

UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE PATENT TRIAL AND APPEAL BOARD

Merck Sharp & Dohme LLC,
Petitioner,

v.

Halozyme Inc.,
Patent Owner.

Case No. PGR2025-00087
U.S. Patent No. 12,371,685

Declaration of Jeffrey P. Kushan

I, Jeffrey P. Kushan, make the following Declaration pursuant to 28 U.S.C. § 1746:

1. I am a partner at the law firm of Sidley Austin LLP.
2. I provide this declaration in connection with the above-identified post grant review proceeding before the United States Patent and Trademark Office and initiated by Merck Sharp & Dohme LLC (“Merck”) against Halozyme Inc. under 35 U.S.C. § 321. Unless otherwise stated, the facts stated in this Declaration are based on my personal knowledge.
3. For each of the exhibits addressed below, an exhibit label and page numbers have been added, but no other alterations have been made. Where the exhibit is a PDF generated from a webpage displayed in a web browser, the PDF may contain information in the header and footer (*e.g.*, the URL, the title of the page being displayed, or similar items), which was generated automatically by the web browser displaying the page.
4. Exhibit 1010 is a true and correct copy of a publication by Ling Zhang, et al., titled “Hyaluronidase Activity of Human Hyal1 Requires Active Site Acidic and Tyrosine Residues” (“Zhang”). This paper was published as a chapter in “The Journal of Biological Chemistry,” Vol. 284, on pages 9433-9442. A true and correct copy of this paper was obtained from the following URL:

<https://www.sciencedirect.com/science/article/pii/S0021925820323425>. As the

Zhang paper itself does not include Supplemental Figure 1 or Supplemental Table 1, I have appended the supplementary material at the end of Exhibit 1010, as pages 9443-9445. Pages 9443-9445 of Exhibit 1010 are a true and correct copy of the PDF file available for download from the following URL:

<https://www.sciencedirect.com/science/article/pii/S0021925820323425#sec1>.

5. EX1015 is a document mapping citations in Merck's Petition to U.S. Patent No. 12,371,685 ("the '685 Patent") to corresponding text in U.S. Patent Application No. 13/694,731 ("the '731 Application"). This mapping was prepared by staff at my law firm working under my supervision, and is true and accurate to the best of my knowledge.

6. Exhibit 1016 is a true and correct copy of a publication by Boris Steipe titled "Consensus-Based Engineering of Protein Stability: From Intrabodies to Thermostable Enzymes" ("Steipe"). This paper was published as a chapter in "Methods in Enzymology," Vol. 388, on pages 176-186. As the Steipe paper itself does not include the year in which it was published, I have appended the publication information at the end of Exhibit 1016, as pages 187-192. Pages 187-192 of Exhibit 1016 are a true and correct copy of the web page available from the following URL:

<https://www.sciencedirect.com/science/article/abs/pii/S0076687904880169>

7. Exhibit 1024 is a true and correct copy of a publication by Sanna Rosengren, et al., titled “Recombinant Human PH20: Baseline Analysis of the Reactive Antibody Prevalence in the General Population Using Healthy Subjects” (“Rosengren 2018”). This paper was published as a chapter in “BioDrugs,” Vol. 32, on pages 83-89. A true and correct copy of this paper was obtained from the following URL: <https://link.springer.com/article/10.1007/s40259-018-0260-y>. As the Rosengren 2018 paper itself does not include Supplemental Table 1, I have appended the supplementary material at the end of Exhibit 1024, as pages 90-91. Pages 90-91 of Exhibit 1024 are a true and correct copy of the PDF file available for download from the following URL:
<https://link.springer.com/article/10.1007/s40259-018-0260-y#Sec17>.

8. Exhibit 1037 is a true and correct copy of a publication by Pascal Benkert, et al., titled “Toward the Estimation of the Absolute Quality of Individual Protein Structure Models” (“Benkert”). This paper was published as a chapter in “Bioinformatics,” Vol. 27, on pages 343-350. A true and correct copy of this paper was obtained from the following URL:
<https://academic.oup.com/bioinformatics/article/27/3/343/320383?login=true>. As the Benkert paper itself does not include the supplementary figures and tables, I have appended the supplementary data at the end of Exhibit 1037, as pages 351-369. Pages 351-369 of Exhibit 1037 are a true and correct copy of the zip file

available for download from the following URL:

<https://academic.oup.com/bioinformatics/article/27/3/343/320383#supplementarydata>.

9. Exhibit 1040 is a true and correct copy of a publication by Yanan He, et al., titled “NMR Structures of Two Designed Proteins with High Sequence Identity but Different Fold and Function” (“He”). This paper was published as a chapter in “PNAS,” Vol. 105, on pages 14412-14417. A true and correct copy of this paper was obtained from the following URL:

<https://www.pnas.org/doi/10.1073/pnas.0805857105>. As the He paper itself does not include the supporting figures and tables, I have appended the supporting information at the end of Exhibit 1040, as pages 14418-14421. Pages 14418-14421 of Exhibit 1040 are a true and correct copy of the PDF file available for download from the following URL:

<https://www.pnas.org/doi/10.1073/pnas.0805857105#supplementary-materials>.

10. Exhibit 1041 is a true and correct copy of a publication by Patrick A. Alexander, et al., titled “A Minimal Sequence Code for Switching Protein Structure and Function” (“Alexander”). This paper was published as a chapter in “PNAS,” Vol. 106, on pages 21149-21154. A true and correct copy of this paper was obtained from the following URL:

<https://www.pnas.org/doi/10.1073/pnas.0906408106>. As the Alexander paper

itself does not include the supporting text, figures, and tables, I have appended the supporting information at the end of Exhibit 1041, as pages 21155-21160. Pages 21155-21160 of Exhibit 1041 are a true and correct copy of the PDF file available for download from the following URL:

<https://www.pnas.org/doi/10.1073/pnas.0906408106#supplementary-materials>.

11. Exhibit 1042 is a true and correct copy of a publication by Biao Ruan, et al., titled “Design and Characterization of a Protein Fold Switching Network” (“Ruan”). This paper was published as a chapter in “Nature Communications,” Vol. 14, on pages 1-14. A true and correct copy of this paper was obtained from the following URL: <https://www.nature.com/articles/s41467-023-36065-3>. As the Ruan paper itself does not include the supplemental figures, tables and descriptions, I have appended the supplementary information at the end of Exhibit 1042, as pages 15-30. Pages 15-30 of Exhibit 1042 are a true and correct copy of the PDF file available for download from the following URL:

<https://www.nature.com/articles/s41467-023-36065-3#Sec29>.

12. Exhibit 1043 is a true and correct copy of a publication by Sievers, et al., titled “Fast, Scalable Generation of High-Quality Protein Multiple Sequence Alignments Using Clustal Omega” (“Sievers”). This paper was published as a chapter in “Molecular Systems Biology,” Vol. 7, on pages 1-6. A true and correct copy of this paper was obtained from the following URL:

<https://www.embopress.org/doi/full/10.1038/msb.2011.75>. As the Sievers paper itself does not include the supplementary information, I have appended the supplementary information at the end of Exhibit 1043, as pages 7-17. Pages 7-17 of Exhibit 1043 are a true and correct copy of the PDF file available for download from the following URL:

<https://www.embopress.org/doi/full/10.1038/msb.2011.75#supplementarymaterials>
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13. Exhibit 1044 is a true and correct copy of a publication by Josip Mihel, et al., titled “PSAIA – Protein Structure and Interaction Analyzer” (“Mihel”). This paper was published as a chapter in “BMC Structural Biology,” Vol. 8, on pages 1-11. A true and correct copy of this paper was obtained from the following URL:

<https://bmcstructbiol.biomedcentral.com/articles/10.1186/14726807-8-21>. The Mihel paper is accompanied by electronic supplementary materials, also available at <https://bmcstructbiol.biomedcentral.com/articles/10.1186/1472-6807-8-21#Sec22>. As the electronic supplementary materials are published as native files, I have included those native files for Exhibit 1044 with the materials being served in the submission of the Petition for Post Grant Review in the PGR2025-00087 proceeding. The native files are available for download from the following URL: <https://bmcstructbiol.biomedcentral.com/articles/10.1186/1472-6807-8-21#Sec22>.

14. Exhibit 1045 is a true and correct copy of a redline that I had created for U.S. Patent Application No. 13/694,731 and U.S. Patent No. 12,371,685 using Litera Compare in Microsoft Word. To create this redline, the text of U.S. Patent Application No. 13/694,731 (as published in U.S. Patent Application Publication 2013-0302275) was copied and compared to the text of U.S. Patent No. 12,371,685, both obtained from the USPTO's Patent Center website. The text of both documents was pasted into separate Word documents. Any text that appeared before the "Background/Summary" heading and the claim language was deleted. The Word document with the text from U.S. Patent Application No. 13/694,731 was designated as the original file and the Word document with the text from U.S. Patent No. 12,371,685 was designated as the modified file. I saved the redline as a PDF and included it here as Exhibit 1045. The redline shows certain differences as a result of formatting changes (principally in the presentation of tables). In my review of the redline (with two exceptions¹), I have not identified any substantive

¹ The '685 Patent alters the list of mutations that should be avoided in enzymatically active PH20 proteins by removing positions 282, 298, and 431 from the list in the '731 Application. *See* EX1045, 78; *also* EX1001, 80:52-64; EX1026, 91:30-92:1. The '685 Patent also changes the list of which mutations to include in modified PH20 polypeptides that exhibit

differences between U.S. Patent Application No. 13/694,731 and U.S. Patent No. 12,371,685, and I believe them to be substantively identical.

- a. The text file that I copied for the '731 Application is available from the following URL:

<https://ppubs.uspto.gov/pubwebapp/authorize.html?redirect=patents/html/20130302275?source=US-PGPUB>.

- b. The text file that I copied for the '685 Patent is available from the following URL:

<https://ppubs.uspto.gov/pubwebapp/authorize.html?redirect=patents/html/12371685?source=USPAT>.

15. Exhibit 1049 (“KEGG, DRUG: Hyaluronidase (human recombinant)”) is a true and correct copy of the web page available from the following URL: <https://www.genome.jp/entry/D06604>.

16. Exhibit 1053 is a true and correct copy of a native file produced by Dr. Sheldon Park, titled “hom_pre2011.txt”.

increased hyaluronidase activity by removing position 320 from the list in the '731 Application. *See* EX1045, 13; *also* EX1001, 13:38-14:24; EX1026, 13:4-37.

17. Exhibit 1054 is a true and correct copy of a native file produced by Dr. Sheldon Park, titled “hom_pre2011_header.txt”.

18. Exhibit 1055 is a true and correct copy of a native file produced by Dr. Sheldon Park, titled “hom_pre2011_header_clean.txt”.

19. Exhibit 1056 is a true and correct copy of a native file produced by Dr. Sheldon Park, titled “hom_pre2011.fasta”.

20. Exhibit 1057 is a true and correct copy of a native file produced by Dr. Sheldon Park, titled “ph20_pre2011.align-clustal_num”.

21. Exhibit 1058 is a true and correct copy of the html display of a native file produced by Dr. Sheldon Park, titled “ph20_pre2011.align-clustal_num”.

22. Exhibit 1061 is a true and correct copy of a publication by Rosengren, et al., titled “Clinical Immunogenicity of rHuPH20, a Hyaluronidase Enabling Subcutaneous Drug Administration” (“Rosengren 2015”). This paper was published as a chapter in “AAPS Journal,” Vol. 17, on pages 1144-1156. A true and correct copy of this paper was obtained from the following URL:

<https://link.springer.com/article/10.1208/s12248-015-9782-0>. As the Rosengren 2015 paper itself does not include the supplemental clinical trial descriptions, I have appended the supplementary material at the end of Exhibit 1061, as pages 1157-1160. Pages 1157-1160 of Exhibit 1061 are a true and correct copy of the

DOCX file available for download from the following URL:

<https://link.springer.com/article/10.1208/s12248-015-9782-0#Sec17>.

23. Exhibit 1064 is a true and correct copy of a set of web pages available from the Internet Archive at the URLs listed below:

- a. Pages 1-2 of Exhibit 1064 (“Basic Local Alignment Search Tool”) are a true and correct copy of the web page available from the following URL:

https://web.archive.org/web/20110721055636/http://blast.ncbi.nlm.nih.gov/Blast.cgi?CMD=Web&PAGE_TYPE=BlastHome

- b. Page 3 of Exhibit 1064 (“Help”) is a true and correct copy of the web page available from the following URL:

https://web.archive.org/web/20110721055521/http://blast.ncbi.nlm.nih.gov/Blast.cgi?CMD=Web&PAGE_TYPE=BlastDocs

- c. Pages 4-22 of Exhibit 1064 (“Blast Program Selection Guide”) are a true and correct copy of the web page available from the following URL:

https://web.archive.org/web/20110721055500/http://blast.ncbi.nlm.nih.gov/Blast.cgi?CMD=Web&PAGE_TYPE=BlastDocs&DOC_TYPE=ProgSelectionGuide

- d. Pages 23-28 of Exhibit 1064 (“BLASTP Suite”) are a true and correct copy of the web page available from the following URL:

https://web.archive.org/web/20110728070830/http://blast.ncbi.nlm.nih.gov/Blast.cgi?PROGRAM=blastp&BLAST_PROGRAMS=blastp&PAGE_TYPE=BlastSearch&SHOW_DEFAULTS=on&LINK_LOC=blasthome

24. Exhibit 1065 is a true and correct copy of a set of web pages available from the Internet Archive at the URLs listed below:

- a. Pages 1-3 of Exhibit 1065 (“Clustal Omega”) are a true and correct copy of the web page available from the following URL:

<https://web.archive.org/web/20111022151531/http://www.clustal.org/omega/>

- b. Pages 4-13 of Exhibit 1065 (“Introduction”) are a true and correct copy of the web page available from the following URL:

<https://web.archive.org/web/20120110130931/http://www.clustal.org/omega/README>

25. Exhibit 1066 is a true and correct copy of a set of web pages available from the Internet Archive at the URLs listed below:

- a. Pages 1-2 of Exhibit 1066 (“SWISS-MODEL”) are a true and correct copy of the web page available from the following URL:

<https://web.archive.org/web/20110519141121/http://swissmodel.expasy.org/?pid=smh01&uid=&token=>

- b. Pages 3-4 of Exhibit 1066 (“Introduction to SWISS-MODEL Workspace”) are a true and correct copy of the web page available from the following URL:

<https://web.archive.org/web/20110519140410/http://swissmodel.expasy.org/?pid=smd11&uid=&token=>

- c. Pages 5-12 of Exhibit 1066 (“Help – Introduction to SWISS-MODEL Workspace”) are a true and correct copy of the web page available from the following URL:

<https://web.archive.org/web/20110519144707/http://swissmodel.expasy.org/?pid=smd02&uid=&token=>

- d. Pages 13-24 of Exhibit 1066 (“Tutorial – Introduction”) are a true and correct copy of the web page available from the following URL:

<https://web.archive.org/web/20110519144916/http://swissmodel.expasy.org/?pid=smd03&uid=&token=>

- e. Pages 25-26 of Exhibit 1066 (“SwissModel Automatic Modelling Mode”) are a true and correct copy of the web page available from the following URL:

https://web.archive.org/web/20110519141354/http://swissmodel.expasy.org/workspace/index.php?func=modelling_simple1

- f. Pages 27-28 of Exhibit 1066 (“Protein Structure & Model Assessment Tools”) are a true and correct copy of the web page available from the following URL:

https://web.archive.org/web/20110519144444/http://swissmodel.expasy.org/workspace/index.php?func=tools_structureassessment1&userid=USERID&token=TOKEN

- g. Pages 29-38 of Exhibit 1066 (“Template Library – Introduction to SWISS-MODEL Workspace”) are a true and correct copy of the web page available from the following URL:

https://web.archive.org/web/20110925072951/http://swissmodel.expasy.org/workspace/index.php?func=special_help&=#QMEAN6

- h. Pages 39-42 of Exhibit 1066 (“QMEAN Server – Quick Help”) are a true and correct copy of the web page available from the following URL:

<https://web.archive.org/web/20110924165101/http://swissmodel.expasy.org/qmean/cgi/index.cgi?page=help>

- i. Pages 43-44 of Exhibit 1066 (“Visualisation”) are a true and correct copy of the web page available from the following URL:

<https://web.archive.org/web/20110519144341/http://swissmodel.expasy.org/repository/?pid=smd08>

26. Exhibit 1067 is a true and correct copy of a set of web pages available from the Internet Archive at the URLs listed below:

- a. Page 1 of Exhibit 1067 (“PyMol”) is a true and correct copy of the web page available from the following URL:

<https://web.archive.org/web/20110701072314/http://pymol.org/>

- b. Pages 2-3 of Exhibit 1067 (“Support”) are a true and correct copy of the web page available from the following URL:

<https://web.archive.org/web/20110709092136/http://www.pymol.org/support>

- c. Pages 4-5 of Exhibit 1067 (“PyMOL Wiki”) are a true and correct copy of the web page available from the following URL:

https://web.archive.org/web/20110716184103/http://www.pymolwiki.org/index.php/Main_Page

- d. Pages 6-7 of Exhibit 1067 (“Commands”) are a true and correct copy of the web page available from the following URL:

<https://web.archive.org/web/20110714225113/http://www.pymolwiki.org/index.php/Category:Commands>

- e. Page 8 of Exhibit 1067 (“Center”) is a true and correct copy of the web page available from the following URL:
<https://web.archive.org/web/20110529094111/http://www.pymolwiki.org/index.php/Center>
- f. Pages 9-12 of Exhibit 1067 (“Color”) are a true and correct copy of the web page available from the following URL:
<https://web.archive.org/web/20110529095125/http://www.pymolwiki.org/index.php/Color>
- g. Pages 13-14 of Exhibit 1067 (“Create”) are a true and correct copy of the web page available from the following URL:
<https://web.archive.org/web/20110404080403/http://www.pymolwiki.org/index.php/Create>
- h. Page 15 of Exhibit 1067 (“Disable”) is a true and correct copy of the web page available from the following URL:
<https://web.archive.org/web/20110809113427/http://www.pymolwiki.org/index.php/Disable>
- i. Page 16 of Exhibit 1067 (“Enable”) is a true and correct copy of the web page available from the following URL:
<https://web.archive.org/web/20110809113452/http://www.pymolwiki.org/index.php/Enable>

- j. Pages 17-18 of Exhibit 1067 (“Extend”) are a true and correct copy of the web page available from the following URL:
<https://web.archive.org/web/20111013065541/http://www.pymolwiki.org/index.php/Extend>
- k. Pages 19-21 of Exhibit 1067 (“Get Area”) are a true and correct copy of the web page available from the following URL:
https://web.archive.org/web/20110515092633/http://www.pymolwiki.org/index.php/Get_Area
- l. Pages 22-23 of Exhibit 1067 (“Get Model”) are a true and correct copy of the web page available from the following URL:
https://web.archive.org/web/20071024002140/http://www.pymolwiki.org/index.php/Get_Model
- m. Pages 24-25 of Exhibit 1067 (“Hide”) are a true and correct copy of the web page available from the following URL:
<https://web.archive.org/web/20110523082224/http://www.pymolwiki.org/index.php/Hide>
- n. Pages 26-27 of Exhibit 1067 (“Select”) are a true and correct copy of the web page available from the following URL:
<https://web.archive.org/web/20110714221710/http://www.pymolwiki.org/index.php/Select>

- o. Pages 28-29 of Exhibit 1067 (“Set”) are a true and correct copy of the web page available from the following URL:
<https://web.archive.org/web/20101006204019/http://www.pymolwiki.org/index.php/Set>
- p. Page 30 of Exhibit 1067 (“Set Name”) is a true and correct copy of the web page available from the following URL:
https://web.archive.org/web/20110426091639/http://www.pymolwiki.org/index.php/Set_Name
- q. Pages 31-32 of Exhibit 1067 (“Show”) are a true and correct copy of the web page available from the following URL:
<https://web.archive.org/web/20110714224117/http://www.pymolwiki.org/index.php/Show>
- r. Pages 33-39 of Exhibit 1067 (“Cartoon”) are a true and correct copy of the web page available from the following URL:
<https://web.archive.org/web/20110728104502/http://www.pymolwiki.org/index.php/Cartoon>
- s. Pages 40-41 of Exhibit 1067 (“Lines”) are a true and correct copy of the web page available from the following URL:
<https://web.archive.org/web/20110522111856/http://www.pymolwiki.org/index.php/Lines>

- t. Pages 42-44 of Exhibit 1067 (“Spheres”) are a true and correct copy of the web page available from the following URL:
<https://web.archive.org/web/20110809121448/http://www.pymolwiki.org/index.php/Spheres>
- u. Pages 45-46 of Exhibit 1067 (“Sticks”) are a true and correct copy of the web page available from the following URL:
<https://web.archive.org/web/20110522120033/http://www.pymolwiki.org/index.php/Sticks>
- v. Pages 47-51 of Exhibit 1067 (“Surface”) are a true and correct copy of the web page available from the following URL:
<https://web.archive.org/web/20110607231738/http://www.pymolwiki.org/index.php/Surface>
- w. Page 52 of Exhibit 1067 (“Plugins”) is a true and correct copy of the web page available from the following URL:
<https://web.archive.org/web/20110728104325/http://www.pymolwiki.org/index.php/Category:Plugins>
- x. Pages 53-57 of Exhibit 1067 (“APBS”) are a true and correct copy of the web page available from the following URL:
<https://web.archive.org/web/20110728103647/http://www.pymolwiki.org/index.php/APBS>

- y. Page 58 of Exhibit 1067 (“TOPTOC”) is a true and correct copy of the web page available from the following URL:
<https://web.archive.org/web/20110606042538/http://www.pymolwiki.org/index.php/TOPTOC>
 - z. Page 59 of Exhibit 1067 (“Biochemical Properties”) is a true and correct copy of the web page available from the following URL:
https://web.archive.org/web/20110610033151/http://www.pymolwiki.org/index.php/Category:Biochemical_Properties
 - aa. Page 60 of Exhibit 1067 (“Nonstandard Amino Acids”) is a true and correct copy of the web page available from the following URL:
https://web.archive.org/web/20101129073634/http://www.pymolwiki.org/index.php/Nonstandard_Amino_Acids
 - bb. Pages 61-62 of Exhibit 1067 (“Mutagenesis”) are a true and correct copy of the web page available from the following URL:
<https://web.archive.org/web/20101121002000/http://www.pymolwiki.org/index.php/Mutagenesis>
27. Exhibits 1069-1075 are true and correct copies of html files produced by Dr. Sheldon Park, which were opened in an internet browser, and saved as PDF files.

I, Jeffrey P. Kushan, do hereby declare and state, that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, under Section 1001 of Title 18 of the United States Code.

Dated: November 10, 2025

Respectfully Submitted,

/Jeffrey P. Kushan

Jeffrey P. Kushan

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