeutic effect. Although the relevant issue in that case was inventive step, the considerations relevant to

sufficiency of disclosure remain the same (see e.g. T 116/18, reasons 13.3.1). Specifically, in T 0488/16, the application as filed was found to lack any evidence at all that any of the very broadly defined compounds of the claims of the application as filed, let alone the single compound claimed (dasatinib), was active as an inhibitor of the specific protein kinase inhibitors concerned.

2.1.4 Thus, in contrast to the facts underlying the present case, in the above-mentioned decisions, no evidence had been presented demonstrating a biological effect for the claimed compounds. In the present case, biological activity data is presented for the large number of compounds exemplified. Even accepting that not all examples fall within the scope of the present claims, as argued by the appellant in opposition proceedings with reference to D2 (letter dated 16 August 2017, point 10), the data presented for the claimed compounds is considered sufficient to support the therapeutic application for which they were tested. As set out in T 609/02, absolute proof that a compound could be approved as a drug before it may be claimed as such (in a medical use claim) is not required. Rather, for demonstrating sufficient disclosure of a therapeutic application, the patent must provide some information in the form of, for example, experimental tests, to the avail that the claimed compound has a direct effect on a metabolic mechanism specifically involved in the disease, this mechanism being either known from the prior art or demonstrated in the patent per se. Showing a pharmaceutical effect in vitro may be sufficient if there is a clear and accepted established relationship between the shown physiological activities (in the present case, ER activity) and the disease (T 609/02, reasons, 9).

2.1.5 Therefore, the data in table 11 of the patent sufficiently demonstrates the effect of the claimed compounds on the specific ER activity tested. Consequently, the appellant's argument that the effect would not be present for further compounds falling within the scope of the claims, but not tested, amounts to an unsubstantiated allegation, and therefore must fail.

2.1.6 The appellant also argued that even for the tested compounds, the data of table 11 did not allow the skilled person to identify which compounds actually provided a suitable effect in the tests employed, i.e. whether a sufficient biological effect had been achieved. The board notes however that with regard to the minority of compounds tested in table 11 achieving a "B" rating in the respective assay in table 1 ("B" denoting an IC_{50} > 100nm), it can only be concluded that these compounds are less active than compounds rated "A", but not that they are "inactive", as implied by the appellant, and therefore unsuitable for the claimed therapeutic indication. The data in table 11 shows that even if some of the claimed compounds display less strong ER activity, they still reduce the viability of breast cancer cells in vitro. Furthermore, although the appellant labelled the in vitro tests of the patent as "very rough", the results in table 11 clearly reflect therapeutic applications in diseases and conditions involving ER activity, as set out above. There is therefore no reason to doubt that the biological tests in the patent demonstrate the suitability of the claimed compounds for therapeutic application in ER-regulated conditions.

2.1.7 It is established case law that a successful objection of lack of sufficiency of disclosure presupposes that there are serious doubts, substantiated by verifiable facts. In the present case, no such facts have been submitted by the appellant. Furthermore, the board found the appellant's arguments based on the case law of the Boards of Appeal to be unconvincing.

Consequently, the board found the invention defined in claim 15 to be sufficiently disclosed.

2.2 Second medical use claim 18

Claim 18 is essentially directed to a compound (of any one of claims 1 to 10) for use in the treatment of a long list of specific conditions, including, *inter alia*, alcoholism, migraine, aortic aneurysm, susceptibility to myocardial infarction, aortic valve sclerosis, cardiovascular disease, coronary artery disease, hypertension, deep vein thrombosis, Graves' Disease, arthritis, multiple sclerosis, cirrhosis, hepatitis B, chronic liver disease, bone density, cholestasis, hypospadias, obesity, osteoarthritis, osteopenia, osteoporosis, Alzheimer's disease, Parkinson's disease, migraine, vertigo, anorexia nervosa, attention deficit hyperactivity disorder (ADHD), dementia, major depressive disorder and psychosis.

2.2.1 The appellant's objections in relation to claim 18 included those outlined above in relation to claim 15, which failed to convince the board.

The appellant also argued in relation to the second medical use claims, citing in particular decision T 2059/13, that the biological tests of table 11 of the

patent (demonstrating ER activity against specific breast cell lines as set out above), were not sufficient to support the effectiveness of the claimed compounds against all conditions claimed, in particular those listed above.

2.2.2 The respondent counter-argued that the patent rendered it plausible that the estrogen receptor is involved in all of the conditions listed in claim 18. Evidence was provided in the patent, in which it was stated that the estrogen receptor can interact with DNA either directly or indirectly (paragraph [0055]), thus indicating its versatility in the regulation of processes in the body.

2.2.3 The board's view is as follows. In T 2059/13, cited by the appellant, it was accepted that the compound in question (aripiprazole) successfully bound to the 5-HT1A receptor. However, there was no evidence in the patent nor in the cited prior art of any link between said receptor and bipolar disorder, the subject-matter of the second medical use claim (reasons, 4.4.4 and 4.4.5). Consequently, sufficiency of disclosure was denied.

2.2.4 The situation in the present case in relation to many of the conditions listed in claim 18 is similar. In paragraph [0005] of the patent, it is stated that the compounds of the invention are useful in the treatment or prevention of diseases or conditions in which the actions of estrogens or estrogen receptors are involved. ER activation in various cancer cells is described in the patent paragraphs [0045] to [0050] and [0055] to [0068], and references to the prior art are provided demonstrating the link between ERs and specific estrogen-dependent cancers (e.g. paragraphs [0055]-[0057]). Existing treatments based on the link

between ER activity and said cancers (e.g. paragraph [0057]) are also described. Biological data is presented demonstrating the activity of the claimed compounds in breast cancer cell lines (examples 84-87 and table 11), thereby credibly linking the ER activity of the claimed compounds with diseases and conditions having a direct link to said activity. This data however only relates to (estrogen-dependent) breast cancer cell lines. With regard to a direct link between ER activity and the conditions other than estrogen-dependent cancer listed in claim 18, apart from mere verbal statements (e.g. paragraphs [0006] and [0061]), the patent is silent - both in terms of biological data demonstrating said link, and any reference to common general knowledge linking ER activity to the **specific** conditions listed. The situation in the contested patent is therefore similar to that underlying case T 2059/13, addressed above, in that the patent does not demonstrate the suitability of the claimed compounds for the treatment of claimed conditions other than estrogen-dependent cancer.

A similar line was taken in T 0488/16 (reasons, 4.5), in which the board stated "*... a mere verbal statement that 'compounds have been found active' in the absence of any verifiable technical evidence is not sufficient to render it credible that the technical problem the application purports to solve ... is indeed solved*".

Also in T 609/02 (reasons, 9), addressed above, it was stated that "*showing a pharmaceutical effect in vitro may be sufficient ... **if there is a clear and accepted established relationship between the shown physiological activities and the disease***" (emphasis added by the present board). In the present case, there

is no such established relationship between the ER receptor and many of the conditions listed in claim 18.

2.2.5 The respondent also cited D9 and D10, (referenced in paragraphs [0055] and [0056] of the patent) to support its position that the invention defined in claim 18 was sufficiently disclosed in relation to all of the conditions listed therein. Specifically, D9 and D10 confirmed the skilled person's general understanding that the estrogen receptor plays a role in a wide variety of processes in the body. This information, in combination with the evidence in the patent rendered it credible that the claimed compounds could be applied in all of the therapeutic uses claimed.

According to D9:

"*Estrogens regulate many cellular processes in a wide variety of target tissues during growth, development, and differentiation. Estrogens are mainly involved in the regulation and development of the female reproductive tract but also play a role in the central nervous system, cardiovascular systems, and in bone metabolism...*" (page 1073, left hand column, first paragraph), and

"*The NF-kB family of transcriptional factors are involved in the immune and skeletal systems and inflammatory response ... NFkB binds to kB elements and regulates the expression of target genes ...* [the estrogen receptor α] *has been shown to inhibit NF-kB in an E_2-dependent manner.*" (page 1074, paragraph bridging left and right columns)

Similarly, according to D10:

"*Estrogens exert a wide variety of effects on growth, development, and differentiation, including important regulatory functions within the reproductive systems of both females and males, in mammary gland development and differentiation, as anti-atherosclerotic agents, in central nervous system functions, and in the regulation of hypothalamic-gonadal axis*" (page 227, left hand column, first paragraph).

2.2.6 The board does not agree. These general statements in D9 and D10 are not sufficiently specific to conclude that the pharmaceutical effect observed in the patent against breast cancer reflects a therapeutic application for all of the conditions listed in claim 18. More specifically, that estrogens may be generally known to play a role in the various processes in the body cannot be equated to direct and unambiguous evidence of a specific effect of ER activity on the metabolic mechanisms of many of the diseases and conditions listed in claim 18, let alone a positive effect required for therapy. Such diseases and conditions include for example, but not limited to, alcoholism, migraine, aortic aneurysm, susceptibility to myocardial infarction, aortic valve sclerosis, cardiovascular disease, coronary artery disease, hypertension, deep vein thrombosis, Graves' Disease, arthritis, multiple sclerosis, cirrhosis, hepatitis B, chronic liver disease, bone density, cholestasis, hypospadias, obesity, osteoarthritis, osteopenia, osteoporosis, Alzheimer's disease, Parkinson's disease, migraine, vertigo, anorexia nervosa, attention deficit hyperactivity disorder (ADHD), dementia, major depressive disorder and psychosis.

2.2.7 In this context the respondent furthermore argued that neither the board nor the appellant had shown that there were serious doubts, substantiated by verifiable facts, regarding the alleged link between ER activity and the diseases and conditions listed in claim 18. However, a parallel can be drawn between this argument and that raised in T 488/16 (reasons, 4.10) in which the proprietor argued that the burden of proof lay with the opponent. The board in that case decided that since persuasive arguments had been put forward by the opponent, its burden had been discharged. Similarly, in the present case as set out above, there is no credible evidence on file directly linking the ER activity of the claimed compounds with all of the conditions listed in contested claim 18. In view of this, and since those conditions are totally different from ER-dependent cancers, it must be assumed that the therapeutic effects claimed (the treatment of those diseases) cannot be obtained.

2.2.8 It follows that with regard to the second medical use directed to therapeutic applications other than estrogen-dependent cancer, the invention defined in claim 18 is insufficiently disclosed.

2.3 In conclusion, the invention defined in contested claim 18 is not disclosed in a manner sufficiently clear and complete for it to be carried out by a person skilled in the art.

Auxiliary requests 1, 2, 3 and 4 - Sufficiency of disclosure

Although renumbered accordingly, second medical use claim 18 of the main request is present in the sets of claims of the auxiliary requests 1, 2, 3 and 4 (as claim 16, 18, 15 and 10, respectively).

It follows therefore that the same conclusion applies for the respective claim of each of these requests. The invention defined in those claims is consequently not sufficiently disclosed.

Auxiliary request 5

3. Sufficiency of disclosure

The set of claims of auxiliary request 5 differs from the main request in the deletion of second medical use claims 16-18.

No objections concerning sufficiency of disclosure were raised in respect of claims 1-14. Furthermore, it was concluded in relation to the set of claims of the main request, above, that claim 15 met the requirements of sufficient disclosure. It follows therefore that the same conclusion applies to claims 1-15 of auxiliary request 5.

The invention defined in claims 1-15 of auxiliary request 5 is consequently sufficiently disclosed.

4. Inventive step - Article 56 EPC

4.1 The appellant submitted that the subject-matter of compound and composition claims (i.e. claims 1-14; statement of grounds of appeal, point 13) lacked inventive step on the basis that

- for the skilled person, there was no justified expectation that the compounds and compositions claimed actually solved a technical problem (referencing decision T 1329/04 and T 0488/16); and

- even if a technical problem could be formulated, solving it was obvious in view of prior art ER degraders GW-5638 and GW-7604 disclosed in D1 (figure 1, bottom left) and D4 (figure 1).

In relation to the first issue, the appellant submitted that "*a comparison with the prior art as is done in the problem-and-solution approach is not suitable. Instead, the assessment should be done in line with T 0488/16*" (statement of grounds of appeal, point 14).

This is not correct. In T 0488/16 it was concluded that the patent did not contain any evidence that the claimed compound dasatinib was useful for the treatment associated therewith, in particular cancer (reasons, 5.5). The lack of evidence however did not preclude the deciding board from applying the problem-solution approach starting from document (7) (reason, 5.2). Consequently, the problem to be solved was defined (vis à vis document (7)) in a less ambitious way, namely as the provision of a further chemical compound (reasons, 5.6).

In the present case, inventive step will be assessed in the same way as in T 0488/16, namely by identifying a suitable closest prior art, establishing the distinguishing feature/s of the claimed subject-matter, and determining whether the alleged effects thereof have been credible achieved. Finally, the objective technical problem is to be formulated, and the obviousness of the solution assessed.

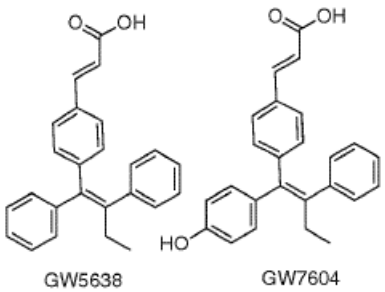
4.2 Closest prior art and distinguishing features

It was undisputed that D1 or D4 could serve as closest prior art. Since D1 and D4 concern the activity of

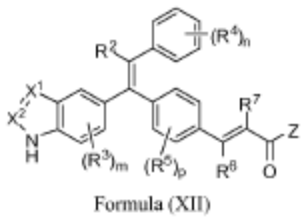
certain compounds at the estrogen receptor (D1, page 427, first paragraph; D4, "Introduction"), the board sees no reason to differ.

4.2.1 It was also undisputed that ER degraders GW-5638 and GW-7604, depicted below, both disclosed in D1 (figure 1, bottom left) or D4 (figure 1), represented the closest prior art embodiments. Since the relevant compounds disclosed in D1 and D4 are identical, the board in the following refers only to D4, although the same considerations apply equally to D1.

4.2.2 The distinguishing features of the claimed compounds over those of D4 were not a matter of dispute: the compounds of formula (XII) of contested claim 1 have a nitrogen-containing ring fused to a phenyl group, which corresponds to the phenyl group in the bottom left of the structures GW-5638 and GW-7604 in D4. The relevant structures are depicted below. According to contested claim 1, the nitrogen-containing ring in the structure of formula (XII) can contain from one to three nitrogen atoms (depending on the definitions of X^1 and X^2 in formula XII).



GW5638 GW7604



Formula (XII)

4.3 Problem solved

The appellant submitted that for the skilled person, there was no justified expectation that the compounds and compositions claimed solved a technical problem.

4.3.1 According to the respondent, the effect of the distinguishing features was that the claimed compounds (also) displayed ER activity. This was disputed by the appellant, who argued that said effect was not rendered credible, since the application as filed did not provide sufficient information to make it plausible for the skilled person that the whole range of claimed compounds possessed the alleged activity (citing T 0488/16).

4.3.2 Concerning the appellant's argument that a technical problem was not solved by the claimed subject-matter, the board's view is similar to that set out above with regard to sufficiency of disclosure. Specifically, the biological data provided in the patent (table 11) renders it credible that the claimed compounds possess ER activity across the scope of claim 1. Also for similar reasons as provided above, the facts in T 0488/16 are different to those underlying the present compound claims: in that decision no data was provided in the application as filed to support the allegation that the sole claimed compound displayed a particular therapeutic effect. In the present patent in contrast, sufficient data has been provided. Furthermore, the relevance of T 1329/04, also cited by the appellant in this regard (but without specific arguments), is not clear to the board. In that case, the objective technical problem, the isolation of a further protein belonging to a specific protein family (reasons, 4), was not considered solved, since it had not been demonstrated that the protein isolated was indeed a member of said family (reasons, 9). This situation lies in contrast to that underlying the contested patent in which sufficient data has been presented supporting the alleged effect as set out above.

4.3.3 Similarly to arguments submitted in the context of sufficiency of disclosure, above, the appellant also argued that in view of the results in table 11 of the patent, some compounds "may" not be sufficiently active to be of practical value in medicine. As set out above, a minority of compounds tested in table 11 achieved a "B" rating in the respective assay ("B" denoting an IC_{50} > 100nm). However, although such compounds are less active than compounds rated "A", it cannot be concluded therefrom that "B" compounds are "inactive" as implied by the appellant, and therefore unsuitable for the claimed therapeutic indication. Rather, said compounds display less strong ER activity. The board notes in this regard that the appellant failed to submit any evidence demonstrating that any of the tested compounds could be considered "inactive".

4.3.4 The objective technical problem underlying contested claims 1-14 is therefore the provision of further compounds (and corresponding compositions) with ER activity.

4.4 Obviousness

4.4.1 The appellant briefly argued that even if a technical problem could be formulated, solving it would have been obvious to the skilled person in view of prior art ER degraders GW-5638 and GW-7604 disclosed in D1 (figure 1, bottom left) and D4 (figure 1).

4.4.2 In this regard the board agrees with both the opposition division (paragraph 4.6 of the contested decision) and the respondent (reply, paragraph 3.6). There is no teaching nor motivation in D4 or elsewhere suggesting that in order to solve the above problem, a specific phenyl group in the prior art compounds GW-5638 and GW-7604 could be fused to a nitrogen-containing heterocycle, thereby forming a bicyclic fused heterocyclic moiety with ER activity.

4.4.3 Although implicit in the formulation of the objective technical problem set out above, it must be emphasised that in the present case, no additional surprising effect over the prior art compounds is necessary to demonstrate inventive step. Rather, the claimed compounds represent non-obvious alternatives to those disclosed in D4 as set out above.

The subject-matter of claims 1-14 therefore involves an inventive step.

4.5 The set of claims of auxiliary request 5 is allowable.

Order

For these reasons it is decided that:

1. The decision under appeal is set aside.

2. The case is remitted to the opposition division with the order to maintain the patent as amended on the basis of

   - claims 1-15 of auxiliary request 5 submitted with the letter dated 19 November 2021,
   - amended page 123 of the granted patent submitted with the letter dated 15 September 2017, and
   - a description to be further adapted thereto, if necessary.

The Registrar: The Chairman:

N. Maslin M. O. Müller

Decision electronically authenticated