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DECISION
of 26 August 2004

Case Number: T 0783/00 - 3.3.1

Application Number: 95921669.8

Publication Number: 0766683

IPC: C07D 473/00

Language of the proceedings: EN

Title of invention:

Novel substituted purinyl derivatives with immunomodulating activity

Applicant:

BIOCHEM PHARMA INC

Opponent:

-

Headword:

Purines/BIOCHEM

Relevant legal provisions:

EPC Art. 111, 123(2)

Keyword:

"Amendments (allowable) - proper basis in original application"

"Remittal (yes) - fresh case"

Decisions cited:

G 0010/93

Catchword:

-



Case Number: T 0783/00 - 3.3.1

D E C I S I O N
of the Technical Board of Appeal 3.3.1
of 26 August 2004

Appellant:

BIOCHEM PHARMA INC
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Representative:

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Decision under appeal:

Decision of the Examining Division of the
European Patent Office posted 23 March 2000
refusing European application No. 95921669.8
pursuant to Article 97(1) EPC.

Composition of the Board:

Chairman: J. M. Jonk
Members: R. Freimuth
S. C. Perryman

Summary of Facts and Submissions

- I. The appeal lodged on 19 May 2000 lies from the decision of the Examining Division posted on 23 March 2000 refusing European patent application No. 95 921 669.8 (European publication No. 766 683), which was filed as international application published as WO 95/35297.
- II. The decision of the Examining Division was based on the original set of 49 claims according to the then pending request wherein claim 1 was directed to compounds defined by way of a *Markush*-formula. The Examining Division found that this claimed subject-matter lacked novelty and inventive step in view of the prior art cited.
- III. At the oral proceedings before the Board held on 26 August 2004 the Appellant (Applicant) no longer maintained the former request. He submitted one single fresh set of 11 claims superseding any previous request. Claim 1 of that request read as follows:
- "1. A compound selected from the group consisting of:
- | | |
|---------------|--|
| Compound #III | N-5-(6-N-Chloropurin-9-yl)-pentanol |
| Compound #V | N-5-(6-N,N-Dimethylaminopurin-9-yl)-
pentanol |
| Compound #1 | N,N-Dimethylaminopurinyl Pentoxycarbonyl
D-Arginine |
| Compound #2 | N-5-(6-N,N-Dimethylaminopurin-9-yl)-
pentoxycarbonyl-L-Arginine |
| Compound #3 | N-5-(6-N-Methylaminopurin-9-yl)-
pentoxycarbonyl-D-Arginine |
| Compound #3a | N-5-(6-N-Methylaminopurin-9-yl)-pentanol |

Compound #4	N-5-(6-N-Methylaminopurin-9-yl)- pentoxycarbonyl-L-Arginine
Compound #5	N-5-(6-N-Aminopurin-9-yl)- pentoxycarbonyl-D-Arginine
Compound #5a	N-5-(6-N-Aminopurin-9-yl)-pentanol
Compound #7	N-5-(6-N-Hydrazinopurin-9-yl)- pentoxycarbonyl-D-Arginine
Compound #7a	N-5-(6-N-Hydrazinopurin-9-yl)-pentanol
Compound #8	N-5-(6-N-Hydrazinopurin-9-yl)- pentoxycarbonyl-L-Arginine;
Compound #9	N-5-(6-N-Chloropurin-9-yl)- pentoxycarbonyl-D-Arginine;
Compound #10	N-5-(6-N-Chloropurin-9-yl)- pentoxycarbonyl-L-Arginine;
Compound #11	Hydroxypurinyl Pentoxycarbonyl D-Arginine
Compound #12	N-5-(6-N-Mercaptopurin-9-yl)- pentoxycarbonyl-D-Arginine;
Compound #13	N-5-(6-N-Mercaptopurin-9-yl)- pentoxycarbonyl-L-Arginine;
Compound #14	N-5-(6-N,N-Dimethylaminopurin-9-yl)- pentoxycarbonyl-Glycine;
Compound #15	N-5-(6-N,N-Dimethylaminopurin-9-yl)-7'- ethoxy-ethoxycarbonyl-D-Arginine;
Compound #16	(2S,4S)-2-(6-N,N-Dimethylaminopurin-9- yl)-4-(methyloxycarbonyl-D-Arginine)- 1,3-dioxolane;
Compound #17	N-5-(6-N,N-Dimethylamino-8-bromopurin-9- yl)-pentoxycarbonyl-L-Arginine;
Compound #18	N-5-(6-N,N-Dimethylamino-8-bomopurin-9- yl)-pentoxycarbonyl-D-Arginine;
Compound #19	N-5-(Purin-9-yl)-pentanol;
Compound #20	N-5-(Purin-9-yl)-pentoxycarbonyl-D- Arginine;

- Compound #21 N-5-(Purin-9-yl)-pentoxycarbonyl-L-Arginine;
- Compound #22 N-5-(6-N,N-Dimethylaminopurin-9-yl)-pentoxycarbonyl-L-Valyl-L-Prolyl-L-Leucine;
- Compound #23 N-5-(6-N,N-Dimethylaminopurin-9-yl)-pentoxycarbonyl-L-Isoleucyl-L-Prolyl-L-Isoleucine;
- Compound #24 N-5-(6-N-Cyclopropylaminopurin-9-yl)-pentanol;
- Compound #25 N-5-(6-N-Cyclopropylaminopurin-9-yl)-pentoxycarbonyl-D-Arginine;
- Compound #26 N-5-(6-N-Cyclopropylaminopurin-9-yl)-pentoxycarbonyl-L-Arginine;
- Compound #27 N-5-(6-N-Azetidinepurin-9-yl)-pentanol;
- Compound #28 N-5-(6-N-Azetidinepurin-9-yl)-pentoxycarbonyl-D-Arginine;
- Compound #29 N-5-(6-N-Azetidinepurin-9-yl)-pentoxycarbonyl-L-Arginine;
- Compound #30 trans-(6-N-Chloropurin-9-yl)-4-methyl-cyclohexyl-methanol;
- Compound #31 trans-(6-N,N-Dimethylaminopurin-9-yl)-4-methyl-cyclohexyl-methanol;
- Compound #32 trans-(6-N,N-Dimethylaminopurin-9-yl)-4-methyl-cyclohexyl-methyloxycarbonyl-D-Arginine;
- Compound #34 trans-(6-N-Methoxypurin-9-yl)-4-methyl-cyclohexyl-methanol;
- Compound #35 cis-(6-N,N-Dimethylaminopurin-9-yl)-4-methyl-cyclohexyl-methanol;
- Compound #36 cis-(6-N,N-Dimethylaminopurin-9-yl)-4-methyl-cyclohexyl-methyloxycarbonyl-D-arginine;

- Compound #37 N-5-(6-N,N-Dimethylaminopurin-9-yl)-
pentoxycarbonyl-D-Citrulline;
- Compound #38 N-5-(6-N-Methylaziridinepurin-9-yl)-
pentanol;
- Compound #39 N-5-(6-N-Methylaziridinepurin-9-yl)-
pentoxycarbonyl-D-Arginine;
- Compound #40 N-5-(6-N,N-Dimethylaminopurin-9-yl)-
thioethoxy-ethoxycarbonyl-D-Arginine;
- Compound #41 Meta-(6-N,N-Dimethylaminopurin-9-yl)-
methyl-benzyloxycarbonyl-D-Arginine;
- Compound #42 N-5-(6-N,N-Dimethylaminopurin-9-yl)-3-
pentynyl-1-oxycarbonyl-D-Arginine;
- Compound #43 N-5-[6-(1-methyl-2-acetoxy)-
ethylaminopurin-9-yl]-pentanol;
- Compound #44 N-5-[6-(1-methyl-2-acetoxy)-
ethylaminopurin-9-yl]-pentoxycarbonyl-D-
Arginine;
- Compound #45 N-5-(2,6-Dichloropurin-9-yl)-pentanol;
- Compound #46 N-5-(2,6-Dichloropurin-9-yl)-
pentoxycarbonyl-D-Arginine;
- Compound #47 N-5-(2,6-Dichloropurin-9-yl)-
pentoxycarbonyl-L-Arginine;
- Compound #48 N-5-(2-Amino-6-N,N-Dimethylaminopurin-9-
yl)-pentanol;
- Compound #49 N-5-(6-N,N-Dimethylamino-8-
methylthiopurin-9-yl)-pentanol;
- Compound #50 N-5-(6-N,N-Dimethylamino-8-
methylthiopurin-9-yl)-pentoxycarbonyl-D-
Arginine;
- Compound #51 N-5-(6-N-Methoxypurin-9-yl)-pentanol;
- Compound #52 N-5-(6-N-Methoxypurin-9-yl)-
pentoxycarbonyl-D-Arginine;
- Compound #53 N-5-(2-chloro-6-methoxypurin-9-yl)-
pentoxycarbonyl-D-Arginine;

- Compound #54 N-5-(6-N,N-Dimethylaminopurin-9-yl)-
pentoxycarbonyl-D-Ornithine;
- Compound #55 N-5-(6-N,N-Dimethylaminopurin-9-yl)-
pentoxycarbonyl-L-Ornithine;
- Compound #56 N-5-(6-N,N-Dimethylaminopurin-9-yl)-
pentoxycarbonyl-L-Valine;
- Compound #57 N-5-(6-N,N-Dimethylaminopurin-9-yl)-
pentoxycarbonyl-D-Valine;
- Compound #58 N-5-(6-N,N-Dimethylaminopurin-9-yl)-
pentoxycarbonylethylamine hydrochloride;
- Compound #59 N-5-(6-N-Mercaptopurin-9-yl)-pentanol;
- Compound #60 N-5-(6-N-Methylthiopurin-9-yl)-pentanol;
- Compound #62 N-4-(6-N,N Dimethyaminopurin-9-yl)-
butanol
- Compound #63 N-4-(6-N,N-Dimethylaminopurin-9-yl)-
butoxycarbonyl-D-Arginine;
- Compound #64 N-4-(6-N,N-Dimethylaminopurin-9-yl)-
butoxycarbonyl-L-Arginine;
- Compound #65 N-6-(6-N-Chloropurin-9-yl)-hexanol;
- Compound #66 N-6-(6-N,N-Dimethylaminopurin-9-yl)-
hexanol;
- Compound #67 N-6-(6-N,N-Dimethylaminopurin-9-yl)-
hexyloxycarbonyl-D-Arginine;
- Compound #68 N-6-(6-N,N-Dimethylaminopurin-9-yl)-
hexyloxycarbonyl-L-Arginine;
- Compound #72 N-5-(6-N,N-Dimethylaminopurin-9-yl)-
pentylamine hydrochloride salt;
- Compound #73 N-5-(6-Methylaziridinepurin-9-yl)-
pentyloxycarbonyl-L-Arginine;
- Compound #74 (2S,4S)-2-(6-N,N-Dimethylaminopurin-9-
yl)-4-hydroxymethyl-1,3-dioxolane;
- Compound #75 (1S,3R) and (1R,3S)-1-(6-N,N-
Dimethylaminopurin-9-yl)-methyl-3-
cyclopentane methanol;

- Compound #76 (1S,3R) and (1R,3S)-1-(6-N,N-Dimethylaminopurin-9-yl)-methyl-3-(methyloxycarbonyl-D-Arginine)-cyclopentane;
- Compound #77 (6-N,N-Dimethylaminopurin-9-yl)-7-ethylaminoethanol;
- Compound #78 (6-N,N-Dimethylaminopurin-9-yl)-7-ethylaminoethoxycarbonyl-D-Arginine;
- Compound #79 (6-N,N-Dimethylaminopurin-9-yl)-7-ethylaminoethoxycarbonyl-L-Arginine;
- Compound #80 N-5-(6-N,N-Dimethylaminopurin-9-yl)-3-pentyl-1-ol;
- Compound #81 N-5-(6-N,N-Dimethylaminopurin-9-yl)-3-pentynyl-1-oxycarbonyl-L-Arginine;
- Compound #82 (6-N,N-Dimethylaminopurin-9-yl)-7-thioethoxy-ethanol;
- Compound #83 (6-N,N-Dimethylaminopurin-9-yl)-7-thioethoxy-ethoxycarbonyl-L-Arginine;
- Compound #84 (2S,4S) and (2R,4R)-2-(6-N,N-Dimethylaminopurin-9-yl)-4-(methoxycarbonyl-D-Arginine)-1,3-oxathiolane;
- Compound #85 (6-N,N-Dimethylaminopurin-9-yl)-7-ethoxy-ethoxyethanol;
- Compound #86 (6-N,N-Dimethylaminopurin-9-yl)-7-ethoxy-ethoxycarbonyl-D-Arginine;
- Compound #87 (6-N,N-Dimethylaminopurin-9-yl)-7-ethoxy-ethoxycarbonyl-L-Arginine; and
- Compound #88 N-5-(6-N,N-Dimethylamino-8-bromopurin-9-yl)-pentanol;

or a pharmaceutically acceptable derivative thereof."

Claims 2 to 5 of that fresh set of claims were dependent on claim 1 and claims 6 to 11 were directed to pharmaceutical compositions comprising a compound as defined in claim 1.

The Appellant submitted that this fresh set of claims reflected the preferred scope of the present invention. Thus, present claim 1 has been restricted to the list of individual compounds found in original dependent claim 27. Therefore the provisions of Article 123 (2) EPC have been met. Due to the substantial amendments made to the subject-matter claimed the fresh set of claims overcame the objections raised in the decision under appeal, thereby requiring substantive examination to be done on a new basis.

- IV. The Appellant requested that the decision under appeal be set aside and the case be remitted for further prosecution on the basis of the sole request submitted at oral proceedings of 26 August 2004.
- V. At the end of the oral proceedings the decision of the Board was announced.

Reasons for the Decision

- 1. The appeal is admissible.
- 2. *Amendments (123(2) EPC)*

Fresh claim 1 is based on original claim 27 in combination with original claim 1. Claims 2 to 5 are supported by original claims 28, 8 and 29. Claims 6 and

8 to 10 are disclosed in original claims 37 and 30 to 32. Claim 7 has a proper basis in original claim 38 in combination with page 28, line 15 of the description as filed. Claim 11 is backed up by original claim 33 and page 28, lines 8 to 12 of the application as filed.

Therefore, the amendments made to the claims do not generate subject-matter extending beyond the content of the application as filed and the Board concludes that the requirements of Article 123(2) EPC are satisfied.

3. *Remittal*

- 3.1 Having so decided, the Board has not, however, taken a decision on the whole matter, since substantial amendments have been made to independent claim 1 which amended claim was presented for the first time at the oral proceedings before the Board. The decision under appeal dealt exclusively with lack of novelty and inventive step of claim 1 according to the then pending request and did not consider claim 1 in the present form as such request was never submitted to the first instance. The amendments leading to fresh claim 1, in particular in restricting the scope of that claim from the previous *Markush*-formula to a list of 85 individual chemical compounds, have the effect that the reasons given in the contested decision for refusing the present application no longer apply since the present claims have never been challenged under Article 54 and 56 EPC for lack of novelty and inventive step.

Thus, the Board considers that the substantial amendments made by the Appellant remove all the objections raised in the decision under appeal and that

present claim 1 generates a fresh case not yet addressed in examination proceedings and requiring reexamination.

While Article 111(1), second sentence, first alternative, EPC gives the Boards of Appeal the power to decide in *ex-parte* proceedings on fresh issues where the application has been refused on other issues, proceedings before the Boards of Appeal in *ex-parte* cases are primarily concerned with examining the contested decision (see decision G 10/93, OJ EPO 1995, 172, points 4 and 5 of the reasons), fresh issues normally being left to the Examining Division to consider after a referral back, so that the Appellant has the opportunity for these to be examined and decided upon without "loss of an instance".

Under these circumstances, the examination not having been concluded and the Appellant having requested remittal, the Board considers it appropriate to exercise the power conferred on it by Article 111(1), second sentence, second alternative, EPC to remit the case to the Examining Division for further prosecution.

- 3.2 The Board has noticed the following issues as needing consideration when resuming examination proceedings. The first instance, when reconsidering the substantive issues, in particular inventive step, should take into account the document J. Med. Chem. 1997, pages 2884 to 2894 submitted by the Appellant-Applicant disclosing that only some of the claimed compounds appear to show the particular immunomodulating activity aimed at. Furthermore, the question may arise whether or not the list of individual compounds in claim 1 is in keeping

with the requirement of unity according to Article 82 EPC. Last but not least, the chemical names given to the compounds listed in the claims need redrafting in view of the requirements of Article 84 EPC since they are simply incorrect and not in line with the rules of chemical nomenclature; for example, compound #1 is labelled differently in claims 1 and 2, though it is the same chemical compound.

Order

For these reasons it is decided that:

1. The decision under appeal is set aside.
2. The case is remitted to the first instance for further prosecution on the basis of the sole request submitted at oral proceedings on 26 August 2004.

The Registrar:

The Chairman:

N. Maslin

J. Jonk