UNITED STATES PATENT AND TRADEMARK OFFICE

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BEFORE THE PATENT TRIAL AND APPEAL BOARD

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MYLAN PHARMACEUTICALS INC.,

Petitioner,

v.

BAUSCH HEALTH IRELAND LIMITED,

Patent Owner.

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Case IPR2022-00722
U.S. Patent No. 7,041,786

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DECLARATION OF KUNWAR SHAILUBHAI

I, Kunwar Shailubhai, under penalty of perjury, declare as follows:

I.   INTRODUCTION

1.   I am of legal age and otherwise competent to make this declaration.

2.   I am the first named inventor on U.S. Patent No. 7,041,786 (Ex. 1001, "the '786 patent"). I have been asked to submit a declaration attesting to how the data disclosed in Table 4 in the specification of the '786 patent and other relevant data related to the peptides disclosed in the '786 patent were generated.

II.   EDUCATION AND WORK EXPERIENCE

3.   I graduated from the Maharaja Sayajirao University of Baroda with a Ph.D. in Microbiology in 1984 and from the University of Missouri-Saint Louis with an M.B.A. in 2002.

4.   I am currently employed by the Pennsylvania Biotechnology Center and Baruch S. Blumberg Institute as a Senior Advisor and Professor.

III.   BIOLOGICAL ACTIVITY DATA IN TABLE 4 OF THE '786 PATENT

5.   I was involved in synthesizing and testing of guanylate cyclase ("GC-C") receptor agonists that enhance intracellular production of cyclic guanosine monophosphate ("cGMP"), including the peptides of the experimental examples reported in the '786 patent. As such, I have first-hand knowledge of how the peptides reported below were made and tested.

6.   I directed the synthesis and testing of the GC-C receptor agonist

peptides in order to examine biological activity as disclosed in Table 4 of the '786

patent.

7.   Human T84 colon carcinoma cells were obtained from the American

Type Culture Collection. (*Id.* at 15:27-29). Cells were grown in a 1:1 mixture of

Ham's F-12 medium and Dulbecco's modified Eagle's medium ("DMEM")

supplemented with 10% fetal bovine serum, 100 U penicillin/ml, and 100 μg/ml

streptomycin. (*Id.* at 15:29-32). The cells were fed fresh medium every third day

and split at a confluence of approximately 80%. (*Id.* at 15:32-34).

8.   Peptides were custom synthesized by Multiple Peptide Systems, San

Diego, California, and by Princeton Biomolecules, Langhorne, Pennsylvania. (*Id.*

at 15:36-38). Biological activity of the synthetic peptides was assayed. (*Id.* at

15:38-39). The confluent monolayers of T84 cells in 24-well plates were washed

twice with 250 μl of DMEM containing 50 mM HEPES (pH 7.4), pre-incubated at

37°C for 10 minutes with 250 μl DMEM containing 50 mM HEPES (pH 7.4) and 1

mM isobutylmethylxanthine ("IBMX"), followed by incubation with peptides (0.1

nM to 10 μM) for 30 minutes. (*Id.* at 15:40-46). The medium was aspirated, and

the reaction was terminated by the addition of 3% perchloric acid. (*Id.* at 15:46-

47). Following centrifugation, and neutralization with 0.1 N NaOH, the

supernatant was used directly for measurements of cGMP using an ELISA kit

(Caymen Chemical, Ann Arbor, Michigan). (*Id.* at 15:47-50).

     9.   As indicated in the following table, the peptides were custom

synthesized and purified (>95% purity) using a published procedure (procedure

from Klodt, et al., *J. Peptide Res.* 50:222-230 (1997)). (*Id.* at 15:53-54, 18:32).

Peptides were evaluated in the T84 cell-based assay for their ability to enhance

intracellular levels of cGMP. (*Id.* at 15:55-56). The results of this test are shown

in Table 4 below.

Peptide agc	
SEQ ID NO.*	
1	
6	
7	
20	
14	
4	
21	

*SEQ ID's for SP301, S

sequences for these anal

**Intracellular cGMP lev

1 micromolar solution o

The value observed for S

(*Id.* at 16:1-19). I note that the p value below Table 4 contains a typographical

error and should say $p < 0.05$. (*Id.* at 16:19).

IV. DATA IN STUDY NUMBER SP-PH-001

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11. ██

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13. ████████████████████████████████████

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