Internal distribution code:

(A) [-] Publication in OJ
(B) [-] To Chairmen and Members
(C) [-] To Chairmen
(D) [X] No distribution

Datasheet for the decision of 4 April 2014

Case Number: T 0499/12 - 3.3.01

Application Number: 04784319.8

Publication Number: 1664091

IPC: C07K5/10, C07K5/08, A61K38/07, A61P31/12

Language of the proceedings: EN

Title of invention:
INHIBITORS OF SERINE PROTEASES, PARTICULARLY HCV NS3-NS4A PROTEASE

Applicant:
Vertex Pharmaceuticals Inc.

Headword:
HCV NS3-NS4A protease inhibitors/VERTEX

Relevant legal provisions:
EPC Art. 123(2), 54, 56

Keyword:
Amended claims at appeal, specific compounds: novelty, inventive step (yes)

Europäisches Patentamt
European Patent Office
Office européen des brevets

Beschwerdekammern
Boards of Appeal
Chambres de recours

European Patent Office
D-80298 MUNICH
GERMANY
Tel. +49 (0) 89 2399-0
Fax +49 (0) 89 2399-4465

Case Number: T 0499/12 - 3.3.01

D E C I S I O N
of Technical Board of Appeal 3.3.01
of 4 April 2014

Appellant: (Applicant)	Vertex Pharmaceuticals Inc. 50 Northern Avenue Boston, MA 02210 (US)
Representative:	Burrichter, A. COHAUSZ & FLORACK Patent- und Rechtsanwälte Partnerschaftsgesellschaft Bleichstrasse 14 40211 Düsseldorf (DE)
Decision under appeal:	**Decision of the Examining Division of the European Patent Office posted on 10 October 2011 refusing European patent application No. 04784319.8 pursuant to Article 97(2) EPC.**

Composition of the Board:

Chairman: A. Lindner
Members: L. Seymour
L. Bühler

Summary of Facts and Submissions

I. The present appeal lies from the decision of the examining division refusing the European patent application No. 04 784 319.8, which was filed as the international application published as WO 2005/028502 with filing date of 17 September 2004 and claiming priority of 18 September 2003 from the US patent application number 60/504,405.

II. The following documents were cited during the examination procedure (cf. decision under appeal, point XI; note: document (2) is omitted, since it identical to document (8)):

(1) WO 03/035060

(3) W. Han et al., Bioorg. Med. Chem. Lett., 2000, 10, 711-713

(4) WO 2004/092162

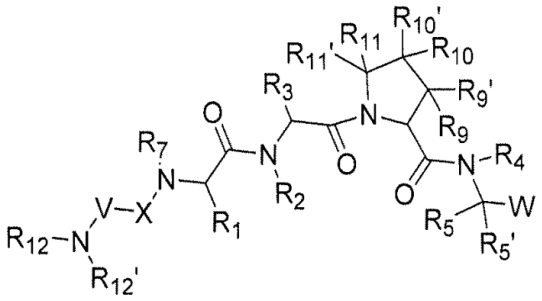
(5) WO 03/087092

(6) WO 02/08244

(7) WO 02/08256

(8) WO 03/006490

III. The decision under appeal was based on the main and sole request filed with letter dated 12 August 2011. Claim 1 of this request related to a compound defined by means of the following Markush formula I (definition of variables omitted by the board for reasons of conciseness):



I

In its analysis of inventive step, the examining division identified the closest prior art as being document (8), and defined the problem to be solved as lying in the provision of alternative NS3-NS4 serine protease inhibitors. The proposed solution, characterised in the definition of the terminal group (R_{12},R_{12}')N-V-, was found to be obvious in the light of document (8) alone, as falling within the customary variations that would be contemplated by the skilled person.

IV. The appellant (applicant) lodged an appeal against this decision.

V. Summons to attend oral proceedings before the board were sent on 6 December 2013, followed by a communication dated 20 December 2013.

VI. With letter dated 16 January 2014, the appellant filed a main request and three auxiliary requests, and provided arguments in favour of inventive step.
In response to a further communication dated 28 January 2014, the appellant stated in its letter of 29 January 2014 that the previous third auxiliary request was now its main and sole request. With letter of 6 February 2014, the appellant filed an amended description.

VII. With a communication dated 11 February 2014, the board provided a version of an adapted description containing all the amendments considered to be necessary in order to fully bring this in line with the new main request.

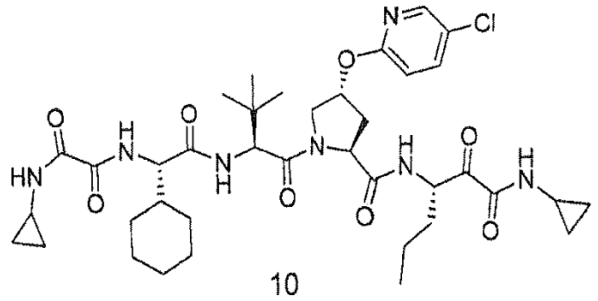
VIII. With letter dated 12 February 2014, received on 13 February 2014, the appellant stated that it agreed to the description amended by the board. Two description pages containing further amendments were additionally filed.

IX. By communication dated 17 February 2014, the appellant was informed that the oral proceedings appointed for 19 February 2014 were cancelled.

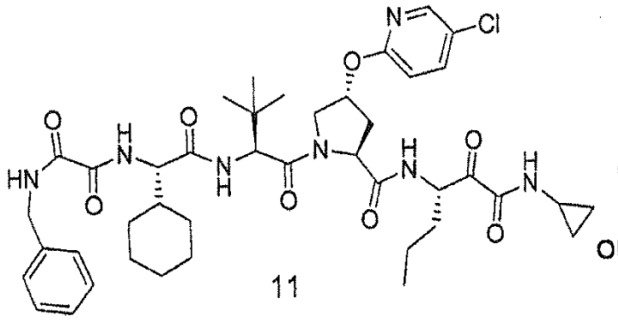
X. With letter of 19 March 2014, the appellant filed a set of claims as a replacement main request, which differed from the request originally filed as auxiliary request 3 with letter of 16 January 2014 (cf. above point VI) in a correction to claim 1.

Claim 1 of the main request reads as follows:

"1. A compound selected from:

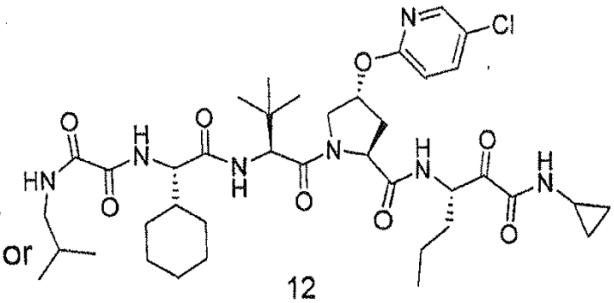


10



11

or



12

or a pharmaceutically acceptable salt thereof."

XI. The appellant (applicant) requested in writing that the decision under appeal be set aside and that a patent be granted on the basis of the main request filed with letter dated 19 March 2014.

Reasons for the Decision

1. The appeal is admissible.

Main and sole request

2. *Amendements (Article 123(2) EPC)*

Claim 1 is based on claims 1 and 45 as originally filed. The basis for remaining claims 2 to 7 is to be found in claims 46 to 50 and 53 as originally filed.

Consequently, the subject-matter of the main request meets the requirements of Article 123(2) EPC.

3. *Novelty (Articles 52(1), 54 EPC)*

Since none of the prior art documents cited during the examination procedure (cf. above point II) disclose the specific compounds now listed in claim 1 (cf. above point X), the subject-matter of the main request is considered to be novel.

4. *Inventive step (Articles 52(1), 56 EPC)*

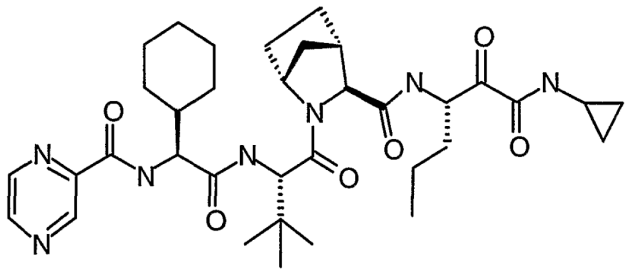
4.1 Document (4) was published after the present filing date, and document (5) after the present priority date, which is validly claimed for the subject-matter of the main request. Therefore, these documents are not to be regarded as state of the art according to Article 54(2) EPC, and are not relevant to the question of inventive step.

4.2 The subject-matter of claim 1 relates to three specifically defined peptide derivatives (cf. above point X). These are useful in inhibiting hepatitis C virus NS3-NS4A protease (cf. present application, paragraph [0002]).

4.3 The board considers, in agreement with the appellant and the examining division, that document (8) can be seen as representing the closest state of the art.

Document (8) also relates to peptidomimetic compounds having the same activity as the present compounds, which are characterised by a bridged bicyclic moiety at the P2 position (see e.g. page 1, lines 6 to 13 and

claim 1). A number of specific examples are listed in Table 1 (pages 45 to 51), including compound 2, which is reproduced here since it is illustrative of the structurally closest compounds to those now claimed:



4.4 The problem to be solved in the light of document (8) may be defined as lying in the provision of alternative NS3-NS4 serine protease inhibitors.

It is noted in this context that, in its letter of 16 January 2014, the appellant additionally defined the problem to be solved in terms of providing an improvement over the prior art. However, it is not apparent that the conditions employed in the assay protocols according to document (8) and the present application are strictly comparable (cf. examples 8 and 4, respectively). It follows that a comparison of the data displayed in the respective Tables 1 cannot be regarded as being conclusive.

4.5 The solution proposed relates to compounds as defined in claim 1 characterised in the presence of an oxamide group (i.e. R(H)N-CO-CO-N(H)-) instead of a heteroaryl-CO-N(H)- group as a terminal moiety, and of the (5-chloropyridin-2-yl)oxy substituent at the pyrrolidine ring, instead of a bridging substituent.

Based on the experimental results reported in Table 1 of the application in suit (see paragraph [0281]), the

board is satisfied that the problem posed has been solved.

4.6 Finally, it remains to be investigated whether the proposed solution is obvious to the skilled person in the light of the prior art.

As outlined above in point 4.3, document (8) teaches compounds characterised in having a bridged bicyclic moiety at the P2 position. This document alone cannot therefore render the claimed subject-matter obvious.

The further cited documents (1), (3), (6) and (7), which all relate to the same technical field as the application in suit, also do not suggest the present compounds:

The teaching of document (1), like document (8), is confined to derivatives exhibiting polycyclic ring systems at the P2 position.

Document (3) also does not provide any teaching with respect to the present derivatisation at the pyrrolidine ring, or regarding a terminal oxamide group (cf. Table 1).

In documents (6) and (7), the derivatisation at the pyrrolidine ring with oxy substituents is envisaged (see e.g. document (6), claim 20; document (7), claim 52). However, the compounds disclosed therein are structurally remote from the present compounds (see e.g. document (6), pages 141 to 180; document (7), compounds 40 to 42 on pages 68, 69). There is no suggestion directing the skilled person to the present (5-chloropyridin-2-yl)oxy and oxamide groups.

Consequently, documents (1), (3), (6) and (7) do not provide the skilled person with any incentive to modify the structurally closest prior art compounds according to document (8), such as compound 2 depicted above in point 4.3, in order to arrive at the compounds now claimed.

4.7 In view of the above considerations, the board concludes that the subject-matter of claim 1 of the main request involves an inventive step. The same applies to the remaining claims, relating to pharmaceutical compositions and uses thereof.

Accordingly, the subject-matter of the main request meets the requirements of Articles 52(1) and 56 EPC.

Order

For these reasons it is decided that:

1. The decision under appeal is set aside.

2. The case is remitted to the department of first instance with the order to grant a patent in the following version:

   - Description pages 1 to 5, 50 to 55, 64 to 71, 75, and 77 to 102 attached to communication dated 11 February 2014

   - Description pages 6 and 76 filed with letter dated 12 February 2014, received on 13 February 2014

   - Claims 1 to 7 filed with letter dated 19 March 2014

The Registrar: The Chairman:

M. Schalow A. Lindner

Decision electronically authenticated