

WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY

International application No.

PCT/KR2019/009215

Box No. 1

Basis of this opinion

1. With regard to the **language**, this opinion has been established on the basis of:
 - ☒ the international application in the language in which it was filed
 - ☐ a translation of the international application into _____, which is the language of a translation furnished for the purposes of international search (Rules 12.3(a) and 23.1(b)).
2. ☐ This opinion has been established taking into account the **rectification of an obvious mistake** authorized by or notified to this Authority under Rule 91 (Rule 43bis.1(b)).
3. ☒ With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, this opinion has been established on the basis of a sequence listing:
 - a. ☒ forming part of the international application as filed:
 - ☒ in the form of an Annex C/ST.25 text file.
 - ☐ on paper or in the form of an image file.
 - b. ☐ furnished together with the international application under PCT Rule 13ter.1(a) for the purposes of international search only in the form of an Annex C/ST.25 text file.
 - c. ☐ furnished subsequent to the international filing date for the purposes of international search only:
 - ☐ in the form of an Annex C/ST.25 text file (Rule 13ter.1(a)).
 - ☐ on paper or in the form of an image file (Rule 13ter.1(b) and Administrative Instructions, Section 713).
4. ☐ In addition, in the case that more than one version or copy of a sequence listing has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that forming part of the application as filed or does not go beyond the application as filed, as appropriate, were furnished.
5. Additional comments:

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Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non obvious), or to be industrially applicable have not been examined in respect of:

☐ the entire international application

☒ claims Nos. 18, 12-29

because:

☐ the said international application, or the said claims Nos. _____ relate to the following subject matter which does not require an international search (*specify*):

☒ the description, claims or drawings (*indicate particular elements below*) or said claims Nos. 22-24, 26-29 are so unclear that no meaningful opinion could be formed (*specify*):

Claims 22-24 and 26-29 refer to claims violating PCT Rule 6.4(a). Therefore, claims 22-24 and 26-29 are unclear.

☐ the claims, or said claims Nos. _____ are so inadequately supported by the description that no meaningful opinion could be formed (*specify*):

☒ no international search report has been established for said claims Nos. 18, 21-29

☐ a meaningful opinion could not be formed without the sequence listing; the applicant did not, within the prescribed time limit:

☐ furnish a sequence listing in the form of an Annex C/ST.25 text file, and such listing was not available to the International Searching Authority in the form and manner acceptable to it; or the sequence listing furnished did not comply with the standard provided for in Annex C of the Administrative Instructions.

☐ furnish a sequence listing on paper or in the form of an image file complying with the standard provided for in Annex C of the Administrative Instructions, and such listing was not available to the International Searching Authority in the form and manner acceptable to it; or the sequence listing furnished did not comply with the standard provided for in Annex C of the Administrative Instructions.

☐ pay the required late furnishing fee for the furnishing of a sequence listing in response to an invitation under Rule 13ter.1(a) or (b).

☐ See Supplemental Box for further details.

**WRITTEN OPINION OF THE
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**Box No. V Reasoned statement under Rule 43bis.1(a)(i) with regard to novelty, inventive step or industrial applicability;
citations and explanations supporting such statement**

1. Statement

Novelty (N)	Claims	<u>1-17, 19, 20</u>	YES
	Claims	<u>None</u>	NO
Inventive step (IS)	Claims	<u>1-17, 19, 20</u>	YES
	Claims	<u>None</u>	NO
Industrial applicability (IA)	Claims	<u>1-17, 19, 20</u>	YES
	Claims	<u>None</u>	NO

2. Citations and explanations:

Reference is made to the following documents:

D1: US 2015-0010529 A1 (WEI, Ge) 08 January 2015

D2: KR 10-2013-0116386 A (HALOZYME, INC.) 23 October 2013

D3: US 2010-0143457 A1 (WEI, Ge et al.) 10 June 2010

D4: WO 2013-102144 A2 (HALOZYME, INC.) 04 July 2013

D5: MCATEE, Caitlin O. et al. Emerging roles for
hyaluronidase in cancer metastasis and therapy.
Advances in Cancer Research. 2014, vol. 123, pages 1-
34

I. Novelty and Inventive Step (PCT Article 33(2) and (3))

1. Claims 1-17, 19 and 20

The PH20 variant including an amino acid residue
substitution or the fragment thereof, set forth in claim
1, is not disclosed in any of D1-D5, and could not be
readily derived by a person skilled in the art.
Claims 2-17, 19 and 20 are dependent on claim 1.

Therefore, claims 1-17, 19 and 20 are novel and involve

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Box No. V

Reasoned statement under Rule 43bis.1(a)(i) with regard to novelty, inventive step or industrial applicability;
citations and explanations supporting such statement

an inventive step.

II. Industrial Applicability (PCT Article 33(4))

Claims 1-17, 19 and 20 are industrially applicable.

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Box No. VII **Certain defects in the international application**

The following defects in the form or contents of the international application have been noted:

Multiple dependent claims cannot serve as a basis for other multiple dependent claims, and thus claims 18, 21 and 25 do not meet the requirement of PCT Rule 6.4(a).

INTERNATIONAL SEARCH REPORT

International application No.

PCT/KR2019/009215

Box No. II Observations where certain claims were found unsearchable (Continuation of item 2 of first sheet)

This international search report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☐ Claims Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:
2. ☒ Claims Nos.: 22-24, 26-29
because they relate to parts of the international application that do not comply with the prescribed requirements to such an extent that no meaningful international search can be carried out, specifically:
Claims 22-24 and 26-29 refer to a claim violating PCT Rule 6.4(a). Thus, claims 22-24 and 26-29 are unclear.
3. ☒ Claims Nos.: 18, 21, 25
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box No. III Observations where unity of invention is lacking (Continuation of item 3 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

1. ☐ As all required additional search fees were timely paid by the applicant, this international search report covers all searchable claims.
2. ☐ As all searchable claims could be searched without effort justifying additional fees, this Authority did not invite payment of additional fees.
3. ☐ As only some of the required additional search fees were timely paid by the applicant, this international search report covers only those claims for which fees were paid, specifically claims Nos.:
4. ☐ No required additional search fees were timely paid by the applicant. Consequently, this international search report is restricted to the invention first mentioned in the claims: it is covered by claims Nos.:

Remark on Protest

- ☐ The additional search fees were accompanied by the applicant's protest and, where applicable, the payment of a protest fee.
- ☐ The additional search fees were accompanied by the applicant's protest but the applicable protest fee was not paid within the time limit specified in the invitation.
- ☐ No protest accompanied the payment of additional search fees.

INTERNATIONAL SEARCH REPORT

International application No.

PCT/KR2019/009215

A. CLASSIFICATION OF SUBJECT MATTER

C12N 9/26(2006.01); A61K 38/16(2006.01); A61K 45/06(2006.01); A61P 35/00(2006.01)

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

C12N 9/26; A61K 31/337; A61K 38/46; A61K 38/47; A61K 38/16; A61K 45/06; A61P 35/00

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Korean utility models and applications for utility models: IPC as above

Japanese utility models and applications for utility models: IPC as above

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)

eKOMPASS (KIPO internal) & Keywords: Hyaluronidase, variation, substitution, enzyme activity, cancer

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	US 2015-0010529 A1 (WEI, Ge) 08 January 2015 See paragraphs [0005], [0009], and figure 1.	1-17,19,20
A	KR 10-2013-0116386 A (HALOZYME, INC.) 23 October 2013 See the entire document.	1-17,19,20
A	US 2010-0143457 A1 (WEI, Ge et al.) 10 June 2010 See the entire document.	1-17,19,20
A	WO 2013-102144 A2 (HALOZYME, INC.) 04 July 2013 See the entire document.	1-17,19,20
A	MCATEE, Caitlin O. et al. Emerging roles for hyaluronidase in cancer metastasis and therapy. <i>Advances in Cancer Research</i> . 2014, vol. 123, pages 1-34 See the entire document.	1-17,19,20

☐ Further documents are listed in the continuation of Box C.☒ See patent family annex.

* Special categories of cited documents:

“A” document defining the general state of the art which is not considered to be of particular relevance

“E” earlier application or patent but published on or after the international filing date

“L” document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

“O” document referring to an oral disclosure, use, exhibition or other means

“P” document published prior to the international filing date but later than the priority date claimed

“F” later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

“X” document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

“Y” document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art

“G” document member of the same patent family

Date of the actual completion of the international search

29 OCTOBER 2019 (29.10.2019)

Date of mailing of the international search report

29 OCTOBER 2019 (29.10.2019)

Name and mailing address of the ISA/KR



Korean Intellectual Property Office
Government Complex Daejeon Building 4, 189, Cheongseon-ro, Seo-gu,
Daejeon, 35208, Republic of Korea
Facsimile No. +82-42-481-8578

Authorized officer

Telephone No.

INTERNATIONAL SEARCH REPORT
Information on patent family members

International application No.
PCT/KR2019/009215

Patent document cited in search report	Publication date	Patent family member	Publication date
US 2015-0010529 A1	08/01/2015	TW 201534726 A WO 2015-003167 A1	16/09/2015 08/01/2015
KR 10-2013-0116386 A	23/10/2013	AU 2009-236635 A1 AU 2009-236635 B2 CA 2721229 A1 CN 102065886 A CN 103381267 A EP 2285402 A2 EP 2662090 A1 EP 3192525 A1 JP 2011-519351 A JP 2014-041131 A JP 2016-074664 A JP 5898146 B2 JP 6262700 B2 KR 10-1647932 B1 KR 10-2010-0135291 A KR 10-2015-0024436 A KR 10-2016-0052812 A NZ 588638 A NZ 601248 A SG 187427 A1 US 10328130 B2 US 2010-0003238 A1 US 2012-0171153 A1 WO 2009-128917 A2 WO 2009-128917 A3	22/10/2009 13/02/2014 22/10/2009 16/05/2011 06/11/2013 23/02/2011 13/11/2013 19/07/2017 07/07/2011 06/03/2014 12/05/2016 06/04/2016 17/01/2016 11/08/2015 24/12/2010 06/03/2015 12/05/2016 26/09/2012 27/06/2014 28/02/2013 25/06/2019 07/01/2010 05/07/2012 22/10/2009 14/01/2010
US 2010-0143457 A1	10/06/2010	AU 2009-333918 A1 AU 2009-333918 B2 CA 2746181 A1 CA 2746181 C CA 2915763 A1 CN 102307993 A CN 102307993 B CN 103205407 A CN 103205407 B CO 6341652 A2 DK 3037529 T3 EP 2367936 A1 EP 2367936 B1 EP 3037529 A1 EP 3037529 B1 ES 2573462 T3 JP 2012-511327 A JP 2014-126277 A JP 5670913 B2 JP 5685765 B2	07/07/2011 05/06/2014 08/07/2010 15/03/2016 08/07/2010 04/01/2012 25/06/2014 17/07/2013 16/03/2016 21/11/2011 20/05/2019 28/09/2011 02/03/2016 29/06/2016 27/03/2019 06/06/2016 24/05/2012 10/07/2014 18/02/2015 15/03/2016

INTERNATIONAL SEARCH REPORT
Information on patent family members

International application No.
PCT/KR2019/009215

Patent document cited in search report	Publication date	Patent family member	Publication date
WO 2013-102144 A2	04/07/2013	KR 10-1493644 E1	13/02/2015
		KR 10-1546563 B1	28/08/2015
		KR 10-2011-0099126 A	06/09/2011
		KR 10-2014-0021046 A	19/02/2014
		LT 3037529 T	27/05/2019
		MX 2011006110 A	24/06/2011
		NZ 583641 A	25/01/2013
		RS 58728 B1	26/06/2019
		SG 172064 A1	28/07/2011
		SG 194364 A1	29/11/2013
		SI 3037529 T1	26/06/2019
		US 2012-0213767 A1	23/08/2012
		US 8927249 B2	06/01/2015
		US 9284543 B2	15/03/2016
		WO 2010-077297 A1	06/07/2010
		ZA 201104116 B	19/12/2018
		AU 2012-362141 A1	10/07/2014
		AU 2012-362141 B2	21/09/2017
		AU 2017-245352 A1	02/11/2017
		AU 2017-245352 B2	01/08/2019
WO 2013-102144 A2	04/07/2013	BR 112014016195 A2	13/06/2017
		CA 2861919 A1	04/07/2013
		CA 2861919 C	02/04/2019
		CN 104244968 A	24/12/2014
		CN 104244968 B	25/07/2017
		DK 2797622 T3	16/01/2017
		EA 030252 B1	31/07/2018
		EA 201400772 A1	30/07/2015
		EP 2797622 A2	05/11/2014
		EP 2797622 B1	12/10/2016
		EP 3130347 A1	15/02/2017
		EP 3130347 B1	18/09/2019
		ES 2608582 T3	21/04/2017
		JP 2015-504666 A	16/02/2015
		JP 2017-112999 A	29/06/2017
		JP 6067746 B2	25/01/2017
		JP 6422933 B2	14/11/2018
		MX 2014007966 A	17/10/2014
		MX 361727 B	14/12/2018
		NZ 626126 A	24/06/2016
WO 2013-102144 A2	04/07/2013	SG 10201604470T A	28/07/2016
		SG 11201403714T A	30/07/2014
		US 2013-0302275 A1	14/11/2013
		US 2016-0362670 A1	15/12/2016
		US 9447401 B2	20/09/2016
		WO 2013-102144 A3	06/02/2014

Electronic Acknowledgement Receipt	
EFS ID:	39936198
Application Number:	16912590
International Application Number:	
Confirmation Number:	9651
Title of Invention:	PH20 POLYPEPTIDE VARIANTS, FORMULATIONS AND USES THEREOF
First Named Inventor/Applicant Name:	GE WEI
Customer Number:	13565
Filer:	Stephanie L. Seidman/Hyun Jeung Ji
Filer Authorized By:	Stephanie L. Seidman
Attorney Docket Number:	33320.03087.US27/3087D
Receipt Date:	08-JUL-2020
Filing Date:	25-JUN-2020
Time Stamp:	15:36:51
Application Type:	Utility under 35 USC 111(a)

Payment information:

Submitted with Payment		no			
File Listing:					
Document Number	Document Description	File Name	File Size(Bytes)/ Message Digest	Multi Part /.zip	Pages (if appl.)
1	Transmittal Letter	3087Dtra.pdf	25546	no	1
			df178268f2e37a0b6a483e38e69f0bbecc6776c		
Warnings:					

Information:					
2	Information Disclosure Statement (IDS) Form (SB08)	3087Dids.pdf	34124	no	2
			576a1d64881e750209574eb35bfd136c433d067e		
Warnings:					
Information:					
This is not an USPTO supplied IDS fillable form					
3	Information Disclosure Statement (IDS) Form (SB08)	3087Dp49.pdf	282638	no	24
			fedb37e5b2ef800bb997cee4c24b2e3762cfed3293a		
Warnings:					
Information:					
This is not an USPTO supplied IDS fillable form					
4	Non Patent Literature	GL.pdf	105998	no	2
			085d5cb53dfcc935e5d2a7882bec54665f37db60		
Warnings:					
Information:					
5	Non Patent Literature	UA.pdf	1470188	no	2
			d8b945d3a9c1436eee17532307b2ebbc006a5949		
Warnings:					
Information:					
6	Non Patent Literature	UB.pdf	1672487	no	2
			bd07160a916b9a1fecb2ce58cfa6225f5fb8939e		
Warnings:					
Information:					
7	Non Patent Literature	UC.pdf	6141444	no	10
			653200504f2e41523fec02615dadb5c347e92692		
Warnings:					
Information:					
Total Files Size (in bytes):			9732425		

This Acknowledgement Receipt evidences receipt on the noted date by the USPTO of the indicated documents, characterized by the applicant, and including page counts, where applicable. It serves as evidence of receipt similar to a Post Card, as described in MPEP 503.

New Applications Under 35 U.S.C. 111

If a new application is being filed and the application includes the necessary components for a filing date (see 37 CFR 1.53(b)-(d) and MPEP 506), a Filing Receipt (37 CFR 1.54) will be issued in due course and the date shown on this Acknowledgement Receipt will establish the filing date of the application.

National Stage of an International Application under 35 U.S.C. 371

If a timely submission to enter the national stage of an international application is compliant with the conditions of 35 U.S.C. 371 and other applicable requirements a Form PCT/DO/EO/903 indicating acceptance of the application as a national stage submission under 35 U.S.C. 371 will be issued in addition to the Filing Receipt, in due course.

New International Application Filed with the USPTO as a Receiving Office

If a new international application is being filed and the international application includes the necessary components for an international filing date (see PCT Article 11 and MPEP 1810), a Notification of the International Application Number and of the International Filing Date (Form PCT/RO/105) will be issued in due course, subject to prescriptions concerning national security, and the date shown on this Acknowledgement Receipt will establish the international filing date of the application.

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Inventors	: Wei <i>et al.</i>	Art Unit	: 1652
Serial No.	: 16/912,590	Examiner	: Not Yet Assigned
Filed	: June 25, 2020	Conf. No.	: 9651
		Cust. No.	: 13565
Title	: PH20 POLYPEPTIDE VARIANTS, FORMULATIONS AND USES THEREOF		

Mail Stop Amendment

Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

INFORMATION DISCLOSURE STATEMENT TRANSMITTAL LETTER

Dear Sir:

Transmitted herewith are an Information Disclosure Statement (2 pages), Forms PTO-1449 (24 pages), and cited non-U.S. patent documents for filing in connection with the above-identified application. Because this Information Disclosure Statement is filed before the receipt of a First Office Action on the Merits for the above-captioned application, a fee is not required. However, should it be determined that a fee for filing these papers is required, the Commissioner is authorized to charge Deposit Account No. 50-0911.

☒ The Commissioner is hereby authorized to charge any fees that may be due in connection with this paper or with this application during its entire pendency to Deposit Account No. 50-0911.

Respectfully submitted,

/Stephanie Seidman/

Stephanie Seidman
Reg. No. 33,779

Attorney Docket No.: 33320.03087.US27/3087D

Address all correspondence to: 13565

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CERTIFICATE OF TRANSMISSION VIA EFS-WEB

I hereby certify that this paper is being transmitted via the Electronic Filing System (EFS-WEB) to the United States Patent and Trademark Office on July 08, 2020.

/Hyun Jeung Ji/
Hyun Jeung Ji



UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
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Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NUMBER	FILING OR 371(C) DATE	FIRST NAMED APPLICANT	ATTY. DOCKET NO./TITLE
16/912,590	06/25/2020	GE WEI	33320.03087.US27/3087D

CONFIRMATION NO. 9651

PUBLICATION NOTICE



OC000000120511392

13565
Dentons US LLP
4655 Executive Drive
Suite 700
San Diego, CA 92121

Title:PH20 POLYPEPTIDE VARIANTS, FORMULATIONS AND USES THEREOF

Publication No.US-2020-0318091-A1

Publication Date:10/08/2020

NOTICE OF PUBLICATION OF APPLICATION

The above-identified application will be electronically published as a patent application publication pursuant to 37 CFR 1.211, et seq. The patent application publication number and publication date are set forth above.

The publication may be accessed through the USPTO's publically available Searchable Databases via the Internet at www.uspto.gov. The direct link to access the publication is currently <http://www.uspto.gov/patft/>.

The publication process established by the Office does not provide for mailing a copy of the publication to applicant. A copy of the publication may be obtained from the Office upon payment of the appropriate fee set forth in 37 CFR 1.19(a)(1). Orders for copies of patent application publications are handled by the USPTO's Public Records Division. The Public Records Division can be reached by telephone at (571) 272-3150 or (800) 972-6382, by facsimile at (571) 273-3250, by mail addressed to the United States Patent and Trademark Office, Public Records Division, Alexandria, VA 22313-1450 or via the Internet.

In addition, information on the status of the application, including the mailing date of Office actions and the dates of receipt of correspondence filed in the Office, may also be accessed via the Internet through the Patent Electronic Business Center at www.uspto.gov using the public side of the Patent Application Information and Retrieval (PAIR) system. The direct link to access this status information is currently <https://portal.uspto.gov/pair/PublicPair>. Prior to publication, such status information is confidential and may only be obtained by applicant using the private side of PAIR.

Further assistance in electronically accessing the publication, or about PAIR, is available by calling the Patent Electronic Business Center at 1-866-217-9197.

Office of Data Management, Application Assistance Unit (571) 272-4000, or (571) 272-4200, or 1-888-786-0101



UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
16/912,590	06/25/2020	GE WEI	33320.03087.US27/3087D	9651
13565	7590	10/15/2020	EXAMINER	
Dentons US LLP 4655 Executive Drive Suite 700 San Diego, CA 92121			LIU, SAMUEL W	
			ART UNIT	PAPER NUMBER
			1656	
			NOTIFICATION DATE	DELIVERY MODE
			10/15/2020	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

MLAIPSD@Dentons.com
lucy.begalla@dentons.com
rosalind.smith@dentons.com

<i>Office Action Summary</i>	Application No. 16/912,590	Applicant(s) WEI et al.	
	Examiner SAMUEL W LIU	Art Unit 1656	AIA (FITF) Status No

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 2 MONTHS FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).

Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) ☒ Responsive to communication(s) filed on 6/25/2020.
☐ A declaration(s)/affidavit(s) under **37 CFR 1.130(b)** was/were filed on ____.

2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.

3) ☐ An election was made by the applicant in response to a restriction requirement set forth during the interview on ____; the restriction requirement and election have been incorporated into this action.

4) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims*

5) ☒ Claim(s) 1-22 is/are pending in the application.
 5a) Of the above claim(s) none is/are withdrawn from consideration.

6) ☐ Claim(s) ____ is/are allowed.

7) ☐ Claim(s) ____ is/are rejected.

8) ☐ Claim(s) ____ is/are objected to.

9) ☒ Claim(s) 1-22 are subject to restriction and/or election requirement

* If any claims have been determined allowable, you may be eligible to benefit from the **Patent Prosecution Highway** program at a participating intellectual property office for the corresponding application. For more information, please see http://www.uspto.gov/patents/init_events/pph/index.jsp or send an inquiry to PPHfeedback@uspto.gov.

Application Papers

10) ☐ The specification is objected to by the Examiner.

11) ☐ The drawing(s) filed on ____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
 Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
 Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

Priority under 35 U.S.C. § 119

12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
Certified copies:
 a) ☐ All b) ☐ Some** c) ☐ None of the:
 1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

** See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)

2) ☐ Information Disclosure Statement(s) (PTO/SB/08a and/or PTO/SB/08b)
 Paper No(s)/Mail Date _____.

3) ☐ Interview Summary (PTO-413)
 Paper No(s)/Mail Date _____.

4) ☐ Other: _____.

Notice of Pre-AIA or AIA Status

The present application is being examined under the pre-AIA first to invent provisions.

Election/Restrictions

Restriction is required under 35 U.S.C. 121.

Group I, claims 1-21, drawn to a modified PH20 polypeptide, classified in CPC C07K 14/00, C12Y 302/02035.

Group II, claim 22, drawn to drawn to a method of treating a disease or a condition and a method of increasing delivery of therapeutic agents comprising administering the pharmaceutical composition comprising the PH20 polypeptide, classified in CPC A61K 47/42, C12Y 302/02035.

Species election

This application contains claims directed to the following patentably distinct species:

Claim 22 (Group II) is directed to the different species, i.e., **(i) a method of treating different “diseases”** including a tumor, cardiovascular disorder; an ophthalmic disorder; a pulmonary disease and edema, and different “**conditions**” including an excess of glycosaminoglycans or glycosaminoglycan accumulation in the brain; **and (ii) a method of increasing delivery of therapeutic agents**; they differ from one another in pathology and treatment methods and treatment outcomes. For example, cardiovascular disorder and cancer are different disease states as evidenced by col.6, lines 17-18, US Pat. No. 6615063.

Claim 13 (Group I) is directed to the different species, i.e., different modified polypeptides comprising SEQ ID NOs:576-586; they differ from one another in amino acid sequences and biological functions.

These species are not obvious variants of one other based on the current record in enzymology, biology, biochemistry, and genetics.

Applicant is required under 35 U.S.C. 121 to elect a disclosed species for prosecution on the merits to which the claims shall be restricted if no generic claim is finally held to be allowable. If Group II is elected, applicant is required to elect “a method” from the species (i) and (ii) (see above); and further, if the method (i) of treating “disease” or “condition” is elected, applicant is required to elect one disease **or** one condition for examination.

There is an examination and search burden for these patentably distinct species due to their mutually exclusive characteristics. The species require a different field of search (e.g.,

searching different classes/subclasses or electronic resources, or employing different search queries); and/or the prior art applicable to one species would not likely be applicable to another species; and/or the species are likely to raise different non-prior art issues under 35 U.S.C. 101 and/or 35 U.S.C. 112, first paragraph.

Applicant is advised that the reply to this requirement to be complete must include (i) an election of a species to be examined even though the requirement may be traversed (37 CFR 1.143) and (ii) identification of the claims encompassing the elected species, including any claims subsequently added. An argument that a claim is allowable or that all claims are generic is considered nonresponsive unless accompanied by an election.

The election of the species may be made with or without traverse. To preserve a right to petition, the election must be made with traverse. If the reply does not distinctly and specifically point out supposed errors in the election of species requirement, the election shall be treated as an election without traverse. Traversal must be presented at the time of election in order to be considered timely. Failure to timely traverse the requirement will result in the loss of right to petition under 37 CFR 1.144. If claims are added after the election, applicant must indicate which of these claims are readable on the elected species.

Should applicant traverse on the ground that the species are not patentably distinct, applicant should submit evidence or identify such evidence now of record showing the species to be obvious variants or clearly admit on the record that this is the case. In either instance, if the examiner finds one of the species unpatentable over the prior art, the evidence or admission may be used in a rejection under 35 U.S.C. 103(a) of the other species. Upon the allowance of a generic claim, applicant will be entitled to consideration of claims to additional species which depend from or otherwise require all the limitations of an allowable generic claim as provided by 37 CFR 1.141.

The inventions are distinct, each from the other because of the following reasons:

Invention I and Invention II are related as product and process of use. The inventions can be shown to be distinct if either or both of the following can be shown: (1) the process for using the product as claimed can be practiced with another materially different product or (2) the product as claimed can be used in a materially different process of using that product (MPEP § 806.05(h)). In the instant case, the polypeptide of Group I can be utilized in a materially different processes such as raising an antibody recognizing the polypeptide thereof, for example.

Restriction for examination purposes as indicated is proper because all these inventions listed in this action are independent or distinct for the reasons given above and there would be a serious search burden and/or examination if restriction were not required because at least following reasons(s) apply:

- the inventions have acquired a separate status in the art in view of their different classification
- the inventions have acquired a separated status in the art due to their recognized divergent subject matter
- the inventions require a different field of search (e.g., searching different classes/subclasses or electronic resource, or employing different search strategies or search queries).

Should applicant traverse on the ground that the inventions are not patentably distinct, applicant should submit evidence or identify such evidence now of record showing the inventions to be obvious variants or clearly admit on the record that this is the case. In either instance, if the examiner finds one of the inventions unpatentable over the prior art, the evidence or admission may be used in a rejection under 35 U.S.C. 103(a) of the other invention.

The examiner has required restriction between product and process claims. Where applicant elects claims directed to the product/apparatus, and all product/apparatus claims are subsequently found allowable, withdrawn process claims that include all the limitations of the allowable product/apparatus claims should be considered for rejoinder. All claims directed to a nonelected process invention must include all the limitations of an allowable product/apparatus claim for that process invention to be rejoined.

In the event of rejoinder, the requirement for restriction between the product/apparatus claims and the rejoined process claims will be withdrawn, and the rejoined process claims will be fully examined for patentability in accordance with 37 CFR 1.104. Thus, to be allowable, the rejoined claims must meet all criteria for patentability including the requirements of 35 U.S.C. 101, 102, 103 and 112. Until all claims to the elected product/apparatus are found allowable, an otherwise proper restriction requirement between product/apparatus claims and process claims may be maintained. Withdrawn process claims that are not commensurate in scope with an allowable product/apparatus claim will not be rejoined. See MPEP § 821.04. Additionally, in order for rejoinder to occur, applicant is advised that the process claims should be amended during prosecution to require the limitations of the product/apparatus claims. Failure to do so may result in no rejoinder. Further, note that the prohibition against double patenting rejections of 35 U.S.C. 121 does not apply where the restriction requirement is withdrawn by the examiner before the patent issues. See MPEP § 804.01.

Further, note that the prohibition against double patenting rejections of 35 U.S.C. 121 does not apply where the restriction requirement is withdrawn by the examiner before the patent issues. See MPEP § 804.01. Applicant is reminded that upon the cancellation of claims to a non-elected invention, the inventorship must be amended in compliance with 37 CFR 1.48(b) if one or more of the currently named inventors is no longer an inventor of at least one claim remaining in the application. Any amendment of inventorship must be accompanied by a petition under 37 CFR 1.48(b) and by the fee required under 37 CFR 1.17(i).

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Samuel Liu whose telephone number is (571) 272-0949. The examiner can normally be reached on Monday-Friday, 9 am to 5:30 pm. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor Manjunath N. Rao can be reached on 571-272-0939.

/Samuel Wei Liu/
Patent Examiner, Art Unit 1656
October 7, 2020

/PAUL J HOLLAND/
Primary Examiner, Art Unit 1656

<i>Notice of References Cited</i>	Application/Control No. 16/912,590		Applicant(s)/Patent Under Reexamination WEI et al.	
	Examiner SAMUEL W LIU		Art Unit 1656	Page 1 of 1

U.S. PATENT DOCUMENTS

*		Document Number Country Code-Number-Kind Code	Date MM-YYYY	Name	CPC Classification	US Classification
*	A	US-6615063-B1	09-2003	Ntziachristos; Vasilis	A61B5/0073	600/312
	B					
	C					
	D					
	E					
	F					
	G					
	H					
	I					
	J					
	K					
	L					
	M					

FOREIGN PATENT DOCUMENTS

*		Document Number Country Code-Number-Kind Code	Date MM-YYYY	Country	Name	CPC Classification
	N					
	O					
	P					
	Q					
	R					
	S					
	T					

NON-PATENT DOCUMENTS

*		Include as applicable: Author, Title Date, Publisher, Edition or Volume, Pertinent Pages)
	U	
	V	
	W	
	X	

*A copy of this reference is not being furnished with this Office action. (See MPEP § 707.05(a).)
Dates in MM-YYYY format are publication dates. Classifications may be US or foreign.

U.S. Patent and Trademark Office
PTO-892 (Rev. 01-2001)

Notice of References Cited

Part of Paper No. 20200929

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Inventors	: Wei <i>et al.</i>	Art Unit	: 1656
Serial No.	: 16/912,590	Examiner	: Liu, Samuel W.
Filed	: June 25, 2020	Conf. No.	: 9651
		Cust. No.	: 13565
Title	: PH20 POLYPEPTIDE VARIANTS, FORMULATIONS AND USES THEREOF		

Mail Stop Amendment

Commissioner for Patents

P.O. Box 1450

Alexandria, VA 22313-1450

ELECTION AND PRELIMINARY AMENDMENT

Dear Sir:

Responsive to the Office Action dated October 15, 2020, setting forth a Restriction Requirement, Applicant elects, without traverse, Group I, Claims 1-21 and new claims 23 and 24, drawn to a modified PH20 polypeptide, and to pharmaceutical compositions comprising the modified PH20 polypeptide. Applicant further elects, for search purposes a PH20 polypeptide that comprises the replacement corresponding to 309N, such as the polypeptide set forth in SEQ ID NO: 581, and any polypeptides that contain the replacement corresponding to 309N and having at least 95% sequence identity to SEQ ID NO:581, such as recited in claim 23, or where the unmodified polypeptide has at least 95% sequence identity to SEQ ID NO: 32 or to SEQ ID NO:35, such as recited in claims 9-11 and 24. Claims 1-21, 23, and 24 of elected Group I read on the elected species.

Amendments to the Claims begin on page 2 of this paper

Remarks/Arguments begin on page 5 of this paper.

CERTIFICATE OF TRANSMISSION VIA EFS-WEB

I hereby certify that this paper is being transmitted via the Electronic Filing System (EFS-WEB) to the United States Patent and Trademark Office on **October 26, 2020**.

/Jimmy Schaub/
Jimmy Schaub

Electronic Patent Application Fee Transmittal				
Application Number:		16912590		
Filing Date:		25-Jun-2020		
Title of Invention:		PH20 POLYPEPTIDE VARIANTS, FORMULATIONS AND USES THEREOF		
First Named Inventor/Applicant Name:		GE WEI		
Filer:		Stephanie L. Seidman/Jimmy Schaub		
Attorney Docket Number:		33320.03087.US27/3087D		
Filed as Large Entity				
Filing Fees for Utility under 35 USC 111(a)				
Description	Fee Code	Quantity	Amount	Sub-Total in USD(\$)
Basic Filing:				
Pages:				
Claims:				
CLAIMS IN EXCESS OF 20	1202	2	100	200
Miscellaneous-Filing:				
Petition:				
Patent-Appeals-and-Interference:				
Post-Allowance-and-Post-Issuance:				

Description	Fee Code	Quantity	Amount	Sub-Total in USD(\$)
Extension-of-Time:				
Miscellaneous:				
Total in USD (\$)				200

Electronic Acknowledgement Receipt	
EFS ID:	40937292
Application Number:	16912590
International Application Number:	
Confirmation Number:	9651
Title of Invention:	PH20 POLYPEPTIDE VARIANTS, FORMULATIONS AND USES THEREOF
First Named Inventor/Applicant Name:	GE WEI
Customer Number:	13565
Filer:	Stephanie L. Seidman/Jimmy Schaub
Filer Authorized By:	Stephanie L. Seidman
Attorney Docket Number:	33320.03087.US27/3087D
Receipt Date:	26-OCT-2020
Filing Date:	25-JUN-2020
Time Stamp:	17:35:49
Application Type:	Utility under 35 USC 111(a)

Payment information:

Submitted with Payment	yes
Payment Type	DA
Payment was successfully received in RAM	\$ 200
RAM confirmation Number	E20200PH36105668
Deposit Account	500911
Authorized User	Jimmy Schaub
The Director of the USPTO is hereby authorized to charge indicated fees and credit any overpayment as follows: 37 CFR 1.16 (National application filing, search, and examination fees) 37 CFR 1.17 (Patent application and reexamination processing fees)	

37 CFR 1.19 (Document supply fees)					
37 CFR 1.20 (Post Issuance fees)					
37 CFR 1.21 (Miscellaneous fees and charges)					
File Listing:					
Document Number	Document Description	File Name	File Size(Bytes)/ Message Digest	Multi Part /.zip	Pages (if appl.)
1	Transmittal Letter	3087Dtra.PDF	139490	no	1
			51fa72c5221e307c156f344efe903c9071ee6338		
Warnings:					
Information:					
2		3087Drrr.PDF	154519	yes	6
			e024427aaacd4620a9fe48bea2652ebcb6167428		
	Multipart Description/PDF files in .zip description				
	Document Description		Start	End	
	Applicant Arguments/Remarks Made in an Amendment		5	6	
	Claims		2	4	
	Response to Election / Restriction Filed		1	1	
Warnings:					
Information:					
3	Fee Worksheet (SB06)	fee-info.pdf	30752	no	2
			d289e7301b09aa377bd3539d157748f763753221		
Warnings:					
Information:					
Total Files Size (in bytes):			324761		

This Acknowledgement Receipt evidences receipt on the noted date by the USPTO of the indicated documents, characterized by the applicant, and including page counts, where applicable. It serves as evidence of receipt similar to a Post Card, as described in MPEP 503.

New Applications Under 35 U.S.C. 111

If a new application is being filed and the application includes the necessary components for a filing date (see 37 CFR 1.53(b)-(d) and MPEP 506), a Filing Receipt (37 CFR 1.54) will be issued in due course and the date shown on this Acknowledgement Receipt will establish the filing date of the application.

National Stage of an International Application under 35 U.S.C. 371

If a timely submission to enter the national stage of an international application is compliant with the conditions of 35 U.S.C. 371 and other applicable requirements a Form PCT/DO/EO/903 indicating acceptance of the application as a national stage submission under 35 U.S.C. 371 will be issued in addition to the Filing Receipt, in due course.

New International Application Filed with the USPTO as a Receiving Office

If a new international application is being filed and the international application includes the necessary components for an international filing date (see PCT Article 11 and MPEP 1810), a Notification of the International Application Number and of the International Filing Date (Form PCT/RO/105) will be issued in due course, subject to prescriptions concerning national security, and the date shown on this Acknowledgement Receipt will establish the international filing date of the application.

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Inventors	: Wei <i>et al.</i>	Art Unit	: 1656
Serial No.	: 16/912,590	Examiner	: Samuel W. LIU
Filed	: June 25, 2020	Conf. No.	: 9651
		Cust. No.	: 13565
Title	: PH20 POLYPEPTIDE VARIANTS, FORMULATIONS AND USES THEREOF		

Mail Stop Amendment

Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

TRANSMITTAL LETTER

Dear Sir:

Responsive to the *Office Action*, dated October 15, 2020, transmitted herewith is a Response to Restriction Requirement (6 pages) for filing in connection with the above-identified application.

- ☒ **Fee for two (2) additional claims in excess of 20 (2 x \$100).....\$200.00 (Large Entity)**
- ☒ The Commissioner is hereby authorized to charge the fees for excess claims, or any fees that may be due in connection with this paper or with this application during its entire pendency, to Deposit Account No. 50-0911.

Respectfully submitted,

/Stephanie Seidman/

Stephanie Seidman

Reg. No. 33,779

Attorney Docket No.: 33320.03087.US27/3087D

Address all correspondence to: 13565

Stephanie Seidman

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CERTIFICATE OF TRANSMISSION VIA EFS-WEB

I hereby certify that this paper is being transmitted via the Electronic Filing System (EFS-WEB) to the United States Patent and Trademark Office on October 26, 2020

/Jimmy Schaub/

Jimmy Schaub

Inventor(s) : Wei *et al.*
Serial No. : 16/912,590
Filed : June 25, 2020

Attorney Docket No.: 33320.03087.US27/3087D
Election and Preliminary Amendment

REMARKS

Any fees that may be due in connection with the filing of this paper or with this application may be charged to Deposit Account No. 50-0911. If a Petition for Extension of Time is needed, this paper is to be considered such Petition.

A Supplemental Information Disclosure Statement is filed under separate cover.

Claims 1-24 are pending; claims 23 and 24, which call out particular embodiments of the elected species are added. Claim 22, which is withdrawn from consideration as drawn to non-elected subject matter, is retained for possible joinder. Claim 1 is amended for clarity. Claim 4 is amended to correctly recite the mutations at position 309 that increase hyaluronidase activity. Basis can be found for example in Table 9, which lists exemplary replacements that the increase hyaluronidase activity. Among these are the replacements E, G, H, L, M, and N at the residue corresponding to 309, where 309 is reference with respect to SEQ ID NO:3, which sets forth the sequence of mature PH20 that has a C-terminus at residue 482 and also SEQ ID NO:7, which sets forth full length mature PH20, which terminates at residue 509. SEQ ID NO: 6 sets forth precursor PH20, which includes the signal sequence (residues 1-35); residue 309 in SEQ ID NOs: 3, 7, and 576-581, corresponds to residue 344 in SEQ ID NO:6.

As stated on page 1, Applicant elects Group 1, and, for search purposes, a species of modified PH20 polypeptides that comprises the replacement corresponding to 309N (with reference to SEQ ID NO:3 or 7), such as the polypeptide set forth in SEQ ID NO:581, and also polypeptides that comprise the replacement and have at least 95% sequence identity to the polypeptide of SEQ ID NO:581, or polypeptides that comprise the replacement corresponding to 309N, where the unmodified polypeptide has at least 95% sequence identity to SEQ ID NO:32 or to SEQ ID NO:35. SEQ ID NO: 32 sets forth the sequence of unmodified PH20 having residues 36-465 and SEQ ID NO:35 sets forth unmodified PH20 having residues 36-468, each relative to the unmodified PH20 polypeptide of SEQ ID NO:7, which sets forth the sequence of mature PH20. SEQ ID NO: 6 sets forth the sequence of full length PH20 that includes the signal peptide, residues 1-35.

Each of the polypeptides of SEQ ID NOs: 576-580 contains the replacements E, G, H, L, and M, respectively, at residue 309. The application shows that each of these replacements at the residue corresponding to 309 confers increased hyaluronidase activity on a PH20 polypeptide comprising such replacement. See, *e.g.*, Table 9, Example 4. Thus, all of the claimed polypeptides share the common feature of a replacement at the residue corresponding

Inventor(s) : Wei *et al.*
Serial No. : 16/912,590
Filed : June 25, 2020

Attorney Docket No.: 33320.03087.US27/3087D
Election and Preliminary Amendment

to 309 (with reference to mature PH20, or position 344 with reference to precursor PH20 that includes the signal sequence), and all claimed polypeptides exhibit increased hyaluronidase activity compared to the corresponding polypeptide that does not include the replacement at residue 309.

In view of the election and remarks herein, examination on the merits and allowance of the application respectfully are requested.

Respectfully submitted,
/Stephanie Seidman/
Stephanie Seidman
Reg. No. 33,779

Attorney Docket No. 33320.03087.US27/3087D
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Inventor(s) : Wei *et al.*
Serial No. : 16/912,590
Filed : June 25, 2020

Attorney Docket No.: 33320.03087.US27/3087D
Election and Preliminary Amendment

AMENDMENTS TO THE CLAIMS:

Please amend claims 1 and 4, and add claims 23 and 24 as follows:

LISTING OF CLAIMS:

1. (Currently Amended) A modified PH20 polypeptide, comprising one or more amino acid replacements in an unmodified PH20 polypeptide, wherein:
the unmodified PH20 polypeptide consists of the sequence of amino acids set forth in SEQ ID NO: 3, 7 or 32-66;
the modified PH20 polypeptide exhibits increased hyaluronidase activity compared to the unmodified PH20 polypeptide not containing the amino acid replacement(s);
the amino acid replacement(s) confer(s) the increased hyaluronidase activity;
an amino acid replacement(s) confers the increased hyaluronidase activity and is at a position corresponding to residue 309, with reference to amino acid positions set forth in SEQ ID NO:3, ~~which confers increased hyaluronidase activity;~~
corresponding amino acid positions are identified by alignment of the PH20 polypeptide with the polypeptide having the sequence of amino acids set forth in SEQ ID NO:3; and
the modified PH20 polypeptide has at least 91% sequence identity to the sequence of amino acids set forth as SEQ ID NO: 3, 7, or 32-66.
2. (Original) The modified PH20 polypeptide of claim 1, wherein the modified PH20 polypeptide has at least 95% sequence identity to the sequence of amino acids set forth as SEQ ID NO: 3, 7, or 32-66.
3. (Original) The modified PH20 polypeptide of claim 2 that is a soluble PH20 polypeptide.
4. (Currently Amended) The modified PH20 polypeptide of claim 1, wherein the replacement is selected from among L at a position corresponding to position 309; N at a position corresponding to position 309; E~~Q~~ at a position corresponding to position 309; R~~G~~ at a position corresponding to position 309; H at a position corresponding to 309; and M~~T~~ at a position corresponding to position 309.
5. (Original) The modified PH20 polypeptide of claim 4, wherein the replacement at the position corresponding to 309 is N.
6. (Original) The modified PH20 polypeptide of claim 1, wherein the unmodified PH20 polypeptide consists of the sequence of amino acids set forth in SEQ ID NO: 3 or 32-66.

Inventor(s) : Wei *et al.*
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Election and Preliminary Amendment

7. (Original) The modified PH20 polypeptide of claim 2, wherein the unmodified PH20 polypeptide consists of the sequence of amino acids set forth in SEQ ID NO: 3 or 32-66.
8. (Original) The modified PH20 polypeptide of claim 5, wherein the unmodified PH20 polypeptide consists of the sequence of amino acids set forth in SEQ ID NO: 3 or 32-66.
9. (Original) The modified PH20 polypeptide of claim 1, wherein the unmodified PH20 polypeptide consists of the sequence of amino acids set forth in SEQ ID NO:35 or a sequence that has at least 95% sequence identity to SEQ ID NO:35.
10. (Original) The modified PH20 polypeptide of claim 1, wherein the unmodified PH20 polypeptide consists of the sequence of amino acids set forth in SEQ ID NO:32 or a sequence that has at least 95% sequence identity to SEQ ID NO:32.
11. (Original) The modified PH20 polypeptide of claim 5, wherein the unmodified PH20 polypeptide consists of the sequence of amino acids set forth in SEQ ID NO:35 or a sequence that has at least 95% sequence identity to SEQ ID NO:35.
12. (Original) The modified PH20 polypeptide of claim 1, wherein the modified PH20 polypeptide exhibits increased hyaluronidase activity that is at least 120% of the hyaluronidase activity compared to the unmodified PH20 polypeptide not containing the amino acid replacement or replacements.
13. (Original) A modified PH20 polypeptide of claim 1, comprising a sequence of amino acids set forth in any of SEQ ID NOS:576-586, or a sequence of amino acids that exhibits at least 91% sequence identity to a sequence of amino acids set forth in any of SEQ ID NOS: 576-586 and that contains the amino acid replacement N at residue 309 with reference to corresponding positions in a polypeptide of any of SEQ ID NOS: 3 and 32-66.
14. (Original) A modified PH20 polypeptide of claim 1, comprising a sequence of amino acids set forth in SEQ ID NO:581, or a sequence of amino acids that exhibits at least 91% sequence identity to a sequence of amino acids set forth in SEQ ID NO:581 and that contains the amino acid replacement N at residue 309 with reference to corresponding positions in a polypeptide of any of SEQ ID NOS: 3 and 32-66.
15. (Original) The modified PH20 polypeptide of claim 1 that comprises one or more of a modification selected from among glycosylation, sialation, albumination, farnesylation, carboxylation, hydroxylation, and phosphorylation.
16. (Original) The modified PH20 polypeptide of claim 1 that comprises an N-acetylglucosamine moiety linked to each of at least three asparagine (N) residues.

Inventor(s) : Wei *et al.*
Serial No. : 16/912,590
Filed : June 25, 2020

Attorney Docket No.: 33320.03087.US27/3087D
Election and Preliminary Amendment

17. (Original) The modified PH20 polypeptide of claim 1 that is conjugated to a polymer.
18. (Original) The modified PH20 polypeptide of claim 16, wherein the polymer is dextran or polyethylene glycol (PEG).
19. (Original) The modified PH20 polypeptide of claim 1, comprising a heterologous signal sequence in place of the native signal sequence.
20. (Original) A chimeric polypeptide, comprising the modified PH20 polypeptide of claim 1.
21. (Original) A pharmaceutical composition, comprising the modified PH20 polypeptide of claim 1.
22. (Withdrawn) A method of treatment, comprising administering a pharmaceutical composition of claim 21, wherein the method is selected from a method that treats an excess of glycosaminoglycans; a tumor; glycosaminoglycan accumulation in the brain; a cardiovascular disorder; an ophthalmic disorder; pulmonary disease or edema; and a method of increasing delivery of therapeutic agents.
23. (New) A modified PH20 polypeptide of claim 1, comprising a sequence of amino acids set forth in SEQ ID NO:581, or a sequence of amino acids that exhibits at least 95% sequence identity to a sequence of amino acids set forth in SEQ ID NO:581 and that contains the amino acid replacement N at residue 309 with reference to corresponding positions in a polypeptide of any of SEQ ID NOS: 3 and 32-66.
24. (New) The modified PH20 polypeptide of claim 5, wherein the unmodified PH20 polypeptide consists of the sequence of amino acids set forth in SEQ ID NO:32 or a sequence that has at least 95% sequence identity to SEQ ID NO:32.

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant	: Wei <i>et al.</i>	Art Unit	: 1656
Serial No.	: 16/912,590	Examiner	: Liu, Samuel W.
Filed	: June 25, 2020	Conf. No.	: 9651
		Cust. No.	: 13565
Title	: PH20 POLYPEPTIDE VARIANTS, FORMULATIONS AND USES THEREOF		

Mail Stop Amendment

Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

**SUPPLEMENTAL INFORMATION DISCLOSURE STATEMENT IN
ACCORDANCE WITH 37 C.F.R. §§ 1.97-1.98**

Dear Sir:

Because this Supplemental Information Disclosure Statement is filed before the receipt of a First Office Action on the Merits for the above-captioned application, a fee is not required. However, should it be determined that a fee for filing these papers is required, the Commissioner is authorized to charge Deposit Account No. 50-0911.

In accordance with the duty of disclosure imposed by 37 C.F.R. § 1.56 to inform the Patent Office of all information known by Applicant or Applicant's representative that may be material to the examination of the subject application, Applicant's representative hereby provides this Supplemental Information Disclosure Statement that is prepared in accordance with 37 C.F.R. §§ 1.97-1.98. Form PTO-1449 (1 page) and copies of the cited non-U.S. patent documents are provided herewith in connection with the above-captioned application.

The documents cited on the Form PTO-1449 are in the English language. Hence, in accordance with the requirements of 37 C.F.R. § 1.98, no further explanation of the listed items is necessary.

Although these documents and applications are made known to the Patent and Trademark Office in compliance with Applicant's duty of disclosure, such disclosure is not to be construed as an admission by Applicant or Applicant's representative that any of the documents, singly or in any combination thereof, is effective as prior art against the subject application. In accordance with 37 C.F.R. § 1.97(g) and (h), the filing of this Supplemental Information Disclosure Statement shall not be construed to mean that a search has been made or that no other material information as defined in 37 C.F.R. § 1.56(b) exists.

CERTIFICATE OF TRANSMISSION VIA EFS-WEB

I hereby certify that this paper is being transmitted via the Electronic Filing System (EFS-WEB) to the United States Patent and Trademark Office on **October 26, 2020**

/Hyun Jeung Ji/
Hyun Jeung Ji

Applicant : Wei *et al.*
Serial No. : 16/912,590
Filed : June 25, 2020

Attorney Docket No.: 33320.03087.US27/3087D
Supplemental Information Disclosure Statement

Applicant respectfully requests that the Examiner review the foregoing documents and they be made of record in the file history of the above-captioned application.

Respectfully submitted,

/Stephanie Seidman/

Stephanie Seidman

Reg. No. 33,779

Attorney Docket No.: 33320.03087.US27/3087D

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Substitute Form PTO-1449 (Modified) List of Patents and Publications for Applicant's Information Disclosure Statement (37 CFR §1.98(b))	U.S. Department of Commerce Patent and Trademark Office		Attorney Docket No. 33320.03087.US27/3087D	Application No. 16/912,590
	Inventor(s) Wei <i>et al.</i>			
	Filing Date June 25, 2020		Group Art Unit 1656	

U.S. Patent Documents							
Examiner Initial	Desig. ID	Document Number	Publication Date	Patentee	Class	Subclass	Filing Date If Appropriate
	AA	2020/0255814	08/13/2020	Wei et al.	435	069.100	03/19/2020

Foreign Patent Documents or Published Foreign Patent Applications						
Examiner Initial	Desig. ID	Document Number	Publication Date	Country or Patent Office	Translation	
					Yes	No
None						

Other Documents (include Author, Title, Date, and Place of Publication)		
Examiner Initial	Desig. ID	Document
	AB	Letter/Written Disclosure of the Supplemental Information Disclosure Statement for the above-referenced application, filed herewith on Oct. 26, 2020, 2 pages.
	AC	Notice of Allowance, issued Jul. 16, 2020, in connection with corresponding U.S. Patent Application No. 15/226,489, 13 pages.
	AD	Written Submissions, filed Oct. 09, 2020, responsive to Hearing Notice, issued Aug. 10, 2020, in connection with corresponding Indian Patent Application No. 6272/DELNP/2014, 27 pages.

Examiner Signature	Date Considered
EXAMINER: Initial if citation considered, whether or not citation is in conformance with MPEP 609; Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.	

Electronic Acknowledgement Receipt	
EFS ID:	40948522
Application Number:	16912590
International Application Number:	
Confirmation Number:	9651
Title of Invention:	PH20 POLYPEPTIDE VARIANTS, FORMULATIONS AND USES THEREOF
First Named Inventor/Applicant Name:	GE WEI
Customer Number:	13565
Filer:	Stephanie L. Seidman/Hyun Jeung Ji
Filer Authorized By:	Stephanie L. Seidman
Attorney Docket Number:	33320.03087.US27/3087D
Receipt Date:	26-OCT-2020
Filing Date:	25-JUN-2020
Time Stamp:	18:02:15
Application Type:	Utility under 35 USC 111(a)

Payment information:

Submitted with Payment		no			
File Listing:					
Document Number	Document Description	File Name	File Size(Bytes)/ Message Digest	Multi Part /.zip	Pages (if appl.)
1	Transmittal Letter	3087Dtra.pdf	25718	no	1
			da26780b2c5edd19f94da587e32fc2c5366def46		
Warnings:					

Information:					
2	Information Disclosure Statement (IDS) Form (SB08)	3087Dids.pdf	29583	no	2
			4f46b1114b70868fbf181091d8ea14d8d77ba5d9		
Warnings:					
Information:					
This is not an USPTO supplied IDS fillable form					
3	Information Disclosure Statement (IDS) Form (SB08)	3087Dp49.pdf	30536	no	1
			9e1bcb3793208d2b6228e9be805eba21cab3827c		
Warnings:					
Information:					
This is not an USPTO supplied IDS fillable form					
4	Non Patent Literature	AB.pdf	101332	no	2
			c2801bb4ac1f4068326745656dd1a00ff277e38c		
Warnings:					
Information:					
This is not an USPTO supplied IDS fillable form					
5	Non Patent Literature	AC.pdf	750051	no	13
			fc9f0ff6931826858cd2fb2d2d406f6a78606028		
Warnings:					
Information:					
6	Non Patent Literature	AD.pdf	381866	no	27
			16c56545ef63e6ca84b6042350a684ca11f36129		
Warnings:					
Information:					
Total Files Size (in bytes):			1319086		

This Acknowledgement Receipt evidences receipt on the noted date by the USPTO of the indicated documents, characterized by the applicant, and including page counts, where applicable. It serves as evidence of receipt similar to a Post Card, as described in MPEP 503.

New Applications Under 35 U.S.C. 111

If a new application is being filed and the application includes the necessary components for a filing date (see 37 CFR 1.53(b)-(d) and MPEP 506), a Filing Receipt (37 CFR 1.54) will be issued in due course and the date shown on this Acknowledgement Receipt will establish the filing date of the application.

National Stage of an International Application under 35 U.S.C. 371

If a timely submission to enter the national stage of an international application is compliant with the conditions of 35 U.S.C. 371 and other applicable requirements a Form PCT/DO/EO/903 indicating acceptance of the application as a national stage submission under 35 U.S.C. 371 will be issued in addition to the Filing Receipt, in due course.

New International Application Filed with the USPTO as a Receiving Office

If a new international application is being filed and the international application includes the necessary components for an international filing date (see PCT Article 11 and MPEP 1810), a Notification of the International Application Number and of the International Filing Date (Form PCT/RO/105) will be issued in due course, subject to prescriptions concerning national security, and the date shown on this Acknowledgement Receipt will establish the international filing date of the application.

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant	: Wei <i>et al.</i>	Art Unit	: 1656
Serial No.	: 16/912,590	Examiner	: Liu, Samuel W.
Filed	: June 25, 2020	Conf. No.	: 9651
		Cust. No.	: 13565
Title	: PH20 POLYPEPTIDE VARIANTS, FORMULATIONS AND USES THEREOF		

Mail Stop Amendment

Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

SUPPLEMENTAL INFORMATION DISCLOSURE STATEMENT TRANSMITTAL LETTER

Dear Sir:

Transmitted herewith are a Supplemental Information Disclosure Statement (2 pages), Form PTO-1449 (1 page), and cited non-U.S. patent documents in connection with the above-identified application. Because this Supplemental Information Disclosure Statement is filed before the receipt of a First Office Action on the Merits for the above-captioned application, a fee is not required. However, should it be determined that a fee for filing these papers is required, the Commissioner is authorized to charge Deposit Account No. 50-0911.

☒ The Commissioner is hereby authorized to charge any fees that may be due in connection with this paper or with this application during its entire pendency to Deposit Account No. 50-0911.

Respectfully submitted,

/Stephanie Seidman/

Stephanie Seidman
Reg. No. 33,779

Attorney Docket No.: 33320.03087.US27/3087D

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CERTIFICATE OF TRANSMISSION VIA EFS-WEB

I hereby certify that this paper is being transmitted via the Electronic Filing System (EFS-WEB) to the United States Patent and Trademark Office on **October 26 2020**.

/Hyun Jeung Ji/
Hyun Jeung Ji

PATENT APPLICATION FEE DETERMINATION RECORD Substitute for Form PTO-875				Application or Docket Number 16/912,590		Filing Date 06/25/2020		☐ To be Mailed					
ENTITY: ☒ LARGE ☐ SMALL ☐ MICRO													
APPLICATION AS FILED - PART I													
		(Column 1)		(Column 2)									
FOR		NUMBER FILED		NUMBER EXTRA		RATE (\$)		FEE (\$)					
☐ BASIC FEE (37 CFR 1.16(a), (b), or (c))		N/A		N/A		N/A							
☐ SEARCH FEE (37 CFR 1.16(k), (l), or (m))		N/A		N/A		N/A							
☐ EXAMINATION FEE (37 CFR 1.16(o), (p), or (q))		N/A		N/A		N/A							
TOTAL CLAIMS (37 CFR 1.16(i))		minus 20 = *				x \$100 =							
INDEPENDENT CLAIMS (37 CFR 1.16(h))		minus 3 = *				x \$460 =							
☐ APPLICATION SIZE FEE (37 CFR 1.16(s))		If the specification and drawings exceed 100 sheets of paper, the application size fee due is \$310 (\$155 for small entity) for each additional 50 sheets or fraction thereof. See 35 U.S.C. 41(a)(1)(G) and 37 CFR 1.16(s).											
☐ MULTIPLE DEPENDENT CLAIM PRESENT (37 CFR 1.16(j))													
* If the difference in column 1 is less than zero, enter "0" in column 2.						TOTAL							
APPLICATION AS AMENDED - PART II													
		(Column 1)		(Column 2)		(Column 3)							
AMENDMENT	10/26/2020		CLAIMS REMAINING AFTER AMENDMENT		HIGHEST NUMBER PREVIOUSLY PAID FOR		PRESENT EXTRA		RATE (\$)		ADDITIONAL FEE (\$)		
	Total (37 CFR 1.16(i))		* 24		Minus ** 22		= 2		x \$100 =		200		
	Independent (37 CFR 1.16(h))		* 1		Minus *** 3		= 0		x \$480 =		0		
	☐ Application Size Fee (37 CFR 1.16(s))												
	☐ FIRST PRESENTATION OF MULTIPLE DEPENDENT CLAIM (37 CFR 1.16(j))												
										TOTAL ADD'L FEE		200	
AMENDMENT			CLAIMS REMAINING AFTER AMENDMENT		HIGHEST NUMBER PREVIOUSLY PAID FOR		PRESENT EXTRA		RATE (\$)		ADDITIONAL FEE (\$)		
	Total (37 CFR 1.16(i))		*		Minus **		=		x \$0 =				
	Independent (37 CFR 1.16(h))		*		Minus ***		=		x \$0 =				
	☐ Application Size Fee (37 CFR 1.16(s))												
	☐ FIRST PRESENTATION OF MULTIPLE DEPENDENT CLAIM (37 CFR 1.16(j))												
										TOTAL ADD'L FEE			
* If the entry in column 1 is less than the entry in column 2, write "0" in column 3.										LIE			
** If the "Highest Number Previously Paid For" IN THIS SPACE is less than 20, enter "20".										/MARSHA R RICHARDS/			
*** If the "Highest Number Previously Paid For" IN THIS SPACE is less than 3, enter "3".													
The "Highest Number Previously Paid For" (Total or Independent) is the highest number found in the appropriate box in column 1.													

This collection of information is required by 37 CFR 1.16. The information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.14. This collection is estimated to take 12 minutes to complete, including gathering, preparing, and submitting the completed application form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, U.S. Department of Commerce, P.O. Box 1450, Alexandria, VA 22313-1450. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. **SEND TO: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.**

If you need assistance in completing the form, call 1-800-PTO-9199 and select option 2.



UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
16/912,590	06/25/2020	GE WEI	33320.03087.US27/3087D	9651
13565	7590	12/09/2020	EXAMINER	
Dentons US LLP 4655 Executive Drive Suite 700 San Diego, CA 92121			LIU, SAMUEL W	
			ART UNIT	PAPER NUMBER
			1656	
			NOTIFICATION DATE	DELIVERY MODE
			12/09/2020	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

MLAIPSD@Dentons.com
lucy.begalla@dentons.com
rosalind.smith@dentons.com

<i>Office Action Summary</i>	Application No. 16/912,590	Applicant(s) WEI et al.	
	Examiner SAMUEL W LIU	Art Unit 1656	AIA (FITF) Status No

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTHS FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).

Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) ☒ Responsive to communication(s) filed on 10/26/2020.
☐ A declaration(s)/affidavit(s) under **37 CFR 1.130(b)** was/were filed on ____.

2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.

3) ☐ An election was made by the applicant in response to a restriction requirement set forth during the interview on ____; the restriction requirement and election have been incorporated into this action.

4) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims*

5) ☒ Claim(s) 1-24 is/are pending in the application.
 5a) Of the above claim(s) 22 is/are withdrawn from consideration.

6) ☐ Claim(s) ____ is/are allowed.

7) ☒ Claim(s) 1-21 and 23-24 is/are rejected.

8) ☐ Claim(s) ____ is/are objected to.

9) ☐ Claim(s) ____ are subject to restriction and/or election requirement

* If any claims have been determined allowable, you may be eligible to benefit from the **Patent Prosecution Highway** program at a participating intellectual property office for the corresponding application. For more information, please see http://www.uspto.gov/patents/init_events/pph/index.jsp or send an inquiry to PPHfeedback@uspto.gov.

Application Papers

10) ☒ The specification is objected to by the Examiner.

11) ☒ The drawing(s) filed on 6/25/2020 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.
 Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
 Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

Priority under 35 U.S.C. § 119

12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
Certified copies:
 a) ☐ All b) ☐ Some** c) ☐ None of the:
 1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

** See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)

 2) ☒ Information Disclosure Statement(s) (PTO/SB/08a and/or PTO/SB/08b)
 Paper No(s)/Mail Date 10/26/2020 & 7/8/2020

3) ☐ Interview Summary (PTO-413)
 Paper No(s)/Mail Date _____
 4) ☐ Other: _____

Notice of Pre-AIA or AIA Status

The present application is being examined under the pre-AIA first to invent provisions.

Status of the claims: Claims 1-24 are pending.

The amendment filed 10/26/2020 which amends claims 1 and 4, and adds new claims 23-24 has been entered.

CONTINUING DATA

This application is a CON of 15226489 filed 8/2/2016 which is a DIV of 13694731 filed 12/28/2012 (now US Pat. No. 9447401) which claims benefit of 61796208 filed 11/01/2012, and claims benefit of 61631313 filed 12/30/2011; wherein provisional application 61631313 has support for the elected invention (see below). In addition, this application is a DIV of 13694731 filed 12/28/2012.

IDS

The references cited in the information disclosure statement (IDS) filed 10/26/2020, and the IDS filed 7/8/2020 which can be found in the parent application 15226489 have been considered by Examiner.

Election/Restriction

Applicants' election (filed 10/26/2020) of Group I, claims 1-21 and election of the species: substitution I **309N** (wherein sequence numbering is in accordance with SEQ ID NO:3) for examination is acknowledged. New claims 23-24 are drawn to the elected invention.

Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)). Claim 22 is withdrawn from further consideration, there being no allowable generic or linking claim. Therefore, claims 1-21 and 23-24 and elected species are under examination.

Objection to specification

The disclosure is objected to because of the following informalities:

The use of the trademark (HydaseTM, VitraseTM and WydaseTM, see p.2, lines 8-9) has been noted in this application. It should be capitalized wherever it appears and be accompanied by the generic terminology. Although the use of trademarks is permissible in patent applications, the proprietary nature of the marks should be respected and every effort made to prevent their use in any manner which might adversely affect their validity as trademarks.

At page 3, line 24, "SEQ ID NOS" should be changed to "SEQ ID NOs"; similar changes should be made throughout the specification.

Objection to claims

In claim 1, "...unmodified PH20 polypeptide consists of the sequence of amino acid set forth in SEQ ID NO:3, 7 or 32-66" is suggested to be changed to "...unmodified PH20 polypeptide consists of the amino acid sequence selected from the group consisting of SEQ ID NO:3, 7 and 32-66".

Also, in claim 1, "...amino acid positions set forth in SEQ ID NO:3" is suggested to be changed to "... amino acid positions of SEQ ID NO:3".

Further, in claim 1, "...91% sequence identity to the sequence of amino acids set forth as SEQ ID NO: 3, 7 or 32-66" is suggested to be changed to "...91% sequence identity to the amino acid sequence selected from the group consisting of SEQ ID NO: 3, 7 and 32-66".

In claim 2, "...sequence of amino acids set forth as SEQ ID NO:..." - is suggested to be changed to "...amino acid sequence selected from the group consisting of SEQ ID NO:..."

In claim 4, "...H at a position corresponding to 309" is suggested to be changed to "...H at a position corresponding to position 309". Similarly, in claim 5, "...corresponding to 309 is N" is suggested to be changed to "...corresponding to position 309 is N".

In claims 6-8, "...the unmodified PH20 polypeptide consists of the sequence of amino acid set forth in SEQ ID NO:3, 7 or 32-66" is suggested to be changed to "...the modified PH20 polypeptide consists of the amino acid sequence selected from the group consisting of SEQ ID NO:3, 7 and 32-66".

In claims 9 and 11, "...unmodified PH20 polypeptide consists of the sequence of amino acids set forth in SEQ ID NO:35..." is suggested to be changed to "...unmodified PH20 polypeptide consists of the amino acid sequence of SEQ ID NO:35..."

In claim 10, "...unmodified PH20 polypeptide consists of the sequence of amino acids set forth in SEQ ID NO:32..." is suggested to be changed to "...unmodified PH20 polypeptide consists of the amino acid sequence of SEQ ID NO:32..."

In claim 13, "...or a sequence of amino acids that exhibits at least 91% sequence identity to a sequence of amino acids set forth in any of SEQ ID NOS:576-586...in a polypeptide of any of SEQ ID NOS: 3 and 32-66" is suggested to be changed to "...or an amino acid sequence that exhibits at least 91% sequence identity to an amino acid sequence selected from the group consisting of SEQ ID NOS:576-586... in an amino acid sequence selected from the group consisting of SEQ ID NOS: 3 and 32-66".

In claim 14, "...a sequence of amino acids set forth in SEQ ID NO:581, or a sequence of amino acids that exhibits at least 91% sequence identity to a sequence of amino acids set forth in SEQ ID NO:581 and that contains ...in a polypeptide of any of SEQ ID NOS: 3 and 32-66" is suggested to be changed to "...an amino acid sequence of SEQ ID NO:581, or an

amino acid sequence that exhibits at least 91% sequence identity to the amino acid sequence of SEQ ID NO:581 and that contains ... in an amino acid sequence selected from the group consisting of SEQ ID NOs: 3 and 32-66".

In claims 15, "...one or more of a modification..." should be changed to "...one or more of modification..."; and "...that comprises one or more of a modification..." is suggested to be changed to "...that further comprises one or more modification...".

In claim 16, "...that comprises an ..." should be changed to "...that further comprises an ...".

In claim 23, "...a sequence of amino acids set forth in SEQ ID NO:581, or a sequence of amino acids that exhibits at least 95% sequence identity to a sequence of amino acids set forth in SEQ ID NO:581 and that ...in a polypeptide of any of SEQ ID NOS: 3 and 32-66" is suggested to be changed to "...an amino acid sequence of SEQ ID NO:581, or an amino acid sequence that exhibits at least 95% sequence identity to an amino acid sequence set forth in SEQ ID NO:581 and that ...in an amino acid sequence selected from the group consisting of SEQ ID NOs: 3 and 32-66".

In claim 24, "...consists of the sequence of amino acids set forth in SEQ ID NO:32 or a sequence that has at least 95% sequence identity to SEQ ID NO:32" is suggested to be changed to "...consists of the amino acid sequence set forth in SEQ ID NO:32 or an amino acid sequence that has at least 95% sequence identity to SEQ ID NO:32".

Duplicate Claims –Warning

Applicant is advised that should claims 13 and 14 be found allowable, claims 13 and 14 will be objected to under 37 CFR 1.75 as being a substantial duplicate thereof. When two claims in an application are duplicates or else are so close in content that they both cover the same thing, despite a slight difference in wording, it is proper after allowing one claim to object to the other as being a substantial duplicate of the allowed claim. See MPEP § 706.03(k).

The reasons that the claims 13 and 14 are substantially duplicate are the following.

Although claim 13 recites the portion that the modified PH20 polypeptide "*comprising a sequence of amino acids set forth in any of SEQ ID NOs:567-586*" (lines 1-2, claim **13**) which is absent in claim **14**, the claim **13 as a whole** is given broadest reasonable interpretation (BRI) as being directed to the modified PH20 polypeptide "*comprising a sequence of amino acids that exhibits at least 91% sequence identity to a sequence of amino acids set forth in any of SEQ ID NO:576-586 and that contains the amino acid replacement N at residue 309 with reference to corresponding positions in a polypeptide of any of SEQ ID NOs:3 and 32-66*" (lines 2-5, claim **13**). In view of the limitation "and that contains the amino acid replacement N at residue 309," the scope of claim 13 is limited to SEQ ID NO: 581, or a sequence of amino acids that exhibits at least 91% sequence identity to SEQ ID NO: 581. Note that SEQ ID NOs: 576-586 are identical

with the exception of the amino acid at position 309. As a result, limiting position 309 to N for any of the recited sequences in claim 13, and/or having at least 91% sequence identity to SEQ ID NOs: 576-586 that contains N at position 309, results in a claim wherein the modified PH20 polypeptide is SEQ ID NO: 581, or a sequence having at least 91% sequence identity to it. This is the same scope as claim 14.

Therefore, the above “Duplicate Claims –Warning” is proper.

Claim Rejections - 35 USC § 112(d)

The following is a quotation of 35 U.S.C. 112(d):

(d) REFERENCE IN DEPENDENT FORMS.—Subject to subsection (e), a claim in dependent form shall contain a reference to a claim previously set forth and then specify a further limitation of the subject matter claimed. A claim in dependent form shall be construed to incorporate by reference all the limitations of the claim to which it refers.

The following is a quotation of 35 U.S.C. 112 (pre-AIA), fourth paragraph:

Subject to the [fifth paragraph of 35 U.S.C. 112 (pre-AIA)], a claim in dependent form shall contain a reference to a claim previously set forth and then specify a further limitation of the subject matter claimed. A claim in dependent form shall be construed to incorporate by reference all the limitations of the claim to which it refers.

Claims 9-11, 13-14, and 23 are rejected under 35 U.S.C. 112(d) or pre-AIA 35 U.S.C. 112, 4th paragraph, as being of improper dependent form for failing to further limit the subject matter of the claim upon which it depends, or for failing to include all the limitations of the claim upon which it depends.

Claims 9-11 recite “...or a sequence that has at least 95% sequence identity to SEQ ID NO:35 (claims 9, 11) or SEQ ID NO:32 (claim10); wherein said “a sequence...” is given broadest reasonable interpretation as being drawn to the amino acid sequence of “unmodified PH20 polypeptide” which fails to further limit the unmodified PH20 polypeptide of SEQ D NO:32 or 35 set forth at lines 3-4 of claim 1 from which claims 9-11 depends (it is noted that claim 11 depends from claim 5, whereas claim 5 depends form claim 4 that depends from claim 1); i.e., the structural variation resulted from “...95% sequence identity...” (claims 9-11) renders the scope of the claims 9-11 broader than the scope of the “unmodified PH20 polypeptide” of claim 1. Thus, claims 9-11 fail to further limit the subject matter of the claim 1, i.e., claims 9-11 are of improper dependent form.

Claim 13 as written is directed to “a **modified** PH20 polypeptide of claim 1, comprising a sequence of amino acids set forth in any of SEQ ID NOs:576-586...” wherein said “a sequence...” is given broadest reasonable interpretation (BRI) as being drawn to “a fragment” of

any one of SEQ ID NOs:576-586 which has the broader scope than that of “the **modified** PH20 polypeptide has at least 91% sequence identity to the sequence of amino acids set forth as SEQ ID NO: 3, 7, or 32-66”, wherein said “a *fragment*” (a *subsequence* of SEQ ID NO: 3, 7, or 32-66) renders the sequence identity lower than “91% (claim 1); and thus, claim **13** fails to further limit the subject matter of the claim 1, i.e., claim 13 is of improper dependent form.

Similarly, see also claims 14 and 23 which recite “a sequence of amino acids set forth in SEQ ID NO:581...” wherein said “a sequence...” is given BRI as being drawn to “a *fragment*”. For the same reason stated above, claims **14** and **23** are written as improper dependent forms.

Claim Rejections - 35 USC § 112(b)

The following is a quotation of 35 U.S.C. 112(b):

(B) CONCLUSION.—The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the inventor or a joint inventor regards as the invention.

The following is a quotation of 35 U.S.C. 112 (pre-AIA), second paragraph:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 18 and 19 are rejected under 35 U.S.C. 112(b) or 35 U.S.C. 112 (pre-AIA), second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which the inventor or a joint inventor, or for pre-AIA the applicant regards as the invention.

Claim 18 lacks antecedent basis for “...the polymer...” in claim 16 which claim 18 depends.

Claim 19 lacks antecedent basis for “...a heterologous signal sequence in place of the native signal sequence” in claim **1** from which claim 19 depends, because none of SEQ ID NOs: 3, 7 and 32-66 contains the heterologous signal sequence. It is noted that the specification only discloses SEQ ID NO:6 comprising the “signal sequence” (see PG PUB [0119], instant specification) whereas claim 1 does not recite said SEQ ID NO:6.

Claim Rejection –Obviousness Type Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the “right to exclude” granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either

anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on nonstatutory double patenting provided the reference application or patent either is shown to be commonly owned with the examined application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement. See MPEP § 717.02 for applications subject to examination under the first inventor to file provisions of the AIA as explained in MPEP § 2159. See MPEP § 2146 *et seq.* for applications not subject to examination under the first inventor to file provisions of the AIA. A terminal disclaimer must be signed in compliance with 37 CFR 1.321(b).

The USPTO Internet website contains terminal disclaimer forms which may be used. Please visit www.uspto.gov/patent/patents-forms. The filing date of the application in which the form is filed determines what form (e.g., PTO/SB/25, PTO/SB/26, PTO/AIA/25, or PTO/AIA/26) should be used. A web-based eTerminal Disclaimer may be filled out completely online using web-screens. An eTerminal Disclaimer that meets all requirements is auto-processed and approved immediately upon submission. For more information about eTerminal Disclaimers, refer to www.uspto.gov/patents/process/file/efs/guidance/eTD-info-I.jsp.

[1] Claims 1-14, 17-18, 21, 23 and 24 are provisionally rejected on the ground of nonstatutory double patenting as being unpatentable over claims 3, 5, 11-12, 23 and 28 of copending Application No. 15226489 ('**489**). This is a provisional nonstatutory double patenting rejection because the patentably indistinct claims have not in fact been patented. Although the claims at issue are not identical, they are not patentably distinct from each other because of the reasons set forth below.

Examiner remark: application '**489** has been granted for patent. However, when this Office action is prepare, Examiner cannot view the issued patent thereof; and thus, the ODP rejection is based on the application '**489**.

Claims 3, 5 and 28 of '**489** disclose a modified PH20 polypeptide having increased hyaluronidase activity that is at least 120% of the hyaluronidase activity compared to the unmodified PH20 polypeptide that does not contain amino acid replacement(s) (i.e., substitution(s)), wherein modified PH20 is soluble (claim 28 of '**489**) and wherein the modified PH20 polypeptide comprises amino acid substitution at residue Ile **309** which has been substituted by Asn (N) (i.e., I309N) according to the unmodified amino acid sequence of SEQ ID NO:3 wherein the modified PH20 polypeptide has at least 95% sequence identity to the

amino acid sequence selected from the group consisting of SEQ ID NO:3, 7 and 32-66, which are the comment subject matters of instant claims 1-8 and 12.

Claim 5 of '489 discloses the amino acid sequence (SEQ ID NO:581) of the modified PH20 comprising I309N which has 100% sequence identity to instant SEQ ID NO:581 (*elected species*, instant claim 13) (see *Sequence alignment* below, wherein Qy is instant SEQ ID NO:581; and Db is SEQ ID NO:581 of '489) which contains the amino acid substitution N at residue 309. Thus, claim 5 of '489 discloses the common subject matter of instant claims 13-14 and 23.

Application US/15226489A; Publication No. US20160362670A1

APPLICANT: Ge Wei et al.

SEQ ID NO **581**

OTHER INFORMATION: Mature PH20 36-482 with N at a position corresponding to amino acid residue **309**

Query Match 100.0%; Length 447;

```
Qy      1 LNFRAAPPVIPNVFLWAWNAPSEFCLGKFDEPLDMSLFSFIGSPRINATGQGVTFYVDR 60
      ||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db      1 LNFRAAPPVIPNVFLWAWNAPSEFCLGKFDEPLDMSLFSFIGSPRINATGQGVTFYVDR 60

Qy     61 LGYYPYIDSITGVTVNGGIPQKISLQDHLDKAKKDITFYMPVDNLGMAVIDWEEWRPTWA 120
      ||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db     61 LGYYPYIDSITGVTVNGGIPQKISLQDHLDKAKKDITFYMPVDNLGMAVIDWEEWRPTWA 120

Qy    121 RNWKPKDVYKNRSIELVQQQNVQLSLTEATEKAKQEFKAGKDFLVETIKLGKLLRPNHL 180
      ||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db    121 RNWKPKDVYKNRSIELVQQQNVQLSLTEATEKAKQEFKAGKDFLVETIKLGKLLRPNHL 180

Qy    181 WGYLFPDCYNHHYKPGYNGSCFNVEIKRNDLSWLWNESTALYPSIYLNTQQSPVAAT 240
      ||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db    181 WGYLFPDCYNHHYKPGYNGSCFNVEIKRNDLSWLWNESTALYPSIYLNTQQSPVAAT 240

Qy    241 LYVRNRVREAIRVSKIPDAKSPLPVFAYTRIVFTDQVLKFLSQDELVYTFGETVALGASG 300
      ||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db    241 LYVRNRVREAIRVSKIPDAKSPLPVFAYTRIVFTDQVLKFLSQDELVYTFGETVALGASG 300

Qy    301 IVIWGTLNMRSMKSCLLLDNYMETILNPYIINVTLAAKMCSQVLCQEQGVCIRKNWNSS 360
      ||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db    301 IVIWGTLNMRSMKSCLLLDNYMETILNPYIINVTLAAKMCSQVLCQEQGVCIRKNWNSS 360

Qy    361 DYLHLNPDNFAIQLEKGGKFTVRGKPTLEDLEQFSEKFCSCYSTLSCKEKADVKTDAV 420
      ||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db    361 DYLHLNPDNFAIQLEKGGKFTVRGKPTLEDLEQFSEKFCSCYSTLSCKEKADVKTDAV 420

Qy    421 DVCIADGVCIDAFLKPPMETEEPQIFY 447
      ||||||||||||||||||||||||||||
Db    421 DVCIADGVCIDAFLKPPMETEEPQIFY 447
```

Claims 11-12 of '489 disclose that the modified PH20 is conjugated to a polymer such as dextran or PEG which is the common subject matter of instant claims 17-18.

Claim 23 of '489 discloses a pharmaceutical composition comprising the modified PH20 polypeptide, which is the common subject matter of instant claim 21.

Since instant SEQ ID NO:3 consists of 447 amino acids; instant SEQ ID NO: 32 (instant claims 10, 24) consists of 430 amino acid and is identical to SEQ ID NO:3 except for truncation (residues 431-447) at C-terminal region thereof; and instant SEQ ID NO: 35 (instant claims 9, 11) consists of 433 amino acid and is identical to SEQ ID NO:3 except for truncation (residues 434-447) at C-terminal region thereof, claims 3, 5 and 28 of '489 are obvious variation of instant claims 9-11 and 24.

[2] Claims 1-4, 7, 9-12, 15-18, 21 and 24 are rejected on the ground of nonstatutory double patenting as being unpatentable over claims 1-5, 10-11, 16-17, 19-20 and 22-23 of U.S. Patent No.9447401 ('401). Although the claims at issue are not identical, they are not patentably distinct from each other because of the following reasons.

Claims 1-5 and 10-11 of '401 disclose a modified PH20 polypeptide comprising amino acid substitution (replacement) at residue 309 (claims 10-11 of '401) and having at least 95% sequence identity to SEQ ID NO:3 (claim 3 of '401), SEQ ID NO:3 of '401 has 100% sequence identity to instant SEQ ID NO:3 wherein the modified PH20 is soluble (claim 2 of '401). MPEP states that "when the structure recited in the reference is substantially identical to that of the claims, claimed properties or functions are presumed to be inherent" (MPEP 2112.01(I)). In this case, since the modified PH20 of '401 contain amino acid substitution at residue 309, i.e., Glu (E) at position 309 (instant claim 4) (see disclosure of claim 11 of '401); it is reasonable to consider that the modified PH20 ('401) is substantially same in structure as that of the claims 1 and 4, per MPEP the property "increased hyaluronidase activity" set forth in instant claim 1 is inherent. Thus, the claims 1-5 and 10-11 of '401 disclose common subject matters of instant claims 1-4, 7 and 12. Since instant SEQ ID NO:3 consists of 447 amino acids; instant SEQ ID NO: 32 (instant claims 10, 24) consists of 430 amino acid and is identical to SEQ ID NO:3 except for truncation (residues 431-447) at C-terminal region thereof; and instant SEQ ID NO: 35 (instant claims 9, 11) consists of 433 amino acid and is identical to SEQ ID NO:3 except for truncation (residues 434-447) at C-terminal region thereof, claims 1-5 and 10-11 of '401 are obvious variation of instant claims 9-11 and 24.

Claim 16 of '401 discloses that the modified PH20 polypeptide is further modified by a modification selected from glycosylation, sialation, albumination, farnesylation, carboxylation, hydroxylation and phosphorylation, which is the common subject matter of instant claims 15.

Claim 17 of '401 discloses that the modified PH20 polypeptide is glycosylated, whereby the polypeptide comprises at least an N-acetylglucosamine moiety linked to each of at least three asparagine (N) residues, which is the common subject matter of instant claims 16.

Claims 19-20 of '401 disclose that the modified PH20 polypeptide is conjugated to a polymer such as dextran or PEG which is the common subject matter of instant claims 17-18.

Claims 22-23 of '401 discloses a pharmaceutical composition comprising the modified PH20 polypeptide, which is the common subject matter of instant claim 21.

Conclusion

No claims are allowed.

During examination, US 20110053247, US 20090028829 and US 20120093770 were also reviewed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to SAMUEL W LIU whose telephone number is (571)272-0949. The examiner can normally be reached on M-F 8:30 am-5:30 pm.

Examiner interviews are available via telephone, in-person, and video conferencing using a USPTO supplied web-based collaboration tool. To schedule an interview, applicant is encouraged to use the USPTO Automated Interview Request (AIR) at <http://www.uspto.gov/interviewpractice>.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Manjunath Rao can be reached on 571-272-0939. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <https://ppair-my.uspto.gov/pair/PrivatePair>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Samuel Wei Liu/
Patent Examiner, Art Unit 1656
November 17, 2020

/SCARLETT Y GOON/
Quality Assurance Specialist, Art Unit 1600

Notice of References Cited	Application/Control No. 16/912,590		Applicant(s)/Patent Under Reexamination WEI et al.	
	Examiner SAMUEL W LIU		Art Unit 1656	Page 1 of 1

U.S. PATENT DOCUMENTS

*		Document Number Country Code-Number-Kind Code	Date MM-YYYY	Name	CPC Classification	US Classification
*	A	US-20110053247-A1	03-2011	Baker; David	C12Y302/01036	435/201
*	B	US-20090028829-A1	01-2009	Gruskin; Elliott A.	C12N9/88	424/93.7
*	C	US-20120093770-A1	04-2012	Bookbinder; Louis H.	A61P31/08	424/85.2
	D					
	E					
	F					
	G					
	H					
	I					
	J					
	K					
	L					
	M					

FOREIGN PATENT DOCUMENTS

*		Document Number Country Code-Number-Kind Code	Date MM-YYYY	Country	Name	CPC Classification
	N					
	O					
	P					
	Q					
	R					
	S					
	T					

NON-PATENT DOCUMENTS

*		Include as applicable: Author, Title Date, Publisher, Edition or Volume, Pertinent Pages)
	U	
	V	
	W	
	X	

*A copy of this reference is not being furnished with this Office action. (See MPEP § 707.05(a).)
Dates in MM-YYYY format are publication dates. Classifications may be US or foreign.

U.S. Patent and Trademark Office
PTO-892 (Rev. 01-2001)

Notice of References Cited

Part of Paper No. 20201106

<i>Search Notes</i> 	Application/Control No. 16/912,590	Applicant(s)/Patent Under Reexamination WEI et al.
	Examiner SAMUEL W LIU	Art Unit 1656

CPC - Searched*		
Symbol	Date	Examiner

CPC Combination Sets - Searched*		
Symbol	Date	Examiner
C12N 9/2474	11/12/2020	SWL

US Classification - Searched*			
Class	Subclass	Date	Examiner

* See search history printout included with this form or the SEARCH NOTES box below to determine the scope of the search.

Search Notes		
Search Notes	Date	Examiner
STIC sequence search for SEQ ID NOs:3, 7, 32-39 and 581-585.	11/10/2020	SWL
WEST search ad google prior art search for (PH20 protein or hyaluronidase or EC 3.2.1.35 or sperm adhesion molecule 1 (SPAM1) / PH20 variant or PH20 mutant or modified PH20 polypeptide / substitution at residue 309 or amino acid substitution I309N (according to SEQ ID NO:3 for amino acid sequence numbering).	11/17/2020	SWL
PALM inventor name search, and reviewed application Nos. 16824572 and 14323932, and US Pat. Nos. 8927249, 9284543 and 9447401.	11/12/2020	SWL

Interference Search			
US Class/CPC Symbol	US Subclass/CPC Group	Date	Examiner

/SAMUEL W LIU/ Examiner, Art Unit 1656	
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<i>Search Notes</i> 	Application/Control No. 16/912,590	Applicant(s)/Patent Under Reexamination WEI et al.
	Examiner SAMUEL W LIU	Art Unit 1656

/SAMUEL W LIU/ Examiner, Art Unit 1656	
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Web Search History

date, time	web site	search string
11/18/2020 11:41:46 PM	Google	(sperm adhesion molecule 1 (SPAM1) or PH20) and (variant or mutant)
11/18/2020 11:42:30 PM	Google	(sperm adhesion molecule 1 (SPAM1) or PH20) and (variant or mutant) and amino acid residue 309 substitution
11/18/2020 11:43:30 PM	Google	(sperm adhesion molecule 1 (SPAM1) or PH20) and (variant or mutant) and I309 substitution
11/18/2020 11:44:24 PM	Google	PH20 (variant or mutant) and amino acid substitution at residue 309 or I309N
11/18/2020 11:44:54 PM	Google	PH20 (variant or mutant) and amino acid substitution at residue 309
11/19/2020 3:56:59 AM	Google	(PH20 protein or hyaluronidase or EC 3.2.1.35) and variant or mutant and substitution at 309

Copy

Attorney Docket No.: 33320.03087.US27/3087D

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Inventors : Wei *et al.* Art Unit : 1652
Serial No. : 16/912,590 Examiner : Not Yet Assigned
Filed : June 25, 2020 Conf. No. : 9651
Cust. No. : 13565
Title : **PH20 POLYPEPTIDE VARIANTS, FORMULATIONS AND USES
THEREOF**

Mail Stop Amendment

Commissioner for Patents

P.O. Box 1450

Alexandria, VA 22313-1450

/S.W.L./

09/30/2020

**INFORMATION DISCLOSURE STATEMENT IN
ACCORDANCE WITH 37 C.F.R. §§ 1.97-1.98**

Dear Sir:

Because this Information Disclosure Statement is filed before the receipt of a First Office Action on the Merits for the above-captioned application, a fee is not required. However, should it be determined that a fee for filing these papers is required, the Commissioner is authorized to charge Deposit Account No. 50-0911.

In accordance with the duty of disclosure imposed by 37 C.F.R. § 1.56 to inform the Patent Office of all information known by Applicant or Applicant's representative that may be material to the examination of the subject application, Applicant's representative hereby provides this Information Disclosure Statement that is prepared in accordance with 37 C.F.R. §§ 1.97-1.98. Forms PTO-1449 (24 pages) and copies of the cited non-U.S. patent documents are provided herewith in connection with the above-captioned application. In accordance with 37 C.F.R. §1.98(d), copies of the references listed on the Forms PTO-1449 that are marked with a double asterisk (**) are not provided herewith as they have been previously provided in connection with U.S. Application Serial No. 13/694,731, 15/226,489, and/or 16/824,572, which are relied upon for an earlier filing date in accordance with 35 U.S.C. §120.

The documents cited on the Forms PTO-1449 are in the English language, with the exception of the items noted below. Item FP (CN 102065886A) is in the Chinese language and an English language equivalent (Item GD, WO 2009/128917) was previously provided in connection with U.S. Application Serial No. 13/694,731. Item FU (JP 2007-153797) is in the Japanese language and an English Derwent Abstract (Item HY) for Japanese Publication No. JP 2007-153797 was previously provided in connection with U.S. Application Serial No.

CERTIFICATE OF TRANSMISSION VIA EFS-WEB

I hereby certify that this paper is being transmitted via the Electronic Filing System (EFS-WEB) to the United States Patent and Trademark Office on July 08, 2020.

/Hyun Jeung Ji/
Hyun Jeung Ji

Copy

Inventors : Wei *et al.*
Serial No. : 16/912,590
Filed : June 25, 2020

Attorney Docket No.: 33320.03087.US27/3087D
Information Disclosure Statement

13/694,731. Item FV (KR 10-2020-0017538) is in the Korean language and a machine generated English translation was previously provided in connection with U.S. Application Serial No. 15/226,489. Hence, in accordance with the requirements of 37 C.F.R. § 1.98, no further explanation of the listed items is necessary.

Applicant also makes known to the Examiner the following pending U.S. Applications that have one or more common inventors and/or an owner in common:

	U.S.S.N.	Filing Date	Publ. No.	Publ. Date	Docket No.	
/S.W.L./	16/373,562	04/02/2019	2019-0224286	7/25/2019	3051L	
/S.W.L./	15/444,151	02/27/2017	2017/0218069 2018/0044419	08/03/2017 02/15/2018	3087B	/SAMUEL W LIU/
/S.W.L./	16/824,572	3/19/2020	n/a	n/a	3087C	09/30/2020

Although these documents and applications are made known to the Patent and Trademark Office in compliance with Applicant's duty of disclosure, such disclosure is not to be construed as an admission by Applicant or Applicant's representative that any of the documents, singly or in any combination thereof, is effective as prior art against the subject application. In accordance with 37 C.F.R. § 1.97(g) and (h), the filing of this Information Disclosure Statement shall not be construed to mean that a search has been made or that no other material information as defined in 37 C.F.R. § 1.56(b) exists.

Applicant respectfully requests that the Examiner review the foregoing documents and they be made of record in the file history of the above-captioned application.

Respectfully submitted,

/Stephanic Scidman/
Stephanic Scidman
Reg. No. 33,779

Attorney Docket No.: 33320.03087.US27/3087D

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It is noted that this portion of the IDS is duplicated which three references have been considered by Examiner.

/SAMUEL W LIU/

09/30/2020

Substitute Form PTO-1449 (Modified)	U.S. Department of Commerce Patent and Trademark Office	Attorney Docket No. 33320.03087.US27/3087D	Application No. 16/912,590
List of Patents and Publications for Applicant's Information Disclosure Statement (37 CFR §1.98(b))		Inventor(s) Wei <i>et al.</i>	
		Filing Date June 25, 2020	Group Art Unit 1656

U.S. Patent Documents							
Examiner Initial	Desig. ID	Document Number	Publication Date	Patentee	Class	Subclass	Filing Date If Appropriate
	AA	2020/0255814	08/13/2020	Wei et al.	435	069.100	03/19/2020

Foreign Patent Documents or Published Foreign Patent Applications						
Examiner Initial	Desig. ID	Document Number	Publication Date	Country or Patent Office	Translation	
					Yes	No
None						

Other Documents (include Author, Title, Date, and Place of Publication)		
Examiner Initial	Desig. ID	Document
	AB	Letter/Written Disclosure of the Supplemental Information Disclosure Statement for the above-referenced application, filed herewith on Oct. 26, 2020, 2 pages.
	AC	Notice of Allowance, issued Jul. 16, 2020, in connection with corresponding U.S. Patent Application No. 15/226,489, 13 pages.
	AD	Written Submissions, filed Oct. 09, 2020, responsive to Hearing Notice, issued Aug. 10, 2020, in connection with corresponding Indian Patent Application No. 6272/DELNP/2014, 27 pages.

Examiner Signature /SAMUEL W LIU/	Date Considered 11/06/2020
EXAMINER: Initial if citation considered, whether or not citation is in conformance with MPEP 609; Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.	

Substitute Form PTO-1449 (Modified) List of Patents and Publications for Applicant's Information Disclosure Statement (37 CFR §1.98(b))	U.S. Department of Commerce Patent and Trademark Office		Attorney Docket No. 33320.03087.US27/3087D	Application No. 16/912,590
	Inventor(s) Wei <i>et al.</i>			
	Filing Date June 25, 2020		Group Art Unit 1656	

U.S. Patent Documents							
Examiner Initial	Desig. ID	Document Number	Publication Date	Patentee	Class	Subclass	Filing Date If Appropriate
	AA	2020/0255814	08/13/2020	Wei et al.	435	069.100	03/19/2020

Foreign Patent Documents or Published Foreign Patent Applications						
Examiner Initial	Desig. ID	Document Number	Publication Date	Country or Patent Office	Translation	
					Yes	No
None						

Other Documents (include Author, Title, Date, and Place of Publication)		
Examiner Initial	Desig. ID	Document
	AB	Letter/Written Disclosure of the Supplemental Information Disclosure Statement for the above-referenced application, filed herewith on Oct. 26, 2020, 2 pages.
	AC	Notice of Allowance, issued Jul. 16, 2020, in connection with corresponding U.S. Patent Application No. 15/226,489, 13 pages.
	AD	Written Submissions, filed Oct. 09, 2020, responsive to Hearing Notice, issued Aug. 10, 2020, in connection with corresponding Indian Patent Application No. 6272/DELNP/2014, 27 pages.

ALL REFERENCES CONSIDERED EXCEPT WHERE LINED THROUGH. /S.W.L./

Examiner Signature /SAMUEL W LIU/	Date Considered 11/06/2020
EXAMINER: Initial if citation considered, whether or not citation is in conformance with MPEP 609; Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.	



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BIB DATA SHEET

CONFIRMATION NO. 9651

SERIAL NUMBER	FILING or 371(c) DATE	CLASS	GROUP ART UNIT	ATTORNEY DOCKET NO.		
16/912,590	06/25/2020	424	1656	33320.03087.US27/3087D		
APPLICANTS HALOZYME, INC., SAN DIEGO, CA; INVENTORS GE WEI, SAN DIEGO, CA; H. MICHAEL SHEPARD, SAN DIEGO, CA; QIPING ZHAO, SAN DIEGO, CA; ROBERT JAMES CONNOR, OCEANSIDE, CA;						
** CONTINUING DATA ***** This application is a CON of 15/226,489 08/02/2016 which is a DIV of 13/694,731 12/28/2012 PAT 9447401 which claims benefit of 61/796,208 11/01/2012 and claims benefit of 61/631,313 12/30/2011 This application 16/912,590 06/25/2020 is a DIV of 13/694,731 12/28/2012 PAT 9447401 which claims benefit of 61/796,208 11/01/2012 and claims benefit of 61/631,313 12/30/2011 ** FOREIGN APPLICATIONS ***** ** IF REQUIRED, FOREIGN FILING LICENSE GRANTED ** 07/02/2020						
Foreign Priority claimed ☐ Yes ☒ No 35 USC 119(a-d) conditions met ☐ Yes ☒ No Verified and /SAMUEL W LIU/ Acknowledged Examiner's Signature		☐ Met after Allowance Initials	STATE OR COUNTRY CA	SHEETS DRAWINGS 13	TOTAL CLAIMS 22	INDEPENDENT CLAIMS 1
ADDRESS Dentons US LLP 4655 Executive Drive Suite 700 San Diego, CA 92121 UNITED STATES						
TITLE PH20 POLYPEPTIDE VARIANTS, FORMULATIONS AND USES THEREOF						
FILING FEE RECEIVED 3720	FEES: Authority has been given in Paper No. _____ to charge/credit DEPOSIT ACCOUNT No. _____ for following:			☐ All Fees ☐ 1.16 Fees (Filing) ☐ 1.17 Fees (Processing Ext. of time) ☐ 1.18 Fees (Issue) ☐ Other _____ ☐ Credit		

WEST Search History for Application 16912590

Creation Date: 2020111903:49

Prior Art Searches

Query	DB	Hits	Op.	Plur.	Thes.	Date
(H20 or sperm adhesion molecule 1 or SPAM1) and (variant or mutant or engineer\$3 or mutated or modified) and substitution	PGPB, USPT, USOC	5191	ADJ	YES		11-19-2020
((H20 or sperm adhesion molecule 1 or SPAM1) and (variant or mutant or engineer\$3 or mutated or modified) and substitution) and PH20 with (substitut\$3 or replace\$5) with (I309 or 309)	PGPB, USPT, USOC	7	ADJ	YES		11-19-2020
PH20 with (variant or mutant or modified) with amino acid with (substitut\$3 or replace\$5)	PGPB, USPT, USOC	n/a	ADJ	YES		11-19-2020
PH20 with (variant or mutant or modified) with amino acid with (substitut\$3 or replace\$5)	PGPB, USPT, USOC	7	ADJ	YES		11-19-2020
PH20 with (variant or mutant or modified) with (substitut\$3 or replace\$5)	PGPB, USPT, USOC	13	ADJ	YES		11-19-2020
(PH20 with (variant or mutant or modified) with (substitut\$3 or replace\$5)) and @ad<20111230	PGPB, USPT, USOC	2	ADJ	YES		11-19-2020
(PH20 with (variant or mutant or modified) and (substitut\$3 or replace\$5)) and @ad<20111230	PGPB, USPT, USOC	34	ADJ	YES		11-19-2020
(PH20 with (variant or mutant or modified) and (substitut\$3 or replace\$5) and @ad<20111230) and (position or amino acid or residue) with 309	PGPB, USPT, USOC	0	ADJ	YES		11-19-2020

Doc Code: DIST.E.FILE Document Description: Electronic Terminal Disclaimer - Filed		PTO/SB/26 U.S. Patent and Trademark Office Department of Commerce
Electronic Petition Request	TERMINAL DISCLAIMER TO OBIATE A DOUBLE PATENTING REJECTION OVER A "PRIOR" PATENT	
Application Number	16912590	
Filing Date	25-Jun-2020	
First Named Inventor	GE WEI	
Attorney Docket Number	33320.03087.US27/3087D	
Title of Invention	PH20 POLYPEPTIDE VARIANTS, FORMULATIONS AND USES THEREOF	
☒ Filing of terminal disclaimer does not obviate requirement for response under 37 CFR 1.111 to outstanding Office Action ☒ This electronic Terminal Disclaimer is not being used for a Joint Research Agreement.		
Owner	Percent Interest	
HALOZYME, INC.	100%	
The owner(s) with percent interest listed above in the instant application hereby disclaims, except as provided below, the terminal part of the statutory term of any patent granted on the instant application which would extend beyond the expiration date of the full statutory term of prior patent number(s) 10865400 9447401 as the term of said prior patent is presently shortened by any terminal disclaimer. The owner hereby agrees that any patent so granted on the instant application shall be enforceable only for and during such period that it and the prior patent are commonly owned. This agreement runs with any patent granted on the instant application and is binding upon the grantee, its successors or assigns. In making the above disclaimer, the owner does not disclaim the terminal part of the term of any patent granted on the instant application that would extend to the expiration date of the full statutory term of the prior patent, "as the term of said prior patent is presently shortened by any terminal disclaimer," in the event that said prior patent later: - expires for failure to pay a maintenance fee; - is held unenforceable; - is found invalid by a court of competent jurisdiction; - is statutorily disclaimed in whole or terminally disclaimed under 37 CFR 1.321; - has all claims canceled by a reexamination certificate; - is reissued; or - is in any manner terminated prior to the expiration of its full statutory term as presently shortened by any terminal disclaimer.		

☒ Terminal disclaimer fee under 37 CFR 1.20(d) is included with Electronic Terminal Disclaimer request. ☐ I certify, in accordance with 37 CFR 1.4(d)(4), that the terminal disclaimer fee under 37 CFR 1.20(d) required for this terminal disclaimer has already been paid in the above-identified application.	
Applicant claims the following fee status: ☐ Small Entity ☐ Micro Entity ☒ Regular Undiscounted I hereby declare 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, or both, under Section 1001 of Title 18 of the United States Code and that such willful false statements may jeopardize the validity of the application or any patent issued thereon.	
THIS PORTION MUST BE COMPLETED BY THE SIGNATORY OR SIGNATORIES I certify, in accordance with 37 CFR 1.4(d)(4) that I am: ☒ An attorney or agent registered to practice before the Patent and Trademark Office who is of record in this application Registration Number <u>33779</u> ☐ A sole inventor ☐ A joint inventor; I certify that I am authorized to sign this submission on behalf of all of the inventors as evidenced by the power of attorney in the application ☐ A joint inventor; all of whom are signing this request	
Signature	/Stephanie Seidman/
Name	Stephanie Seidman

*Statement under 37 CFR 3.73(b) is required if terminal disclaimer is signed by the assignee (owner).
 Form PTO/SB/96 may be used for making this certification. See MPEP § 324.

Electronic Patent Application Fee Transmittal				
Application Number:		16912590		
Filing Date:		25-Jun-2020		
Title of Invention:		PH20 POLYPEPTIDE VARIANTS, FORMULATIONS AND USES THEREOF		
First Named Inventor/Applicant Name:		GE WEI		
Filer:		Stephanie L. Seidman/Rosalind Smith		
Attorney Docket Number:		33320.03087.US27/3087D		
Filed as Large Entity				
Filing Fees for Utility under 35 USC 111(a)				
Description	Fee Code	Quantity	Amount	Sub-Total in USD(\$)
Basic Filing:				
STATUTORY OR TERMINAL DISCLAIMER	1814	1	170	170
Pages:				
Claims:				
Miscellaneous-Filing:				
Petition:				
Patent-Appeals-and-Interference:				
Post-Allowance-and-Post-Issuance:				

Description	Fee Code	Quantity	Amount	Sub-Total in USD(\$)
Extension-of-Time:				
Miscellaneous:				
Total in USD (\$)				170

Doc Code: DISQ.E.FILE
Document Description: Electronic Terminal Disclaimer – Approved

Application No.: 16912590

Filing Date: 25-Jun-2020

Applicant/Patent under Reexamination: WEI

Electronic Terminal Disclaimer filed on March 15, 2021

☒ APPROVED

This patent is subject to a terminal disclaimer

☐ DISAPPROVED

Approved/Disapproved by: Electronic Terminal Disclaimer automatically approved by EFS-Web

U.S. Patent and Trademark Office

Electronic Acknowledgement Receipt	
EFS ID:	42135701
Application Number:	16912590
International Application Number:	
Confirmation Number:	9651
Title of Invention:	PH20 POLYPEPTIDE VARIANTS, FORMULATIONS AND USES THEREOF
First Named Inventor/Applicant Name:	GE WEI
Customer Number:	13565
Filer:	Stephanie L. Seidman/Rosalind Smith
Filer Authorized By:	Stephanie L. Seidman
Attorney Docket Number:	33320.03087.US27/3087D
Receipt Date:	15-MAR-2021
Filing Date:	25-JUN-2020
Time Stamp:	18:28:26
Application Type:	Utility under 35 USC 111(a)

Payment information:

Submitted with Payment	yes
Payment Type	DA
Payment was successfully received in RAM	\$170
RAM confirmation Number	E20213EI28211149
Deposit Account	500911
Authorized User	Rosalind Smith
The Director of the USPTO is hereby authorized to charge indicated fees and credit any overpayment as follows: 37 CFR 1.16 (National application filing, search, and examination fees) 37 CFR 1.17 (Patent application and reexamination processing fees)	

37 CFR 1.19 (Document supply fees)
 37 CFR 1.20 (Post Issuance fees)
 37 CFR 1.21 (Miscellaneous fees and charges)

File Listing:

Document Number	Document Description	File Name	File Size(Bytes)/ Message Digest	Multi Part /.zip	Pages (if appl.)
1	Terminal Disclaimer-Filed (Electronic)	eTerminal-Disclaimer.pdf	33629	no	2
			043553ef9e692e10c6535ad86fd8616e9704c77		

Warnings:

Information:

2	Fee Worksheet (SB06)	fee-info.pdf	30610	no	2
			98cf941d8469cc8f87ffba175f339ad88af6e96d		

Warnings:

Information:

Total Files Size (in bytes):			64239
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This Acknowledgement Receipt evidences receipt on the noted date by the USPTO of the indicated documents, characterized by the applicant, and including page counts, where applicable. It serves as evidence of receipt similar to a Post Card, as described in MPEP 503.

New Applications Under 35 U.S.C. 111

If a new application is being filed and the application includes the necessary components for a filing date (see 37 CFR 1.53(b)-(d) and MPEP 506), a Filing Receipt (37 CFR 1.54) will be issued in due course and the date shown on this Acknowledgement Receipt will establish the filing date of the application.

National Stage of an International Application under 35 U.S.C. 371

If a timely submission to enter the national stage of an international application is compliant with the conditions of 35 U.S.C. 371 and other applicable requirements a Form PCT/DO/EO/903 indicating acceptance of the application as a national stage submission under 35 U.S.C. 371 will be issued in addition to the Filing Receipt, in due course.

New International Application Filed with the USPTO as a Receiving Office

If a new international application is being filed and the international application includes the necessary components for an international filing date (see PCT Article 11 and MPEP 1810), a Notification of the International Application Number and of the International Filing Date (Form PCT/RO/105) will be issued in due course, subject to prescriptions concerning national security, and the date shown on this Acknowledgement Receipt will establish the international filing date of the application.

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant	: Wei <i>et al.</i>	Art Unit	: 1656
Serial No.	: 16/912,590	Examiner	: Liu, Samuel W.
Filed	: June 25, 2020	Conf. No.	: 9651
		Cust. No.	: 13565
Title	: PH20 POLYPEPTIDE VARIANTS, FORMULATIONS AND USES THEREOF		

Mail Stop Amendment

Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

**SUPPLEMENTAL INFORMATION DISCLOSURE STATEMENT IN
ACCORDANCE WITH 37 C.F.R. §§ 1.97-1.98**

Dear Sir:

Because this Supplemental Information Disclosure Statement is filed after the receipt of a First Office Action on the Merits for the above-captioned application, the Commissioner is authorized to charge the fee for filing the Supplemental Information Disclosure Statement to Deposit Account No. 50-0911.

In accordance with the duty of disclosure imposed by 37 C.F.R. § 1.56 to inform the Patent Office of all information known by Applicant or Applicant's representative that may be material to the examination of the subject application, Applicant's representative hereby provides this Supplemental Information Disclosure Statement that is prepared in accordance with 37 C.F.R. §§ 1.97-1.98. A Form PTO-1449 (1 page) and copies of the cited non-U.S. patent documents are provided herewith in connection with the above-captioned application.

The documents cited on the Form PTO-1449 are in the English language. Hence, in accordance with the requirements of 37 C.F.R. § 1.98, no further explanation of the listed items is necessary.

Although these documents and applications are made known to the Patent and Trademark Office in compliance with Applicant's duty of disclosure, such disclosure is not to be construed as an admission by Applicant or Applicant's representative that any of the documents, singly or in any combination thereof, is effective as prior art against the subject application. In accordance with 37 C.F.R. § 1.97(g) and (h), the filing of this Information Disclosure Statement shall not be construed to mean that a search has been made or that no other material information as defined in 37 C.F.R. § 1.56(b) exists.

CERTIFICATE OF TRANSMISSION VIA EFS-WEB

I hereby certify that this paper is being transmitted via the Electronic Filing System (EFS-WEB) to the United States Patent and Trademark Office on March 17, 2021.

/Hyun Jeung Ji/
Hyun Jeung Ji

Inventors : Wei *et al.*
Serial No. : 16/912,590
Filed : June 25, 2020

Attorney Docket No.: 33320.03087.US27/3087D
Supplemental Information Disclosure Statement

Applicant respectfully requests that the Examiner review the foregoing documents and they be made of record in the file history of the above-captioned application.

Respectfully submitted,

/Stephanie Seidman/
Stephanie Seidman
Reg. No. 33,779

Attorney Docket No.: 33320.03087.US27/3087D

Address all correspondence to: 13565

Stephanie Seidman
Dentons US LLP
4655 Executive Drive, Ste. 700
San Diego, California 92121
Telephone: (619) 595-8010
Facsimile: (619) 595-8135
email: stephanie.seidman@dentons.com

Substitute Form PTO-1449 (Modified)		U.S. Department of Commerce Patent and Trademark Office		Attorney Docket No. 33320.03087.US27/ 3087D		Application No. 16/912,590	
List of Patents and Publications for Applicant's Information Disclosure Statement (37 CFR §1.98(b))				Inventors <i>Wei et al.</i>			
				Filing Date June 25, 2020		Group Art Unit 1656	
U.S. Patent Documents							
Examiner Initial	Desig. ID	Document Number	Publication Date	Patentee	Class	Subclass	Filing Date If Appropriate
	AA	2020/0368330	11/26/2020	Frost et al.	424	078.170	07/16/2020

Foreign Patent Documents or Published Foreign Patent Applications						
Examiner Initial	Desig. ID	Document Number	Publication Date	Country or Patent Office	Translation	
					Yes	No
None						

Other Documents (include Author, Title, Date, and Place of Publication)		
Examiner Initial	Desig. ID	Document
	AB	Letter/Written Disclosure of the Information Disclosure Statement for the above-referenced application, filed herewith on March 17, 2021, 2 pages.
	AC	Rosengren et al., "Clinical Immunogenicity of rHuPH20, a Hyaluronidase Enabling Subcutaneous Drug Administration," AAPS J. 17(5):1144-56 (2015).
	AD	Office Action, issued Oct. 27, 2020, in connection with U.S. Patent Application No. 16/824,572, 9 pages.
	AE	Response, filed Jan. 27, 2021, to Office Action, issued Oct. 27, 2020, in connection with U.S. Patent Application No. 16/824,572, 23 pages.
	AF	Notice of Allowance, mailed Feb. 18, 2021, and Examiner-Initiated Interview Summary, summarizing the interview held on Feb. 10, 2021, issued in connection with U.S. Patent Application No. 16/824,572, 10 pages.
	AG	Amended claims and abstract, filed Nov. 19, 2020, responsive to Examiner request, in connection with Indian Patent Application No. 6272/DELNP/2014, 22 pages.
	AH	Certificate of Grant, issued Dec. 28, 2020, in connection with Indian Patent Application No. 6272/DELNP/2014, 1 page.
	AI	Certificate of Grant, issued Oct. 01, 2020, in connection with Israeli Patent Application No. 233192, 3 pages.
	AJ	Notification Prior to Acceptance, issued Dec. 14, 2020, in connection with Israeli Patent Application No. 274798 [English reporting letter; original document as issued in Hebrew; and English translation of allowed claims], 10 pages.

Examiner Signature	Date Considered
EXAMINER: Initial if citation considered, whether or not citation is in conformance with MPEP 609; Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.	

Electronic Patent Application Fee Transmittal				
Application Number:		16912590		
Filing Date:		25-Jun-2020		
Title of Invention:		PH20 POLYPEPTIDE VARIANTS, FORMULATIONS AND USES THEREOF		
First Named Inventor/Applicant Name:		GE WEI		
Filer:		Stephanie L. Seidman/Hyun Jeung Ji		
Attorney Docket Number:		33320.03087.US27/3087D		
Filed as Large Entity				
Filing Fees for Utility under 35 USC 111(a)				
Description	Fee Code	Quantity	Amount	Sub-Total in USD(\$)
Basic Filing:				
Pages:				
Claims:				
Miscellaneous-Filing:				
Petition:				
Patent-Appeals-and-Interference:				
Post-Allowance-and-Post-Issuance:				
Extension-of-Time:				

Description	Fee Code	Quantity	Amount	Sub-Total in USD(\$)
Miscellaneous:				
SUBMISSION- INFORMATION DISCLOSURE STMT	1806	1	260	260
Total in USD (\$)				260

Electronic Acknowledgement Receipt	
EFS ID:	42211462
Application Number:	16912590
International Application Number:	
Confirmation Number:	9651
Title of Invention:	PH20 POLYPEPTIDE VARIANTS, FORMULATIONS AND USES THEREOF
First Named Inventor/Applicant Name:	GE WEI
Customer Number:	13565
Filer:	Stephanie L. Seidman/Hyun Jeung Ji
Filer Authorized By:	Stephanie L. Seidman
Attorney Docket Number:	33320.03087.US27/3087D
Receipt Date:	17-MAR-2021
Filing Date:	25-JUN-2020
Time Stamp:	20:24:50
Application Type:	Utility under 35 USC 111(a)

Payment information:

Submitted with Payment	yes
Payment Type	DA
Payment was successfully received in RAM	\$260
RAM confirmation Number	E20213GK25263590
Deposit Account	500911
Authorized User	Hyun Jeung Ji
The Director of the USPTO is hereby authorized to charge indicated fees and credit any overpayment as follows: 37 CFR 1.16 (National application filing, search, and examination fees) 37 CFR 1.17 (Patent application and reexamination processing fees)	

37 CFR 1.19 (Document supply fees)					
37 CFR 1.20 (Post Issuance fees)					
37 CFR 1.21 (Miscellaneous fees and charges)					
File Listing:					
Document Number	Document Description	File Name	File Size(Bytes)/ Message Digest	Multi Part /.zip	Pages (if appl.)
1	Transmittal Letter	3087Dtra.pdf	25258	no	1
			92cc36ddb7eb14c307796f4cf7f0295dd848d9f1		
Warnings:					
Information:					
2	Information Disclosure Statement (IDS) Form (SB08)	3087Dids.pdf	29458	no	2
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Warnings:					
Information:					
This is not an USPTO supplied IDS fillable form					
3	Information Disclosure Statement (IDS) Form (SB08)	3087Dp49.pdf	33922	no	1
			2043f5c3a6d03fccd4700fd3c7032eefd3cf7966		
Warnings:					
Information:					
This is not an USPTO supplied IDS fillable form					
4	Non Patent Literature	AB.pdf	101325	no	2
			f3358f8d01a4895c79327fbd158122975df39175		
Warnings:					
Information:					
5	Non Patent Literature	AC.pdf	653835	no	13
			67005e5c7babcf63aebdea310b1116744c912c723		
Warnings:					
Information:					
6	Non Patent Literature	AD.pdf	377285	no	9
			71f0c139eea18181cccd9b213f2e62eb454cbf0		

Warnings:					
Information:					
7	Non Patent Literature	AE.pdf	313310	no	23
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Warnings:					
Information:					
8	Non Patent Literature	AF.pdf	581104	no	10
			1e4b69647e123889c9c6c0e3de4e09cb806248d3		
Warnings:					
Information:					
9	Non Patent Literature	AG.pdf	9475115	no	22
			3cc5abcc2e9df919188d6718e565c33534b8c5da		
Warnings:					
Information:					
10	Non Patent Literature	AH.pdf	1363172	no	1
			119e433db6803cb7aac84e7b8ced38da6aff46d6d		
Warnings:					
Information:					
11	Non Patent Literature	AI.pdf	220396	no	3
			02ab05d332ad6af76f155841c09b01832c7eaf6789		
Warnings:					
Information:					
12	Non Patent Literature	AJ.pdf	5907433	no	10
			8ca93a08a1332f915e9ac9469f6f9c102e11d05d		
Warnings:					
Information:					
13	Fee Worksheet (SB06)	fee-info.pdf	30757	no	2
			6eb72d0b4953ec35506bc940ce3e73d399c590da		
Warnings:					
Information:					

This Acknowledgement Receipt evidences receipt on the noted date by the USPTO of the indicated documents, characterized by the applicant, and including page counts, where applicable. It serves as evidence of receipt similar to a Post Card, as described in MPEP 503.

New Applications Under 35 U.S.C. 111

If a new application is being filed and the application includes the necessary components for a filing date (see 37 CFR 1.53(b)-(d) and MPEP 506), a Filing Receipt (37 CFR 1.54) will be issued in due course and the date shown on this Acknowledgement Receipt will establish the filing date of the application.

National Stage of an International Application under 35 U.S.C. 371

If a timely submission to enter the national stage of an international application is compliant with the conditions of 35 U.S.C. 371 and other applicable requirements a Form PCT/DO/EO/903 indicating acceptance of the application as a national stage submission under 35 U.S.C. 371 will be issued in addition to the Filing Receipt, in due course.

New International Application Filed with the USPTO as a Receiving Office

If a new international application is being filed and the international application includes the necessary components for an international filing date (see PCT Article 11 and MPEP 1810), a Notification of the International Application Number and of the International Filing Date (Form PCT/RO/105) will be issued in due course, subject to prescriptions concerning national security, and the date shown on this Acknowledgement Receipt will establish the international filing date of the application.

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant : Wei *et al.* Art Unit : 1656
Serial No. : 16/912,590 Examiner : Liu, Samuel W.
Filed : June 25, 2020 Conf. No. : 9651
Cust. No. : 13565
Title : **PH20 POLYPEPTIDE VARIANTS, FORMULATIONS AND USES
THEREOF**

Mail Stop Amendment

Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

**SUPPLEMENTAL INFORMATION DISCLOSURE STATEMENT TRANSMITTAL
LETTER**

Dear Sir:

Transmitted herewith are a Supplemental Information Disclosure Statement (2 pages), Form PTO-1449 (1 page), and cited non-U.S. patent documents for filing in connection with the above-identified application. Because this Supplemental Information Disclosure Statement is filed after the receipt of a First Office Action on the Merits in the above-referenced application, the Commissioner is authorized to charge Deposit Account No. 50-0911, as stated below:

☒ The Commissioner is hereby authorized to charge any fees that may be due in connection with this paper or with this application during its entire pendency to Deposit Account No. 50-0911.

Respectfully submitted,

/Stephanie Seidman/

Stephanie Seidman
Reg. No. 33,779

Attorney Docket No.: 33320.03087.US27/3087D

Address all correspondence to: 13565

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Dentons US LLP
4655 Executive Drive, Ste. 700
San Diego, California 92121
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Facsimile: (619) 595-8135
email: stephanie.seidman@dentons.com

CERTIFICATE OF TRANSMISSION VIA EFS-WEB

I hereby certify that this paper is being transmitted via the Electronic Filing System (EFS-WEB) to the United States Patent and Trademark Office on March 17, 2021.

/Hyun Jeung Ji/
Hyun Jeung Ji

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Inventors	: Wei <i>et al.</i>	Art Unit	: 1656
Serial No.	: 16/912,590	Examiner	: Samuel W. LIU
Filed	: June 25, 2020	Conf. No.	: 9651
		Cust. No.	: 13565
Title	: PH20 POLYPEPTIDE VARIANTS, FORMULATIONS AND USES THEREOF		

Mail Stop Amendment

Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

TRANSMITTAL LETTER

Dear Sir:

Responsive to the *Non-Final Office Action*, mailed December 9, 2020, transmitted herewith is an *Amendment and Response* (24 pages) for filing in connection with the above-identified application.

- ☒ **One-Month Extension of Time Fee by a Large Entity...\$220.00**
- ☒ **Two Additional Claims Large Entity (\$100 x 2).....\$200.00**
- ☒ The Commissioner is authorized to charge the extension of time fee for response within first month, excess claim fees, and any other fees that may be due in connection with this paper or with this application during its entire pendency to Deposit Account No. 50-0911.

Respectfully submitted,

/Stephanie Seidman/

Stephanie Seidman
Reg. No. 33,779

Attorney Docket No.: 33320.03087.US27/3087D
Address all correspondence to: 13565
Stephanie Seidman
Dentons US LLP
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San Diego, California 92121
Telephone: (619) 595-8010
Facsimile: (619) 595-8135
email: stephanie.seidman@dentons.com

CERTIFICATE OF TRANSMISSION VIA EFS-WEB

I hereby certify that this paper is being transmitted via the Electronic Filing System (EFS-WEB) to the United States Patent and Trademark Office on **March 17, 2021**.

/Jimmy Schaub/
Jimmy Schaub

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Inventors	: Wei <i>et al.</i>	Art Unit	: 1656
Serial No.	: 16/912,590	Examiner	: Liu, Samuel W.
Filed	: June 25, 2020	Conf. No.	: 9651
		Cust. No.	: 13565
Title	: PH20 POLYPEPTIDE VARIANTS, FORMULATIONS AND USES THEREOF		

Mail Stop Amendment

Commissioner for Patents

P.O. Box 1450

Alexandria, VA 22313-1450

AMENDMENT AND RESPONSE

Dear Sir:

Responsive to the Office Action, dated December 09, 2020, entry of the amendment and consideration of the following remarks respectfully are requested.

Amendments to the Specification begin on page **2** of this paper.

Amendments to the Claims begin on page **9** of this paper.

Remarks/Arguments begin on page **13** of this paper.

CERTIFICATE OF TRANSMISSION VIA EFS-WEB

I hereby certify that this paper is being transmitted via the Electronic Filing System (EFS-WEB) to the United States Patent and Trademark Office on **March 17, 2021**

/Jimmy Schaub/
Jimmy Schaub

Inventor(s) : Wei *et al.*
Serial No. : 16/912,590
Filed : June 25, 2020

Attorney Docket No.: 33320.03087.US27/3087D
Amendment and Response

AMENDMENTS TO THE SPECIFICATION:

Page and line numbers are designated with reference to the specification as originally filed on June 25, 2020. Please amend the specification as follows:

Replace the paragraph beginning at page 1, line 33, with the following amended paragraph:

Hyaluronan (hyaluronic acid; HA) is a polypeptide that is found in the extracellular matrix of many cells, especially in soft connective tissues. HA also is found predominantly in skin, cartilage, and in synovial fluid in mammals. Hyaluronan also is the main constituent of the vitreous of the eye. HA has a role in various physiological processes, such as in water and plasma protein homeostasis (Laurent TC *et al.* (1992) *FASEB J* 6: 2397-2404). Certain diseases are associated with expression and/or production of hyaluronan. Hyaluronan-degrading enzymes, such as hyaluronidases, are enzymes that degrade hyaluronan. By catalyzing HA degradation, hyaluronan-degrading enzymes (*e.g.*, hyaluronidases) can be used to treat diseases or disorders associated with accumulation of HA or other glycosaminoglycans. Also, since HA is a major component of the interstitial barrier, hyaluronan-degrading enzymes (*e.g.*, hyaluronidase) increase tissue permeability and therefore can be used to increase the dispersion and delivery of therapeutic agents. Various hyaluronidases have been used therapeutically (*e.g.*, hyaluronidases sold under the trademarks Hydase[®][[TM]](bovine testicular hyaluronidase), Vitrase[®][[TM]] (ovine hyaluronidase), and Wydase[®][[TM]](bovine hyaluronidase)), typically as dispersing and spreading agents in combination with other therapeutic agents. Many of these are ovine or bovine forms, which can be immunogenic for treatment of humans. Improved hyaluronan-degrading enzymes, such as hyaluronidases, and compositions thereof that can be used for treatment are needed.

Replace the paragraph beginning at page 52, line 28, with the following amended paragraph:

As used herein, soluble human PH20 (sHuPH20) includes human PH20 polypeptides that lack a contiguous sequence of amino acids from the C-terminus of human PH20 that includes all or a portion of the glycosylphosphatidylinositol (GPI) anchor sequence (C-terminally truncated PH20 polypeptides) such that upon expression, the polypeptides are soluble under physiological conditions. For example, soluble human PH20 polypeptides are C-terminally truncated polypeptides of human PH20 set forth as SEQ ID NO:6 in its precursor form or in SEQ ID NO:7 in its mature form lacking the signal sequence, or allelic variants thereof (*e.g.* set forth in any of SEQ ID NOS: 68-72). Solubility can be assessed by any

Inventor(s) : Wei *et al.*
Serial No. : 16/912,590
Filed : June 25, 2020

Attorney Docket No.: 33320.03087.US27/3087D
Amendment and Response

suitable method that demonstrates solubility under physiologic conditions. Exemplary of such methods is the Triton® X-114 assay, that assesses partitioning into the aqueous phase and that is described above. In addition, a soluble human PH20 polypeptide is, if produced in CHO cells, such as CHO-S cells, a polypeptide that is expressed and is secreted into the cell culture medium. Soluble human PH20 polypeptides, however, are not limited to those produced in CHO cells, but can be produced in any cell or by any method, including recombinant expression and polypeptide synthesis. Reference to secretion in CHO cells is definitional. Hence, if a polypeptide could be expressed and secreted in CHO cells and is soluble in the media, *i.e.*, partitions into the aqueous phase when extracted with Triton® X-114 detergent, it is a soluble PH20 polypeptide whether or not it is so-produced. The precursor polypeptides for sHuPH20 polypeptides can include a signal sequence, such as a heterologous or non-heterologous (*i.e.*, native) signal sequence. Exemplary of the precursors are those that include a signal sequence, such as the native 35 amino acid signal sequence at amino acid positions 1-35 (see, *e.g.*, amino acids 1-35 of SEQ ID NO:6).

Replace the paragraph beginning at page 75, line 25, with the following amended paragraph:

As used herein, “fast-acting insulin” refers to any insulin that exhibits peak insulin levels at or about not more than four hours following subcutaneous administration to a subject. Fast-acting insulins include any insulin or any fast-acting insulin composition for acute administration to a diabetic subject in response to an actual, perceived, or anticipated hyperglycemic condition in the subject arising at the time of, or within about four hours following, administration of the fast-acting insulin (such as a prandial hyperglycemic condition resulting or anticipated to result from, consumption of a meal), whereby the fast-acting insulin is able to prevent, control or ameliorate the acute hyperglycemic condition. Fast-acting insulins include recombinant insulins and isolated insulins (also referred to as “regular” insulins) such as the insulin sold as human insulin, porcine insulins and bovine insulins, as well as rapid acting insulin analogs (also termed fast-acting insulin analogs herein) designed to be rapid acting by virtue of amino acid changes. Exemplary regular insulin preparations include, but are not limited to, human regular insulins, such as those sold under the trademarks Humulin® R, Novolin® R and Velosulin®, Insulin Human, USP and Insulin Human Injection, USP, as well as acid formulations of insulin, such as, for example, Toronto Insulin, Old Insulin, and Clear Insulin, and regular pig insulins, such as Iletin II® insulin (porcine insulin). Regular insulins

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typically have an onset of action of between 30 minutes to an hour, and a peak insulin level of 2-5 hours post administration.

Replace the paragraph beginning at page 84, line 32, with the following amended paragraph:

PH20 can exist in membrane-bound or membrane-associated form, or can be secreted into the media when expressed from cells, and thereby can exist in soluble form. Soluble PH20 can be detected and discriminated from insoluble, membrane-bound PH20 using methods well known in the art, including, but not limited to, those using a Triton® X-114 assay. In this assay, soluble PH20 hyaluronidases partition into the aqueous phase of a Triton® X-114 detergent solution warmed to 37 °C (Bordier *et al.*, (1981) J. Biol. Chem., 256:1604-7) while membrane-anchored PH20 hyaluronidases partition into the detergent rich phase. Thus, in addition to using algorithms to assess whether a PH20 polypeptide is naturally GPI-anchored and hence membrane-bound, solubility experiments also can be performed.

Replace the paragraph beginning at page 85, line 4, with the following amended paragraph:

Soluble PH20 enzymes include hyaluronidases that contain a GPI-anchor attachment signal sequence, but that are loosely attached to the membrane such that they do not contain a phospholipase sensitive anchor. For example, soluble PH20 polypeptides include ovine or bovine PH20. Various forms of such soluble PH20 hyaluronidases have been prepared and approved for therapeutic use in subjects, including humans. For example, animal-derived hyaluronidase preparations include Vitrase® hyaluronidase (ISTA Pharmaceuticals), which is a purified ovine testicular hyaluronidase, and Amphadase® hyaluronidase (Amphastar Pharmaceuticals), which is a bovine testicular hyaluronidase. Soluble PH20 enzymes also include truncated forms of non-human or human membrane-associated PH20 hyaluronidases that lack one or more amino acid residues of a glycosylphosphatidylinositol (GPI) anchor attachment signal sequence and that retain hyaluronidase activity (see *e.g.*, U.S. Patent No. 7,767,429; U.S. Publication No. US20100143457). Thus, instead of having a GPI-anchor covalently attached to the C-terminus of the protein in the ER and being anchored to the extracellular leaflet of the plasma membrane, these polypeptides are secreted when expressed from cells and are soluble. In instances where the soluble hyaluronan degrading enzyme retains a portion of the GPI anchor attachment signal sequence, 1, 2, 3, 4, 5, 6, 7, 8, 9, 10 or more amino acid residues in the GPI-anchor attachment signal sequence can be retained, provided the polypeptide is soluble (*i.e.*, secreted when expressed from cells) and active.

Replace the paragraph beginning at page 86, line 23, with the following amended paragraph:

In particular, a soluble human PH20 polypeptide is a polypeptide that is truncated after amino acid 482 of the sequence set forth in SEQ ID NO:6. Such a polypeptide can be generated from a nucleic acid molecule containing a signal sequence and encoding amino acids 36-482, for example, as set forth in SEQ ID NO:1 (containing an IgG kappa signal sequence) or SEQ ID NO:67 (containing the native signal sequence). Post translational processing removes the signal sequence, leaving a 447 amino acid soluble recombinant human PH20 (SEQ ID NO:3). A product produced upon expression of a vector set forth in SEQ ID NO:4 or 5, and containing a nucleic acid molecule set forth in SEQ ID NO:67, results in a secreted product, designated rHuPH20, in the culture medium that exhibits heterogeneity at the C-terminus such that the product includes a mixture of species that can include any one or more of SEQ ID NOS: 3 and 44-48 in various abundance. Typically, rHuPH20 is produced in cells that facilitate correct N-glycosylation to retain activity, such as mammalian cells, for example CHO cells (*e.g.*, DG44 CHO cells). Hylenex® hyaluronidase (Halozyme) is a human recombinant hyaluronidase produced by genetically engineered Chinese Hamster Ovary (CHO) cells containing nucleic acid encoding a truncated human PH20 polypeptide (designated rHuPH20).

Replace the paragraph beginning at page 174, line 15, with the following amended paragraph:

Single dose formulations of PH20 are known in the art. For example, Hylenex® recombinant hyaluronidase (hyaluronidase human injection) contains, per mL, 8.5 mg NaCl (145 mM), 1.4 mg dibasic sodium phosphate (9.9 mM), 1.0 mg human albumin, 0.9 mg edetate disodium (2.4 mM), 0.3 mg CaCl₂ (2.7 mM) and NaOH to adjust the pH to 7.4. Other formulations of human soluble hyaluronidase, such as the rHuPH20 formulations described in U.S. Pat. Pub. No. US2011/0053247, include 130 mM NaCl, 10 mM Hepes, pH 7.0; or 10 mM histidine, 130 mM NaCl, pH 6.0. Any of the modified PH20 polypeptides provided herein can be similarly formulated.

Replace the paragraph beginning at page 179, line 1, with the following amended paragraph:

In particular examples herein, the formulations contain one or more detergents, such as surfactants, to maintain the stability of the active agent(s) (*e.g.*, PH20 hyaluronidase). For example, surfactants can inhibit aggregation of PH20 and minimize absorptive loss. The

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surfactants generally are non-ionic surfactants. Surfactants that can be included in the formulations herein include, but are not limited to, partial and fatty acid esters and ethers of polyhydric alcohols such as of glycerol, or sorbitol, poloxamers and polysorbates. For example, exemplary surfactants in the -formulations herein include any one or more of poloxamer 188 (PLURONICS® poloxamer such as PLURONIC® F68 poloxamer), TETRONICS® surfactant, polysorbate 20, polysorbate 80, PEG 400, PEG 3000, Tween® surfactant (e.g., Tween® 20 or Tween® 80 surfactants), Triton® X-100 surfactant, SPAN® surfactant, MYRJ® surfactant, BRIJ® surfactant, CREMOPHOR® surfactant, polypropylene glycols or polyethylene glycols. In some examples, the formulations herein contain poloxamer 188, polysorbate 20, polysorbate 80, generally poloxamer 188 (pluronic F68). The formulations provided herein generally contain at least one surfactant, such as 1, 2 or 3 surfactants.

Replace the paragraph beginning at page 196, line 14, with the following amended paragraph:

The solubility of a PH20 polypeptide can be determined by any method known to one of the skill in the art. One method for determining solubility is detergent partitioning. For example, a soluble PH20 polypeptide can be distinguished, for example, by its partitioning into the aqueous phase of a Triton® X-114 detergent solution at 37 °C (Bordier et al., (1981) *J. Biol. Chem.*, 256:1604-1607). Membrane-anchored polypeptides, such as lipid-anchored hyaluronidases, including GPI-anchored hyaluronidases, will partition into the detergent-rich phase, but will partition into the detergent-poor or aqueous phase following treatment with Phospholipase C. Phospholipase C is an enzyme that cleaves the phospho-glycerol bond found in GPI-anchored proteins. Treatment with PLC will cause release of GPI-linked proteins from the outer cell membrane.

Replace the paragraph beginning at page 198, line 20, with the following amended paragraph:

Other methods and uses of a modified PH20 polypeptide include any that are known to one of skill in the art. For example, various forms of PH20 hyaluronidases have been prepared and approved for therapeutic use in humans. For example, animal-derived hyaluronidase preparations include Vitrase® hyaluronidase (ISTA Pharmaceuticals), a purified ovine testicular hyaluronidase, and Amphadase® hyaluronidase (Amphastar Pharmaceuticals), a bovine testicular hyaluronidase. Hylenex® hyaluronidase (Halozyme Therapeutics) is a human recombinant hyaluronidase produced by genetically engineered Chinese Hamster Ovary

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(CHO) cells containing nucleic acid encoding for soluble rHuPH20 (see e.g., U.S. Patent No. 7,767,429). Approved therapeutic uses for hyaluronidases include use as an adjuvant to increase the absorption and dispersion of other therapeutic agents for hypodermoclysis (subcutaneous fluid administration), and as an adjunct in subcutaneous urography for improving resorption of radiopaque agents. In addition to these indications, hyaluronidases can be used as a therapeutic or cosmetic agent for the treatment of additional diseases and conditions. For example, hyaluronidase is commonly used, for example, for peribulbar block in local anesthesia prior ophthalmic surgery. The presence of the enzyme prevents the need for additional blocks and reduces the time to the onset of akinesia (loss of eye movement). Peribulbar and sub-Tenon's block are the most common applications of hyaluronidase for ophthalmic procedures. Hyaluronidase also can promote akinesia in cosmetic surgery, such as blepharoplasties and face lifts. It is understood that soluble PH20 hyaluronidases provided herein, including esPH20 hyaluronidases, can be used in any method of treatment or combination therapy for which a PH20 hyaluronidase is used (see e.g., U.S. Publication Nos. US20040268425; US20050260186; US20060104968; and U.S. Appl. Serial Nos. 12/381,844, published as U.S. Publication No. US20100074885; 12/386,249, published as U.S. Publication No. US20090311237; 12/387,225, published as U.S. Publication No. US20090304665; and 12/386,222, published as U.S. Publication No. US2010003238, each incorporated by reference in their entirety).

Replace the paragraph beginning at page 205, line 19, with the following amended paragraph:

Exemplary antibodies or other therapeutic agents include, but are not limited to, Cetuximab (*e.g.*, IMC-C225; Erbitux®); Trastuzumab (*e.g.*, Herceptin®); Rituximab (*e.g.*, Rituxan®; MabThera®); Bevacizumab (*e.g.*, Avastin®); Alemtuzumab (*e.g.*, Campath®; Campath-1H®; Mabcampath®); Panitumumab (*e.g.*, ABX-EGF; Vectibix®); Ranibizumab (*e.g.*, Lucentis®); Ibritumomab; Ibritumomab tiuxetan (*e.g.*, Zevalin®); Tositumomab; Iodine I 131 Tositumomab (*e.g.*, BEXXAR®); Catumaxomab (*e.g.*, Removab®); Gemtuzumab; Gemtuzumab ozogamicin (*e.g.*, Mylotarg®); Abatacept (*e.g.*, CTLA4-Ig; Orencia®); Belatacept (*e.g.*, L104EA29YIg; LEA29Y; LEA); Ipilimumab (*e.g.*, MDX-010; MDX-101); Tremelimumab (*e.g.*, ticilimumab; CP-675,206); PRS-010 (see *e.g.*, US20090042785); PRS-050 (US7585940; US20090305982); Aflibercept (VEGF Trap, AVE005; Holash *et al.*, (2002) *PNAS* 99:11393-11398); Volociximab (M200); F200 (Chimeric (human/murine) IgG4 Fab fragment of Volociximab (M200)); MORAb-009 Mouse/human chimeric

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IgG1(US20050054048); Soluble fusion protein: Anti-mesothelin Fv linked to a truncated Pseudomonas exotoxin A (SS1P (CAT-5001); US20070189962); Cixutumumab (IMC-A12); Nimotuzumab (h-R3) (Spicer (2005) *Curr Opin Mol Ther* 7:182-191); Zalutumumab (HuMax-EGFR; Lammerts van Bueren *et al.* (2008) *PNAS* 105:6109-14); Necitumumab IMC-11F8 (Li *et al.* (2008) *Structure* 16:216-227); Sym004 (Pedersen *et al.* 2010 *Cancer Res* 70:588-597); and mAb-425.

Replace the paragraph beginning at page 218, line 29, with the following amended paragraph:

The concentrated, diafiltered harvest was inactivated for virus. Prior to viral inactivation, a solution of 10% Triton® X-100 detergent, and 3% tri (n-butyl) phosphate (TNBP) was prepared. The concentrated, diafiltered harvest was exposed to 1% Triton® X-100 detergent, and 0.3% TNBP for 1 hour in a 36 L glass reaction vessel immediately prior to purification on the Q column.

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AMENDMENTS TO THE CLAIMS:

Please amend claims 1, 2, 4-11, 13-16, 18, 19, and 22-24, and add claims 25 and 26 as follows:

LISTING OF CLAIMS:

1. (Currently Amended) A modified PH20 polypeptide, comprising one or more amino acid replacements in an unmodified PH20 polypeptide, wherein:

the unmodified PH20 polypeptide consists of the amino acid sequence selected from the group consisting of sequence of amino acids set forth in SEQ ID NOs: 3, 7 and 32-66;

the modified PH20 polypeptide exhibits increased hyaluronidase activity compared to the unmodified PH20 polypeptide not containing the amino acid replacement(s);

the amino acid replacement(s) confer(s) the increased hyaluronidase activity;

an amino acid replacement confers the increased hyaluronidase activity and is at a position corresponding to residue 309, with reference to amino acid positions of set forth in SEQ ID NO:3;

corresponding amino acid positions are identified by alignment of the PH20 polypeptide with the polypeptide having the sequence of amino acids of set forth in SEQ ID NO:3; and

the modified PH20 polypeptide has at least 91% sequence identity to the amino acid sequence selected from the group consisting of sequence of amino acids set forth as SEQ ID NOs: 3, 7 and 32-66.

2. (Currently Amended) The modified PH20 polypeptide of claim 1, wherein the modified PH20 polypeptide has at least 95% sequence identity to the sequence of amino acids set forth as amino acid sequence selected from the group consisting of SEQ ID NOs: 3, 7, and 32-66.

3. (Original) The modified PH20 polypeptide of claim 2 that is a soluble PH20 polypeptide.

4. (Currently Amended) The modified PH20 polypeptide of claim 1, wherein the replacement is selected from among L at a position corresponding to position 309; N at a position corresponding to position 309; E at a position corresponding to position 309; G at a position corresponding to position 309; H at a position corresponding to position 309; and M at a position corresponding to position 309.

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5. (Currently Amended) The modified PH20 polypeptide of claim 4, wherein the replacement at the position corresponding to position 309 is N.

6. (Currently Amended) The modified PH20 polypeptide of claim 1, wherein the unmodified PH20 polypeptide consists of the amino acid sequence selected from the group consisting of sequence of amino acids set forth in SEQ ID NOs: 3 and 32-66.

7. (Currently Amended) The modified PH20 polypeptide of claim 2, wherein the unmodified PH20 polypeptide consists of the amino acid sequence selected from the group consisting of sequence of amino acids set forth in SEQ ID NOs: 3 and 32-66.

8. (Currently Amended) The modified PH20 polypeptide of claim 5, wherein the unmodified PH20 polypeptide consists of the amino acid sequence selected from the group consisting of sequence of amino acids set forth in SEQ ID NOs: 3 and 32-66.

9. (Currently Amended) The modified PH20 polypeptide of claim 1, wherein the unmodified PH20 polypeptide consists of the amino acid sequence of ~~amino acids set forth in SEQ ID NO:35 or a sequence that has at least 95% sequence identity to SEQ ID NO:35.~~

10. (Currently Amended) The modified PH20 polypeptide of claim 1, wherein the unmodified PH20 polypeptide consists of the amino acid sequence of ~~amino acids set forth in SEQ ID NO:32 or a sequence that has at least 95% sequence identity to SEQ ID NO:32.~~

11. (Currently Amended) The modified PH20 polypeptide of claim 5, wherein the unmodified PH20 polypeptide consists of the amino acid sequence of ~~amino acids set forth in SEQ ID NO:35 or a sequence that has at least 95% sequence identity to SEQ ID NO:35.~~

12. (Original) The modified PH20 polypeptide of claim 1, wherein the modified PH20 polypeptide exhibits increased hyaluronidase activity that is at least 120% of the hyaluronidase activity compared to the unmodified PH20 polypeptide not containing the amino acid replacement or replacements.

13. (Currently Amended) ~~The~~A modified PH20 polypeptide of claim 1, comprising the amino acid sequence selected from the group consisting of a sequence of amino acids set forth in any of SEQ ID NOs:576-586, or an amino acid ~~a sequence of amino acids~~ that exhibits at least 91% sequence identity to the amino acid sequence selected from the group consisting a sequence of amino acids set forth in any of SEQ ID NOS:3 and 32-66-576-586 and that contains the amino acid replacement L, N, E, G, H, M, Q, R, S, T or V at residue 309 ~~with reference to corresponding positions in a polypeptide of any of SEQ ID NOs: 3 and 32-66.~~

14. (Currently Amended) ~~The~~A modified PH20 polypeptide of claim 1, comprising the amino acid sequence of a sequence of amino acids set forth in SEQ ID NO:581, or an

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~~amino acid sequence a sequence of amino acids~~ that exhibits at least 91% sequence identity to ~~the amino acid sequence selected from the group consisting of a sequence of amino acids set forth in SEQ ID NOS: 3 and 32-66~~ SEQ ID NO: 581 and that contains the amino acid replacement N at residue 309, ~~with reference to corresponding positions in a polypeptide of any of SEQ ID NOS: 3 and 32-66.~~

15. (Currently Amended) The modified PH20 polypeptide of claim 1 that further comprises one or more ~~modification of a modification~~ selected from among glycosylation, sialation, albumination, farnesylation, carboxylation, hydroxylation, and phosphorylation.

16. (Currently Amended) The modified PH20 polypeptide of claim 1 that further comprises an N-acetylglucosamine moiety linked to each of at least three asparagine (N) residues.

17. (Original) The modified PH20 polypeptide of claim 1 that is conjugated to a polymer.

18. (Currently Amended) The modified PH20 polypeptide of claim ~~17~~46, wherein the polymer is dextran or polyethylene glycol (PEG).

19. (Currently Amended) The modified PH20 polypeptide of claim 1, further comprising a heterologous signal sequence, wherein the unmodified PH20 polypeptide consists of an amino acid sequence selected from the group consisting of SEQ ID NOS: 3 and 32-66 in place of the native signal sequence.

20. (Original) A chimeric polypeptide, comprising the modified PH20 polypeptide of claim 1.

21. (Original) A pharmaceutical composition, comprising the modified PH20 polypeptide of claim 1.

22. (Withdrawn-Currently Amended) A method of treatment, comprising administering a pharmaceutical composition of claim 21, wherein the method is selected from a method that treats an excess of glycosaminoglycans; a tumor; glycosaminoglycan accumulation in the brain; a cardiovascular disorder; an ophthalmic disorder; and pulmonary disease or edema; and a method of increasing delivery of therapeutic agents.

23. (Currently Amended) ~~A~~The modified PH20 polypeptide of claim 1, comprising ~~the amino acid sequence of a sequence of amino acids set forth in~~ SEQ ID NO: 581, or an amino acid sequence a sequence of amino acids that exhibits at least 95% sequence identity to the amino acid sequence of a sequence of amino acids set forth in SEQ ID NO: 581 and that

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contains the amino acid replacement N at residue 309 ~~with reference to corresponding positions in a polypeptide of any of SEQ ID NOS: 3 and 32-66.~~

24. (Currently Amended) The modified PH20 polypeptide of claim 5, wherein:
the unmodified PH20 polypeptide consists of the amino acid sequence ~~of amino acids~~
set forth in SEQ ID NO:32; and

the amino acid sequence a sequence of the modified PH20 polypeptide that has at least
95% sequence identity to SEQ ID NO:32.

25. (New) The modified PH20 polypeptide of claim 5, wherein:
the unmodified PH20 polypeptide consists of the amino acid sequence set forth in SEQ
ID NO:35; and

the amino acid sequence of the modified PH20 polypeptide has at least 95% sequence
identity to SEQ ID NO:32.

26. (New) The modified PH20 polypeptide of claim 1, further comprising a signal
sequence, wherein the unmodified PH20 polypeptide consists of an amino acid sequence
selected from the group consisting of SEQ ID NOs: 3 and 32-66.

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REMARKS

Any fees that may be due in connection with the filing of this paper or with this application may be charged to Deposit Account No. 50-0911. If a Petition for Extension of Time is needed, this paper is to be considered such Petition.

A Supplemental Information Disclosure Statement is filed under separate cover.

Claims 1-26 are pending. Claims 1-21, 23 and 24 have been examined. Claim 22, which is withdrawn from consideration as drawn to non-elected subject matter, is retained for possible joinder upon allowance of the product claims on which it depends. Claims 1, 2, 4-11, 13-16, 18, 19, 23 and 24 are amended to address the Examiner's objections. Claim 25, directed to a modified PH20 polypeptide that comprises a replacement corresponding to 309N that has at least 95% sequence identity to SEQ ID NO:32, is added. Claim 26 that recites that the polypeptides further comprise a signal sequence, is added. Claim 22 is amended, for clarity, to indicate that the method is for treating the recited conditions and disorders, and the method is for increasing delivery of therapeutic agents. Claims 13, 14 and 23 are amended to recite that the modified PH20 polypeptide has 91% sequence identity to the unmodified, to ensure proper dependency on claim 1. Claims 13, 14 and 23 also are amended to delete the extraneous language identifying reference corresponding amino acid positions, which is recited in claim 1, from which claims 13, 14 and 23 depend. No new matter is added.

OBJECTIONS TO THE SPECIFICATION

Use of Trademarks

The Examiner states that the trademarks Hydase™, Vitrase™ and Wydase™ referenced in the specification, at page 2, lines 8-9, should be capitalized and accompanied by the generic terminology. Applicant respectfully submits that the use of trademarks in the specification generally is in compliance with the Office's policies regarding such use. The use of trademarks in patent applications is addressed in the Manual of Patent Examining Procedures (MPEP), §608.01(v), "Marks Used in Commerce and Trade Names." As the cited section describes (*see* Part II, "Proprietary Nature of Marks Used in Commerce," (emphasis added)):

Marks should be identified by capitalizing each letter of the mark (in the case of word or letter marks) ***or otherwise indicating the description of the mark (in the case of marks in the form of a symbol or device or other nontextual form)***

This is borne out in form paragraph 6.20 recited in the cited section, which provides the following Examiner Note (emphasis added):

1. Capitalize each letter of the word in the bracket ***or, where appropriate, include a proper symbol indicating use in commerce such as TM, SM, or [®] following the word.***

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Applicant respectfully submits that in the instant specification, trademarks are designated by their appropriate symbols. Trademarks generally are properly used as adjectives referencing source throughout the specification. There is clear reference to the generic terminology for the trademarks and, in some instances, the owner of the trademark (*e.g.*, Halozyme Therapeutics is the owner of the Hylenex® trademark) or indications that the product is "sold under" a particular trademark name. These are acceptable ways of designating trademarks, as noted in the above-cited section of the MPEP. For Example, at page 52, lines 6-8, the specification recites:

Examples of commercially available bovine or ovine soluble hyaluronidases are **Vitrasc® hyaluronidase (ovine hyaluronidase) and Amphadase® hyaluronidase (bovine hyaluronidase)** (emphasis added)

Each is identified with a generic term.

At page 75, line 36 to page 76, line 1, the specification recites:

Exemplary regular insulin preparations include, but are not limited to, **human regular insulins, such as those sold under the trademarks Humulin® R, Novolin® R and Velosulin®** (emphasis added)

At page 76, lines 15-18, the specification recites:

Exemplary **rapid acting insulin analogs include**, but are not limited to, for example, **insulin lispro (*e.g.*, Humalog® insulin), insulin aspart (*e.g.*, NovoLog® insulin), and insulin glulisine (*e.g.*, Apidra® insulin) the fast-acting insulin composition sold as VIAject® and VIAtab®** (see, *e.g.*, U.S. Pat. No. 7,279,457). (emphasis added)

At page 84, lines 19-21, the specification recites:

Original bovine testicular extract preparations included, for example, **extracts sold under the trademarks Wydase®, Hylase®, "Dessau," Neopermease®, Alidase® and Hyazyme®.** (emphasis added)

Nevertheless, to advance prosecution, the specification is amended. For example, at page 2, the specification is amended so that Hydase®, Vitrasc® and Wydase®, which designate the marks by appropriate symbols, are followed by marks by generic terms, as required by the Examiner or are referenced as trademarks. Additional recitations of trademarks in the specification, at paragraphs beginning on pages 52, 75, 84, 85, 86, 174, 179, 196, 198, 205 and 218, are amended to employ the trademarks as adjectives and/or to contain generic terminology. All other recitations of trademarks throughout the application are designated by appropriate symbols, and contain the generic terminology, and, thus, do not require amendment.

Use of Sequence Identifiers

The Examiner states that the term "SEQ ID NOS" should be replaced with "SEQ ID NOs" at page 3, line 24, and throughout the specification. Applicant is not aware of any rule

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stating that reference to multiple sequence identity numbers must be denoted as "SEQ ID NOs" and not "SEQ ID NOS." A search of the USPTO database of issued patents identifies hundreds of issued patents in which multiple sequence identifiers are denoted as "SEQ ID NOS" in the specification and/or the claims. A few exemplary issued patents that refer to "SEQ ID NOS" in the specification and/or the claims are as follows: 7,999,070; 8,741,565; 7,456,273; 7,993,849; 7,091,323; 7,432,364; 8,900,829; 7,951,563; 7,932,031; 8,685,689; 8,227,231; and 9,447,401. Applicant therefore respectfully requests withdrawal of this objection, or provision of regulation or rule setting forth this requirement.

OBJECTIONS TO THE CLAIMS

The Examiner objects to several of the claims on various grounds, each of which is addressed below:

(1) In Claim 1, the Examiner states that the recitation "...unmodified PH20 polypeptide consists of the **sequence of amino acids set forth in** SEQ ID NO: 3, 7 or 32-66" should be changed to "...unmodified PH20 polypeptide consists of the **amino acid sequence selected from the group consisting of** SEQ ID NOs: 3, 7 and 32-66." (emphasis added).

Applicant respectfully disagrees with the requirement to replace the recitation "sequence of amino acids" with "amino acid sequence" and submits that the language as recited in the claims accurately characterizes the unmodified PH20 polypeptide. In the phrase "sequence of amino acids," the prepositional phrase "of amino acids" modifies the noun "sequence," thus rendering it clear that the sequence is an amino acid sequence. The phrase "unmodified PH20 polypeptide consists of" precedes "sequence of amino acids," rendering clear that the unmodified PH20 polypeptide consists of the sequence of amino acids set forth as the recited SEQ ID NOs.

The instant application is a continuation of U.S. application Serial No. 15/226,489, which is a divisional of U.S. application Serial No. 13/694,731, now U.S. Patent No. 9,447,401. Issued U.S. Patent No. 9,447,401 includes claims directed to modified PH20 polypeptides; the claims recite "sequence of amino acids" (see *e.g.*, claims 1, 2, 3). Insofar as the claims of the issued patent, which recite "sequence of amino acids," have been deemed patentable by the Patent Office, the claims of the instant application should not be objected to for reciting "sequence of amino acids."

The Examiner is reminded that, as set forth in 35 U.S.C. §282, an issued patent is presumptively valid and meets the requirements of 35 U.S.C. §112. MPEP §1701 states that the Examiner must give full faith and credit to determinations of the Patent Office and cannot

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denigrate the validity of an issued patent. The Examiner's rejection of the claims in the instant application denigrates the validity of issued claims in U.S. Patent No. 9,447,401.

In the interest of advancing prosecution, claim 1 is amended as required by the Examiner. Applicant has complied with the requirement of the Examiner, but notes that a polypeptide is comprised of a sequence of amino acids; it is not comprised of an amino acid sequence, which is a written representation of the amino acid sequence of a polypeptide. Nevertheless in view of the requirement by the Office to use this language, this language should be interpreted to refer to a physical polypeptide, not a written representation.

(2) In claim 1, the Examiner states that the recitation "...amino acid positions set forth in SEQ ID NO:3" should be changed to "... amino acid positions of SEQ ID NO:3." Applicant respectfully disagrees, and submits that the language as recited in the claims accurately characterizes the amino acid positions. The positions of amino acids in a sequence is a property that represents the amino acid residues that make up a protein or polypeptide; it is not a property of a "SEQ ID NO:" A "SEQ ID NO:" merely is a label to designate a sequence. While a protein or polypeptide can be characterized by the sequences of their amino acid residues, and the "SEQ ID NOS" help to locate where in the Sequence Listing the sequences may be read, the "SEQ ID NOS" label amino acid sequences that are recited or set forth. A "SEQ ID NO" does not possess amino acid positions; it is a label. Applicant therefore respectfully submits that the language "amino acid positions set forth in SEQ ID NO:3" (*i.e.*, how the sequence identifying amino acid positions can be located) is accurate and need not be replaced with "amino acid positions of SEQ ID NO:3." In the interest of advancing prosecution, since the amendment is not substantive, claim 1 is amended as required by the Examiner.

(3) In claim 1, the Examiner states that the recitation "...91% sequence identity to the sequence of amino acids set forth as SEQ ID NO: 3, 7 or 32-66" should be changed to "... 91% sequence identity to the amino acid sequence selected from the group consisting of SEQ ID NO: 3, 7 and 32-66." As detailed above in objection (1), Applicant submits that the language of the claims is clear and accurately characterizes the unmodified PH20 polypeptide. The recitation of "selected from among a, b, and c" is acceptable alternative language; there is no requirement in US patent laws or the MPEP to employ Markush language. Markush language is one form of acceptable language for reciting alternatives.

In the interest of advancing prosecution, since the amendment is not substantive, claim 1 is amended as required by the Examiner. Applicant states that this amendment does not change the scope nor substance of the claim. The recitations of "selected from the group

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consisting of SEQ ID NOs: 3, 7, and 32-66” is the same as selected from among a polypeptide whose sequence is “set forth in any of SEQ ID NOs: 3, 7, and 32-66.”

Claim 2 similarly is amended to recite “...amino acid sequence selected from the group consisting of SEQ ID NOs:...” as required by the Examiner.

(4) In claim 4, “...H at a position corresponding to 309” is requested to be changed to “...H at a position corresponding to position 309.” Similarly, in claim 5, “...corresponding to 309 is N” is requested to be changed to “...corresponding to position 309 is N.” Claims 4 and 5 are amended to insert the term “position,” where appropriate, as required by the Examiner.

(5) In claims 6-8, “...the unmodified PH20 polypeptide consists of the sequence of amino acids set forth in SEQ ID NO:3, 7 or 32-66” is requested to be changed to “...the modified PH20 polypeptide consists of the amino acid sequence selected from the group consisting of SEQ ID NO:3, 7 and 32-66.” As detailed above with respect to the rejections to claim 1, Applicant states that the amended requested by the Examiner does not change the scope nor content of the claim. US patent law permits a variety of alternative recitations; Markush language is not required. Applicant submits that the language of the claims is clear and accurately characterizes the unmodified PH20 polypeptide. In the interest of advancing prosecution, claims 6 - 8 are amended as required by the Examiner.

(6) In claims 9 and 11, the Examiner states “...unmodified PH20 polypeptide consists of the sequence of amino acids set forth in SEQ ID NO:35” should be changed to “...unmodified PH20 polypeptide consists of the amino acid sequence of SEQ ID NO:35.” As detailed above with respect to the objections to claim 1, Applicant submits that the language of the claims is clear and accurately characterizes the unmodified PH20 polypeptide. In the interest of advancing prosecution, claims 9 and 11 are amended as required by the Examiner.

Claim 10 similarly is amended to recite “...unmodified PH20 polypeptide consists of the amino acid sequence of SEQ ID NO:32...” as requested by the Examiner.

(7) In claim 13, the Examiner states “...or a sequence of amino acids that exhibits at least 91% sequence identity to a sequence of amino acids set forth in any of SEQ ID NOS: 576-586...in a polypeptide of any of SEQ ID NOs:3 and 32-66” should be changed to “...or an amino acid sequence that exhibits at least 91% sequence identity to an amino acid sequence selected from the group consisting of SEQ ID NOs:576-586...in an amino acid sequence selected from the group consisting of SEQ ID NOs: 3 and 32-66.” As detailed above with respect to the objections to claim 1, Applicant submits that the language of the claim is clear and accurately characterizes the modified and unmodified PH20 polypeptides. In the interest of

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advancing prosecution, claim 13 is amended to include the language required by the Examiner. Claim 13 also is amended to recite that the modified PH20 polypeptide exhibits at least 91% sequence identity to the unmodified, to ensure proper dependency on claim 1.

(8) In claim 14, the Examiner states "...a sequence of amino acids set forth in SEQ ID NO:581, or a sequence of amino acids that exhibits at least 91% sequence identity to a sequence of amino acids set forth in SEQ ID NO:581 and that contains...in a polypeptide of any of SEQ ID NOS: 3 and 32-66" should be changed to "...an amino acid sequence of SEQ ID NO:581, or an amino acid sequence that exhibits at least 91% sequence identity to the amino acid sequence of SEQ ID NO:581 and that contains...in an amino acid sequence selected from the group consisting of SEQ ID NOs: 3 and 32-66." As detailed above with respect to the objections to claim 1, Applicant submits that the language of the claim is clear and accurately characterizes the modified and unmodified PH20 polypeptides. In the interest of advancing prosecution, claim 14 is amended to include the language required by the Examiner. Claim 14 also is amended to recite that the modified PH20 polypeptide exhibits at least 91% sequence identity to the unmodified, to ensure proper dependency on claim 1.

(9) In claim 15, the Examiner states "...one or more of a modification..." should be changed to "...one or more of modification..." and "...that comprises one or more of a modification" should be changed to "...that further comprises one or more modification..."

Applicant respectfully requests reconsideration of the rejection. Claim 15 is amended to recite:

The modified PH20 polypeptide of claim 1 that further comprises one or more modifications selected from among glycosylation, sialation, albumination, farnesylation, carboxylation, hydroxylation, and phosphorylation.

Thus, as amended, the claim clearly indicates that the modified PH20 polypeptide further comprises one or more modifications, and lists post-translational and chemical modifications. The term "modifications" is used rather than "modification," as suggested by the Examiner, because there can be one or more modifications, thus, grammatically the plural form of the word "modification" is appropriate. The language aligns with the language of claim 1, which recites, in part, that the modified PH20 polypeptide comprises "one or more amino acid replacements."

The claim also is amended to include the term "further" preceding the word "comprises," as required by the Examiner, to address the rejection.

(10) In claim 16, the Examiner states "...that comprises an..." should be changed to "that further comprises an..." Claim 16 is amended as required by the Examiner.

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(11) In claim 23, the Examiner states "...a sequence of amino acids set forth in SEQ ID NO:581, or a sequence of amino acids that exhibits at least 95% sequence identity to a sequence of amino acids set forth in SEQ ID NO:581 and that ...in a polypeptide of any of SEQ ID NOS: 3 and 32-66" should be changed to "...an amino acid sequence of SEQ ID NO:581, or an amino acid sequence that exhibits at least 95% sequence identity to an amino acid sequence set forth in SEQ ID NO:581 and that ...in an amino acid sequence selected from the group consisting of SEQ ID NOS: 3 and 32-66."

As detailed above with respect to the objections to claim 1, Applicant submits that the language of the claim is clear and accurately characterizes the modified and unmodified PH20 polypeptides. In the interest of advancing prosecution, claim 23 is amended as required by the Examiner.

(12) In claim 24, the Examiner states "...consists of the sequence of amino acids set forth in SEQ ID NO:32 or a sequence of amino acids that has at least 95% sequence identity to SEQ ID NO:32" should be changed to "...consists of the amino acid sequence set forth in SEQ ID NO:32 or an amino acid sequence that has at least 95% sequence identity to SEQ ID NO:32." As detailed above with respect to the objections to claim 1, Applicant submits that the language of the claim is clear and accurately characterizes the modified PH20 polypeptides. In the interest of advancing prosecution, claim 24 is amended as required by the Examiner. Claim 24 also is amended to recite that the modified PH20 polypeptide has at least 95% sequence identity to the unmodified PH20 polypeptide to ensure proper dependency.

DUPLICATE CLAIMS

The Examiner states that "should claims 13 and 14 be found allowable, claims 13 and 14 will be objected to under 37 CFR 1.75 as being a substantial duplicate thereof." The Examiner states that claims 13 and 14 are substantially duplicates of each other because:

Although claim 13 recites the portion that the modified PH20 polypeptide "comprising a sequence of amino acids set forth in any of SEQ ID NOS:[576]-586" (lines 1-2, claim 13) which is absent in claim 14, the claim 13 as a whole is given broadest reasonable interpretation (BRI) as being directed to the modified PH20 polypeptide "comprising a sequence of amino acids that exhibits at least 91% sequence identity to a sequence of amino acids set forth in any of SEQ ID NO:576-586 and that contains the amino acid replacement N at residue 309 with reference to corresponding positions in a polypeptide of any of SEQ ID NOS:3 and 32-66" (lines 2-5, claim 13). In view of the limitation "and that contains the amino acid replacement N at residue 309," the scope of claim 13 is limited to SEQ ID NO: 581, or a sequence of amino acids that exhibits at least 91% sequence identity to SEQ ID NO: 581. Note that SEQ ID NOS: 576-586 are identical with the exception of the amino acid at position 309. As a result, limiting position 309 to N for any of the recited sequences in claim 13, and/or having at least 91% sequence identity to SEQ ID NOS: 576-586 that contains N at position 309, results in a claim wherein the modified PH20 polypeptide is SEQ ID NO: 581, or a

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sequence having at least 91% sequence identity to it. This is the same scope as claim 14.

Reconsideration and withdrawal of this rejection respectfully is requested in view of the amendments to the claims and the following remarks.

As amended, claim 13 recites:

The modified PH20 polypeptide of claim 1, comprising the amino acid sequence selected from the group consisting of SEQ ID NOs:576-586, or an amino acid sequence that exhibits at least 91% sequence identity to the amino acid sequence selected from the group consisting of SEQ ID NOs:3 and 32-66 and that contains the amino acid replacement L, N, E, G, H, M, Q, R, S, T or V at residue 309.

As amended claim 14 recites:

The modified PH20 polypeptide of claim 1, comprising the amino acid sequence of SEQ ID NO:581, or an amino acid sequence that exhibits at least 91% sequence identity to the amino acid sequence selected from the group consisting of SEQ ID NOs: 3 and 32-66 and that contains the amino acid replacement N at residue 309.

Thus, Claim 13 is directed to a modified PH20 polypeptide comprising the sequence of amino acids set forth as any of SEQ ID NOs: 576-586 or with at least 91% identity to the unmodified sequences that contains a replacement at the residue corresponding to residue 309. Modified PH20 polypeptides designated as SEQ ID NOs: 576-586 comprise a replacement at residue 309, such as replacement with any of L, N, E, G, H, M, Q, R, S, T or V. For example, SEQ ID NO: 576 comprises mature PH20 with E at a position corresponding to residue 309, SEQ ID NO: 577 comprises mature PH20 with G at a position corresponding to residue 309, and SEQ ID NO: 578 comprises mature PH20 with H at a position corresponding to residue 309. Claim 14 is limited to a modified PH20 polypeptide comprising a sequence of amino acids set forth as SEQ ID NO: 581 or with at least 91% identity to the listed unmodified sequences, comprising a replacement with N at residue 309. Thus, claim 14 limits the modified PH20 polypeptide to a polypeptide comprising SEQ ID NO: 581 with a replacement with N at residue 309 or a polypeptide with 91% sequence identity to the unmodified polypeptides and that contains a replacement at N at residue 309. Claim 13 recites that all of the modified PH20 polypeptides include L, N, E, G, H, M, Q, R, S, T or V at residue 309. Thus, claim 14 is directed to a subset of the polypeptides within the scope of claim 13; claims 13 and 14 are not of the same scope.

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THE REJECTION OF CLAIMS 9-11, 13, 14 and 23 UNDER 35 U.S.C. § 112, FOURTH PARAGRAPH

Claims 9-11, 13, 14 and 23 are rejected under 35 U.S.C. § 112, fourth paragraph, as being of improper dependent form for failing to further limit the subject matter of the claim upon which it depends, or for failing to include all the limitations of the claim upon which it depends.

Claims 9-11 are rejected in the recitation “or a sequence that has at least 95% sequence identity to SEQ ID NO:35,” for claims 9 and 11, or “SEQ ID NO:32,” for claim 10. The Examiner states:

wherein said “a sequence...” is given broadest reasonable interpretation as being drawn to the amino acid sequence of “unmodified PH20 polypeptide” which fails to further limit the unmodified PH20 polypeptide of SEQ ID NO:32 or 35 set forth at lines 3-4 of claim 1 from which claims 9-11 depends (it is noted that claim 11 depends from claim 5, whereas claim 5 depends from claim 4 that depends from claim 1); i.e., the structural variation resulted from “...95% sequence identity...” (claims 9-11) renders the scope of the claims 9-11 broader than the scope of the “unmodified PH20 polypeptide” of claim 1. Thus, claims 9-11 fail to further limit the subject matter of the claim 1, i.e., claims 9-11 are of improper dependent form.

Claims 13 and 14 are rejected in the recitation “a **modified** PH20 polypeptide of claim 1, comprising a sequence of amino acids set forth in any of SEQ ID NOs:576-586” for claim 13 or “SEQ ID NO:581” for claim 14. The Examiner states:

wherein said “a sequence...” is given broadest reasonable interpretation (BRI) as being drawn to “a fragment” of any one of SEQ ID NOs:576-586 which has the broader scope than that of “the modified PH20 polypeptide has at least 91% sequence identity to the sequence of amino acids set forth as SEQ ID NO: 3, 7, or 32-66”, wherein said “a fragment” (a subsequence of SEQ ID NO: 3, 7, or 32-66) renders the sequence identity lower than “91% (claim 1); and thus, claim 13 fails to further limit the subject matter of the claim 1, i.e., claim 13 is of improper dependent form.

The Examiner states that claims 14 and 23 are similarly rejected and “[f]or the same reason stated above, claims **14** and **23** are written as improper dependent forms.”

This rejection respectfully is traversed.

Relevant Law

A properly dependent claim includes all limitations of the base claim(s) upon which it depends, and is of a narrower scope. As amended each of claims 9-11, 13, 14, and 23 are properly dependent.

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The Rejected Claims

Claims 9-11

Claims 9-11 are amended to delete the recitation that the unmodified PH20 polypeptide has at least 95% sequence identity to SEQ ID NO: 32 (claim 10) or SEQ ID NO: 35 (claims 9 and 11), to address the rejection. As amended, claims 9 and 11 recite that the unmodified PH20 polypeptide consists of the amino acid sequence of SEQ ID NO:35, and claim 10 recites that the unmodified PH20 polypeptide consists of the amino acid sequence of SEQ ID NO:32.

Claims 9 and 10 depend on claim 1, which recites that the unmodified PH20 polypeptide consists of the amino acid sequence selected from the group consisting of SEQ ID NOs: 3, 7 and 32-66. Claim 11 depends on claim 5, which depends on claim 1. Claims 9-11 recite that the unmodified PH20 polypeptide consists of the amino acid sequence of SEQ ID NO: 35 (claims 9 and 11) or SEQ ID NO: 32 (claim 10); claims 9-11 include all limitations of the base claim(s) and recite a further limitation that the unmodified PH20 polypeptide is limited to SEQ ID NO: 35 (claims 9 and 11) or SEQ ID NO: 32 (claim 10). Thus, claims 9-11 are properly dependent on claim 1, are not broader than the claims on which they depend, and the rejection is obviated by the amendment to the claims.

Claims 13, 14 and 23

Claims 13 and 14 are set forth above. Claims 13, 14, and 23 are amended to recite that the modified PH20 polypeptide comprises the amino acid sequence selected from the group consisting of SEQ ID NOs:576-586 (claim 13) or the amino acid sequence of SEQ ID NO: 581 (claims 14 and 23), to address the rejection. As amended, the claims 13, 14 and 23 are directed to modified mature PH20 polypeptides comprising a replacement at a position corresponding to amino acid residue 309, which are designated as SEQ ID NOs: 576-586, in the sequence listing, and to PH20 polypeptides that have 91% sequence identity to the unmodified PH20 polypeptide and comprise a replacement at 309. The language of the claims, where the modified PH20 polypeptide comprises the sequence of amino acids set forth as SEQ ID NOs: 576-586 (claim 13) or SEQ ID NO: 581 (claims 14 and 23) renders clear that the claimed polypeptides exclude fragments thereof that are inconsistent with or broader than the modified PH20 polypeptides of claim 1. Claims 13, 14 and 23 are directed to modified PH20 polypeptides that contain replacements at residue 309, and also to modified polypeptides that contain the replacement and have 91% sequence identity to the unmodified PH20 polypeptides of SEQ ID NOs: 3 and 32-66. Each of SEQ ID NOS: 576-586 contains only a single amino

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acid replacement relative the unmodified polypeptide of SEQ ID NO:3. Thus, claims 13, 14 and 23 are not broader in scope nor identical in scope to the claims on which they depend.

THE REJECTION OF CLAIMS 18 and 19 UNDER 35 U.S.C. § 112, SECOND PARAGRAPH

Claims 18 and 19 are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which the inventor or a joint inventor, or for pre-AIA the applicant regards as the invention.

Reconsideration and withdrawal of these rejections respectfully is requested in view of the amendments to the claims and the following arguments

The Rejected Claims

Claim 18

Claim 18 is rejected as lacking antecedent basis for the term “polymer” in claim 16, from which claim 18 depends. Claim 18 is amended to depend on claim 17, which recites that the modified PH20 polypeptide is conjugated to a polymer. Therefore, it respectfully is submitted that this ground for rejection is rendered moot.

Claim 19

Claim 19 is rejected as lacking antecedent basis for the recitation “...a heterologous signal sequence in place of the native signal sequence” in claim 1 from which claim 19 depends. The Examiner states that “none of SEQ ID NOs: 3, 7 and 32-66 contains the heterologous signal sequence,” and that the specification “only discloses SEQ ID NO:6 comprising the “signal sequence” (see PG PUB [0119], instant specification) whereas claim 1 does not recite said SEQ ID NO:6.” Claim 19 is amended to recite that the modified PH20 polypeptide further comprises a heterologous signal sequence. Claim 19 recites (emphasis added)

The modified PH20 polypeptide of claim 1, further comprising a heterologous signal sequence wherein the unmodified PH20 polypeptide consists of an amino acid sequence selected from the group consisting of SEQ ID NOs: 3 and 32-66.

None of SEQ ID NOs; 3 and 32-66 include a signal sequence. As amended, claim 19 does not reference a signal sequence of claim 1, from which it depends Claim 19 adds that the modified PH20 polypeptide that the polypeptide further comprises a heterologous signal sequence. Thus, amendment of claim 19 to recite that the modified PH20 polypeptide further comprises a heterologous signal sequence renders the rejection of claim 19, for lacking antecedent basis, moot. Added claim 26 is directed to modified PH20 polypeptides that further comprise a signal sequence to include endogenous and heterologous signal sequences.

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REJECTION FOR OBVIOUSNESS-TYPE DOUBLE PATENTING

Claims 1-14, 17, 18, 21, 23 and 24 are rejected on the ground of obviousness-type double patenting as being unpatentable over claims 3, 5, 11, 12, 23 and 28 of Application No. 15/226,489, now issued Patent No. 10,865,400. Claims 1-4, 7, 9-12, 15-18, 21 and 24 are rejected on the ground of nonstatutory double patenting as being unpatentable over claims 1-5, 10-11, 16-17, 19-20, 22 and 23 of U.S. Patent No. 9,447,401. The Examiner states that although the claims are not identical, they are not patentably distinct from each other. Terminal Disclaimers with respect to each of U.S. Patent Nos. 9,447,401 and 10,865,400 have been filed.

* * *

Consideration of the above remarks, entry of this amendment, and allowance of the application, respectfully are requested.

Respectfully submitted,
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Electronic Patent Application Fee Transmittal				
Application Number:		16912590		
Filing Date:		25-Jun-2020		
Title of Invention:		PH20 POLYPEPTIDE VARIANTS, FORMULATIONS AND USES THEREOF		
First Named Inventor/Applicant Name:		GE WEI		
Filer:		Stephanie L. Seidman/Jimmy Schaub		
Attorney Docket Number:		33320.03087.US27/3087D		
Filed as Large Entity				
Filing Fees for Utility under 35 USC 111(a)				
Description	Fee Code	Quantity	Amount	Sub-Total in USD(\$)
Basic Filing:				
Pages:				
Claims:				
CLAIMS IN EXCESS OF 20	1202	2	100	200
Miscellaneous-Filing:				
Petition:				
Patent-Appeals-and-Interference:				
Post-Allowance-and-Post-Issuance:				

Description	Fee Code	Quantity	Amount	Sub-Total in USD(\$)
Extension-of-Time:				
Extension - 1 month with \$0 paid	1251	1	220	220
Miscellaneous:				
Total in USD (\$)				420

Electronic Acknowledgement Receipt	
EFS ID:	42211828
Application Number:	16912590
International Application Number:	
Confirmation Number:	9651
Title of Invention:	PH20 POLYPEPTIDE VARIANTS, FORMULATIONS AND USES THEREOF
First Named Inventor/Applicant Name:	GE WEI
Customer Number:	13565
Filer:	Stephanie L. Seidman/Jimmy Schaub
Filer Authorized By:	Stephanie L. Seidman
Attorney Docket Number:	33320.03087.US27/3087D
Receipt Date:	17-MAR-2021
Filing Date:	25-JUN-2020
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Application Type:	Utility under 35 USC 111(a)

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Submitted with Payment	yes
Payment Type	DA
Payment was successfully received in RAM	\$ 420
RAM confirmation Number	E20213GL19083909
Deposit Account	500911
Authorized User	Jimmy Schaub
The Director of the USPTO is hereby authorized to charge indicated fees and credit any overpayment as follows: 37 CFR 1.16 (National application filing, search, and examination fees) 37 CFR 1.17 (Patent application and reexamination processing fees)	

37 CFR 1.19 (Document supply fees)					
37 CFR 1.20 (Post Issuance fees)					
37 CFR 1.21 (Miscellaneous fees and charges)					
File Listing:					
Document Number	Document Description	File Name	File Size(Bytes)/ Message Digest	Multi Part /.zip	Pages (if appl.)
1	Transmittal Letter	3087D-TRA-NFOA.PDF	142122	no	1
			648cf95937f48faac5a6af2e38322dc2ec6553e9		
Warnings:					
Information:					
2		3087D-AMA.PDF	312036	yes	24
			97727702a41bcc9e0085294132a60941a20fc863		
	Multipart Description/PDF files in .zip description				
	Document Description		Start	End	
	Applicant Arguments/Remarks Made in an Amendment		1	1	
	Claims		2	8	
	Applicant Arguments/Remarks Made in an Amendment		9	12	
	Applicant Arguments/Remarks Made in an Amendment		13	24	
Warnings:					
Information:					
3	Fee Worksheet (SB06)	fee-info.pdf	32808	no	2
			0e6a853d43a81e15e476791356abb3285e753d9		
Warnings:					
Information:					
Total Files Size (in bytes):			486966		

This Acknowledgement Receipt evidences receipt on the noted date by the USPTO of the indicated documents, characterized by the applicant, and including page counts, where applicable. It serves as evidence of receipt similar to a Post Card, as described in MPEP 503.

New Applications Under 35 U.S.C. 111

If a new application is being filed and the application includes the necessary components for a filing date (see 37 CFR 1.53(b)-(d) and MPEP 506), a Filing Receipt (37 CFR 1.54) will be issued in due course and the date shown on this Acknowledgement Receipt will establish the filing date of the application.

National Stage of an International Application under 35 U.S.C. 371

If a timely submission to enter the national stage of an international application is compliant with the conditions of 35 U.S.C. 371 and other applicable requirements a Form PCT/DO/EO/903 indicating acceptance of the application as a national stage submission under 35 U.S.C. 371 will be issued in addition to the Filing Receipt, in due course.

New International Application Filed with the USPTO as a Receiving Office

If a new international application is being filed and the international application includes the necessary components for an international filing date (see PCT Article 11 and MPEP 1810), a Notification of the International Application Number and of the International Filing Date (Form PCT/RO/105) will be issued in due course, subject to prescriptions concerning national security, and the date shown on this Acknowledgement Receipt will establish the international filing date of the application.

PATENT APPLICATION FEE DETERMINATION RECORD Substitute for Form PTO-875				Application or Docket Number 16/912,590		Filing Date 06/25/2020		☒ To be Mailed					
ENTITY: ☒ LARGE ☐ SMALL ☐ MICRO													
APPLICATION AS FILED - PART I													
		(Column 1)		(Column 2)									
FOR		NUMBER FILED		NUMBER EXTRA		RATE (\$)		FEE (\$)					
☐ BASIC FEE (37 CFR 1.16(a), (b), or (c))		N/A		N/A		N/A							
☐ SEARCH FEE (37 CFR 1.16(k), (l), or (m))		N/A		N/A		N/A							
☐ EXAMINATION FEE (37 CFR 1.16(o), (p), or (q))		N/A		N/A		N/A							
TOTAL CLAIMS (37 CFR 1.16(i))		minus 20 =		*		x \$100 =							
INDEPENDENT CLAIMS (37 CFR 1.16(h))		minus 3 =		*		x \$460 =							
☐ APPLICATION SIZE FEE (37 CFR 1.16(s))		If the specification and drawings exceed 100 sheets of paper, the application size fee due is \$310 (\$155 for small entity) for each additional 50 sheets or fraction thereof. See 35 U.S.C. 41(a)(1)(G) and 37 CFR 1.16(s).											
☐ MULTIPLE DEPENDENT CLAIM PRESENT (37 CFR 1.16(j))													
* If the difference in column 1 is less than zero, enter "0" in column 2.						TOTAL							
APPLICATION AS AMENDED - PART II													
		(Column 1)		(Column 2)		(Column 3)							
AMENDMENT	03/17/2021		CLAIMS REMAINING AFTER AMENDMENT		HIGHEST NUMBER PREVIOUSLY PAID FOR		PRESENT EXTRA		RATE (\$)		ADDITIONAL FEE (\$)		
	Total (37 CFR 1.16(i))		* 26		Minus ** 24		= 2		x \$100 =		200		
	Independent (37 CFR 1.16(h))		* 1		Minus *** 3		= 0		x \$480 =		0		
	☐ Application Size Fee (37 CFR 1.16(s))												
	☐ FIRST PRESENTATION OF MULTIPLE DEPENDENT CLAIM (37 CFR 1.16(j))												
										TOTAL ADD'L FEE		200	
AMENDMENT			CLAIMS REMAINING AFTER AMENDMENT		HIGHEST NUMBER PREVIOUSLY PAID FOR		PRESENT EXTRA		RATE (\$)		ADDITIONAL FEE (\$)		
	Total (37 CFR 1.16(i))		*		Minus **		=		x \$0 =				
	Independent (37 CFR 1.16(h))		*		Minus ***		=		x \$0 =				
	☐ Application Size Fee (37 CFR 1.16(s))												
	☐ FIRST PRESENTATION OF MULTIPLE DEPENDENT CLAIM (37 CFR 1.16(j))												
										TOTAL ADD'L FEE			
* If the entry in column 1 is less than the entry in column 2, write "0" in column 3.										LIE			
** If the "Highest Number Previously Paid For" IN THIS SPACE is less than 20, enter "20".										/ANGELA D JOHNSON/			
*** If the "Highest Number Previously Paid For" IN THIS SPACE is less than 3, enter "3".													
The "Highest Number Previously Paid For" (Total or Independent) is the highest number found in the appropriate box in column 1.													

This collection of information is required by 37 CFR 1.16. The information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.14. This collection is estimated to take 12 minutes to complete, including gathering, preparing, and submitting the completed application form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, U.S. Department of Commerce, P.O. Box 1450, Alexandria, VA 22313-1450. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. **SEND TO: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.**

If you need assistance in completing the form, call 1-800-PTO-9199 and select option 2.



UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
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P.O. Box 1450
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NOTICE OF ALLOWANCE AND FEE(S) DUE

13565 7590 04/14/2021
Dentons US LLP
4655 Executive Drive
Suite 700
San Diego, CA 92121

EXAMINER

LIU, SAMUEL W

ART UNIT

PAPER NUMBER

1656

DATE MAILED: 04/14/2021

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
16/912,590	06/25/2020	GE WEI	33320.03087.US27/3087D	9651

TITLE OF INVENTION: PH20 POLYPEPTIDE VARIANTS, FORMULATIONS AND USES THEREOF

APPLN. TYPE	ENTITY STATUS	ISSUE FEE DUE	PUBLICATION FEE DUE	PREV. PAID ISSUE FEE	TOTAL FEE(S) DUE	DATE DUE
nonprovisional	UNDISCOUNTED	\$1200	\$0.00	\$0.00	\$1200	07/14/2021

THE APPLICATION IDENTIFIED ABOVE HAS BEEN EXAMINED AND IS ALLOWED FOR ISSUANCE AS A PATENT. PROSECUTION ON THE MERITS IS CLOSED. THIS NOTICE OF ALLOWANCE IS NOT A GRANT OF PATENT RIGHTS. THIS APPLICATION IS SUBJECT TO WITHDRAWAL FROM ISSUE AT THE INITIATIVE OF THE OFFICE OR UPON PETITION BY THE APPLICANT. SEE 37 CFR 1.313 AND MPEP 1308.

THE ISSUE FEE AND PUBLICATION FEE (IF REQUIRED) MUST BE PAID WITHIN THREE MONTHS FROM THE MAILING DATE OF THIS NOTICE OR THIS APPLICATION SHALL BE REGARDED AS ABANDONED. THIS STATUTORY PERIOD CANNOT BE EXTENDED. SEE 35 U.S.C. 151. THE ISSUE FEE DUE INDICATED ABOVE DOES NOT REFLECT A CREDIT FOR ANY PREVIOUSLY PAID ISSUE FEE IN THIS APPLICATION. IF AN ISSUE FEE HAS PREVIOUSLY BEEN PAID IN THIS APPLICATION (AS SHOWN ABOVE), THE RETURN OF PART B OF THIS FORM WILL BE CONSIDERED A REQUEST TO REAPPLY THE PREVIOUSLY PAID ISSUE FEE TOWARD THE ISSUE FEE NOW DUE.

HOW TO REPLY TO THIS NOTICE:

I. Review the ENTITY STATUS shown above. If the ENTITY STATUS is shown as SMALL or MICRO, verify whether entitlement to that entity status still applies.

If the ENTITY STATUS is the same as shown above, pay the TOTAL FEE(S) DUE shown above.

If the ENTITY STATUS is changed from that shown above, on PART B - FEE(S) TRANSMITTAL, complete section number 5 titled "Change in Entity Status (from status indicated above)".

For purposes of this notice, small entity fees are 1/2 the amount of undiscounted fees, and micro entity fees are 1/2 the amount of small entity fees.

II. PART B - FEE(S) TRANSMITTAL, or its equivalent, must be completed and returned to the United States Patent and Trademark Office (USPTO) with your ISSUE FEE and PUBLICATION FEE (if required). If you are charging the fee(s) to your deposit account, section "4b" of Part B - Fee(s) Transmittal should be completed and an extra copy of the form should be submitted. If an equivalent of Part B is filed, a request to reapply a previously paid issue fee must be clearly made, and delays in processing may occur due to the difficulty in recognizing the paper as an equivalent of Part B.

III. All communications regarding this application must give the application number. Please direct all communications prior to issuance to Mail Stop ISSUE FEE unless advised to the contrary.

IMPORTANT REMINDER: Maintenance fees are due in utility patents issuing on applications filed on or after Dec. 12, 1980. It is patentee's responsibility to ensure timely payment of maintenance fees when due. More information is available at www.uspto.gov/PatentMaintenanceFees.

PART B - FEE(S) TRANSMITTAL

Complete and send this form, together with applicable fee(s), by mail or fax, or via EFS-Web.

By mail, send to: Mail Stop ISSUE FEE
Commissioner for Patents
P.O. Box 1450
Alexandria, Virginia 22313-1450

By fax, send to: (571)-273-2885

INSTRUCTIONS: This form should be used for transmitting the ISSUE FEE and PUBLICATION FEE (if required). Blocks 1 through 5 should be completed where appropriate. All further correspondence including the Patent, advance orders and notification of maintenance fees will be mailed to the current correspondence address as indicated unless corrected below or directed otherwise in Block 1, by (a) specifying a new correspondence address; and/or (b) indicating a separate "FEE ADDRESS" for maintenance fee notifications.

CURRENT CORRESPONDENCE ADDRESS (Note: Use Block 1 for any change of address)

13565 7590 04/14/2021
Dentons US LLP
4655 Executive Drive
Suite 700
San Diego, CA 92121

Note: A certificate of mailing can only be used for domestic mailings of the Fee(s) Transmittal. This certificate cannot be used for any other accompanying papers. Each additional paper, such as an assignment or formal drawing, must have its own certificate of mailing or transmission.

Certificate of Mailing or Transmission

I hereby certify that this Fee(s) Transmittal is being deposited with the United States Postal Service with sufficient postage for first class mail in an envelope addressed to the Mail Stop ISSUE FEE address above, or being transmitted to the USPTO via EFS-Web or by facsimile to (571) 273-2885, on the date below.

(Typed or printed name)
(Signature)
(Date)

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
16/912,590	06/25/2020	GE WEI	33320.03087.US27/3087D	9651

TITLE OF INVENTION: PH20 POLYPEPTIDE VARIANTS, FORMULATIONS AND USES THEREOF

APPLN. TYPE	ENTITY STATUS	ISSUE FEE DUE	PUBLICATION FEE DUE	PREV. PAID ISSUE FEE	TOTAL FEE(S) DUE	DATE DUE
nonprovisional	UNDISCOUNTED	\$1200	\$0.00	\$0.00	\$1200	07/14/2021

EXAMINER	ART UNIT	CLASS-SUBCLASS
LIU, SAMUEL W	1656	424-094620

1. Change of correspondence address or indication of "Fee Address" (37 CFR 1.363).

☐ Change of correspondence address (or Change of Correspondence Address form PTO/SB/122) attached.

☐ "Fee Address" indication (or "Fee Address" Indication form PTO/SB/47; Rev 03-09 or more recent) attached. **Use of a Customer Number is required.**

2. For printing on the patent front page, list

(1) The names of up to 3 registered patent attorneys or agents OR, alternatively,

1 _____

(2) The name of a single firm (having as a member a registered attorney or agent) and the names of up to 2 registered patent attorneys or agents. If no name is listed, no name will be printed.

2 _____

3 _____

3. ASSIGNEE NAME AND RESIDENCE DATA TO BE PRINTED ON THE PATENT (print or type)

PLEASE NOTE: Unless an assignee is identified below, no assignee data will appear on the patent. If an assignee is identified below, the document must have been previously recorded, or filed for recordation, as set forth in 37 CFR 3.11 and 37 CFR 3.81(a). Completion of this form is NOT a substitute for filing an assignment.

(A) NAME OF ASSIGNEE

(B) RESIDENCE: (CITY and STATE OR COUNTRY)

Please check the appropriate assignee category or categories (will not be printed on the patent) : ☐ Individual ☐ Corporation or other private group entity ☐ Government

4a. Fees submitted: ☐ Issue Fee ☐ Publication Fee (if required) ☐ Advance Order - # of Copies _____

4b. Method of Payment: (Please first reapply any previously paid fee shown above)

☐ Electronic Payment via EFS-Web ☐ Enclosed check ☐ Non-electronic payment by credit card (Attach form PTO-2038)

☐ The Director is hereby authorized to charge the required fee(s), any deficiency, or credit any overpayment to Deposit Account No. _____

5. Change in Entity Status (from status indicated above)

☐ Applicant certifying micro entity status. See 37 CFR 1.29

☐ Applicant asserting small entity status. See 37 CFR 1.27

☐ Applicant changing to regular undiscounted fee status.

NOTE: Absent a valid certification of Micro Entity Status (see forms PTO/SB/15A and 15B), issue fee payment in the micro entity amount will not be accepted at the risk of application abandonment. NOTE: If the application was previously under micro entity status, checking this box will be taken to be a notification of loss of entitlement to micro entity status.

NOTE: Checking this box will be taken to be a notification of loss of entitlement to small or micro entity status, as applicable.

NOTE: This form must be signed in accordance with 37 CFR 1.31 and 1.33. See 37 CFR 1.4 for signature requirements and certifications.

Authorized Signature _____

Date _____

Typed or printed name _____

Registration No. _____



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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
16/912,590	06/25/2020	GE WEI	33320.03087.US27/3087D	9651
13565	7590	04/14/2021	EXAMINER	
Dentons US LLP 4655 Executive Drive Suite 700 San Diego, CA 92121			LIU, SAMUEL W	
			ART UNIT	PAPER NUMBER
			1656	
DATE MAILED: 04/14/2021				

Determination of Patent Term Adjustment under 35 U.S.C. 154 (b) (Applications filed on or after May 29, 2000)

The Office has discontinued providing a Patent Term Adjustment (PTA) calculation with the Notice of Allowance.

Section 1(h)(2) of the AIA Technical Corrections Act amended 35 U.S.C. 154(b)(3)(B)(i) to eliminate the requirement that the Office provide a patent term adjustment determination with the notice of allowance. See Revisions to Patent Term Adjustment, 78 Fed. Reg. 19416, 19417 (Apr. 1, 2013). Therefore, the Office is no longer providing an initial patent term adjustment determination with the notice of allowance. The Office will continue to provide a patent term adjustment determination with the Issue Notification Letter that is mailed to applicant approximately three weeks prior to the issue date of the patent, and will include the patent term adjustment on the patent. Any request for reconsideration of the patent term adjustment determination (or reinstatement of patent term adjustment) should follow the process outlined in 37 CFR 1.705.

Any questions regarding the Patent Term Extension or Adjustment determination should be directed to the Office of Patent Legal Administration at (571)-272-7702. Questions relating to issue and publication fee payments should be directed to the Customer Service Center of the Office of Patent Publication at 1-(888)-786-0101 or (571)-272-4200.

OMB Clearance and PRA Burden Statement for PTOL-85 Part B

The Paperwork Reduction Act (PRA) of 1995 requires Federal agencies to obtain Office of Management and Budget approval before requesting most types of information from the public. When OMB approves an agency request to collect information from the public, OMB (i) provides a valid OMB Control Number and expiration date for the agency to display on the instrument that will be used to collect the information and (ii) requires the agency to inform the public about the OMB Control Number's legal significance in accordance with 5 CFR 1320.5(b).

The information collected by PTOL-85 Part B is required by 37 CFR 1.311. The information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.14. This collection is estimated to take 30 minutes to complete, including gathering, preparing, and submitting the completed application form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, U.S. Department of Commerce, P.O. Box 1450, Alexandria, Virginia 22313-1450. **DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. SEND TO: Commissioner for Patents, P.O. Box 1450, Alexandria, Virginia 22313-1450.** Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it displays a valid OMB control number.

Privacy Act Statement

The Privacy Act of 1974 (P.L. 93-579) requires that you be given certain information in connection with your submission of the attached form related to a patent application or patent. Accordingly, pursuant to the requirements of the Act, please be advised that: (1) the general authority for the collection of this information is 35 U.S.C. 2(b) (2); (2) furnishing of the information solicited is voluntary; and (3) the principal purpose for which the information is used by the U.S. Patent and Trademark Office is to process and/or examine your submission related to a patent application or patent. If you do not furnish the requested information, the U.S. Patent and Trademark Office may not be able to process and/or examine your submission, which may result in termination of proceedings or abandonment of the application or expiration of the patent.

The information provided by you in this form will be subject to the following routine uses:

1. The information on this form will be treated confidentially to the extent allowed under the Freedom of Information Act (5 U.S.C. 552) and the Privacy Act (5 U.S.C. 552a). Records from this system of records may be disclosed to the Department of Justice to determine whether disclosure of these records is required by the Freedom of Information Act.
2. A record from this system of records may be disclosed, as a routine use, in the course of presenting evidence to a court, magistrate, or administrative tribunal, including disclosures to opposing counsel in the course of settlement negotiations.
3. A record in this system of records may be disclosed, as a routine use, to a Member of Congress submitting a request involving an individual, to whom the record pertains, when the individual has requested assistance from the Member with respect to the subject matter of the record.
4. A record in this system of records may be disclosed, as a routine use, to a contractor of the Agency having need for the information in order to perform a contract. Recipients of information shall be required to comply with the requirements of the Privacy Act of 1974, as amended, pursuant to 5 U.S.C. 552a(m).
5. A record related to an International Application filed under the Patent Cooperation Treaty in this system of records may be disclosed, as a routine use, to the International Bureau of the World Intellectual Property Organization, pursuant to the Patent Cooperation Treaty.
6. A record in this system of records may be disclosed, as a routine use, to another federal agency for purposes of National Security review (35 U.S.C. 181) and for review pursuant to the Atomic Energy Act (42 U.S.C. 218(c)).
7. A record from this system of records may be disclosed, as a routine use, to the Administrator, General Services, or his/her designee, during an inspection of records conducted by GSA as part of that agency's responsibility to recommend improvements in records management practices and programs, under authority of 44 U.S.C. 2904 and 2906. Such disclosure shall be made in accordance with the GSA regulations governing inspection of records for this purpose, and any other relevant (i.e., GSA or Commerce) directive. Such disclosure shall not be used to make determinations about individuals.
8. A record from this system of records may be disclosed, as a routine use, to the public after either publication of the application pursuant to 35 U.S.C. 122(b) or issuance of a patent pursuant to 35 U.S.C. 151. Further, a record may be disclosed, subject to the limitations of 37 CFR 1.14, as a routine use, to the public if the record was filed in an application which became abandoned or in which the proceedings were terminated and which application is referenced by either a published application, an application open to public inspection or an issued patent.
9. A record from this system of records may be disclosed, as a routine use, to a Federal, State, or local law enforcement agency, if the USPTO becomes aware of a violation or potential violation of law or regulation.

Notice of Allowability	Application No. 16/912,590	Applicant(s) WEI et al.	
	Examiner SAMUEL W LIU	Art Unit 1656	AIA (FITF) Status No

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address--

All claims being allowable, PROSECUTION ON THE MERITS IS (OR REMAINS) CLOSED in this application. If not included herewith (or previously mailed), a Notice of Allowance (PTOL-85) or other appropriate communication will be mailed in due course. **THIS NOTICE OF ALLOWABILITY IS NOT A GRANT OF PATENT RIGHTS.** This application is subject to withdrawal from issue at the initiative of the Office or upon petition by the applicant. See 37 CFR 1.313 and MPEP 1308.

1. ☒ This communication is responsive to 3/17/2021 & 4/8/2021.
☐ A declaration(s)/affidavit(s) under **37 CFR 1.130(b)** was/were filed on _____.
2. ☐ An election was made by the applicant in response to a restriction requirement set forth during the interview on _____; the restriction requirement and election have been incorporated into this action.
3. ☒ The allowed claim(s) is/are 1-21 and 23-26 . As a result of the allowed claim(s), you may be eligible to benefit from the **Patent Prosecution Highway** program at a participating intellectual property office for the corresponding application. For more information , please see http://www.uspto.gov/patents/init_events/pph/index.jsp or send an inquiry to PPHfeedback@uspto.gov.
4. ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
Certified copies:
a) ☐ All b) ☐ Some *c) ☐ None of the:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this national stage application from the International Bureau (PCT Rule 17.2(a)).
* Certified copies not received: _____.

Applicant has THREE MONTHS FROM THE "MAILING DATE" of this communication to file a reply complying with the requirements noted below. Failure to timely comply will result in ABANDONMENT of this application.
THIS THREE-MONTH PERIOD IS NOT EXTENDABLE.

5. ☐ CORRECTED DRAWINGS (as "replacement sheets") must be submitted.
☐ including changes required by the attached Examiner's Amendment / Comment or in the Office action of Paper No./Mail Date _____.
Identifying indicia such as the application number (see 37 CFR 1.84(c)) should be written on the drawings in the front (not the back) of each sheet. Replacement sheet(s) should be labeled as such in the header according to 37 CFR 1.121(d).
6. ☐ DEPOSIT OF and/or INFORMATION about the deposit of BIOLOGICAL MATERIAL must be submitted. Note the attached Examiner's comment regarding REQUIREMENT FOR THE DEPOSIT OF BIOLOGICAL MATERIAL.

Attachment(s)

1. ☒ Notice of References Cited (PTO-892) 2. ☒ Information Disclosure Statements (PTO/SB/08), Paper No./Mail Date 3/17/2021. 3. ☐ Examiner's Comment Regarding Requirement for Deposit of Biological Material _____. 4. ☒ Interview Summary (PTO-413), Paper No./Mail Date. 4/8/2021.	5. ☒ Examiner's Amendment/Comment 6. ☒ Examiner's Statement of Reasons for Allowance 7. ☐ Other _____.
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/SAMUEL W LIU/ Examiner, Art Unit 1656	/SCARLETT Y GOON/ QAS, Art Unit 1600
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Notice of Pre-AIA or AIA Status

The present application is being examined under the pre-AIA first to invent provisions.

DETAILED ACTION

The amendment filed 3/17/2021 which amends claims 1, 2, 4-11, 13-16, 18-19 and 23-24, and adds claims 25-26 has been entered. The following Office action is applied to the pending claims 1-26.

The terminal disclaimer filed on 3/15/2021 disclaiming the terminal portion of any patent granted on this application, which would extend beyond the expiration date of US Pat. Nos. 10865400 and 9447401 have been reviewed and accepted. It is noted that Application No. 15226489 cited in the ODP rejection in the Office action mailed 12/9/2021 now is US Pat. No. 10865400.

The references cited in the IDS filed 3/17/2021 have been considered by Examiner.

EXAMINER'S AMENDMENT

An Examiner's Amendment to the record appears below. Should the change and/or additions be unacceptable to Applicant, an amendment may be filed as provided by 37 C.F.R. § 1.312. To ensure consideration of such an amendment, it **MUST** be submitted no later than payment of the Issue Fee. Authorization for this Examiner's Amendment was given in communication with Stephanie Seidman on 4/8/2021. Applicants accepted the Examiner's proposed amendment to claims 1, 19 and 26, and agreed to cancel claim 22.

Claim 1 (currently amended). A modified PH20 polypeptide, comprising one or more amino acid replacements in an unmodified PH20 polypeptide, wherein: the unmodified PH20 polypeptide consists of the amino acid sequence selected from the group consisting of SEQ ID NOs: 3, 7 and 32-66; the modified PH20 polypeptide exhibits increased hyaluronidase activity compared to the unmodified PH20 polypeptide not containing the amino acid replacement(s); the amino acid replacement(s) confer(s) the increased hyaluronidase activity; an amino acid replacement confers the increased hyaluronidase activity and is at a position corresponding to residue 309, with reference to amino acid positions of SEQ ID NO:3; corresponding amino acid positions are identified by alignment of the PH20 polypeptide with the polypeptide having the amino acid sequence of ~~amino acids~~ of SEQ ID NO:3; and the modified PH20 polypeptide has at least 91% sequence identity to the amino acid sequence selected from the group consisting of SEQ ID NOs: 3, 7 and 32-66.

Claim 19 (currently amended). The modified PH20 polypeptide of claim 1, further comprising a heterologous signal sequence wherein the unmodified PH20 polypeptide consists of ~~an~~ the amino acid sequence selected from the group consisting of SEQ ID NOs: 3 and 32-66.

Cancel claim 22.

Claim 25 (currently amended). The modified PH20 polypeptide of claim 5, wherein: the unmodified PH20 polypeptide consists of the amino acid sequence set forth in SEQ ID NO:35; and the amino acid sequence of the modified PH20 polypeptide has at least 95% sequence identity to SEQ ID NO:~~32~~ 35.

Claim 26 (currently amended). The modified PH20 polypeptide of claim 1, further comprising a signal sequence, wherein the unmodified PH20 polypeptide consists of ~~an~~ the amino acid sequence selected from the group consisting of SEQ ID NOs: 3 and 32-66.

Rejections withdrawn

The 112(d) rejection of claims 9-11, 13, 14 and 23 is withdrawn in light of the amendment of claims 9-11, 13, 14 and 23.

The 112(b) rejection of 18-19 is withdrawn in light of the amendment of the claims 18-19.

The ODP rejections of claims 1-14, 17-18, 21, 23 and 24 over Application 15226489, and the ODP rejection of claims 1-4, 7, 9-12, 15-18, 21, 23 and 24 over US Pat. No. 9447401 are withdrawn in light of the terminal disclaimers filed on 3/15/2021 (see above).

Reasons allowed

The closest prior art is US20130071394 ('394) which discloses variant PH20 polypeptides (from human or non-human species) or truncated mutant forms thereof wherein the variant PH20 polypeptide ([0026]-[0028], '394) contains amino acid substitutions ([0150], '394). However, '394 does not teach or suggest that the modified PH20 polypeptide comprises the substitution at position 309 wherein the resultant modified PH20 has increased hyaluronidase activity and has at least 91% sequence identity to the unmodified PH20 polypeptide of SEQ ID NO:3 (a mature human PH20 polypeptide) or to the unmodified PH20 polypeptide of SEQ ID NO: 7 (a full-length human PH20 polypeptide) or to one of unmodified PH20 polypeptides of SEQ ID NOs: 32-66 (mature human PH20 polypeptides with amino acid truncation at C-terminal region) as set forth in claim 1. While '394 has taught that the PH20 polypeptide can comprise substitution mutations, '394 does not teach or suggest which amino acid residues are substituted to achieve the increased hyaluronidase activity as recited in the claimed "modified PH20 polypeptide" comprising the amino acid substitution at residue 309 which confers the increased hyaluronidase activity recited in the claim 1. It is noted that all of the unmodified PH20

polypeptides of SEQ ID NOs:3, 7 and 32-66 have the identical sequences at residues 1-465; and thus, the sequence of the modified PH20 comprising the substitution at residue 309 can be determined as compared to the unmodified PH20 polypeptide sequences. Thus, the claimed modified PH20 polypeptide (claim 1) is free from prior art. Therefore, claims 1-21 and 23-26 are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to SAMUEL W LIU whose telephone number is (571)272-0949. The examiner can normally be reached on M-F 8:30 am-5:30 pm.

Examiner interviews are available via telephone, in-person, and video conferencing using a USPTO supplied web-based collaboration tool. To schedule an interview, applicant is encouraged to use the USPTO Automated Interview Request (AIR) at <http://www.uspto.gov/interviewpractice>.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Manjunath Rao can be reached on 571-272-0939. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <https://ppair-my.uspto.gov/pair/PrivatePair>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Samuel Wei Liu/
Patent Examiner, Art Unit 1656
April 8, 2021

/SCARLETT Y GOON/
QAS, Art Unit 1600

<i>Examiner-Initiated Interview Summary</i>	Application No. 16/912,590	Applicant(s) WEI et al.		
	Examiner SAMUEL W LIU	Art Unit 1656	AIA (First Inventor to File) Status No	Page 1 of 1

All Participants (applicant, applicants representative, PTO personnel)	Title	Type
SAMUEL W LIU	Examiner	Telephonic
Stephanie Seidman	Attorney of Record	

Date of Interview: 08 April 2021

Issues Discussed:

Other

Discussed the rejoinder of the process claim 22 which has been previously withdrawn from further consideration. Examiner pointed out that, although the claimed method (claim 22) employs the allowable product “a pharmaceutical composition” comprising the “modified PH20 polypeptide” of claim 1 that is allowable, the claim 22 as written is not in the condition for allowability in this case because the instant claim 22 does not satisfy the requirements of 35 U.S.C. 112(a). Examiner proposed to cancel claim 22. Applicant’s representative accepted the Examiner’s proposal of the cancellation of claim 22.

/SAMUEL W LIU/ Examiner, Art Unit 1656	/SCARLETT Y GOON/ QAS, Art Unit 1600
Applicant is reminded that a complete written statement as to the substance of the interview must be made of record in the application file. It is the applicants responsibility to provide the written statement, unless the interview was initiated by the Examiner and the Examiner has indicated that a written summary will be provided. See MPEP 713.04 Please further see: MPEP 713.04 Title 37 Code of Federal Regulations (CFR) § 1.133 Interviews, paragraph (b) 37 CFR § 1.2 Business to be transacted in writing	

Applicant recordation instructions: It is not necessary for applicant to provide a separate record of the substance of interview.

Examiner recordation instructions: Examiners must summarize the substance of any interview of record. A complete and proper recordation of the substance of an interview should include the items listed in MPEP 713.04 for complete and proper recordation including the identification of the general thrust of each argument or issue discussed, a general indication of any other pertinent matters discussed regarding patentability and the general results or outcome of the interview, to include an indication as to whether or not agreement was reached on the issues raised.

Notice of References Cited	Application/Control No. 16/912,590		Applicant(s)/Patent Under Reexamination WEI et al.	
	Examiner SAMUEL W LIU		Art Unit 1656	Page 1 of 1

U.S. PATENT DOCUMENTS

*		Document Number Country Code-Number-Kind Code	Date MM-YYYY	Name	CPC Classification	US Classification
*	A	US-20130071394-A1	03-2013	Troyer; John K.	A61K39/395	424/134.1
	B					
	C					
	D					
	E					
	F					
	G					
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	I					
	J					
	K					
	L					
	M					

FOREIGN PATENT DOCUMENTS

*		Document Number Country Code-Number-Kind Code	Date MM-YYYY	Country	Name	CPC Classification
	N					
	O					
	P					
	Q					
	R					
	S					
	T					

NON-PATENT DOCUMENTS

*		Include as applicable: Author, Title Date, Publisher, Edition or Volume, Pertinent Pages)
	U	
	V	
	W	
	X	

*A copy of this reference is not being furnished with this Office action. (See MPEP § 707.05(a).)
Dates in MM-YYYY format are publication dates. Classifications may be US or foreign.

Search Notes 	Application/Control No. 16/912,590	Applicant(s)/Patent Under Reexamination WEI et al.
	Examiner SAMUEL W LIU	Art Unit 1656

CPC - Searched*		
Symbol	Date	Examiner
C12N 9/2474	04/07/2021	SWL

CPC Combination Sets - Searched*		
Symbol	Date	Examiner
C12N 9/2474	11/12/2020	SWL

US Classification - Searched*			
Class	Subclass	Date	Examiner

* See search history printout included with this form or the SEARCH NOTES box below to determine the scope of the search.

Search Notes		
Search Notes	Date	Examiner
STIC sequence search for SEQ ID NOs:3, 7, 32-39 and 581-585 (reviewed)	04/07/2021	SWL
Assignee and inventor name search combined with WEST prior art search and google prior art search for (PH20 protein or hyaluronidase or EC 3.2.1.35 or sperm adhesion molecule 1 (SPAM1) / PH20 variant or modified PH20 with substitution at residue 309 / I309N, I309H, I309M, I309G, I309L, I309H (residue numbering according to instant SEQ ID NO:3).	04/08/2021	SWL
PALM inventor name search	04/07/2021	SWL

/SAMUEL W LIU/ Examiner, Art Unit 1656	
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<i>Search Notes</i> 	Application/Control No. 16/912,590	Applicant(s)/Patent Under Reexamination WEI et al.
	Examiner SAMUEL W LIU	Art Unit 1656

Interference Search			
US Class/CPC Symbol	US Subclass/CPC Group	Date	Examiner
	WEST interference search (PGPUB text search) for (PH20 polypeptide protein or hyaluronidase mutant or variant/ amino acid substitution at position 309; residue numbering according to instant SEQ ID NO:3.	04/08/2021	SWL

/SAMUEL W LIU/ Examiner, Art Unit 1656	
---	--

Issue Classification 	Application/Control No. 16/912,590	Applicant(s)/Patent Under Reexamination WEI et al.
	Examiner SAMUEL W LIU	Art Unit 1656

CPC						
Symbol					Type	Version
C12N	/	9	/	2474	F	2013-01-01
A61K	/	38	/	47	I	2013-01-01
A61K	/	38	/	28	I	2013-01-01
A61K	/	45	/	06	I	2013-01-01
C12Y	/	302	/	01035	I	2013-01-01
A61K	/	9	/	0019	I	2013-01-01
A61K	/	47	/	10	I	2013-01-01
C12Q	/	1	/	34	I	2013-01-01
G01N	/	2333	/	926	A	2013-01-01
G01N	/	2333	/	928	A	2013-01-01
Y02A	/	50	/	30	A	2018-01-01
A61K	/	38	/	00	A	2013-01-01

CPC Combination Sets								
Symbol					Type	Set	Ranking	Version
A61K	/	38	/	28	I	1	1	2013-01-01
A61K	/	2300	/	00	I	1	2	2013-01-01
A61K	/	38	/	47	I	2	1	2013-01-01
A61K	/	2300	/	00	I	2	2	2013-01-01

/SAMUEL W LIU/ Examiner, Art Unit 1656 (Assistant Examiner)	09 April 2021 (Date)	Total Claims Allowed: 25	
/SCARLETT Y GOON/ QAS, Art Unit 1600 (Primary Examiner)	09 April 2021 (Date)	O.G. Print Claim(s) 1	O.G. Print Figure none

Issue Classification 	Application/Control No. 16/912,590	Applicant(s)/Patent Under Reexamination WEI et al.
	Examiner SAMUEL W LIU	Art Unit 1656

INTERNATIONAL CLASSIFICATION				
CLAIMED				
C12N	/	9	/	26
NON-CLAIMED				
A61K	/	38	/	00

US ORIGINAL CLASSIFICATION	
CLASS	SUBCLASS

CROSS REFERENCES(S)						
CLASS	SUBCLASS (ONE SUBCLASS PER BLOCK)					

/SAMUEL W LIU/ Examiner, Art Unit 1656 (Assistant Examiner)	09 April 2021 (Date)	Total Claims Allowed: 25	
/SCARLETT Y GOON/ QAS, Art Unit 1600 (Primary Examiner)	09 April 2021 (Date)	O.G. Print Claim(s) 1	O.G. Print Figure none

Issue Classification 	Application/Control No. 16/912,590	Applicant(s)/Patent Under Reexamination WEI et al.
	Examiner SAMUEL W LIU	Art Unit 1656

☐ Claims renumbered in the same order as presented by applicant ☐ CPA ☒ T.D. ☐ R.1.47															
CLAIMS															
Final	Original	Final	Original	Final	Original	Final	Original	Final	Original	Final	Original	Final	Original	Final	Original
1	1	13	10	21	19										
2	2	8	11	22	20										
3	3	14	12	23	21										
5	4	15	13	24	23										
6	5	16	14	9	24										
11	6	17	15	10	25										
4	7	18	16	25	26										
7	8	19	17												
12	9	20	18												

/SAMUEL W LIU/ Examiner, Art Unit 1656 (Assistant Examiner)	09 April 2021 (Date)	Total Claims Allowed: 25	
/SCARLETT Y GOON/ QAS, Art Unit 1600 (Primary Examiner)	09 April 2021 (Date)	O.G. Print Claim(s) 1	O.G. Print Figure none



variant or modified PH20 polypeptide and substitution at 309 or Ile 309


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About 2,150 results (0.32 seconds)

<https://www.freepatentsonline.com> > ...
PH20 POLYPEPTIDE VARIANTS, FORMULATIONS AND ...

Oct 8, 2020 — The modified PH20 polypeptide of claim 1, wherein the replacement is selected from among L at a ... contains the amino acid replacement N at residue 309 with reference to corresponding positions in a ... Met (M), Leu, Tyr, Ile.

<https://patents.google.com> > patent
US10328130B2 - Modified hyaluronidases and uses in ...

The other variants are selected from among polypeptides having at least 60%, 65, 70, ... PH20 soluble hyaluronidase or allelic or species or other variants thereof. ... Differences are defined as nucleic acid or amino acid substitutions, insertions or ... While in 73% (227 of 309) of the cases, the fraction of hyaluronan-positive ...

<https://patents.google.com> > patent
US8431380B2 - Soluble hyaluronidase glycoprotein ...

Minimally active polypeptide domains of the soluble, neutral active SHASECP domains ... Included are modified amino-terminal leader peptides that enhance secretion of ... HYAL1 is the prototypical acid-active enzyme and PH20 is the prototypical ... Phe Val (V) Ile, Leu, Met, Nle, Nv Other substitutions are also permissible ...

<https://patentimages.storage.googleapis.com> > ... PDF
US 2014/0178330 A9

Modified PH20 hyaluronidase polypeptides, including modi. (65) ... Polypeptide Variants, Formulations and Uses Thereof." ... purposes herein, amino acid replacements are denoted by the ... to position 309; Data position corresponding to position 310; ... Ile, Leu. Other substitutions also are permissible and can be deter.

<https://www.ic.gc.ca> > opic-опо > opd > eng > summary
Patent 2964317 Summary - Canadian Patents Database

thereof, comprising a modification(s) in the sequence of amino acids of an ... the variant ADA2 protein comprises an amino acid replacement at one or ... of the polypeptide whose sequence is set forth in of SEQ ID NO:5, wherein ... 262, 264, 266, 267, 277, 293, 296, 309, 317, 321, 352, 366, 371, 372, 373, ... 1 Ile isoleucine

<https://hupo.org> > resources > Documents PDF
Proteolytic Cleavage—Mechanisms, Function, and - Human ...

by T Klein · 2018 · Cited by 71 — Approaches for a Near-Ubiquitous Posttranslational Modification, Theo Klein, ... enzymatic hydrolysis of a peptide bond in a peptide or protein substrate by a ... eqolisin with a bound N-terminal cleavage fragment Ala-Ile-His (pdb code: 1s2tr) ... Marimastat as the label-accepting probe.309,310. A variant ...

<https://www.google.com> > patents
WO2014177460A1 - Human fcγn-binding modified antibodies ...

Human fcγn-binding modified antibodies and methods of use Download PDF ... G Proteins 0.000 description 63; Z38000006467 substitution reactions Methods ... 101710032459 hyaluronidase PH-20 Proteins 0.000 description 1 ... The term "variant (human) Fc-region polypeptide" denotes an amino acid ... L399A Chem.

<https://www.uniprot.org> > uniprot
SPAM1 - Hyaluronidase PH-20 precursor - Homo sapiens ...

Hyaluronidase PH-20 (EC:3.2.1.35 ... Sperm surface protein PH-20 ... Synonyms:HYAL3, PH20 ... Genetic variation databases ... a></p>Signal peptide, 1 -- 35, By similarityAdd BLAST, 35 ...

4/9/2021

variant or modified PH20 polypeptide and substitution at 309 or Ile 309 - Google Search

Amino acid modifications ... it is not in any way intended to be used as a substitute for professional medical advice, diagnosis, ...
Missing: 309 Ile

<https://academic.oup.com/mbe/article/>

Positive Selection for Indel Substitutions in the Rodent Sperm ...

by O Podlaha · 2005 · Cited by 59 — We show that the rate of insertion/deletion (indel) substitutions in exon 1 of the ... indicate that positive selection promoting length variation in Catsper1 may be ... We also modified the McDonald and Kreitman (1991) test to examine whether the ... — 309. Yang, Z. 1997 . PAML: a program package for phylogenetic analysis by ...

https://www.researchgate.net/publication/11290119_R...

(PDF) Regulation of Hyaluronidase Activity by Alternative ...

Mar 24, 2021 — All tumor cells and tissues mainly express HYAL3 variants. HYAL3v1 ... HA-degrading enzyme, PH20 may also interact with HA to increase ...

1 2 3 4 5 6 7 8 9 Next

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Substitute Form PTO-1449 (Modified)		U.S. Department of Commerce Patent and Trademark Office		Attorney Docket No. 33320.03087.US27/ 3087D		Application No. 16/912,590	
List of Patents and Publications for Applicant's Information Disclosure Statement (37 CFR §1.98(b))				Inventors <i>Wei et al.</i>			
				Filing Date June 25, 2020		Group Art Unit 1656	
U.S. Patent Documents							
Examiner Initial	Desig. ID	Document Number	Publication Date	Patentee	Class	Subclass	Filing Date If Appropriate
	AA	2020/0368330	11/26/2020	Frost et al.	424	078.170	07/16/2020

Foreign Patent Documents or Published Foreign Patent Applications						
Examiner Initial	Desig. ID	Document Number	Publication Date	Country or Patent Office	Translation	
					Yes	No
None						

Other Documents (include Author, Title, Date, and Place of Publication)		
Examiner Initial	Desig. ID	Document
	AB	Letter/Written Disclosure of the Information Disclosure Statement for the above-referenced application, filed herewith on March 17, 2021, 2 pages.
	AC	Rosengren et al., "Clinical Immunogenicity of rHuPH20, a Hyaluronidase Enabling Subcutaneous Drug Administration," AAPS J. 17(5):1144-56 (2015).
	AD	Office Action, issued Oct. 27, 2020, in connection with U.S. Patent Application No. 16/824,572, 9 pages.
	AE	Response, filed Jan. 27, 2021, to Office Action, issued Oct. 27, 2020, in connection with U.S. Patent Application No. 16/824,572, 23 pages.
	AF	Notice of Allowance, mailed Feb. 18, 2021, and Examiner-Initiated Interview Summary, summarizing the interview held on Feb. 10, 2021, issued in connection with U.S. Patent Application No. 16/824,572, 10 pages.
	AG	Amended claims and abstract, filed Nov. 19, 2020, responsive to Examiner request, in connection with Indian Patent Application No. 6272/DELNP/2014, 22 pages.
	AH	Certificate of Grant, issued Dec. 28, 2020, in connection with Indian Patent Application No. 6272/DELNP/2014, 1 page.
	AI	Certificate of Grant, issued Oct. 01, 2020, in connection with Israeli Patent Application No. 233192, 3 pages.
	AJ	Notification Prior to Acceptance, issued Dec. 14, 2020, in connection with Israeli Patent Application No. 274798 [English reporting letter; original document as issued in Hebrew; and English translation of allowed claims], 10 pages.

Examiner Signature /SAMUEL W LIU/	Date Considered 04/01/2021
EXAMINER: Initial if citation considered, whether or not citation is in conformance with MPEP 609; Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.	

WEST Search History for Application 16912590

Creation Date: 2021040901:52

Interference Searches

Query	DB	Hits	Op.	Plur.	Thes.	Date
(PH20 adj (polypeptide or protein) or hyaluronidase) and (mutation or replac \$ 4 or substitut \$ 3) with (amino acid or residue or position)	PGPB	5401	ADJ	YES		04-09-2021
((PH20 adj (polypeptide or protein) or hyaluronidase) and (mutation or replac \$ 4 or substitut \$ 3) with (amino acid or residue or position)) and (modified or recombinant or engineered or variant or mutant or mutated) near1 PH20	PGPB	54	ADJ	YES		04-09-2021
((PH20 adj (polypeptide or protein) or hyaluronidase) and (mutation or replac \$ 4 or substitut \$ 3) with (amino acid or residue or position) and (modified or recombinant or engineered or variant or mutant or mutated) near1 PH20) and ((mutation or replac \$ 4 or substitut \$ 3) with 309 or I309 \$ 1)	PGPB	6	ADJ	YES		04-09-2021

Prior Art Searches

Query	DB	Hits	Op.	Plur.	Thes.	Date
(PH20 adj(polypeptide or protein) or hyaluronidase or EC 3.2.1.35 or sperm adhesion molecule 1 or SPAM1) and (mutation or replac\$4 or substitut\$3) with (amino acid or residue or position)	PGPB, USPT, USOC	8294	ADJ	YES		04-09-2021
((PH20 adj(polypeptide or protein) or hyaluronidase or EC 3.2.1.35 or sperm adhesion molecule 1 or SPAM1) and (mutation or replac\$4 or substitut\$3) with (amino acid or residue or position)) and (modified or recombinant or engineered or variant or mutant or mutated) near1 PH20	PGPB, USPT, USOC	86	ADJ	YES		04-09-2021
((PH20 adj(polypeptide or protein) or hyaluronidase or EC 3.2.1.35 or sperm adhesion molecule 1 or SPAM1) and (mutation or replac\$4	PGPB, USPT, USOC	7	ADJ	YES		04-09-2021

or substitut\$3) with (amino acid or residue or position) and (modified or recombinant or engineered or variant or mutant or mutated) near1 PH20) and (mutation or replac\$4 or substitut\$3) with 309						
((PH20 adj(polypeptide or protein) or hyaluronidase or EC 3.2.1.35 or sperm adhesion molecule 1 or SPAM1) and (mutation or replac\$4 or substitut\$3) with (amino acid or residue or position) and (modified or recombinant or engineered or variant or mutant or mutated) near1 PH20 and (mutation or replac\$4 or substitut\$3) with 309) and ((mutation or replac\$4 or substitut\$3) with 309 or I309\$1)	PGPB, USPT, USOC	7	ADJ	YES		04-09-2021
((PH20 adj(polypeptide or protein) or hyaluronidase or EC 3.2.1.35 or sperm adhesion molecule 1 or SPAM1) and (mutation or replac\$4 or substitut\$3) with (amino acid or residue or position) and (modified or recombinant or engineered or variant or mutant or mutated) near1 PH20 and (mutation or replac\$4 or substitut\$3) with 309 and ((mutation or replac\$4 or substitut\$3) with 309 or I309\$1)) and @ad<20111230	PGPB, USPT, USOC	0	ADJ	YES		04-09-2021
HALOZYME adj INC	PGPB, USPT, USOC	138	ADJ	YES		04-09-2021
(HALOZYME adj INC) and (PH20 adj (polypeptide or protein) or hyaluronidase) and (mutation or replac\$4 or substitut\$3) with (amino acid or residue or position)	PGPB, USPT, USOC	n/a	ADJ	YES		04-09-2021
(HALOZYME adj INC) and (PH20 adj (polypeptide or protein) or hyaluronidase) and (mutation or replac\$4 or substitut\$3) with (amino acid or residue or position)	PGPB, USPT, USOC	103	ADJ	YES		04-09-2021
(HALOZYME adj INC and (PH20 adj (polypeptide or protein) or hyaluronidase) and (mutation or replac\$4 or substitut\$3) with (amino acid or residue or position)) and (modified or recombinant or engineered or variant or mutant or mutated) near1 PH20	PGPB, USPT, USOC	48	ADJ	YES		04-09-2021
(HALOZYME adj INC and (PH20 adj (polypeptide or protein) or hyaluronidase) and (mutation or replac\$4 or substitut\$3) with (amino acid or residue or position) and (modified or recombinant or engineered or variant or mutant	PGPB, USPT, USOC	5	ADJ	YES		04-09-2021

or mutated) near1 PH20) and (mutation or replac\$4 or substitut\$3) with 309						
WEI-GE.in. or SHEPARD-H-MICHAEL.in. or ZHAO-QIPING.in. or CONNOR-ROBERT-JAMES.in.	PGPB, USPT, USOC	316	ADJ	YES		04-09-2021
(WEI-GE.in. or SHEPARD-H-MICHAEL.in. or ZHAO-QIPING.in. or CONNOR-ROBERT-JAMES.in.) and (PH20 adj (polypeptide or protein) or hyaluronidase) and (mutation or replac\$4 or substitut\$3) with (amino acid or residue or position)	PGPB, USPT, USOC	33	ADJ	YES		04-09-2021
(WEI-GE.in. or SHEPARD-H-MICHAEL.in. or ZHAO-QIPING.in. or CONNOR-ROBERT-JAMES.in. and (PH20 adj (polypeptide or protein) or hyaluronidase) and (mutation or replac\$4 or substitut\$3) with (amino acid or residue or position)) and (modified or recombinant or engineered or variant or mutant or mutated) near1 PH20	PGPB, USPT, USOC	31	ADJ	YES		04-09-2021
(WEI-GE.in. or SHEPARD-H-MICHAEL.in. or ZHAO-QIPING.in. or CONNOR-ROBERT-JAMES.in. and (PH20 adj (polypeptide or protein) or hyaluronidase) and (mutation or replac\$4 or substitut\$3) with (amino acid or residue or position) and (modified or recombinant or engineered or variant or mutant or mutated) near1 PH20) and ((mutation or replac\$4 or substitut\$3) with 309 or I309\$1)	PGPB, USPT, USOC	8	ADJ	YES		04-09-2021

CPCI A 61 P 27/02 20180101
CPCI A 61 P 29/00 20180101
CPCI C 12 N 9/2474 20130101
CPCI A 61 P 43/00 20180101
CPCI A 61 K 38/28 20130101
CPCI A 61 K 2300/00 20130101
CPCI A 61 K 38/47 20130101
CPCI A 61 K 2300/00 20130101
CPCA G 01 N 2333/926 20130101
CPCA A 61 K 38/00 20130101
CPCA G 01 N 2333/928 20130101
CPCA Y 02 A 50/30 20180101

CPC-COMBINATION-SET(S) :

TYPE RANK CPC
CPCC 1 A 61 K 38/28
2 A 61 K 2300/00
CPCC 1 A 61 K 38/47
2 A 61 K 2300/00

ABSTRACT:

Modified PH20 hyaluronidase polypeptides, including modified polypeptides that exhibit increased stability and/or increased activity, are provided. Also provided are compositions and formulations and uses thereof.

Full	Title	Citation	Front	Review	Classification	Date	Reference	Sequences	Figures	Claims	KMC	Draw D
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☐ 2. Document ID: US 20200255814 A1

L4: Entry 2 of 7

File: PGPB

Aug 13, 2020

PGPUB-DOCUMENT-NUMBER: 20200255814

PGPUB-FILING-TYPE:

DOCUMENT-IDENTIFIER: US 20200255814 A1

TITLE: PH20 POLYPEPTIDE VARIANTS, FORMULATIONS AND USES THEREOF

PUBLICATION-DATE: March 19, 2020

PATENT-FAMILY-ID: 47595052

INVENTOR-INFORMATION:

NAME	CITY	STATE	COUNTRY
WEI; Ge	San Diego	CA	US
Shepard; H. Michael	San Diego	CA	US
Zhao; Qiping	San Diego	CA	US
Connor; Robert James	Oceanside	CA	US

APPLICANT-INFORMATION:

NAME	CITY	STATE	COUNTRY	AUTHORITY	TYPE
HALOZYME, INC.	San Diego	CA	US		

APPL-NO: 16/824572 [PAIM] [DAV] [US Family]
DATE FILED: March 19, 2020

US-CL-CURRENT: 1/1

CPC-CURRENT:

TYPE	CPC	DATE
CPCI	<u>A 61 K 9/0019</u>	20130101
CPCI	<u>A 61 P 35/00</u>	20180101
CPCI	<u>A 61 P 3/04</u>	20180101
CPCI	<u>A 61 P 3/10</u>	20180101
CPCI	<u>A 61 K 47/10</u>	20130101
CPCI	<u>A 61 P 11/00</u>	20180101
CPCI	<u>A 61 P 27/02</u>	20180101
CPCI	<u>C 12 Q 1/34</u>	20130101
CPCI	<u>C 12 Y 302/01035</u>	20130101
CPCI	<u>A 61 P 43/00</u>	20180101
CPCI	<u>A 61 K 38/47</u>	20130101
CPCI	<u>A 61 P 29/00</u>	20180101
CPCI	<u>A 61 K 45/06</u>	20130101
CPCI	<u>A 61 K 38/28</u>	20130101
CPCI	<u>C 12 N 9/2474</u>	20130101
CPCI	<u>A 61 K 38/28</u>	20130101
CPCI	<u>A 61 K 2300/00</u>	20130101
CPCI	<u>A 61 K 38/47</u>	20130101
CPCI	<u>A 61 K 2300/00</u>	20130101
CPCA	<u>Y 02 A 50/30</u>	20180101
CPCA	<u>G 01 N 2333/928</u>	20130101
CPCA	<u>A 61 K 38/00</u>	20130101
CPCA	<u>G 01 N 2333/926</u>	20130101

CPC-COMBINATION-SET(S) :

TYPE	RANK	CPC
CPCC	1	<u>A 61 K 38/28</u>
	2	<u>A 61 K 2300/00</u>
CPCC	1	<u>A 61 K 38/47</u>
	2	<u>A 61 K 2300/00</u>

ABSTRACT:

Modified PH20 hyaluronidase polypeptides, including modified polypeptides that exhibit increased stability and/or increased activity, are provided. Also provided are compositions and formulations and uses thereof.

Full	Title	Citation	Front	Review	Classification	Date	Reference	Sequences	Claims	KeyC	Draw De
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☐ 3. Document ID: US 20160362670 A1

L4: Entry 3 of 7

File: PGPB

Dec 15, 2016

PGPUB-DOCUMENT-NUMBER: 20160362670

PGPUB-FILING-TYPE:

DOCUMENT-IDENTIFIER: US 20160362670 A1

TITLE: PH20 POLYPEPTIDE VARIANTS, FORMULATIONS AND USES THEREOF

PUBLICATION-DATE: August 2, 2016

PATENT-FAMILY-ID: 47595052

INVENTOR-INFORMATION:

NAME	CITY	STATE	COUNTRY
Wei; Ge	San Diego	CA	US
Shepard; H. Michael	San Diego	CA	US
Zhao; Qiping	San Diego	CA	US
Connor; Robert James	Oceanside	CA	US

APPLICANT-INFORMATION:

NAME	CITY	STATE	COUNTRY	AUTHORITY	TYPE
HALOZYME, INC.	San Diego	CA	US		

APPL-NO: 15/226489 [PAIM] [DAV] [US Family]

DATE FILED: August 2, 2016

US-CL-CURRENT: 1/1

CPC-CURRENT:

TYPE	CPC	DATE
CPCI	<u>A 61 P 3/04</u>	20180101
CPCI	<u>A 61 P 43/00</u>	20180101
CPCI	<u>A 61 K 47/10</u>	20130101
CPCI	<u>A 61 P 3/10</u>	20180101
CPCI	<u>A 61 K 45/06</u>	20130101
CPCI	<u>A 61 K 38/47</u>	20130101
CPCI	<u>A 61 K 38/28</u>	20130101
CPCI	<u>A 61 P 27/02</u>	20180101
CPCI	<u>A 61 P 29/00</u>	20180101
CPCI	<u>A 61 P 11/00</u>	20180101
CPCI	<u>C 12 Q 1/34</u>	20130101
CPCI	<u>C 12 Y 302/01035</u>	20130101
CPCI	<u>A 61 P 35/00</u>	20180101
CPCI	<u>A 61 K 9/0019</u>	20130101
CPCI	<u>C 12 N 9/2474</u>	20130101
CPCI	<u>A 61 K 38/28</u>	20130101
CPCI	<u>A 61 K 2300/00</u>	20130101
CPCI	<u>A 61 K 38/47</u>	20130101
CPCI	<u>A 61 K 2300/00</u>	20130101
CPCA	<u>G 01 N 2333/928</u>	20130101
CPCA	<u>Y 02 A 50/30</u>	20180101
CPCA	<u>A 61 K 38/00</u>	20130101
CPCA	<u>G 01 N 2333/926</u>	20130101

CPC-COMBINATION-SET(S) :

TYPE	RANK	CPC
CPCC	1	<u>A 61 K 38/28</u>
	2	<u>A 61 K 2300/00</u>
CPCC	1	<u>A 61 K 38/47</u>
	2	<u>A 61 K 2300/00</u>

ABSTRACT:

Modified PH20 hyaluronidase polypeptides, including modified polypeptides that exhibit increased stability and/or increased activity, are provided. Also provided are compositions and formulations and uses thereof.

Full	Title	Citation	Front	Review	Classification	Date	Reference	Sequences	Claims	MM	Draw
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4. Document ID: US 20140178330 A9

L4: Entry 4 of 7

File: PGPB

Jun 26, 2014

PGPUB-DOCUMENT-NUMBER: 20140178330
PGPUB-FILING-TYPE: us-republication-corrected
DOCUMENT-IDENTIFIER: US 20140178330 A9

TITLE: PH20 Polypeptide Variants, Formulations And Uses Thereof

PUBLICATION-DATE: December 28, 2012

PRIOR-PUBLICATION-INFORMATION:

DOCUMENT-IDENTIFIER DOCUMENT-DATE
US 20130302275 A1 November 14, 2013

PATENT-FAMILY-ID: 47595052

INVENTOR-INFORMATION:

NAME	CITY	STATE	COUNTRY
Wei; Ge	San Diego	CA	US
Shepard; H. Michael	San Diego	CA	US
Zhao; Qiping	San Diego	CA	US
Connor; Robert James	Oceanside	CA	US

APPLICANT-INFORMATION:

NAME	CITY	STATE	COUNTRY	AUTHORITY	TYPE
Wei; Ge	San Diego	CA	US		
Shepard; H. Michael	San Diego	CA	US		
Zhao; Qiping	San Diego	CA	US		
Connor; Robert James	Oceanside	CA	US		

APPL-NO: 13/694731 [PALM] [DAV] [US Family]
DATE FILED: December 28, 2012

US-CL-CURRENT: 424/85.2, 424/130.1, 424/209.1, 424/225.1, 424/85.5, 424/85.6,
424/85.7, 424/94.62, 435/18, 435/201, 435/320.1, 435/325, 536/23.2

CPC-CURRENT:

TYPE	CPC	DATE
CPCI	A 61 K 47/10	20130101
CPCI	A 61 K 9/0019	20130101
CPCI	A 61 K 38/28	20130101
CPCI	A 61 K 38/47	20130101
CPCI	C 12 N 9/2474	20130101
CPCI	A 61 P 35/00	20180101

CPCI	A	<u>61</u>	P	<u>3/10</u>	20180101
CPCI	A	<u>61</u>	P	<u>3/04</u>	20180101
CPCI	A	<u>61</u>	P	<u>11/00</u>	20180101
CPCI	A	<u>61</u>	P	<u>43/00</u>	20180101
CPCI	A	<u>61</u>	P	<u>29/00</u>	20180101
CPCI	C	<u>12</u>	Q	<u>1/34</u>	20130101
CPCI	A	<u>61</u>	K	<u>45/06</u>	20130101
CPCI	C	<u>12</u>	Y	<u>302/01035</u>	20130101
CPCI	A	<u>61</u>	P	<u>27/02</u>	20180101
CPCI	A	<u>61</u>	K	<u>38/28</u>	20130101
CPCI	A	<u>61</u>	K	<u>2300/00</u>	20130101
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CPCI	A	<u>61</u>	K	<u>2300/00</u>	20130101
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CPCA	Y	<u>02</u>	A	<u>50/30</u>	20180101
CPCA	A	<u>61</u>	K	<u>38/00</u>	20130101
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CPC-COMBINATION-SET(S) :

TYPE	RANK	CPC
CPCC	1	A <u>61</u> K <u>38/28</u>
	2	A <u>61</u> K <u>2300/00</u>
CPCC	1	A <u>61</u> K <u>38/47</u>
	2	A <u>61</u> K <u>2300/00</u>

ABSTRACT:

Modified PH20 hyaluronidase polypeptides, including modified polypeptides that exhibit increased stability and/or increased activity, are provided. Also provided are compositions and formulations and uses thereof.

Full	Title	Citation	Front	Review	Classification	Date	Reference	Sequences		Claims	KMC	Draw D
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☐ 5. Document ID: US 20130302275 A1

L4: Entry 5 of 7

File: PGPB

Nov 14, 2013

PGPUB-DOCUMENT-NUMBER: 20130302275

PGPUB-FILING-TYPE:

DOCUMENT-IDENTIFIER: US 20130302275 A1

TITLE: PH20 Polypeptide Variants, Formulations And Uses Thereof

PUBLICATION-DATE: December 28, 2012

PATENT-FAMILY-ID: 47595052

INVENTOR-INFORMATION:

NAME	CITY	STATE	COUNTRY
Wei; Ge	San Diego	CA	US
Shepard; H. Michael	San Diego	CA	US
Zhao; Qiping	San Diego	CA	US
Connor; Robert James	Oceanside	CA	US

APPLICANT-INFORMATION:

NAME	CITY	STATE	COUNTRY	AUTHORITY	TYPE
Wei; Ge	San Diego	CA	US		
Shepard; H. Michael	San Diego	CA	US		
Zhao; Qiping	San Diego	CA	US		
Connor; Robert James	Oceanside	CA	US		

APPL-NO: 13/694731 [PALM] [DAV] [US Family]
 DATE FILED: December 28, 2012

US-CL-CURRENT: 424/85.2; 424/130.1, 424/209.1, 424/225.1, 424/85.5, 424/85.6,
424/85.7, 424/94.62, 435/18, 435/201, 435/320.1, 435/325, 536/23.2

CPC-CURRENT:

TYPE	CPC	DATE
CPCI	A <u>61</u> P <u>3/04</u>	20180101
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CPCI	C <u>12</u> N <u>9/2474</u>	20130101
CPCI	A <u>61</u> K <u>45/06</u>	20130101
CPCI	A <u>61</u> P <u>11/00</u>	20180101
CPCI	A <u>61</u> P <u>29/00</u>	20180101
CPCI	C <u>12</u> Y <u>302/01035</u>	20130101
CPCI	A <u>61</u> P <u>35/00</u>	20180101
CPCI	A <u>61</u> K <u>9/0019</u>	20130101
CPCI	A <u>61</u> K <u>38/47</u>	20130101
CPCI	A <u>61</u> P <u>3/10</u>	20180101
CPCI	A <u>61</u> P <u>27/02</u>	20180101
CPCI	C <u>12</u> Q <u>1/34</u>	20130101
CPCI	A <u>61</u> K <u>38/28</u>	20130101
CPCI	A <u>61</u> P <u>43/00</u>	20180101
CPCI	A <u>61</u> K <u>38/28</u>	20130101
CPCI	A <u>61</u> K <u>2300/00</u>	20130101
CPCI	A <u>61</u> K <u>38/47</u>	20130101
CPCI	A <u>61</u> K <u>2300/00</u>	20130101
CPCA	A <u>61</u> K <u>38/00</u>	20130101
CPCA	G <u>01</u> N <u>2333/926</u>	20130101
CPCA	G <u>01</u> N <u>2333/928</u>	20130101
CPCA	Y <u>02</u> A <u>50/30</u>	20180101

CPC-COMBINATION-SET(S) :

TYPE	RANK	CPC
CPCC	1	A <u>61</u> K <u>38/28</u>
	2	A <u>61</u> K <u>2300/00</u>
CPCC	1	A <u>61</u> K <u>38/47</u>
	2	A <u>61</u> K <u>2300/00</u>

ABSTRACT:

Modified PH20 hyaluronidase polypeptides, including modified polypeptides that exhibit increased stability and/or increased activity, are provided. Also provided are compositions and formulations and uses thereof.

Full	Title	Citation	Front	Review	Classification	Date	Reference	Sequences	Claims	KMC	Draw De
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6. Document ID: US 10865400 B2

L4: Entry 6 of 7

File: USPT

Dec 15, 2020

US-PAT-NO: 10865400

DOCUMENT-IDENTIFIER: US 10865400 B2

TITLE: PH20 polypeptide variants, formulations and uses thereof

DATE-ISSUED: December 15, 2020

PRIOR-PUBLICATION-INFORMATION:

DOCUMENT-IDENTIFIER DOCUMENT-DATE

US 20160362670 A1 December 15, 2016

PATENT-FAMILY-ID: 47595052

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Wei; Ge	San Diego	CA		US
Shepard; H. Michael	San Diego	CA		US
Zhao; Qiping	San Diego	CA		US
Connor; Robert James	Oceanside	CA		US

APPLICANT-INFORMATION:

NAME	CITY	STATE	COUNTRY	AUTHORITY	TYPE
HALOZYME, INC.	San Diego	CA	US		

APPL-NO: 15/226489 [PALM] [DAV] [US Family]

DATE FILED: August 2, 2016

US-CL-CURRENT: 1/1

CPC-CURRENT:

TYPE	CPC	DATE
CPCI	<u>A 61 K 9/0019</u>	20130101
CPCI	<u>A 61 P 3/04</u>	20180101
CPCI	<u>A 61 P 35/00</u>	20180101
CPCI	<u>A 61 P 3/10</u>	20180101
CPCI	<u>A 61 P 29/00</u>	20180101
CPCI	<u>C 12 Y 302/01035</u>	20130101
CPCI	<u>C 12 N 9/2474</u>	20130101
CPCI	<u>A 61 K 47/10</u>	20130101
CPCI	<u>A 61 K 45/06</u>	20130101
CPCI	<u>A 61 K 38/47</u>	20130101
CPCI	<u>A 61 P 27/02</u>	20180101
CPCI	<u>A 61 P 43/00</u>	20180101
CPCI	<u>A 61 P 11/00</u>	20180101
CPCI	<u>C 12 Q 1/34</u>	20130101
CPCI	<u>A 61 K 38/28</u>	20130101
CPCI	<u>A 61 K 38/28</u>	20130101
CPCI	<u>A 61 K 2300/00</u>	20130101
CPCI	<u>A 61 K 38/47</u>	20130101
CPCI	<u>A 61 K 2300/00</u>	20130101

CPCA G 01 N 2333/928 20130101
 CPCA A 61 K 38/00 20130101
 CPCA G 01 N 2333/926 20130101
 CPCA Y 02 A 50/30 20180101

CPC-COMBINATION-SET(S) :

TYPE RANK CPC
 CPCC 1 A 61 K 38/28
 2 A 61 K 2300/00
 CPCC 1 A 61 K 38/47
 2 A 61 K 2300/00

ABSTRACT:

Modified PH20 hyaluronidase polypeptides, including modified polypeptides that exhibit increased stability and/or increased activity, are provided. Also provided are compositions and formulations and uses thereof.

18 Claims, 13 Drawing figures
 Exemplary Claim Number: 1
 Number of Drawing Sheets: 13

Full	Title	Citation	Front	Review	Classification	Date	Reference	Sequences	Figures	Claims	KMC	Draw Data
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☐ 7. Document ID: US 9447401 B2

L4: Entry 7 of 7

File: USPT

Sep 20, 2016

US-PAT-NO: 9447401

DOCUMENT-IDENTIFIER: US 9447401 B2

****Please see Images for: (Certificate of Correction) ****

TITLE: PH20 polypeptide variants, formulations and uses thereof

DATE-ISSUED: September 20, 2016

PRIOR-PUBLICATION-INFORMATION:

DOCUMENT-IDENTIFIER DOCUMENT-DATE

US 20130302275 A1 November 14, 2013

US 20140178330 A9 June 26, 2014

PATENT-FAMILY-ID: 47595052

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Wei; Ge	San Diego	CA		US
Shepard; H. Michael	San Diego	CA		US
Zhao; Qiping	San Diego	CA		US
Connor; Robert James	Oceanside	CA		US

APPLICANT-INFORMATION:

NAME	CITY	STATE	COUNTRY	AUTHORITY	TYPE
Wei; Ge	San Diego	CA	US		

Shepard; H. Michael San Diego CA US
 Zhao; Qiping San Diego CA US
 Connor; Robert James Oceanside CA US

APPL-NO: 13/694731 [PALM] [DAV] [US Family]
 DATE FILED: December 28, 2012

US-CL-CURRENT: 1/1

CPC-CURRENT:

TYPE	CPC	DATE
CPCI	A 61 P 27/02	20180101
CPCI	A 61 K 45/06	20130101
CPCI	A 61 K 9/0019	20130101
CPCI	A 61 P 35/00	20180101
CPCI	C 12 Y 302/01035	20130101
CPCI	A 61 P 3/04	20180101
CPCI	C 12 N 9/2474	20130101
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CPCI	A 61 P 3/10	20180101
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CPCI	A 61 K 2300/00	20130101
CPCI	A 61 K 38/47	20130101
CPCI	A 61 K 2300/00	20130101
CPCA	G 01 N 2333/926	20130101
CPCA	A 61 K 38/00	20130101
CPCA	G 01 N 2333/928	20130101
CPCA	Y 02 A 50/30	20180101

CPC-COMBINATION-SET(S) :

TYPE	RANK	CPC
CPCC	1	A 61 K 38/28
	2	A 61 K 2300/00
CPCC	1	A 61 K 38/47
	2	A 61 K 2300/00

ABSTRACT:

Modified PH20 hyaluronidase polypeptides, including modified polypeptides that exhibit increased stability and/or increased activity, are provided. Also provided are compositions and formulations and uses thereof.

49 Claims, 13 Drawing figures
 Exemplary Claim Number: 1
 Number of Drawing Sheets: 13

Full	Title	Citation	Front	Review	Classification	Date	Reference	Sequences	Claims	KMC	Draw
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Term	Documents
MUTATION	304924
MUTATIONS	301569
"309"	576759
309S	362
REPLAC\$4	0
REPLAC	5864
REPLACA	25
REPLACAB	2
REPLACABLE	2302
REPLACABLY	487
REPLACACED	1
(L3 and ((mutation or replac\$4 or substitut\$3) with 309 or I309 \$1)).PGPB,USPT,USOC.	7

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BIB DATA SHEET

CONFIRMATION NO. 9651

SERIAL NUMBER	FILING or 371(c) DATE	CLASS	GROUP ART UNIT	ATTORNEY DOCKET NO.		
16/912,590	06/25/2020	424	1656	33320.03087.US27/3087D		
RULE						
APPLICANTS HALOZYME, INC., SAN DIEGO, CA; INVENTORS GE WEI, SAN DIEGO, CA; H. MICHAEL SHEPARD, SAN DIEGO, CA; QIPING ZHAO, SAN DIEGO, CA; ROBERT JAMES CONNOR, OCEANSIDE, CA;						
** CONTINUING DATA ***** This application is a CON of 15/226,489 08/02/2016 PAT 10865400 which is a DIV of 13/694,731 12/28/2012 PAT 9447401 which claims benefit of 61/796,208 11/01/2012 and claims benefit of 61/631,313 12/30/2011 This application 16/912,590 06/25/2020 is a DIV of 13/694,731 12/28/2012 PAT 9447401 which claims benefit of 61/796,208 11/01/2012 and claims benefit of 61/631,313 12/30/2011						
** FOREIGN APPLICATIONS *****						
** IF REQUIRED, FOREIGN FILING LICENSE GRANTED ** 07/02/2020						
Foreign Priority claimed ☐ Yes ☒ No 35 USC 119(a-d) conditions met ☐ Yes ☒ No Verified and /SAMUEL W LIU/ Acknowledged Examiner's Signature		☐ Met after Allowance Initials	STATE OR COUNTRY CA	SHEETS DRAWINGS 13	TOTAL CLAIMS 22	INDEPENDENT CLAIMS 1
ADDRESS Dentons US LLP 4655 Executive Drive Suite 700 San Diego, CA 92121 UNITED STATES						
TITLE PH20 POLYPEPTIDE VARIANTS, FORMULATIONS AND USES THEREOF						
FILING FEE RECEIVED 3920	FEES: Authority has been given in Paper No. _____ to charge/credit DEPOSIT ACCOUNT No. _____ for following:			☐ All Fees ☐ 1.16 Fees (Filing) ☐ 1.17 Fees (Processing Ext. of time) ☐ 1.18 Fees (Issue) ☐ Other _____ ☐ Credit		

Web Search History

date, time	web site	search string
4/9/2021 2:00:29 AM	Google	((PH20 adj (polypeptide or protein) or hyaluronidase) and (mutation or replac \$ 4 or substitut \$ 3) with (amino acid or residue or position)) and (modified or recombinant or engineered or variant or mutant or mutated) near1 PH20
4/9/2021 2:03:49 AM	Google	(PH20 polypeptide or hyaluronidase) and (mutation or substitution)
4/9/2021 2:05:57 AM	Google	variant PH20 and substitution at 309 or (I309N, I309H, I309M, I309G, I309L, I309H)
4/9/2021 2:06:00 AM	Google	variant or modified PH20 polypeptide and substitution at 309 or Ile 309



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UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
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Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
16/912,590	06/25/2020	GE WEI	33320.03087.US27/3087D	9651
13565	7590	05/03/2021	EXAMINER	
Dentons US LLP 4655 Executive Drive Suite 700 San Diego, CA 92121			LIU, SAMUEL W	
			ART UNIT	PAPER NUMBER
			1656	
			NOTIFICATION DATE	DELIVERY MODE
			05/03/2021	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

MLAIPSD@Dentons.com
lucy.begalla@dentons.com
rosalind.smith@dentons.com

<i>Applicant-Initiated Interview Summary</i>	Application No. 16/912,590	Applicant(s) WEI et al.		
	Examiner SAMUEL W LIU	Art Unit 1656	AIA (First Inventor to File) Status No	Page 1 of 1

All Participants (applicant, applicants representative, PTO personnel)	Title	Type
SAMUEL W LIU	Examiner	Telephonic
Stephanie Seidman	Attorney of Record	

Date of Interview: 28 April 2021

Issues Discussed:

Other

Applicant's representative requested that Examiner consider the IDS filed 7/8/2020 (24 pages) which has not been signed and dated by Examiner previously. Examiner agreed to send the copy of said IDS dated "9/30/2020" which has been consider by the Examiner (see the attachment for said IDS).

/SAMUEL W LIU/ Examiner, Art Unit 1656	/SCARLETT Y GOON/ QAS, Art Unit 1600
Applicant is reminded that a complete written statement as to the substance of the interview must be made of record in the application file. It is the applicants responsibility to provide the written statement, unless the interview was initiated by the Examiner and the Examiner has indicated that a written summary will be provided. See MPEP 713.04 Please further see: MPEP 713.04 Title 37 Code of Federal Regulations (CFR) § 1.133 Interviews, paragraph (b) 37 CFR § 1.2 Business to be transacted in writing	

Applicant recordation instructions: The formal written reply to the last Office action must include the substance of the interview. (See MPEP section 713.04). If a reply to the last Office action has already been filed, applicant is given a non-extendable period of the longer of one month or thirty days from this interview date, or the mailing date of this interview summary form, whichever is later, to file a statement of the substance of the interview.

Examiner recordation instructions: Examiners must summarize the substance of any interview of record. A complete and proper recordation of the substance of an interview should include the items listed in MPEP 713.04 for complete and proper recordation including the identification of the general thrust of each argument or issue discussed, a general indication of any other pertinent matters discussed regarding patentability and the general results or outcome of the interview, to include an indication as to whether or not agreement was reached on the issues raised.

Substitute Form PTO-1449 (Modified)		U.S. Department of Commerce Patent and Trademark Office		Attorney Docket No. 33320.03087.US27/3087D		Application No. 16/912,590	
List of Patents and Publications for Applicant's Information Disclosure Statement (37 CFR §1.98(b))				Inventors <i>Wei et al.</i>		Group Art Unit 1652	
				Filing Date June 25, 2020			
U.S. Patent Documents							
Examiner Initial	Desig. ID	Document Number	Publication Date	Patentee	Class	Subclass	Filing Date If Appropriate
	AA	3,536,809	10/27/1970	Applezweig	424	28	02/17/1969
	AB	3,598,123	08/10/1971	Zaffaroni	424	435	04/01/1969
	AC	3,630,200	12/28/1971	Higuchi	424	427	06/09/1969
	AD	3,710,795	01/16/1973	Higuchi et al.	424	424	09/29/1970
	AE	3,845,770	11/05/1974	Theeuwes et al.	424	427	06/05/1972
	AF	3,916,899	11/04/1975	Theeuwes et al.	424	424	02/07/1974
	AG	4,002,531	01/11/1977	Royer	435	188	01/22/1976
	AH	4,008,719	02/22/1977	Theeuwes et al.	424	427	02/02/1976
	AI	4,044,126	08/23/1977	Cook et al.	514	180	07/09/1976
	AJ	4,179,337	12/18/1979	Davis et al.	435	181	07/28/1977
	AK	4,364,923	12/21/1982	Cook et al.	424	46	04/30/1981
	AL	4,414,209	11/08/1983	Cook et al.	514	180	06/13/1977
	AM	4,769,027	09/06/1988	Baker et al.	424	493	02/24/1987
	AN	4,952,496	08/28/1990	Studier et al.	435	91.41	12/29/1986
	AO	4,980,286	12/25/1990	Morgan et al.	435	371	01/03/1989
	AP	5,033,252	07/23/1991	Carter	53	425	07/30/1990
	AQ	5,052,558	10/01/1991	Carter	206	439	07/27/1990
	AR	5,059,595	10/22/1991	Le Grazie	424	468	03/20/1990
	AS	5,073,543	12/17/1991	Marshall et al.	514	21	07/21/1988
	AT	5,120,548	06/09/1992	McClelland et al.	424	473	11/07/1989
	AU	5,122,614	06/16/1992	Zalipsky	548	520	04/19/1990
	AV	5,323,907	06/28/1994	Kalvelage	206	531	03/15/1993
	AW	5,324,844	06/28/1994	Zalipsky	548	520	01/08/1992
	AX	5,446,090	08/29/1995	Harris	525	54.1	11/12/1993
	AY	5,591,767	01/07/1997	Mohr et al.	514	413	06/06/1995
	AZ	5,612,460	03/18/1997	Zalipsky	530	391.9	02/17/1994
	BA	5,639,476	06/17/1997	Oshlack et al.	424	468	06/02/1995
	BB	5,643,575	07/01/1997	Martinez et al.	424	194.1	10/27/1993
	BC	5,672,662	09/30/1997	Harris et al.	525	408	10/02/1995
	BD	5,674,533	10/07/1997	Santus et al.	424	493	05/26/1995
Examiner Signature /SAMUEL W LIU/				Date Considered 09/30/2020			
EXAMINER: Initial if citation considered, whether or not citation is in conformance with MPEP 609; Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.							

Substitute Form PTO-1449 (Modified)		U.S. Department of Commerce Patent and Trademark Office		Attorney Docket No. 33320.03087.US27/3087D		Application No. 16/912,590	
List of Patents and Publications for Applicant's Information Disclosure Statement (37 CFR §1.98(b))				Inventors <i>Wei et al.</i>		Group Art Unit 1652	
				Filing Date June 25, 2020			
U.S. Patent Documents							
Examiner Initial	Desig. ID	Document Number	Publication Date	Patentee	Class	Subclass	Filing Date If Appropriate
	BE	5,721,348	02/24/1998	Primakoff et al.	536	22.1	10/21/1991
	BF	5,733,566	03/31/1998	Lewis	424	426	10/30/1995
	BG	5,766,581	06/16/1998	Bartley et al.	424	85.1	03/30/1995
	BH	5,795,569	08/18/1998	Bartley et al.	424	85.1	10/12/1994
	BI	5,808,096	09/15/1998	Zalipsky	548	520	01/21/1997
	BJ	5,854,046	12/29/1998	Au-Young et al.	435	201	01/20/1998
	BK	5,900,461	05/04/1999	Harris	525	54.11	02/23/1998
	BL	5,919,455	07/06/1999	Greenwald et al.	424	178.1	03/20/1997
	BM	5,932,462	08/03/1999	Harris et al.	435	188	05/17/1995
	BN	5,958,750	09/28/1999	Au-Young et al.	435	201	07/03/1996
	BO	5,985,263	11/16/1999	Lee et al.	424	85.2	12/19/1997
	BP	5,990,237	11/23/1999	Bentley et al.	525	54.2	05/20/1998
	BQ	6,057,110	05/02/2000	Au-Young et al.	435	6	12/17/1998
	BR	6,113,906	09/05/2000	Greenwald et al.	424	194.1	12/29/1998
	BS	6,193,963	02/27/2001	Stern et al.	424	94.6	08/21/1997
	BT	6,214,966	04/10/2001	Harris	528	322	09/25/1997
	BU	6,258,351	07/10/2001	Harris	424	78.3	11/05/1997
	BV	6,340,742	01/22/2002	Burg et al.	530	351	06/28/2000
	BW	6,413,507	07/02/2002	Bentley et al.	424	78.02	12/23/1999
	BX	6,420,339	07/16/2002	Gegg et al.	514	12	10/14/1998
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	CF	6,858,736	02/22/2005	Nho et al.	546	290	12/23/2002
	CG	7,105,330	09/12/2006	Stern et al.	435	200	07/18/2003
	CH	7,279,457	10/09/2007	Pohl et al.	514	3	03/11/2005
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List of Patents and Publications for Applicant's Information Disclosure Statement (37 CFR §1.98(b))				Inventors Wei et al.		Group Art Unit 1652	
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	CX	8,568,713	10/29/2013	Frost et al.	424	094.500	05/18/2012
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	DI	2001/0044526	11/22/2001	Shen	530	409	02/21/2001
	DJ	2001/0046481	11/29/2001	Bentley et al.	424	78.18	04/21/2001
	DK	2002/0052430	05/02/2002	Harris et al.	523	406	11/05/2001
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	DO	2003/0114647	06/19/2003	Harris et al.	530	402	04/10/2002
	DP	2003/0143596	07/31/2003	Bentley et al.	435	6	11/07/2002
	DQ	2003/0158333	08/21/2003	Roberts et al.	530	402	10/09/2002
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	DS	2004/0013637	01/22/2004	Bentley et al.	424	78.17	02/10/2003
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** = Copies not provided herewith as they have been previously provided in connection with U.S. Serial Nos. 13/694,731, 15/226,489, and/or 16/824,572, which are relied upon for an earlier filing date in accordance with 35 U.S.C. §120.

X* = An English language equivalent has been previously provided in connection with U.S. Serial No. 13/694,731.

X** = An English Derwent Abstract (Item HY) for Japanese Publication No. JP 2007-153797 has been previously provided in connection with U.S. Serial No. 13/694,731.

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	GP**	Anttila et al., "High levels of stromal hyaluronan predict poor disease outcome in epithelial ovarian cancer," Cancer Research 60:150-155 (2000).					
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	IC**	Elder et. al., "Intra-arterial hyaluronidase in severe peripheral arterial disease," <i>Lancet</i> 648-649 (1980).
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	IJ**	Filocomo et al., "Chimeric Sindbis viruses dependent on the NS3 protease of hepatitis C virus," <i>J.Virology</i> 71:1417-1427 (1997).
	IK**	Forsburg, S., "Codon usage table for <i>Schizosaccharomyces pombe</i> ," <i>Yeast</i> 10(8):1045-1047 (1994).
	IL**	Fransson et al., "Solvent effects on the solubility and physical stability of human insulin-like growth factor I," <i>Pharm Res.</i> 14(5):606-612 (1997).
	IM**	Frost, G. and R. Stern, "A microtiter-based assay for hyaluronidase activity not requiring specialized reagents," <i>Anal. Biochem.</i> 251:263-269 (1997).
	IN**	Gardner et al., "The complete nucleotide sequence of an infectious clone of cauliflower mosaic virus by M13mp7 shotgun sequencing," <i>Nucleic Acids Res.</i> 9:2871-2888 (1981).
	IO**	GenBank Accession No. AAC60607, PH-20 [<i>Homo sapiens</i>], published on Jun. 05, 2000 [online] [retrieved on Dec. 12, 2012][retrieved from URL:< ncbi.nlm.nih.gov/protein/AAC60607 >], 1 page.
	IP**	Gilbert, W. and L. Villa-Komaroff, "Useful Proteins from Recombinant Bacteria," <i>Scientific American</i> 242(4):74-94 (1980).
	IQ**	Girish et al., "Hyaluronidase inhibitors: a biological and therapeutic perspective," <i>Curr Med Chem</i> 16(18):2261-2288 (2009).
	IR**	Gmachl et al., "The human sperm protein PH-20 has hyaluronidase activity," <i>FEBS</i> 336(3):545-548 (1993).
	IS**	Good et al., "Hydrogen ion buffers for biological research," <i>Biochemistry</i> 5(2):467-477 (1966).
	IT**	Gribskov et al., "Sigma factors from <i>E. coli</i> , <i>B. subtilis</i> , phage SP01, and phage T4 are homologous proteins," <i>Nucl. Acids Res.</i> 14(16):6745-6763 (1986).
	IU**	Grosschedl et al., "Introduction of a mu immunoglobulin gene into the mouse germ line: specific expression in lymphoid cells and synthesis of functional antibody," <i>Cell</i> 38:647-658 (1984).
	IV**	Guiotto et al., "An improved procedure for the synthesis of branched polyethylene glycols (PEGs) with the reporter dipeptide Met-betaAla for protein conjugation," <i>Bioorg. Med. Chem. Lett.</i> 12:177-180 (2002).
	IW**	Guntenhoner et al., "A substrate-gel assay for hyaluronidase activity," <i>Matrix</i> 12:388-396 (1992).
	IX**	Guo et al., "Protein tolerance to random amino acid change," <i>Proc. Nat'l. Acad. Sci. USA</i> 101:9205-9210 (2004).
	IY**	Hahn et al., "Generation of a novel poliovirus with a requirement of hepatitis C virus protease NS3 activity," <i>Virology</i> 226:318-326 (1996).
	IZ**	Haller et al., "Escaping the interstitial matrix with enzyme-mediated drug delivery," <i>Drug Delivery Technology</i> , 5(5):1-6 (2005).
	JA**	Hamatake et al., "Establishment of an in vitro assay to characterize hepatitis C virus NS3-4A protease trans-processing activity," <i>Intervirology</i> 39:249-258 (1996).
	JB**	Hammer et al., "Diversity of alpha-fetoprotein gene expression in mice is generated by a combination of separate enhancer elements," <i>Science</i> 235:53-58 (1987).

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	JC**	Hanahan, D., "Heritable formation of pancreatic beta-cell tumours in transgenic mice expressing recombinant insulin/simian virus 40 oncogenes," <i>Nature</i> 315(6015):115-122 (1985).					
	JD**	Harris, J. and R. Chess, "Effect of pegylation on pharmaceuticals," <i>Nat Rev Drug Discov</i> 2(3):214-221 (2003).					
	JE**	Hartman S. and R. Mulligan, "Two dominant-acting selectable markers for gene transfer studies in mammalian cells," <i>Proc Natl Acad Sci</i> 85:8047-8051 (1988).					
	JF**	Have et al., "Cloning and characterization of the cDNA encoding the PH20 protein in the European red fox <i>Vulpes vulpes</i> ," <i>Reproduct Fertil Dev</i> 10:165-172 (1998).					
	JG**	Herrera-Estrella et al., "Expression of chimaeric genes transferred into plant cells using a ti-plasmid-derived vector," <i>Nature</i> 303:209-213 (1983).					
	JH**	Herrera-Estrella et al., "Light-inducible and chloroplast-associated expression of a chimaeric gene introduced into <i>Nicotiana tabacum</i> using a Ti plasmid vector," <i>Nature</i> 310(5973):115-120 (1984).					
	JI**	Hibi et al., "Chondroitinase C activity of <i>Streptococcus intermedius</i> ," <i>FEMS-Microbiol-Lett.</i> 48(2):121-124 (1989).					
	JJ**	Hofinger et al., "Isoenzyme-specific differences in the degradation of hyaluronic acid by mammalian-type hyaluronidases," <i>Glycoconj J</i> 25:101-109 (2008).					
	JK**	Holash et al., "VEGF-Trap: a VEGF blocker with potent antitumor effects," <i>Proc Natl Acad Sci USA</i> 99(17):11393-11398 (2002).					
	JL**	Hooper et al., "Determination of glycosyl-phosphatidylinositol membrane protein anchorage" <i>Proteomics</i> 1:748-755 (2001)					
	JM**	Horn et al., "Intravesical chemotherapy of superficial bladder tumors in a controlled trial with cis-platinum versus cis-platinum plus hyaluronidase," <i>J. Surg. Oncol.</i> 28:304-307 (1985).					
	JN**	Huang et al., "Recombinant Human Hyaluronidase PH20 Does Not Stimulate an Acute Inflammatory Response and Inhibits Lipopolysaccharide-Induced Neutrophil Recruitment in the Air Pouch Model of Inflammation," <i>J Immunol.</i> 192(11):5285-5295 (2014).					
	JO**	Huang, X. and M. Miller. "A time-efficient, linear-space local similarity algorithm." <i>Adv. Appl. Math.</i> 12:337-357 (1991).					
	JP**	Hunnicut et al., "Structural relationship of sperm soluble hyaluronidase to the sperm membrane protein PH-20," <i>Biol Reprod.</i> 54(6):1343-1349 (1996).					
	JQ**	Infante et al., "Phase I trials of PEGylated recombinant human hyaluronidase PH20 in patients with advanced solid tumours," <i>Br J Cancer</i> 118(2):153-161 (2018).					
	JR**	Ito et al., "Cultivation of hepatitis C virus in primary hepatocyte culture from patients with chronic hepatitis C results in release of high titre infectious virus," <i>J. Gen. Virol.</i> 77:1043-1054 (1996).					
	JS**	IUPAC-IUB Commission on Biochemical Nomenclature, "A One-Letter Notation for Amino Acid Sequences: Tentative Rules," <i>J. Biol. Chem.</i> 243:3557-3559 (1968).					
	JT**	IUPAC-IUB, "Abbreviated nomenclature of synthetic polypeptides-polymerized amino acids-revised recommendations," Commission on Biochemical Nomenclature, <i>Biochemistry</i> 11:1726-1731 (1972).					
	JU**	Jadin et al., "A comprehensive model of hyaluronan turnover in the mouse," <i>Matrix Biol</i> 31(2):81-89 (2012).					
	JV**	Jay et al., "Construction of a general vector for efficient expression of mammalian proteins in bacteria: use of a synthetic ribosome binding site," <i>Proc. Natl. Acad. Sci. USA</i> 78:5543-5548 (1981).					
	JW**	Karvinen et al., "Hyaluronan, CD44 and versican in epidermal keratinocyte tumors," <i>British Journal of Dermatology</i> 148:86-94 (2003).					
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	JX**	Kelsey et al., "Species- and tissue-specific expression of human alpha 1-antitrypsin in transgenic mice," <i>Genes And Devel.</i> 1:161-171 (1987).					
	JY**	Kim et al., "Sperm penetration through cumulus mass and zona pellucida," <i>Int J Dev Biol.</i> 52(5-6):677-682 (2008).					
	JZ**	Kodukula et al., "Biosynthesis of phosphatidylinositol glycan-anchored membrane proteins" <i>J. Biol. Chem.</i> 266:4464-4470 (1991).					
	KA**	Kohno et al., "Effects of hyaluronidase on doxorubicin penetration into squamous carcinoma multicellular tumor spheroids and its cell lethality," <i>J. Cancer Res. Oncol.</i> 120:293-297 (1994).					
	KB**	Kollias et al., "Regulated expression of human A gamma-, beta-, and hybrid gamma beta-globin genes in transgenic mice: manipulation of the developmental expression patterns," <i>Cell</i> 46:89-94 (1986).					
	KC**	Krumlauf et al., "Developmental regulation of alpha-fetoprotein genes in transgenic mice," <i>Mol. Cell. Biol.</i> 5:1639-1648 (1985).					
	KD**	Krupers et al., "Complexation of poly(ethylene oxide) with poly(acrylic acid-co-hydroxyethyl methacrylate)s," <i>Eur. Polym J.</i> 32(6):785-790 (1996).					
	KE**	Kyte et al., "A Simple Method for Displaying the Hydropathic Character of a Protein" <i>J. Mol. Biol.</i> 157:105-132 (1982).					
	KF**	Lalancette et al., "Characterization of an 80-kilodalton bull sperm protein identified as PH-20," <i>Biol Reprod.</i> 65(2):628-636 (2001).					
	KG**	Lam et al., "The effect of benzyl alcohol on recombinant human interferon-gamma," <i>Pharm Res.</i> 14(6):725-729 (1997).					
	KH**	Lammerts van Bueren et al., "The antibody zalutumumab inhibits epidermal growth factor receptor signaling by limiting intra- and intermolecular flexibility," <i>Proc Natl Acad Sci U S A.</i> 105(16):6109-6114 (2008). Retraction also included, <i>Proc Natl Acad Sci U S A.</i> 109(14):5548 (2008).					
	KI**	Lathrop et al., "cDNA cloning reveals the molecular structure of a sperm surface protein, PH-20, involved in sperm-egg adhesion and the wide distribution of its gene among mammals," <i>J Cell Biol.</i> 111(6 Pt 2):2939-2949 (1990).					
	KJ**	Laurent, T. and J. Fraser, "Hyaluronan," <i>FASEB J</i> 6:2397-2404 (1992).					
	KK**	Leder et al., "Consequences of widespread deregulation of the c-myc gene in transgenic mice: multiple neoplasms and normal development," <i>Cell</i> 45:485-495 (1986).					
	KL**	Li et al., "Importance of glycosylation and disulfide bonds in hyaluronidase activity of macaque sperm surface PH-20," <i>J. Androl.</i> 23:211-219 (2002).					
	KM**	Li et al., "Structural basis for EGF receptor inhibition by the therapeutic antibody IMC-11F8," <i>Structure.</i> 16(2):216-227 (2008).					
	KN**	Liang et al., "Prediction of antigenic epitopes on protein surfaces by consensus scoring," <i>BMC Bioinformatics.</i> 10:302 (2009), 10 pages.					
	KO**	Lin et al., "A hyaluronidase activity of the sperm plasma membrane protein PH-20 enables sperm to penetrate the cumulus cell layer surrounding the egg," <i>J Cell Biol.</i> 125(5):1157-1163 (1994).					
	KP**	Lin et al., "Molecular cloning of the human and monkey sperm surface protein PH-20," <i>Proc. Natl. Acad. Sci. USA</i> 90:10071-10075 (1993).					
	KQ**	Lipponen et al "High stromal hyaluronan level is associated with poor differentiation and metastasis in prostate cancer," <i>European Journal of Cancer</i> 37:849-856 (2001).					
	KR**	Locke et al., "ENHANZE® drug delivery technology: a novel approach to subcutaneous administration using recombinant human hyaluronidase PH20," <i>Drug Deliv</i> 26(1):98-106 (2019).					
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	KS**	Louveau, I. and F. Gondret, "GH and insulin affect fatty acid synthase activity in isolated porcine adipocytes in culture without any modifications of sterol regulatory element binding protein-1 expression," J Endocrin. 181:271-280 (2004).
	KT**	Lowy et al., "Isolation of transforming DNA: cloning the hamster aprt gene," Cell 22:817-823 (1980).
	KU**	Lu, H. and E. Wimmer., "Poliovirus chimeras replicating under the translational control of genetic elements of hepatitis C virus reveal unusual properties of the internal ribosomal entry site of hepatitis C virus," Proc. Natl. Acad. Sci. USA 93:1412-1417 (1996).
	KV**	Lu, Y. and A. Felix, "Pegylated peptides I: Solid-phase synthesis of N alpha-pegylated peptides using Fmoc strategy," Peptide Res 6:140-146 (1993).
	KW**	Lu, Y. and A. Felix, "Pegylated peptides. II. Solid-phase synthesis of amino-, carboxy- and side-chain pegylated peptides," Int. J. Peptide Protein Res. 43:127-138 (1994).
	KX**	M3WD76 Felca (2015, updated) Hyaluronidase/PH20 from <i>Felis catus</i> , 3 pages.
	KY**	Ma et al., "Fucosylation in prokaryotes and eukaryotes" Glycobiology 16(12):158R-184R (2006)
	KZ**	Maa and Hsu, "Aggregation of recombinant human growth hormone induced by phenolic compounds" Int. J. Pharm. 140(2):155-168 (1996).
	LA**	MacDonald, R., "Expression of the pancreatic elastase I gene in transgenic mice," Hepatology 7:42S-51S(1987).
	LB**	Magram et al., "Developmental regulation of a cloned adult beta-globin gene in transgenic mice," Nature 315:338-340 (1985).
	LC**	Maksimenko et al. "Resistance of dextran-modified hyaluronidase to inhibition by heparin" Biochemistry (Mosc). 66(4):456-463 (2001).
	LD**	Mammalian Gene Collection (MGC) Program Team, "Generation and initial analysis of more than 15,000 full-length human and mouse cDNA sequences," Proc. Natl. Acad. Sci. USA 99:16899-16903 (2002).
	LE**	Marković-Housley et al., "Crystal Structure of Hyaluronidase, a Major Allergen of Bee Venom," Structure 8: 1025-1035 (2000).
	LF**	McIlvaine, WB, "A buffer solution for colorimetric comparison," J. Biol. Chem. 49:183-186 (1921).
	LG**	Mehyar et al., "Modulation of the pharmacokinetics and pharmacodynamics of proteins by polyethylene glycol conjugation," J. Pharm. Pharmaceut. Sci. 3(1):125-136 (2000).
	LH**	Menzel, E. and C. Farr, "Hyaluronidase and its substrate hyaluronan: biochemistry, biological activities and therapeutic uses," Cancer Lett. 131:3-11 (2003).
	LI**	Merrifield, J., "Solid phase peptide synthesis. I. The synthesis of a tetrapeptide," J Am Chem Soc 85:2149-2154 (1963).
	LJ**	Meyer et al., "The soluble hyaluronidase from bull testes is a fragment of the membrane-bound PH-20 enzyme." FEBS Letters 413(2):385-388 (1997).
	LK**	Michelacci et al., "Chondroitinase C from <i>Flavobacterium heparinum</i> ," J. Biol. Chem. 251:1154-1158 (1976).
	LL**	Miller et al., "Use of retroviral vectors for gene transfer and expression," Meth. Enzymol. 217:581-599 (1993).
	LM**	Mizutani et al., "Characterization of hepatitis C virus replication in cloned cells obtained from a human T-cell leukemia virus type 1-infected cell line, MT-2," J.Virol. 70:7219-7223 (1996).
	LN**	Mizutani et al., "Inhibition of hepatitis C virus replication by antisense oligonucleotide in culture cells," Biochem. Biophys. Res. Commun. 212:906-911 (1995).

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	LO**	Molineux, G., "Pegylation: engineering improved biopharmaceuticals for oncology," <i>Pharmacotherapy</i> 23 (8 Pt 2):3S-8S (2003).					
	LP**	Monfardini et al., "A branched monomethoxypoly(ethylene glycol) for protein modification," <i>Bioconjugate Chem.</i> 6:62-69 (1995).					
	LQ**	Nadsombati et al., "Dose-range developmental toxicity of rHuPH20 in mice," <i>Matrix Biology</i> 27:23 (2008).					
	LR**	NCBI Reference Sequence XP_011728213.1, <i>Macaca nemestrina</i> (pig-tailed macaque) PH-20 hyaluronidase. Published on Apr. 24, 2018. Retrieved from URL:< ncbi.nlm.nih.gov/protein/795324051/ [retrieved on Apr. 20, 2020], 2 pages.					
	LS**	Nakayama et al., "CD15 expression in mature granulocytes is determined by alpha 1,3-fucosyltransferase IX, but in promyelocytes and monocytes by alpha 1,3-fucosyltransferase IV," <i>J. Biol. Chem.</i> , 276(19):16100-16106 (2001).					
	LT**	Needleman, S. and C. Wunsch "A general method applicable to the search for similarities in the amino acid sequence of two proteins," <i>J Mol Biol.</i> 48:443-453 (1970).					
	LU**	Nekoroski et al., "A recombinant human hyaluronidase sustained release gel for the treatment of post-surgical edema," <i>Int J Dermatol.</i> 53(6):777-785 (2014). Epub 2013 Oct 29.					
	LV**	Omaetxebarria et al., "Computational approach for identification and characterization of GPI-anchored peptides in proteomics experiments," <i>Proteomics</i> 7(12):1951-1960 (2007).					
	I.W**	Ornitz et al., "Elastase I promoter directs expression of human growth hormone and SV40 T antigen genes to pancreatic acinar cells in transgenic mice," <i>Cold Spring Harbor Symp. Quant. Biol.</i> 50:399-409 (1986).					
	LX**	Ostresh et al., "Peptide libraries: determination of relative reduction rates of protected amino acids in competitive couplings," <i>Biopolymers</i> 34:1681-1689 (1994).					
	LY**	Padavattan, S. "Crystal structure determination of hyaluronidase : a major bee venom allergen, in complex with an IgG Fab fragment and purification and biophysical characterization of bovine testes hyaluronidase," 2006, PhD Thesis, University of Basel, Faculty of Science. DOI: 10.5451/unibas-004349798. 98 pages.					
	LZ**	Paul, A. and D. Sochart, "Improving the results of ganglion aspiration by the use of hyaluronidase," <i>J Hand Surg</i> 22(2):219-221 (1997).					
	MA**	Paulick, M. and C. Bertozzi, "The glycosylphosphatidylinositol anchor: A complex membrane-anchoring structure for proteins," <i>Biochemistry</i> 47:6991-7000 (2008).					
	MB**	Pawlowski et al., "The effects of hyaluronidase upon tumor formation in BALB/c mice painted with 7,12-dimethylbenz-(a)anthracene," <i>Int. J. Cancer</i> 23:105-109 (1979).					
	MC**	Pedersen et al., "Sym004: a novel synergistic anti-epidermal growth factor receptor antibody mixture with superior anticancer efficacy," <i>Cancer Res.</i> 70(2):588-597 (2010).					
	MD**	Pham et al., "Large-scale transient transfection of serum-free suspension-growing HEK293 EBNA1 cells: peptone additives improve cell growth and transfection efficiency," <i>Biotechnology and Bioengineering</i> 84:332-342 (2003).					
	ME**	Phelps et al., "Restricted lateral diffusion of PH-20, a PI-anchored sperm membrane protein," <i>Science</i> 240:1780-1782 (1988).					
	MF**	Pierleoni et al., "PredGPI: a GPI-anchor predictor," <i>BMC Bioinformatics</i> 9:392 (2008).					
	MG**	Pinkert et al., "An albumin enhancer located 10 kb upstream functions along with its promoter to direct efficient, liver-specific expression in transgenic mice," <i>Genes and Devel.</i> 1:268- 276 (1987).					
	MH**	Pirinen et al "Prognostic value of hyaluronan expression in non-small cell lung cancer: Increased stromal expression indicated unfavorable outcome in patients with adenocarcinoma," <i>Int. J. Cancer</i> 95:12-17 (2001).					
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	MI**	Primakoff et al., "Fully effective contraception in male and female guinea pigs immunized with the sperm protein PH-20," <i>Nature</i> 335:543-546 (1988).
	MJ**	Prothmann et al., "Sexual size dimorphism predicts rates of sequence evolution of Sperm Adhesion Molecule 1 (SPAM1, also PH-20) in monkeys, but not in hominoids (apes including humans)," <i>Mol Phy Ev</i> 63:52-63 (2012).
	MK**	Readhead et al., "Expression of a myelin basic protein gene in transgenic shiverer mice: correction of the dysmyelinating phenotype," <i>Cell</i> 48:703-712 (1987).
	ML**	Reitinger et al., "Designed human serum hyaluronidase 1 variant, HYAL1DeltaL, exhibits activity up to pH 5.9," <i>J Biol Chem.</i> 284(29):19173-177 (2009).
	MM**	Remmele et al., "Interleukin-1 receptor (IL-1R) liquid formulation development using differential scanning calorimetry," <i>Pharm Res.</i> 15(2):200-208 (1998).
	MN**	Rhodes et al., "Transformation of maize by electroporation of embryos," <i>Methods Mol Biol</i> 55:121-131 (1995).
	MO**	Richmond, T., "Precompiled codon-usage tables," <i>Genome Biology</i> 1(1):reports241 (2000), 2 pages.
	MP**	Ripka et al., "Two Chinese hamster ovary glycosylation mutants affected in the conversion of GDP-mannose to GDP-fucose," <i>Arch. Biochem. Biophys.</i> 249(2):533-545 (1986).
	MQ**	Roberts et al., "Chemistry for peptide and protein PEGylation," <i>Advanced Drug Delivery Review</i> 54:459-476 (2002).
	MR**	Ropponen et al "Tumor Cell-associated Hyaluronan as an Unfavorable Prognostic Factor in Colorectal Cancer," <i>Cancer Research</i> 58:342-347 (1998).
	MS**	Sato et al., "Cloning and expression in Escherichia coli of the gene encoding the Proteus vulgaris chondroitin ABC lyase," <i>Appl. Microbiol. Biotechnol.</i> 41(1):39-46 (1994).
	MT**	Sato, H., "Enzymatic procedure for site-specific pegylation of proteins," <i>Adv. Drug Deliv. Rev.</i> 54:487-504 (2002).
	MU**	Sawhney et al., "Bioerodible hydrogels based on photopolymerized poly(ethylene glycol)-co poly(hydroxyl acid) Diacrylate Macromers," <i>Macromolecules</i> 26:581-587 (1993).
	MV**	Schanté et al., "Improvement of hyaluronic acid enzymatic stability by the grafting of amino-acids," <i>Carbohydrate Polymers</i> , 87(3):2211-2216 (2012).
	MW**	Scharf et al., "Heat stress promoters and transcription factors," <i>Results Probl Cell Differ</i> 20:125-162 (1994).
	MX**	Scheithauer et al., "In vitro evaluation of the anticancer drug modulatory effect of hyaluronidase in human gastrointestinal cell lines," <i>Anticancer Res.</i> 8:391-396 (1988).
	MY**	Schuller et al., "Pharmacokinetics of intrahepatic 5-fluorouracil + preinjected hyaluronidase," <i>Proc. Amer. Assoc. Cancer Res.</i> 32:173, abstract no. 1034 (1991).
	MZ**	Schwartz and Dayhoff, eds., <i>Atlas of Protein Science and Structure</i> , National Biomedical Research Foundation, pp. 353-358 (1979).
	NA**	Schwartzman, J., "Hyaluronidase: A Review in Its Therapeutic Use in Pediatrics," <i>J. Pediat.</i> 39:491-502 (1951).
	NB**	Seaton et al., "Rat sperm 2B1 glycoprotein (PH20) contains a C-terminal sequence motif for attachment of a glycosyl phosphatidylinositol anchor. Effects of endoproteolytic cleavage on hyaluronidase activity," <i>Biol Reprod.</i> 62(6):1667-1676 (2000).
	NC**	Shani, M., "Tissue-specific expression of rat myosin light-chain," <i>Nature</i> 314:283-286 (1985).
	ND**	Sharp et al., "Codon usage patterns in Escherichia coli, Bacillus subtilis, Saccharomyces cerevisiae, Schizosaccharomyces pombe, Drosophila melanogaster and Homo sapiens; a review of the considerable within-species diversity," <i>Nucleic Acids Res.</i> 16(17):8207-8211 (1988).

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	NE**	Sharp, P. and E. Cowe, "Synonymous codon usage in <i>Saccharomyces cerevisiae</i> ," <i>Yeast</i> 7(7):657-678 (1991).					
	NF**	Shekhar et al., "The matrix reloaded: halozyme's recombinant enzyme helps injected drugs spread faster," <i>Chem. Biol.</i> 14:603-604 (2007).					
	NG**	Shimizu, Y. and H. Yoshikura, "Multicycle infection of hepatitis C virus in cell culture and inhibition by alpha and beta interferons," <i>J. Virol.</i> 68:8406-8408 (1994).					
	NH**	Singh et al., "Mechanisms of m-cresol-induced protein aggregation studied using a model protein cytochrome c," <i>J Pharm Sci.</i> 100(5):1679-1689 (2011); Epub date Jan. 12, 2011.					
	NI**	Smith, T. and M. Waterman, "Comparison of biosequences," <i>Advances in Applied Mathematics</i> 2:482-489 (1981).					
	NJ**	St Croix et al., "Reversal of intrinsic and acquired forms of drug resistance by hyaluronidase treatment of solid tumors," <i>Cancer Lett</i> 131(1):35-44 (1998).					
	NK**	Steinkuhler et al., "Product inhibition of the hepatitis C virus NS3 protease," <i>Biochem.</i> 37:8899-8905 (1998).					
	NL**	Stern et al., "Hyaluronidases: their genomics, structures, and mechanisms of action," <i>Chem Rev</i> 106: 818-839 (2006).					
	NM**	Stern, R., "Devising a pathway for hyaluronan catabolism: are we there yet?" <i>Glycobiology</i> 13:105R-115R (2003).					
	NN**	Sturla et al., "Core fucosylation of N-linked glycans in leukocyte adhesion deficiency/congenital disorder of glycosylation IIc fibroblasts," <i>Glycobiology</i> 15(10):924-935 (2005).					
	NO**	Sudo et al., "Establishment of an in vitro assay system for screening hepatitis C virus protease inhibitors using high performance liquid chromatography," <i>Antiviral Res.</i> 32:9-18 (1996).					
	NP**	Sutton, S. and D. Porter, "Development of the antimicrobial effectiveness as USP chapter <51>," <i>PDA J. Pharm. Sci Technol.</i> , 56(6):300-311 (2002).					
	NQ**	Swift et al., "Tissue-specific expression of the rat pancreatic elastase I gene in transgenic mice," <i>Cell</i> 38(3):639-646 (1984).					
	NR**	Takahashi et al., "A fluorimetric Morgan-Elson assay method for hyaluronidase activity," <i>Anal. Biochem.</i> 322:257-263 (2003).					
	NS**	Takeshita et al., "An enzyme-linked immunosorbent assay for detecting proteolytic activity of hepatitis C virus proteinase," (1997) <i>Anal. Biochem.</i> 247:242-246.					
	NT**	Taliani et al., "A continuous assay of hepatitis C virus protease based on resonance energy transfer depsipeptide substrates," <i>Anal. Biochem.</i> 240:60-67 (1996).					
	NU**	ten Have et al., "Cloning and characterization of the cDNA encoding the PH20 protein in the European red fox <i>Vulpes vulpes</i> ," <i>Reprod Fertil Dev.</i> 10(2):165-172 (1998).					
	NV**	Tkalec et al., "Isolation and expression in <i>Escherichia coli</i> of <i>csIA</i> and <i>csIB</i> , genes coding for the chondroitin sulfate-degrading enzymes chondroitinase AC and chondroitinase B, respectively, from <i>Flavobacterium heparinum</i> ," <i>Applied and Environmental Microbiology</i> 66(1):29-35 (2000).					
	NW**	Tsubery et al., "Prolonging the action of protein and peptide drugs by a novel approach of reversible polyethylene glycol modification," <i>J Biol. Chem</i> 279(37):38118-38124 (2004).					
	NX**	Tsuda et al., "Substrate specificity studies of flavobacterium chondroitinase C and heparitinases towards the glycosaminoglycan—protein linkage region. Use of a sensitive analytical method developed by chromophore-labeling of linkage glycoserines using dimethylaminoazobenzenesulfonyl chloride," <i>Eur. J. Biochem.</i> 262:127-133 (1999).					
	NY**	Tung et al., "Mechanism of infertility in male guinea pigs immunized with sperm PH-20," <i>Biol. Reprod.</i> 56(5):1133-1141 (1997).					
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	NZ**	Udenfriend, S. and K. Kodukula, "Prediction of omega site in nascent precursor of glycosylphosphatidylinositol protein," <i>Methods Enzymol.</i> 250:571-582 (1995).					
	OA**	UniProt Murine PH20 sequence, Retrieved from: <URL: uniprot.org/uniprot/P48794 [retrieved on Sept. 1, 2010] [5 pages].					
	OB**	United States Pharmacopeia. USP <51>. Antimicrobial effectiveness testing. United States Pharmacopeia Convention, Inc, Rockville, MD., 5 pages.					
	OC**	USP XXII-NF XVII, United States Pharmacopeia Convention, Inc, Rockville, MD., pages 644-645 (1990).					
	OD**	Varela et al., "Exome sequencing identifies frequent mutation of the SWI/SNF complex gene PBRM1 in renal carcinoma," <i>Nature</i> 469(7331):539-542 (2011).					
	OE**	Veronese et al., "Branched and Linear Poly(Ethylene Glycol): Influence of the Polymer Structure on Enzymological, Pharmacokinetic, and Immunological Properties of Protein Conjugates," <i>J. Bioactive Compatible Polymers</i> 12:197-207 (1997).					
	OF**	Von Sivaraman Padavattan (2006) Thesis of University of Basel, "Crystal structure determination of hyaluronidase, a major bee venom allergen, in complex with an IgG Fab fragment and purification and biophysical characterization of bovine testes hyaluronidase," 100 pages.					
	OG**	Wagner et al., "Nucleotide sequence of the thymidine kinase gene of herpes simplex virus type 1," <i>Proc. Natl. Acad. Sci. USA</i> 78:1441-1445 (1981).					
	OH**	Wang et al., "The molecular physiology of hepatic nuclear factor 3 in the regulation of gluconeogenesis," <i>J. Biol. Chem.</i> 275(19):14717-14721 (2000).					
	OI**	Watson et al., <i>Molecular Biology of the Gene</i> , 4th Edition, The Benjamin/Cummings Pub. Co., p. 224 (1987).					
	OJ**	Weiss et al., "Activities of monomeric insulin analogs at position A8 are uncorrelated with their thermodynamic stabilities," <i>J. Biol. Chem.</i> 276(43):40018-40024 (2001).					
	OK**	Wells et al., "Additivity of Mutational Effects in Proteins," <i>Biochem</i> 29:8509-8517 (1990).					
	OL**	White et al., "Comparison of the glycosyl-phosphatidylinositol cleavage/attachment site between mammalian cells and parasitic protozoa," <i>J. Cell Sci.</i> 113(Pt.4):721-727 (2000).					
	OM**	Wigler et al., "Transfer of purified herpes virus thymidine kinase gene to cultured mouse cells," <i>Cell</i> 11:223-232 (1977).					
	ON**	Wigler et al., "Transformation of mammalian cells with an amplifiable dominant-acting gene," <i>Proc Natl Acad Sci. USA</i> 77:3567-3570 (1980).					
	OO**	Yamamoto et al., "Identification of a functional promoter in the long terminal repeat of Rous sarcoma virus," <i>Cell</i> 22:787-797 (1980).					
	OP**	Yamane-Ohnuki et al., "Establishment of FUT8 knockout Chinese hamster ovary cells: an ideal host cell line for producing completely defucosylated antibodies with enhanced antibody-dependent cellular cytotoxicity," <i>Biotech. Bioeng.</i> 87:614-622 (2004).					
	OQ**	Yang, X. and X. Yu, "An introduction to epitope prediction methods and software," <i>Rev Med Virol.</i> 19(2):77-96 (2009).					
	OR**	Yocum et al., "Assessment and implication of the allergic sensitivity to a single dose of recombinant human hyaluronidase injection: A double-blind placebo-controlled clinical trial," <i>J Infus Nursing</i> 30:293-299 (2007).					
	OS**	Yudin et al., "Characterization of the active site of monkey sperm hyaluronidase," <i>Reproduction.</i> 121(5):735-743 (2001).					
	OT**	Zalipsky, S., "Chemistry of polyethylene glycol conjugates with biologically active molecules," <i>Adv. Drug Del. Rev.</i> 16:157-182 (1995).					
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Other Documents (include Author, Title, Date, and Place of Publication)

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	OU**	Zanker et al., "Induction of response in previous chemotherapy resistant patients by hyaluronidase," Proc. Amer. Assoc. Cancer Res. 27:390 Abstract 1550 (1986).
	OV**	Zhang et al., "Hyaluronidase Activity of Hyman HyalI Requires Active Site Acidic and Tyrosine residues," J Biol Chem 284(14):9433-9442 (2009).
	OW**	Zhao, X. and J. Harris, "Novel degradable poly(ethylene glycol) esters for delivery," in Poly(ethylene glycol), Chemistry and Biological Applications, ACS Symposium Series 680, Hams, J. and S. Zalipsky, (eds), 458-472 (1997).
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	OY**	Bee et al., "Recombinant human PH20 is well tolerated at higher intravenous and subcutaneous doses in cynomolgus monkeys," EUFEPS 2008, Munich, Germany. Poster and individual panels, 9 pages.
	OZ **	Bookbinder et al., "Biochemical characterization of recombinant human PH20 (SPAM1) hyaluronidase," Hyaluronan (ISHAS) 2007, Charleston, SC. Abstract, 1 page.
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	PB**	Bookbinder et al., "Enhancing drug transport through temporary matrix depolymerization," Keystone Symposia 2005. (poster and abstract- 13 pages).
	PC**	Bookbinder et al., "Enhancing drug transport through temporary matrix depolymerization," Keystone Symposia 2005, Abstract, 1 page.
	PD**	Bookbinder et al., "Evaluation of the compatibility and pharmacokinetics of co-formulated biologics with recombinant human hyaluronidase: Dose Response," American Association of Pharmaceutical Scientists Conference, November 2006. Abstract, 2 pages.
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	PF**	Byerley et al., "'Cutting out the bull'. Recombinant human hyaluronidase: Moving to an animal-free system," Association of Clinical Embryologists, 2006, Dublin, Ireland. Abstract published in Human Fertility, 9(2):110 (2006).
	PG**	Frost et al., "Punctuated equilibrium: The evolution of recombinant human hyaluronidase," Ophthalmic Anesthesia Society, 2006, Chicago, IL, abstract, 1 page.
	PH**	Frost et al., "Punctuated equilibrium: The evolution of recombinant human hyaluronidase," Ophthalmic Anesthesia Society, 2006, Chicago, IL, presentation, 35 pages.
	PI**	Haller et al., "Enhance technology – a revolution in drug dispersion," Biotechnology Industry Organization (BIO) Annual Meeting, June 19-22, 2005, Philadelphia, PA. Abstract, 3 pages.
	PJ**	Haller et al., "Recombinant human hyaluronidase for the interstitial transport of therapeutics," American Association of Pharmaceutical Scientists Conference, June 2006, San Antonio, TX, Abstract, 2 pages.
	PK**	Haller et al., "Recombinant human hyaluronidase for the interstitial transport of therapeutics," Controlled Release Society Conference, Vienna, Austria, 2006, Abstract, 2 pages.
	PL**	Haller et al., "Revolutionizing drug dispersion with enhance technology," American Association of Pharmaceutical Scientists Annual Meeting, Nov 6-10, 2005, Nashville, TN, Poster, 1 page.
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	PN**	Haller et al., "The effects of recombinant human hyaluronidase on drug dispersion," American Association of Pharmaceutical Scientists Annual Meeting, Abstract in AAPS Journal 7(S2) May 5, 2005; 3 pages.					
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	PP**	Haller, M., "Focus on enhanced and innovative recombinant human enzymes," Japanese Export Trade Organization, September 2004, Chicago, IL., Presentation, 16 pages.					
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	PR**	Haller, M., "Enzyme-facilitated parenteral drug transport," Strategic Research Institute's 10th Anniversary Drug Delivery Technology and Deal-making Summit 2005, New Brunswick, NJ. Presentation, 24 pages.					
	PS**	Hofer et al., "Human recombinant hyaluronidase increases the convection of molecules up to 0.2 µm in athymic nude mice," American Association for Laboratory Animal Science, 2006, Salt Lake City, UT. Abstract published in J. Am. Assoc. Lab. Animal Sci., 45:120, Abstract P97 (2006), 1 page.					
	PT**	Hofer, "Human Recombinant Hyaluronidase Increases the Convection of Molecules up to 0.2 µm in Athymic Nude Mice," American Association for Laboratory Animal Science, 2006, Salt Lake City, UT. Abstract published in J. Am. Assoc. Lab. Animal Sci., 45:120, 2006. Poster P97, 1 page.					
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	PW**	Keller et al., "Pharmacokinetic, pharmacodynamic and toxicologic effects of a recombinant human hyaluronidase (rHuPH20) in rodent and non-human primate models," Hyaluronan (ISHAS) 2007, Charleston, SC, Poster and individual panels, 14 pages.					
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	PY**	Morrow et al., "Human Hyaluronidase Coinjection Accelerates Insulin Pharmacokinetics and Glucodynamics of 3 Rapid Insulin Analogs," American Diabetes Association Scientific Sessions, held on June 28, 2010 in Orlando, FL., Abstract # 353-OR, 2 pages.					
	PZ**	Nadsombati et al., "Evaluation of developmental and prenatal/postnatal reproduction toxicity of rHuPH20 in mice," American College of Toxicology 30th annual meeting, 2009, November 1-4, Palm Springs, CA, Abstract, 1 page.					
	QA**	Nagy et al., "Prospective, randomized study on bovine and recombinant human (Cumulase®) Hyaluronidases," American Society of Reproductive Medicine, 2006, New Orleans, LA, 06-A-886-ASRM, 2 pages.					
	QB**	Nagy, Z., "Prospective study on rHuPH20," European Society of Human Reproduction & Embryology Annual Meeting, June 19-22, 2005, Copenhagen, Denmark. Abstract O-213, 1 page.					
	QC**	"PEGPH20: The Science & The Strategy," presented at J. P. Morgan Healthcare Conference on Jan. 7, 2015. Presentation. 81 pages.					
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	QD**	Pinkstaff et al., "Recombinant human hyaluronidase for drug and fluid dispersion," American Association of Pharmaceutical Scientists Annual Meeting, November 2006, Boston, MA, Abstract, 2 pages.					
	QE**	Pinkstaff et al., "Recombinant human hyaluronidase for drug and fluid dispersion," American Association of Pharmaceutical Scientists Annual Meeting, November 2006, Boston, MA, Poster and individual panels, 8 pages.					
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	QG**	Torley, H., "Halozyne Therapeutics, Inc. The next chapter begins: creating value through growth," Presented at the 32nd Annual J.P. Morgan Healthcare Conference January 2014, 26 pages.					
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	QJ**	Wei et al., "Structure function analysis of the human hyaluronidase enzymes," Presented at American Society for Matrix Biology Biennial Meeting, San Diego, CA, December 9, 2008, Poster B4 and individual panels, 5 pages.					
	QK**	Wilson, M., "Enhance technology – an enzymatic drug delivery system (DDS)," Japanese Export Trade Organization, November 2005, Santa Clara, CA. Oral presentation, 22 pages.					
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	QM**	News Release, Halozyne Therapeutics, Inc "Halozyne Licenses New Enhance Target For \$30 Million Upfront Payment, Future Milestones And Royalties," Published Sept. 14, 2017 [online] Retrieved from:<URL: halozyne.com/investors/news-releases/news-release-details/2017/Halozyne-Licenses-New-Enhance-Target-For-30-Million-Upfront-Payment-Future-Milestones-And-Royalties/default.aspx [retrieved on Sept. 14, 2017], 3 pages.					
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	QP**	News Article, "Alteogen Inc. to Develop Herceptin Biosimilar for Subcutaneous Injection," Published on Aug. 23, 2018 [online] Retrieved from: <URL:thebell.co.kr/free/Content/ArticleView.asp?key=201808220100037100002360 [Original document retrieved from the internet and English translation], 4 pages.					
	QQ**	News Article, "[Promising biocompany] Alteogen Inc. tries to differentiate itself with specialized bio technology and strategy," Published on Sept. 17, 2018 [online] Retrieved from: <URL:cdaily.co.kr/news/read?newsId=01105366619341104&mediaCodeNo=257&OutLnkChk=Y [Original document retrieved from the internet and English translation], 4 pages.					
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	QR**	News Release, Halozyne Therapeutics, Inc., "Halozyne Publication In The Journal Clinical Cancer Research Highlights New Nonclinical Data Supporting Multiple Effects Of PEGPH20 On The Tumor Microenvironment," Published Oct. 04, 2018 [online] Retrieved from: <URL: halozyne.com/investors/news-releases/news-release-details/2018/Halozyne-Publication-In-The-Journal-Clinical-Cancer-Research-Highlights-New-Nonclinical-Data-Supporting-Multiple-Effects-Of-PEGPH20-On-The-Tumor-Microenvironment/default.aspx [retrieved on Oct. 5, 2018], 4 pages.					
	QS**	News Article, "Alteogen, Inc. challenges to the ethical drug market by utilizing 'Human Hyaluronidase'," Published on Oct. 29 2018 [online] Retrieved from: <URL:fnnews.com/news/201810290941498520 [Original document retrieved from the internet and English translation], 6 pages.					
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	QU**	News Article, "Maximizing patient convenience by changing intravenous injection to subcutaneous injection Alteogen expects increased exports of the technology this year," Published on Jan. 20, 2019 [online] Retrieved from: <URL:news.hankyung.com/article/2019012023181 [Original documents retrieved from the internet and English translation], 5 pages.					
	QV**	News Release, Halozyne Therapeutics, Inc., "Halozyne Announces Actions To Focus Strategy On ENHANZE® Drug Delivery Technology," Published Nov. 04, 2019 [online], Retrieved from: <URL: halozyne.com/investors/news-releases/news-release-details/2019/Halozyne-Announces-Actions-To-Focus-Strategy-On-ENHANZE-Drug-Delivery-Technology/default.aspx [retrieved on Nov. 11, 2019], 4 pages.					
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	QX**	English translation of News Article, "Alteogen files a PCT application for subcutaneous pharmaceutical composition," Published on Mar. 24, 2020 [online], retrieved from <URL: medipana.com/news/news_viewer.asp?NewsNum=254556&MainKind=A&NewsKind=5&vCount=12&vKind [retrieved on Mar. 26, 2020], 2 pages.					
	QY**	Partial International Search Report, sent by facsimile Sept. 9, 2013, in connection with International Patent Application No. PCT/US2012/072182, 6 pages.					
	QZ**	International Search Report and Written Opinion, mailed Dec. 17, 2013, in connection with International Patent Application No. PCT/US2012/072182, 18 pages.					
	RA**	Response, dated March 17, 2014, to Written Opinion, mailed Dec. 17, 2013, in connection with International Patent Application No. PCT/US2012/072182, 94 pages.					
	RB**	Second Written Opinion, mailed May 21, 2014, in connection with International Patent Application No. PCT/US2012/072182, 8 pages.					
	RC**	Response, dated July 21, 2014, to second Written Opinion, mailed May 21, 2014, in connection with International Patent Application No. PCT/US2012/072182, 72 pages.					
	RD**	Second Written Opinion, mailed Jul. 30, 2014, in connection with International Patent Application No. PCT/US2012/072182, 9 pages.					
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	RF**	International Preliminary Report on Patentability, mailed Sept. 12, 2014, in connection with International Patent Application No. PCT/US2012/072182, 11 pages.			
	RG**	Office Action, mailed November 2, 2015, in connection with U.S. Patent Application Serial No. 13/694,731, 14 pages.			
	RH**	Response, filed Apr. 20, 2016, to Office Action, mailed Nov. 2, 2015, in connection with U.S. Patent Application Serial No. 13/694,731, 43 pages.			
	RI**	Notice of Allowance, mailed May 20, 2016, in connection with U.S. Patent Application Serial No. 13/694,731, 16 pages.			
	RJ**	Office Action, issued May 15, 2019, in connection with U.S. Patent Application No. 15/226,489, 16 pages.			
	RK**	Response, filed Oct. 15, 2019, to Office Action, issued May 15, 2019, in connection with U.S. Patent Application No. 15/226,489, 30 pages.			
	RL**	Office Action, issued Jan. 23, 2020, in connection with U.S. Patent Application No. 15/226,489, 19 pages.			
	RM**	Response, filed Apr. 24, 2020, to Office Action, issued Jan. 23, 2020, in connection with U.S. Patent Application No. 15/226,489, 25 pages.			
	RN**	Examination Report, issued Jan. 13, 2017, in connection with Australian Patent Application No. 2012362141, 3 pages.			
	RO**	Response, filed Aug. 14, 2017, to Examination Report, issued Jan. 13, 2017, in connection with Australian Patent Application No. 2012362141, 43 pages.			
	RP**	Notice of Acceptance, dated Sept. 11, 2017, issued in connection with Australian Patent Application No. 2012362141, 3 pages.			
	RQ**	Office Action (claimed deemed allowable), dated Oct. 19, 2018, issued in connection with Australian Patent Application No. 2017245352, 7 pages.			
	RR**	Notice of Acceptance, issued Jul. 17, 2019, in connection with Australian Patent Application No. 2017245352, 3 pages.			
	RS**	Examiner's Report, issued March 1, 2016, in connection with Canadian Patent Application No. 2861919, 7 pages.			
	RT**	Response, filed Jul. 14, 2016, to Examiner's Report, issued Mar. 1, 2016, in connection with Canadian Patent Application No. 2861919, 37 pages.			
	RU**	Examiner's Report, issued Jan. 24, 2017, in connection with Canadian Patent Application No. 2861919, 4 pages.			
	RV**	Response, filed Jul. 24, 2017, to Examiner's Report, issued Jan. 24, 2017, in connection with Canadian Patent Application No. 2861919, 26 pages.			
	RW**	Examiner's Report, issued Jan. 23, 2018, in connection with Canadian Patent Application No. 2861919, 4 pages.			
	RX**	Response, filed Jun. 21, 2018, to Examiner's Report, dated Jan. 23, 2018, issued in connection with Canadian Patent Application No. 2861919, 39 pages.			
	RY**	Notice of Allowance, dated Dec. 12, 2018, issued in connection with Canadian Patent Application No. 2861919, 1 page.			
	RZ**	Office Action, issued May 25, 2015, in connection with Chinese Patent Application No. 201280070954.9 [English language translation and original document in Chinese], 7 pages.			
	SA**	Response, filed Oct. 9, 2015, to Office Action, issued May 25, 2015, in connection with Chinese Patent Application No. 201280070954.9 [English instructions and document as filed in Chinese], 37 pages.			
	SB**	Office Action, issued Feb. 3, 2016, in connection with Chinese Patent Application No. 201280070954.9 [English language translation and original document in Chinese], 6 pages.			
Examiner Signature		/SAMUEL W LIU/		Date Considered 09/30/2020	
EXAMINER: Initial if citation considered, whether or not citation is in conformance with MPEP 609; Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.					

Substitute Form PTO-1449 (Modified)	U.S. Department of Commerce Patent and Trademark Office	Attorney Docket No. 33320.03087.US27/3087D	Application No. 16/912,590
List of Patents and Publications for Applicant's Information Disclosure Statement (37 CFR §1.98(b))		Inventors <i>Wei et al.</i>	
		Filing Date June 25, 2020	Group Art Unit 1652

Other Documents (include Author, Title, Date, and Place of Publication)

Examiner Initial	Desig. ID	Document
	SC**	Response, filed Jun. 20, 2016, to Office Action, issued Feb. 3, 2016, in connection with Chinese Patent Application No. 201280070954.9 [English language instructions, document as filed in Chinese and claims, as filed, in English], 58 pages.
	SD**	Office Action, issued Oct. 17, 2016, in connection with Chinese Patent Application No. 201280070954.9 [English language translation and original document in Chinese], 4 pages.
	SE**	Response, filed Dec. 27, 2016, to Office Action, issued Oct. 17, 2016, in connection with Chinese Patent Application No. 201280070954.9 [English language instructions and document as-filed in Chinese], 18 pages.
	SF**	Letter, dated Mar. 15, 2017, reporting Telephonic Interview with Examiner in connection with Chinese Patent Application No. 201280070954.9, 1 page.
	SG**	Response, filed Mar. 23, 2017 to Telephonic Interview with Examiner in connection with Chinese Patent Application No. 201280070954.9, 10 pages.
	SH**	Notice of Granting Patent Right for Invention, issued April 28, 2017, in connection with Chinese Patent Application No. 201280070954.9 [English translation and original document in Chinese], 4 pages.
	SI**	Notice of Allowance, dated Dec. 7, 2017, issued in connection with Eurasian Patent Application No. 201400772 [English letter and original document in Russian], 2 pages.
	SJ**	Response, filed Mar. 3, 2015, to Communication Pursuant to Rules 161(1) and 162 EPC, issued Sept. 4, 2014, in connection with European Patent Application No. 12816624.6, 40 pages.
	SK**	Communication Pursuant to Rule 71(3) (Intention to Grant), issued Apr. 22, 2016, in connection with European Patent Application No. 12816624.6, 5 pages.
	SL**	Extended European Search Report, dated Jan. 12, 2017, issued in connection with European Patent Application No. 16189970.3, 11 pages.
	SM**	Response, filed Aug. 15, 2017, to Extended European Search Report, dated Jan. 12, 2017, issued in connection with European Patent Application No. 16189970.3, 55 pages.
	SN**	Examination Report, dated Sept. 14, 2017, issued in connection with European Patent Application No. 16189970.3, 3 pages.
	SO**	Response, dated Oct. 13, 2017, to Examination Report, dated Sept. 14, 2017, issued in connection with European Patent Application No. 16189970.3, 19 pages.
	SP**	Communication Pursuant to Article 94(3) EPC (claims deemed allowable), dated Feb. 26, 2018, issued in connection with European Patent Application No. 16189970.3, 3 pages.
	SQ**	Response, filed Sept. 10, 2018, to Communication Pursuant to Article 94(3) EPC (claims deemed allowable), issued Feb. 26, 2018, issued in connection with European Patent Application No. 16189970.3, 821 pages.
	SR**	Communication Pursuant to Article 71(3) EPC (Intention to Grant), dated Apr. 08, 2019, issued in connection with European Patent Application No. 16189970.3, 7 pages.
	SS**	Decision to Grant, issued Aug. 22, 2019, in connection with European Patent Application No. 16189970.3, 2 pages.
	ST**	Examination Report, issued Dec. 4, 2018, in connection with Indian Patent Application No. 6272/DELNP/2014, 6 pages.
	SU**	Response, filed Sept. 4, 2019, to Examination Report, issued Dec. 4, 2018, in connection with Indian Patent Application No. 6272/DELNP/2014, 79 pages.
	SV**	Office Action, dated Aug. 3, 2016, in connection with Israeli Patent Application No. 233192 [English language translation], 3 pages.
	SW**	Response, filed Jan. 3, 2017, to Office Action, dated Aug. 3, 2016, in connection with Israeli Patent Application No. 233192 [English language translation], 32 pages.

Examiner Signature /SAMUEL W LIU/	Date Considered 09/30/2020
EXAMINER: Initial if citation considered, whether or not citation is in conformance with MPEP 609; Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.	

Substitute Form PTO-1449 (Modified)		U.S. Department of Commerce Patent and Trademark Office		Attorney Docket No. 33320.03087.US27/3087D		Application No. 16/912,590	
List of Patents and Publications for Applicant's Information Disclosure Statement (37 CFR §1.98(b))				Inventors <i>Wei et al.</i>			
				Filing Date June 25, 2020		Group Art Unit 1652	
Other Documents (include Author, Title, Date, and Place of Publication)							
Examiner Initial	Desig. ID	Document					
	SX**	Office Action, dated Nov. 20, 2017, issued in connection with Israeli Patent Application No. 233192 [English language translation], 2 pages.					
	SY**	Response, filed May 21, 2018, to Office Action, dated Nov. 20, 2017, issued in connection with Israeli Patent Application No. 233192 [English language translation], 22 pages.					
	SZ**	Office Action (claims deemed allowable), dated Feb. 20, 2019, issued in connection with Israeli Patent Application No. 233192 [English letter reporting Office Action and original document in Hebrew], 5 pages.					
	TA**	Official Action, issued Jan. 19, 2016, in connection with Japanese Patent Application No. 2014-550526 [English translation and original document in Japanese], 8 pages.					
	TB**	Response, filed Jul. 15, 2016, to Official Action, issued Jan. 19, 2016, in connection with Japanese Patent Application No. 2014-550526 [English instructions and document as filed in Japanese], 138 pages.					
	TC**	Decision to Grant, issued Nov. 22, 2016, in connection with Japanese Patent Application No. 2014-550526 [Letter reporting decision to grant and original document in Japanese], 5 pages.					
	TD**	Office Action, issued Dec 12, 2017, in connection with Japanese Patent Application No. 2016-247708 [English translation and original document in Japanese], 6 pages.					
	TE**	Response, filed May 22, 2018, to Office Action, issued Dec. 12, 2017, in connection with Japanese Patent Application No. 2016-247708 [English instructions with amended claims, documents as-filed in Japanese and English translation of claims as-filed], 90 pages.					
	TF**	Decision to Grant, issued Sept. 18, 2018, in connection with Japanese Patent Application No. 2016-247708 [English reporting letter and original document in Japanese], 4 pages.					
	TG**	Office Action, dated May 25, 2018, in connection with Mexican Patent Application No. MX/a/2014/007966 [English translation and original document in Spanish], 6 pages.					
	TH**	Response, filed Oct. 10, 2018, to Office Action, dated May 25, 2018, in connection with Mexican Patent Application No. MX/a/2014/007966 [English instructions and document as-filed in Spanish], 13 pages.					
	TI**	Notice of Allowance, issued Oct. 18, 2018, in connection with Mexican Patent Application No. MX/a/2014/007966 [English reporting letter and original document in Spanish], 4 pages.					
	TJ**	Examination Report, dated Mar. 26, 2015, in connection with New Zealand Patent Application No. 626126, 32 pages.					
	TK**	Response, dated May 16, 2016, to Examination Report, dated Mar. 26, 2015, in connection with New Zealand Patent Application No. 626126, 70 pages.					
	TL**	Notice of Acceptance, dated Jun. 8, 2016, in connection with New Zealand Patent Application No. 626126, 1 page.					
	TM**	Letters Patent, issued Sept. 27, 2016, in connection with New Zealand Patent No. 626126, 1 page.					
	TN**	Examination Report, dated Jul. 27, 2017, issued in connection with New Zealand Patent Application No. 720075, 4 pages.					
	TO**	Response, filed Feb. 26, 2018, to Examination Report, dated Jul. 27, 2017, issued in connection with New Zealand Patent Application No. 720075, 88 pages.					
	TP**	Notice of Acceptance, dated Mar. 10, 2020, issued in connection with New Zealand Patent Application No. 720075, 1 page.					
	TQ**	Search Report and Written Opinion, dated Dec. 4, 2015, in connection with Singaporean Patent Application No. 11201403714T, 7 pages.					
	TR**	Response, filed May 23, 2016, to Search Report and Written Opinion, dated Dec. 4, 2015, in connection with Singaporean Patent Application No. 11201403714T, 21 pages.					

Examiner Signature /SAMUEL W LIU/	Date Considered 09/30/2020
EXAMINER: Initial if citation considered, whether or not citation is in conformance with MPEP 609; Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.	

Substitute Form PTO-1449 (Modified)		U.S. Department of Commerce Patent and Trademark Office		Attorney Docket No. 33320.03087.US27/3087D	Application No. 16/912,590
List of Patents and Publications for Applicant's Information Disclosure Statement				Inventors Wei <i>et al.</i>	
				Filing Date June 25, 2020	Group Art Unit 1652
(37 CFR §1.98(b))					
Other Documents (include Author, Title, Date, and Place of Publication)					
Examiner Initial	Desig. ID	Document			
	TS**	Written Opinion, dated Sept. 18, 2017, in connection with Singapore Patent Application No. 11201403714T, 9 pages.			
	TT**	Response, filed Oct. 27, 2017, to Written Opinion, dated Sept. 18, 2017, in connection with Singapore Patent Application No. 11201403714T, 6 pages.			
	TU**	Corrected Notice of Eligibility for Grant and Examination Report, dated Jul. 02, 2018, in connection with Singapore Patent Application No. 11201403714T, 8 pages.			
	TV**	Certificate of Grant, dated Oct. 3, 2018, in connection with Singapore Patent Application No. 11201403714T [Grant Certificate and Granted Claims], 6 pages.			
	TW**	Search Report and Written Opinion, issued Oct. 20, 2017, in connection with Singapore Patent Application No. 10201604470T, 14 pages.			
	TX**	Response, filed Mar. 20, 2018, to Search Report and Written Opinion, issued Oct. 20, 2017, in connection with Singapore Patent Application No. 10201604470T [Response, replacement specification pages, amended claims and cited document], 105 pages.			
	TY**	Examination Report, dated Aug. 6, 2018, and Notice of Eligibility for Grant, dated Aug. 7, 2018, issued in connection with Singapore Patent Application No. 10201604470T, 6 pages.			
	TZ**	English translation of Official Action, issued Mar. 20, 2020, in connection with Korean Application No. 10-2020-7002955.			
	UA	English translation of News Article, "Alteogen files a PCT application for subcutaneous pharmaceutical composition," Published on Mar. 24, 2020 [online], retrieved from <URL: medipana.com/news/news_viewer.asp?NewsNum=254556&MainKind=A&NewsKind=5&vCount=12&vKind [retrieved on Mar. 26, 2020], 2 pages.			
	UB	Hearing Notice, issued Jun. 17, 2020, in connection with Indian Patent Application No. 6272/DELNP/2014, 2 pages.			
	UC	English Translation of International Search Report and Written Opinion, issued Oct. 29, 2019, in connection with International application No. PCT/KR2019/009215, 10 pages.			
** = Copies not provided herewith as they have been previously provided in connection with U.S. Serial Nos. 13/694,731, 15/226,489, and/or 16/824,572, which are relied upon for an earlier filing date in accordance with 35 U.S.C. §120.					

Examiner Signature /SAMUEL W LIU/	Date Considered 09/30/2020
EXAMINER: Initial if citation considered, whether or not citation is in conformance with MPEP 609; Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.	

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Inventor(s)	: Ge Wei <i>et al.</i>	Art Unit	: 1656
Serial No.	: 16/912,590	Examiner	: Samuel W. Liu
Filed	: June 25, 2020	Conf. No.	: 9651
		Cust. No.	: 13565
Title	: PH20 POLYPEPTIDE VARIANTS, FORMULATIONS AND USES THEREOF		

Mail Stop Missing Parts

Commissioner for Patents

P.O. Box 1450

Alexandria, VA 22313-1450

REQUEST FOR CORRECTED FILING RECEIPT

Dear Sir:

Transmitted herewith is this *Request for Corrected Filing Receipt*, a copy of the *Filing Receipt*, mailed July 6, 2020, with annotated corrections, and an updated *Application Data Sheet*, marked to show the changes to the residence and mailing address information of inventor H. Michael Shepard.

Please update the Second Inventor's City and State of Residence to read as follows:

H. Michael Shepard, Springfield, OR;

Applicant requests the city and state of the residence of inventor H. Michael Shepard be updated from "San Diego, CA" to "Springfield, OR". A marked-up updated *Application Data Sheet* (ADS) is filed herewith to provide the Office with H. Michael Shepard's new residence and mailing address information.

Applicant respectfully requests provision of an updated filing receipt to reflect the updated information.

Respectfully submitted,

/Stephanie Seidman/

Stephanie Seidman

Reg. No. 33,779

Attorney Docket No. 33320.03087.US27/3087D

Address all correspondence to: 13565

Stephanie Seidman

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San Diego, California 92121

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CERTIFICATE OF TRANSMISSION VIA EFS-WEB

I hereby certify that this paper is being transmitted via the Electronic Filing System (EFS-WEB) to the United States Patent and Trademark Office on **May 05, 2021**.

/Rosalind E. Smith/

Rosalind E. Smith

Inventor(s) : Ge Wei *et al.*
Serial No. : 16/912,590
Filed : June 25, 2020

Attorney Docket No.: 33320.03087.US27/3087D
Request for Corrected Filing Receipt

Attachment 1

**Copy of *Updated Filing Receipt*, mailed July 6, 2020,
with Annotated Corrections**

COPY



UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
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www.uspto.gov

APPLICATION NUMBER	FILING or 371(c) DATE	GRP ART UNIT	FIL FEE REC'D	ATTY. DOCKET NO	TOT CLAIMS	IND CLAIMS
16/912,590	06/25/2020	1652	3520	33320.03087.US27/3087D	22	1

CONFIRMATION NO. 9651

FILING RECEIPT



0000000118220624

13565
Dentons US LLP
4655 Executive Drive
Suite 700
San Diego, CA 92121

Date Mailed: 07/06/2020

Receipt is acknowledged of this non-provisional utility patent application. The application will be taken up for examination in due course. Applicant will be notified as to the results of the examination. Any correspondence concerning the application must include the following identification information: the U.S. APPLICATION NUMBER, FILING DATE, NAME OF FIRST INVENTOR, and TITLE OF INVENTION. Fees transmitted by check or draft are subject to collection.

Please verify the accuracy of the data presented on this receipt. If an error is noted on this Filing Receipt, please submit a written request for a corrected Filing Receipt, including a properly marked-up ADS showing the changes with strike-through for deletions and underlining for additions. If you received a "Notice to File Missing Parts" or other Notice requiring a response for this application, please submit any request for correction to this Filing Receipt with your reply to the Notice. When the USPTO processes the reply to the Notice, the USPTO will generate another Filing Receipt incorporating the requested corrections provided that the request is grantable.

Inventor(s)

GE WEI, SAN DIEGO, CA;
H. MICHAEL SHEPARD, ~~SAN DIEGO, CA;~~ SPRINGFIELD, OR;
QIPING ZHAO, SAN DIEGO, CA;
ROBERT JAMES CONNOR, OCEANSIDE, CA;

Applicant(s)

HALOZYME, INC., SAN DIEGO, CA;

Power of Attorney:

Stephanie Seidman--33779
Frank Miskiel--53332
James Turner--74602

Domestic Priority data as claimed by applicant

This application is a CON of 15/226,489 08/02/2016
which is a DIV of 13/694,731 12/28/2012 PAT 9447401
which claims benefit of 61/796,208 11/01/2012
and claims benefit of 61/631,313 12/30/2011
This application 16/912,590
is a DIV of 13/694,731 12/28/2012 PAT 9447401
which claims benefit of 61/796,208 11/01/2012
and claims benefit of 61/631,313 12/30/2011

Foreign Applications for which priority is claimed (You may be eligible to benefit from the **Patent Prosecution Highway** program at the USPTO. Please see <http://www.uspto.gov> for more information.) - None.

Foreign application information must be provided in an Application Data Sheet in order to constitute a claim to foreign priority. See 37 CFR 1.55 and 1.76.

Permission to Access Application via Priority Document Exchange: Yes

Permission to Access Search Results: Yes

Applicant may provide or rescind an authorization for access using Form PTO/SB/39 or Form PTO/SB/69 as appropriate.

If Required, Foreign Filing License Granted: 07/02/2020

The country code and number of your priority application, to be used for filing abroad under the Paris Convention, is **US 16/912,590**

Projected Publication Date: 10/08/2020

Non-Publication Request: No

Early Publication Request: No
Title

PH20 POLYPEPTIDE VARIANTS, FORMULATIONS AND USES THEREOF

Preliminary Class

435

Statement under 37 CFR 1.55 or 1.78 for AIA (First Inventor to File) Transition Applications: No

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Since the rights granted by a U.S. patent extend only throughout the territory of the United States and have no effect in a foreign country, an inventor who wishes patent protection in another country must apply for a patent in a specific country or in regional patent offices. Applicants may wish to consider the filing of an international application under the Patent Cooperation Treaty (PCT). An international (PCT) application generally has the same effect as a regular national patent application in each PCT-member country. The PCT process **simplifies** the filing of patent applications on the same invention in member countries, but **does not result** in a grant of "an international patent" and does not eliminate the need of applicants to file additional documents and fees in countries where patent protection is desired.

Almost every country has its own patent law, and a person desiring a patent in a particular country must make an application for patent in that country in accordance with its particular laws. Since the laws of many countries differ in various respects from the patent law of the United States, applicants are advised to seek guidance from specific foreign countries to ensure that patent rights are not lost prematurely.

Applicants also are advised that in the case of inventions made in the United States, the Director of the USPTO must issue a license before applicants can apply for a patent in a foreign country. The filing of a U.S. patent application serves as a request for a foreign filing license. The application's filing receipt contains further information and guidance as to the status of applicant's license for foreign filing.

Applicants may wish to consult the USPTO booklet, "General Information Concerning Patents" (specifically, the section entitled "Treaties and Foreign Patents") for more information on timeframes and deadlines for filing foreign patent applications. The guide is available either by contacting the USPTO Contact Center at 800-786-9199, or it can be viewed on the USPTO website at <http://www.uspto.gov/web/offices/pac/doc/general/index.html>.

For information on preventing theft of your intellectual property (patents, trademarks and copyrights), you may wish to consult the U.S. Government website, <http://www.stopfakes.gov>. Part of a Department of Commerce initiative, this website includes self-help "toolkits" giving innovators guidance on how to protect intellectual property in specific countries such as China, Korea and Mexico. For questions regarding patent enforcement issues, applicants may call the U.S. Government hotline at 1-866-999-HALT (1-866-999-4258).

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Title 35, United States Code, Section 184

Title 37, Code of Federal Regulations, 5.11 & 5.15

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Application Data Sheet 37 CFR 1.76		Attorney Docket Number	33320.03087.US27/3087D
		Application Number	<u>16/912,590</u>
Title of Invention	PH20 POLYPEPTIDE VARIANTS, FORMULATIONS AND USES THEREOF		

The application data sheet is part of the provisional or nonprovisional application for which it is being submitted. The following form contains the bibliographic data arranged in a format specified by the United States Patent and Trademark Office as outlined in 37 CFR 1.76.

Inventor Information:

Inventor 1				
Legal Name				
Prefix	Given Name	Middle Name	Family Name	Suffix
	Ge		Wei	
Residence Information (Select One) ☒ US Residency ☐ Non US Residency ☐ Active US Military Service				
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Mailing Address of Inventor:				
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City	San Diego	State/Province	CA	
Postal Code	92131	Country	US	
Inventor 2				
Legal Name				
Prefix	Given Name	Middle Name	Family Name	Suffix
	H.	Michael	Shepard	
Residence Information (Select One) ☒ US Residency ☐ Non US Residency ☐ Active US Military Service				
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Address 2				
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Postal Code	~~92129~~ <u>97478</u>	Country	US	
Inventor 3				
Legal Name				
Prefix	Given Name	Middle Name	Family Name	Suffix
	Qiping		Zhao	
Residence Information (Select One) ☒ US Residency ☐ Non US Residency ☐ Active US Military Service				
City	San Diego	State/Province	CA	Country of Residence US
Mailing Address of Inventor:				
Address 1	11240 Windbrook Way			
Address 2				

Application Data Sheet 37 CFR 1.76		Attorney Docket Number		33320.03087.US27/3087D	
		Application Number		16/912,590	
Title of Invention		PH20 POLYPEPTIDE VARIANTS, FORMULATIONS AND USES THEREOF			
City	San Diego		State/Province	CA	
Postal Code	92131		Country	US	
Inventor 4					
Legal Name					
Prefix	Given Name	Middle Name	Family Name	Suffix	
	Robert	James	Connor		
Residence Information (Select One) ☒ US Residency ☐ Non US Residency ☐ Active US Military Service					
City	Oceanside	State/Province	CA	Country of Residence	US
Mailing Address of Inventor:					
Address 1	451 Lexington Circle				
Address 2					
City	Oceanside		State/Province	CA	
Postal Code	92057		Country	US	
All Inventors Must Be Listed – Add Additional Inventor Information blocks for each inventor.					

Correspondence Information:

Enter either Customer Number or complete the Correspondence Information section below. For further information see 37 CFR 1.33(a).	
Customer Number	13565
Email Address	stephanie.seidman@dentons.com
Email Address	mlaipsd@dentons.com

Application Information:

Title of the Invention	PH20 POLYPEPTIDE VARIANTS, FORMULATIONS AND USES THEREOF		
Attorney Docket Number	33320.03087.US27/3087D	Small Entity Status Claimed	☐
Application Type	☒ Nonprovisional ☐ Provisional		
Subject Matter	☒ Utility ☐ Plant ☐ Design		
Total Number of Drawing Sheets (if any)	13	Suggested Figure for Publication (if any)	

Representative Information:

Please Select One:	☐ Customer Number		☒ US Patent Practitioner		☐ Limited Recognition (37 CFR 11.9)	
Prefix	Given Name	Middle Name	Family Name	Suffix		
	Stephanie		Seidman			
Registration Number:		33,779				
Prefix	Given Name	Middle Name	Family Name	Suffix		
	Frank	J.	Miskiel			
Registration Number:		53,332				
Prefix	Given Name	Middle Name	Family Name	Suffix		
	James	M.	Turner			
Registration Number:		74,602				

Application Data Sheet 37 CFR 1.76		Attorney Docket Number	33320.03087.US27/3087D
		Application Number	<u>16/912,590</u>
Title of Invention	PH20 POLYPEPTIDE VARIANTS, FORMULATIONS AND USES THEREOF		

Domestic Benefit/National Stage Information:

This section allows for the applicant to either claim benefit under 35 U.S.C. 119(e), 120, 121, or 365(c) or indicate National Stage entry from a PCT application. Providing this information in the application data sheet constitutes the specific reference required by 35 U.S.C. 119(e) or 120, and 37 CFR 1.78.							
Present Application No.		Continuity Type		Prior Application No.		Filing Date (YYYY-MM-DD)	
Present Application No.	Continuity Type	Prior Application No.		Filing Date (YYYY-MM-DD)	Patent Number	Issue Date (YYYY-MM-DD)	
<i>This application</i>	is a Continuation of	15/226,489		2016-08-02	<u>10,865,400</u>	<u>2020-12-15</u>	
Prior Application No. 15/226,489 - Status:				☒ Patented ☐ Pending ☐ Abandoned ☐ Expired			
Application Number	Continuity Type	Prior Application No.		Filing Date (YYYY-MM-DD)	Patent Number	Issue Date (YYYY-MM-DD)	
15/226,489	is a Divisional of	13/694,731		2012-12-28	9,447,401	2016-09-20	
Prior Application No. 13/694,731 - Status:				☒ Patented ☐ Pending ☐ Abandoned ☐ Expired			
Application Number	Continuity Type	Prior Application No.		Filing Date (YYYY-MM-DD)			
13/694,731	claims priority to	61/796,208		2012-11-01			
Prior Application No. 61/796,208 - Status:				☐ Patented ☐ Pending ☐ Abandoned ☒ Expired			
Application Number	Continuity Type	Prior Application No.		Filing Date (YYYY-MM-DD)			
13/694,731	claims priority to	61/631,313		2011-12-30			
Prior Application No. 61/631,313 - Status:				☐ Patented ☐ Pending ☐ Abandoned ☒ Expired			
Present Application Number	Continuity Type	Prior Application No.		Filing Date (YYYY-MM-DD)	Patent Number	Issue Date (YYYY-MM-DD)	
<i>This application</i>	is a Divisional of	13/694,731		2012-12-28	9,447,401	2016-09-20	
Prior Application No. 13/694,731 - Status:				☒ Patented ☐ Pending ☐ Abandoned ☐ Expired			
Application Number	Continuity Type	Prior Application No.		Filing Date (YYYY-MM-DD)			
13/694,731	claims priority to	61/796,208		2012-11-01			
Prior Application No. 61/796,208 - Status:				☐ Patented ☐ Pending ☐ Abandoned ☒ Expired			
Application Number	Continuity Type	Prior Application No.		Filing Date (YYYY-MM-DD)			
13/694,731	claims priority to	61/631,313		2011-12-30			
Prior Application No. 61/631,313 - Status:				☐ Patented ☐ Pending ☐ Abandoned ☒ Expired			
Foreign Priority Information:							
This section allows for the applicant to claim benefit of foreign priority and to identify any prior foreign application for which priority is not claimed. Providing this information in the application data sheet constitutes the claim for priority as required by 35 U.S.C. 119(b) and 37 CFR 1.55.							
Application Number	Country	Filing Date (YYYY-MM-DD)		Priority Claimed		Access Code (if applicable)	
				☐ Yes ☐ No			

Application Data Sheet 37 CFR 1.76		Attorney Docket Number	33320.03087.US27/3087D
		Application Number	<u>16/912,590</u>
Title of Invention	PH20 POLYPEPTIDE VARIANTS, FORMULATIONS AND USES THEREOF		

Statement under 37 CFR 1.55 or 1.78 for AIA (First Inventor to File) Transition Applications:

☐ If checked, this application (1) claims priority to or the benefit of an application filed before March 16, 2013 and (2) also contains, or contained at any time, a claim to a claimed invention that has an effective filing date on or after March 16, 2013.

Authorization or Opt-Out of Authorization to Permit Access:

When this Application Data Sheet is properly signed and filed with the application, applicant has provided written authority to permit a participating foreign intellectual property (IP) office access to the instant application-as-filed (see paragraph A in subsection 1 below) and the European Patent Office (EPO) access to any search results from the instant application (see paragraph B in subsection 1 below). Should applicant choose not to provide an authorization identified in subsection 1 below, applicant must opt-out of the authorization by checking the corresponding box A or B or both in subsection 2 below.

NOTE: This section of the Application Data Sheet is **ONLY** reviewed and processed with the **INITIAL** filing of an application. After the initial filing of an application, an Application Data Sheet cannot be used to provide or rescind authorization for access by a foreign IP office(s). Instead, Form PTO/SB/39 or PTO/SB/69 must be used as appropriate.

1. Authorization to Permit Access by a Foreign Intellectual Property Office(s)

A. Priority Document Exchange (PDX) - Unless box A in subsection 2 (opt-out of authorization) is checked, the undersigned hereby grants the USPTO authority to provide the European Patent Office (EPO), the Japan Patent Office (JPO), the Korean Intellectual Property Office (KIPO), the State Intellectual Property Office of the People's Republic of China (SIPO), the World Intellectual Property Organization (WIPO), and any other foreign intellectual property office participating with the USPTO in a bilateral or multilateral priority document exchange agreement in which a foreign application claiming priority to the instant patent application is filed, access to: (1) the instant patent application-as-filed and its related bibliographic data, (2) any foreign or domestic application to which priority or benefit is claimed by the instant application and its related bibliographic data, and (3) the date of filing of this Authorization. See 37 CFR 1.14(h)(1).

B. Search Results from U.S. Application to EPO - Unless box B in subsection 2 (opt-out of authorization) is checked, the undersigned hereby grants the USPTO authority to provide the EPO access to the bibliographic data and search results from the instant patent application when a European patent application claiming priority to the instant patent application is filed. See 37 CFR 1.14(h)(2).

The applicant is reminded that the EPO's Rule 141(1) EPC (European Patent Convention) requires applicants to submit a copy of search results from the instant application without delay in a European patent application that claims priority to the instant application.

2. Opt-Out of Authorizations to Permit Access by a Foreign Intellectual Property Office(s)

☐ **A.** Applicant **DOES NOT** authorize the USPTO to permit a participating foreign IP office access to the instant application-as-filed. If this box is checked, the USPTO will not be providing a participating foreign IP office with any documents and information identified in subsection 1A above.

☐ **B.** Applicant **DOES NOT** authorize the USPTO to transmit to the EPO any search results from the instant patent application. If this box is checked, the USPTO will not be providing the EPO with search results from the instant application.

NOTE: Once the application has published or is otherwise publicly available, the USPTO may provide access to the application in accordance with 37 CFR 1.14.

Applicant Information:

Providing assignment information in this section does not substitute for compliance with any requirement of part 3 of Title 37 of CFR to have an assignment recorded by the Office.

Applicant 1

If the applicant is the inventor (or the remaining joint inventor or inventors under 37 CFR 1.45), this section should not be completed. The information to be provided in this section is the name and address of the legal representative who is the applicant under 37 CFR 1.43; or the name and address of the assignee, person to whom the inventor is under an obligation to assign the invention, or person who otherwise shows sufficient proprietary interest in the matter who is the applicant under 37 CFR 1.46. If the applicant is an applicant under 37 CFR 1.46 (assignee, person to whom the inventor is obligated to assign, or person who otherwise shows sufficient proprietary interest) together with one or more joint inventors, then the joint inventor or inventors who are also the applicant should be identified in this section.

☒ Assignee	☐ Legal Representative under 35 U.S.C. 117	☐ Joint Inventor
☐ Person to whom the inventor is obligated to assign	☐ Person who shows sufficient proprietary interest	
If applicant is the legal representative, indicate the authority to file the patent application, the inventor is:		
☐ Deceased	☐ Legally incapacitated	

Application Data Sheet 37 CFR 1.76		Attorney Docket Number	33320.03087.US27/3087D
		Application Number	<u>16/912,590</u>
Title of Invention	PH20 POLYPEPTIDE VARIANTS, FORMULATIONS AND USES THEREOF		
Name of the Deceased or Legally Incapacitated Inventor:			
If the Applicant is an Organization check here.			☒
Organization Name:	HALOZYME, INC.		
Mailing Address Information For Applicant:			
Address 1	11388 Sorrento Valley Road		
Address 2			
City	San Diego	State/Province	CA
Country	US	Postal Code	92121
Phone Number	858-794-8889	Fax Number	858-704-8311
Email Address			
If needed, Additional Applicant Data may be added within this form.			

Signature:

NOTE: This form must be signed in accordance with 37 CFR 1.33. See 37 CFR 1.4 for signature requirements and certifications					
Signature	/Stephanie Seidman/			Date (YYYY-MM-DD)	2021-05-05
First Name	Stephanie	Last Name	Seidman	Registration Number	33,779
Additional Signatures may be added within this form.					

This collection of information is required by 37 CFR 1.76. The information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.14. **SEND TO: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.**

Electronic Acknowledgement Receipt	
EFS ID:	42642325
Application Number:	16912590
International Application Number:	
Confirmation Number:	9651
Title of Invention:	PH20 POLYPEPTIDE VARIANTS, FORMULATIONS AND USES THEREOF
First Named Inventor/Applicant Name:	GE WEI
Customer Number:	13565
Filer:	Stephanie L. Seidman/Rosalind Smith
Filer Authorized By:	Stephanie L. Seidman
Attorney Docket Number:	33320.03087.US27/3087D
Receipt Date:	05-MAY-2021
Filing Date:	25-JUN-2020
Time Stamp:	13:47:42
Application Type:	Utility under 35 USC 111(a)

Payment information:

Submitted with Payment		no			
File Listing:					
Document Number	Document Description	File Name	File Size(Bytes)/ Message Digest	Multi Part /.zip	Pages (if appl.)
1	Transmittal Letter	3087Dtra_05-05-21.pdf	137885	no	1
			d9468ddd9f720d954fb40e9a1914a6c8811 1ec4e		
Warnings:					

Information:					
2	Request for Corrected Filing Receipt	3087Drcfr_05-05-21.pdf	396581	no	6
			842c398d12490b5affe2445c3bd7ceb86dc0831b		
Warnings:					
Information:					
3	Application Data Sheet	3087Dads_05-05-21.pdf	160490	no	5
			9d78da0f6ee3696b84f8b7691505397851c79c7f		
Warnings:					
Information:					
This is not an USPTO supplied ADS fillable form					
Total Files Size (in bytes):			694956		
This Acknowledgement Receipt evidences receipt on the noted date by the USPTO of the indicated documents, characterized by the applicant, and including page counts, where applicable. It serves as evidence of receipt similar to a Post Card, as described in MPEP 503. <u>New Applications Under 35 U.S.C. 111</u> If a new application is being filed and the application includes the necessary components for a filing date (see 37 CFR 1.53(b)-(d) and MPEP 506), a Filing Receipt (37 CFR 1.54) will be issued in due course and the date shown on this Acknowledgement Receipt will establish the filing date of the application. <u>National Stage of an International Application under 35 U.S.C. 371</u> If a timely submission to enter the national stage of an international application is compliant with the conditions of 35 U.S.C. 371 and other applicable requirements a Form PCT/DO/EO/903 indicating acceptance of the application as a national stage submission under 35 U.S.C. 371 will be issued in addition to the Filing Receipt, in due course. <u>New International Application Filed with the USPTO as a Receiving Office</u> If a new international application is being filed and the international application includes the necessary components for an international filing date (see PCT Article 11 and MPEP 1810), a Notification of the International Application Number and of the International Filing Date (Form PCT/RO/105) will be issued in due course, subject to prescriptions concerning national security, and the date shown on this Acknowledgement Receipt will establish the international filing date of the application.					

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Inventor(s)	: Ge Wei <i>et al.</i>	Art Unit	: 1656
Serial No.	: 16/912,590	Examiner	: Samuel W. Liu
Filed	: June 25, 2020	Conf. No.	: 9651
		Cust. No.	: 13565
Title	: PH20 POLYPEPTIDE VARIANTS, FORMULATIONS AND USES THEREOF		

Mail Stop Missing Parts

Commissioner for Patents

P.O. Box 1450

Alexandria, VA 22313-1450

TRANSMITTAL LETTER

Dear Sir:

Transmitted herewith are a *Request for Corrected Filing Receipt*, a copy of the *Filing Receipt*, mailed July 6, 2020, with annotated corrections, and an updated *Application Data Sheet*, for filing in connection with the above-captioned application.

The residence and mailing address of inventor H. Michael Shepard has changed and provision of an updated Filing Receipt is requested to reflect the updated information. A marked-up updated *Application Data Sheet* is filed herewith to provide the Office with inventor H. Michael Shepard's change of address.

A fee for filing this request should not be due. However, should it be determined that a fee for filing these papers is required, the Commissioner is authorized to charge Deposit Account No. 50-0911, as stated below.

☒ The Commissioner is hereby authorized to charge any fees that may be due in connection with this and the attached papers or with this application during its entire pendency to Deposit Account No. 50-0911.

Respectfully submitted,

/Stephanie Seidman/

Stephanie Seidman

Reg. No. 33,779

Attorney Docket No. 33320.03087.US27/3087D

Address all correspondence to: 13565

Stephanie Seidman

Dentons US LLP

4655 Executive Drive, Suite 700

San Diego, CA 92121

Telephone: (619) 595-8010

Facsimile: (619) 595-8135

email: stephanie.seidman@dentons.com

CERTIFICATE OF TRANSMISSION VIA EFS-WEB

I hereby certify that this paper is being transmitted via the Electronic Filing System (EFS-WEB) to the United States Patent and Trademark Office on **May 05, 2021**.

/Rosalind E. Smith/

Rosalind E. Smith



UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NUMBER	FILING or 371(c) DATE	GRP ART UNIT	FIL FEE REC'D	ATTY. DOCKET NO	TOT CLAIMS	IND CLAIMS
16/912,590	06/25/2020	1656	3920	33320.03087.US27/3087D	22	1

CONFIRMATION NO. 9651

CORRECTED FILING RECEIPT



0000000123417403

13565
Dentons US LLP
4655 Executive Drive
Suite 700
San Diego, CA 92121

Date Mailed: 05/07/2021

Receipt is acknowledged of this non-provisional utility patent application. The application will be taken up for examination in due course. Applicant will be notified as to the results of the examination. Any correspondence concerning the application must include the following identification information: the U.S. APPLICATION NUMBER, FILING DATE, NAME OF FIRST INVENTOR, and TITLE OF INVENTION. Fees transmitted by check or draft are subject to collection.

Please verify the accuracy of the data presented on this receipt. If an error is noted on this Filing Receipt, please submit a written request for a corrected Filing Receipt, including a properly marked-up ADS showing the changes with strike-through for deletions and underlining for additions. If you received a "Notice to File Missing Parts" or other Notice requiring a response for this application, please submit any request for correction to this Filing Receipt with your reply to the Notice. When the USPTO processes the reply to the Notice, the USPTO will generate another Filing Receipt incorporating the requested corrections provided that the request is grantable.

Inventor(s)

GE WEI, SAN DIEGO, CA;
H. MICHAEL SHEPARD, Springfield, OR;
QIPING ZHAO, SAN DIEGO, CA;
ROBERT JAMES CONNOR, OCEANSIDE, CA;

Applicant(s)

HALOZYME, INC., SAN DIEGO, CA;

Power of Attorney:

Stephanie Seidman--33779
Frank Miskiel--53332
James Turner--74602

Domestic Priority data as claimed by applicant

This application is a CON of 15/226,489 08/02/2016 PAT 10865400
which is a DIV of 13/694,731 12/28/2012 PAT 9447401
which claims benefit of 61/796,208 11/01/2012
and claims benefit of 61/631,313 12/30/2011
This application 16/912,590
is a DIV of 13/694,731 12/28/2012 PAT 9447401
which claims benefit of 61/796,208 11/01/2012
and claims benefit of 61/631,313 12/30/2011

Foreign Applications for which priority is claimed (You may be eligible to benefit from the **Patent Prosecution Highway** program at the USPTO. Please see <http://www.uspto.gov> for more information.) - None.
Foreign application information must be provided in an Application Data Sheet in order to constitute a claim to foreign priority. See 37 CFR 1.55 and 1.76.

Permission to Access Application via Priority Document Exchange: Yes

Permission to Access Search Results: Yes

Applicant may provide or rescind an authorization for access using Form PTO/SB/39 or Form PTO/SB/69 as appropriate.

If Required, Foreign Filing License Granted: 07/02/2020

The country code and number of your priority application, to be used for filing abroad under the Paris Convention, is **US 16/912,590**

Projected Publication Date: Not Applicable

Non-Publication Request: No

Early Publication Request: No
Title

PH20 POLYPEPTIDE VARIANTS, FORMULATIONS AND USES THEREOF

Preliminary Class

424

Statement under 37 CFR 1.55 or 1.78 for AIA (First Inventor to File) Transition Applications: No

PROTECTING YOUR INVENTION OUTSIDE THE UNITED STATES

Since the rights granted by a U.S. patent extend only throughout the territory of the United States and have no effect in a foreign country, an inventor who wishes patent protection in another country must apply for a patent in a specific country or in regional patent offices. Applicants may wish to consider the filing of an international application under the Patent Cooperation Treaty (PCT). An international (PCT) application generally has the same effect as a regular national patent application in each PCT-member country. The PCT process **simplifies** the filing of patent applications on the same invention in member countries, but **does not result** in a grant of "an international patent" and does not eliminate the need of applicants to file additional documents and fees in countries where patent protection is desired.

Almost every country has its own patent law, and a person desiring a patent in a particular country must make an application for patent in that country in accordance with its particular laws. Since the laws of many countries differ in various respects from the patent law of the United States, applicants are advised to seek guidance from specific foreign countries to ensure that patent rights are not lost prematurely.

Applicants also are advised that in the case of inventions made in the United States, the Director of the USPTO must issue a license before applicants can apply for a patent in a foreign country. The filing of a U.S. patent application serves as a request for a foreign filing license. The application's filing receipt contains further information and guidance as to the status of applicant's license for foreign filing.

Applicants may wish to consult the USPTO booklet, "General Information Concerning Patents" (specifically, the section entitled "Treaties and Foreign Patents") for more information on timeframes and deadlines for filing foreign patent applications. The guide is available either by contacting the USPTO Contact Center at 800-786-9199, or it can be viewed on the USPTO website at <http://www.uspto.gov/web/offices/pac/doc/general/index.html>.

For information on preventing theft of your intellectual property (patents, trademarks and copyrights), you may wish to consult the U.S. Government website, <http://www.stopfakes.gov>. Part of a Department of Commerce initiative, this website includes self-help "toolkits" giving innovators guidance on how to protect intellectual property in specific countries such as China, Korea and Mexico. For questions regarding patent enforcement issues, applicants may call the U.S. Government hotline at 1-866-999-HALT (1-866-999-4258).

LICENSE FOR FOREIGN FILING UNDER
Title 35, United States Code, Section 184
Title 37, Code of Federal Regulations, 5.11 & 5.15

GRANTED

The applicant has been granted a license under 35 U.S.C. 184, if the phrase "IF REQUIRED, FOREIGN FILING LICENSE GRANTED" followed by a date appears on this form. Such licenses are issued in all applications where the conditions for issuance of a license have been met, regardless of whether or not a license may be required as set forth in 37 CFR 5.15. The scope and limitations of this license are set forth in 37 CFR 5.15(a) unless an earlier license has been issued under 37 CFR 5.15(b). The license is subject to revocation upon written notification. The date indicated is the effective date of the license, unless an earlier license of similar scope has been granted under 37 CFR 5.13 or 5.14.

This license is to be retained by the licensee and may be used at any time on or after the effective date thereof unless it is revoked. This license is automatically transferred to any related applications(s) filed under 37 CFR 1.53(d). This license is not retroactive.

The grant of a license does not in any way lessen the responsibility of a licensee for the security of the subject matter as imposed by any Government contract or the provisions of existing laws relating to espionage and the national security or the export of technical data. Licensees should apprise themselves of current regulations especially with respect to certain countries, of other agencies, particularly the Office of Defense Trade Controls, Department of State (with respect to Arms, Munitions and Implements of War (22 CFR 121-128)); the Bureau of Industry and Security, Department of Commerce (15 CFR parts 730-774); the Office of Foreign Assets Control, Department of Treasury (31 CFR Parts 500+) and the Department of Energy.

NOT GRANTED

No license under 35 U.S.C. 184 has been granted at this time, if the phrase "IF REQUIRED, FOREIGN FILING LICENSE GRANTED" DOES NOT appear on this form. Applicant may still petition for a license under 37 CFR 5.12, if a license is desired before the expiration of 6 months from the filing date of the application. If 6 months has lapsed from the filing date of this application and the licensee has not received any indication of a secrecy order under 35 U.S.C. 181, the licensee may foreign file the application pursuant to 37 CFR 5.15(b).

SelectUSA

The United States represents the largest, most dynamic marketplace in the world and is an unparalleled location for business investment, innovation, and commercialization of new technologies. The U.S. offers tremendous resources and advantages for those who invest and manufacture goods here. Through SelectUSA, our nation works to promote and facilitate business investment. SelectUSA provides information assistance to the international investor community; serves as an ombudsman for existing and potential investors; advocates on behalf of U.S. cities, states, and regions competing for global investment; and counsels U.S. economic development organizations on investment attraction best practices. To learn more about why the United States is the best country in the world to develop technology, manufacture products, deliver services, and grow your business, visit <http://www.SelectUSA.gov> or call +1-202-482-6800.

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Inventors	: Ge WEI <i>et al.</i>	Art Unit	: 1656
Serial No.	: 16/912,590	Examiner	: Samuel W. LIU
Filed	: June 25, 2020	Conf. No.	: 9651
		Cust. No.	: 13565
Title	: PH20 POLYPEPTIDE VARIANTS, FORMULATIONS AND USES THEREOF		

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Commissioner for Patents
U.S. Patent and Trademark Office
P.O. Box 1450
Alexandria, VA 22313-1450

AMENDMENT PURSUANT TO 37 C.F.R. §1.312

Dear Sir:

Responsive to the *Notice of Allowance*, mailed April 14, 2021, the following amendment and consideration of the following remarks respectfully are requested.

Amendments to the claims begin on page 2 of this paper.

Remarks begin on page 5 of this paper.

CERTIFICATE OF TRANSMISSION VIA EFS-WEB

I hereby certify that this paper is being transmitted via the Electronic Filing System (EFS-WEB) to the United States Patent and Trademark Office on **May 21, 2021**.

/Rosalind E. Smith/

Rosalind E. Smith

Electronic Acknowledgement Receipt	
EFS ID:	42792316
Application Number:	16912590
International Application Number:	
Confirmation Number:	9651
Title of Invention:	PH20 POLYPEPTIDE VARIANTS, FORMULATIONS AND USES THEREOF
First Named Inventor/Applicant Name:	GE WEI
Customer Number:	13565
Filer:	Stephanie L. Seidman/Rosalind Smith
Filer Authorized By:	Stephanie L. Seidman
Attorney Docket Number:	33320.03087.US27/3087D
Receipt Date:	21-MAY-2021
Filing Date:	25-JUN-2020
Time Stamp:	19:16:51
Application Type:	Utility under 35 USC 111(a)

Payment information:

Submitted with Payment		no			
File Listing:					
Document Number	Document Description	File Name	File Size(Bytes)/ Message Digest	Multi Part /.zip	Pages (if appl.)
1	Transmittal Letter	3087Dtra_05-21-21.pdf	161999	no	1
			a8bc3bb2be1c83f33f62df86bb20a794a0719bc9		
Warnings:					

Information:					
2		3087Damd312_05-21-21.pdf	151217	yes	5
			86a35b4b6706525173bbafae0432240fba6d4f04		
	Multipart Description/PDF files in .zip description				
	Document Description		Start	End	
	Applicant Arguments/Remarks Made in an Amendment		5	5	
	Claims		2	4	
	Amendment after Notice of Allowance (Rule 312)		1	1	
Warnings:					
Information:					
Total Files Size (in bytes):			313216		
This Acknowledgement Receipt evidences receipt on the noted date by the USPTO of the indicated documents, characterized by the applicant, and including page counts, where applicable. It serves as evidence of receipt similar to a Post Card, as described in MPEP 503. <u>New Applications Under 35 U.S.C. 111</u> If a new application is being filed and the application includes the necessary components for a filing date (see 37 CFR 1.53(b)-(d) and MPEP 506), a Filing Receipt (37 CFR 1.54) will be issued in due course and the date shown on this Acknowledgement Receipt will establish the filing date of the application. <u>National Stage of an International Application under 35 U.S.C. 371</u> If a timely submission to enter the national stage of an international application is compliant with the conditions of 35 U.S.C. 371 and other applicable requirements a Form PCT/DO/EO/903 indicating acceptance of the application as a national stage submission under 35 U.S.C. 371 will be issued in addition to the Filing Receipt, in due course. <u>New International Application Filed with the USPTO as a Receiving Office</u> If a new international application is being filed and the international application includes the necessary components for an international filing date (see PCT Article 11 and MPEP 1810), a Notification of the International Application Number and of the International Filing Date (Form PCT/RO/105) will be issued in due course, subject to prescriptions concerning national security, and the date shown on this Acknowledgement Receipt will establish the international filing date of the application.					

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Inventor	: Ge WEI <i>et al.</i>	Art Unit	: 1656
Serial No.	: 16/912,590	Examiner	: Samuel W. LIU
Filed	: June 25, 2020	Conf. No.	: 9651
		Cust. No.	: 13565
Title	: PH20 POLYPEPTIDE VARIANTS, FORMULATIONS AND USES THEREOF		

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Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

TRANSMITTAL LETTER

Dear Sir:

Transmitted herewith is an *Amendment Pursuant to 37 C.F.R. § 1.312* (5 pages) for filing in connection with the above-identified application.

☒ The Commissioner is hereby authorized to charge any fees that may be due in connection with this paper or with this application during its entire pendency to Deposit Account No. 50-0911.

Respectfully submitted,

/Stephanie Seidman/
Stephanie Seidman
Reg. No. 33,779

Attorney Docket No. 33320.03087.US27/3087D
Address all correspondence to: 13565
Stephanie Seidman
Dentons US LLP
4655 Executive Drive, Ste. 700
San Diego, California 92121
Telephone: (619) 595-8010
Facsimile: (619) 595-8135
email: stephanie.seidman@dentons.com

CERTIFICATE OF TRANSMISSION BY EFS-WEB

I hereby certify that this paper is being transmitted via the Electronic Filing System (EFS-WEB) to the United States Patent and Trademark Office on **May 21, 2021**.

/Rosalind E. Smith/
Rosalind E. Smith

Inventor(s): Wei *et al.*
Serial No. : 16/912,590
Filed : June 25, 2020

Attorney Docket No.: 33320.03087.US27/3087D
Amendment Pursuant to 37 C.F.R. §1.312

REMARKS

Any fees that may be due in connection with this paper or this application during its entire pendency should be charged to Deposit Account No. 50-0911. If a Petition for extension of time is needed, this paper is to be considered such Petition.

Amendment of the Claims:

Applicant acknowledges the *Notice of Allowance*, mailed April 14, 2021, in which claims 1-21 and 23-26 are allowed. The listing of claims incorporates the Examiner's amendments in the *Notice of Allowance*, mailed April 14, 2021. In reviewing the claims for payment of the issue fee, minor obvious typographical errors and inconsistencies were identified. Claims 1, 13-15, 19 and 23 are amended to correct these errors. Claim 1 is amended to correct the obvious typographical error in the recitation of "SEQ ID NOs" that was introduced in the Examiner's Amendment. Claim 1 also is amended to render it clear that an amino acid replacement at position 309 confers increased hyaluronidase activity. Claim 14 is amended to recite that the modified polypeptide has least 91% sequence identity to the reference amino acid sequence, to conform to the language of claim 1, on which it depends. Claim 15 is amended to correct the spelling of the word "sialylation." Claim 19 is amended to include the comma that was inadvertently deleted in the Examiner's Amendment. Claims 13, 14 and 23 are amended to recite that the replacement is at a position corresponding to residue 309, to conform to the language of claim 1, on which they depend. Since the amendments correct minor errors, for clarity, they do not affect patentability of the claims. No new matter is added.

* * *

Entry of the amendments and remarks into the file history of the above-captioned application respectfully is requested.

Respectfully submitted,

/Stephanie Seidman/

Stephanie Seidman

Reg. No. 33,779

Attorney Docket No.: 33320.03087.US27/3087D

Address all correspondence to: 13565

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AMENDMENTS TO THE CLAIMS:

Please amend claims 1, 13-15, 19 and 23, as indicated below. This listing of claims replaces all prior versions and listing of claims in the application.

LISTING OF CLAIMS:

1. (Currently Amended) A modified PH20 polypeptide, comprising one or more amino acid replacements in an unmodified PH20 polypeptide, wherein:
 - the unmodified PH20 polypeptide consists of the amino acid sequence selected from the group consisting of SEQ ID NOs~~SEP ID NOs~~: 3, 7 and 32-66;
 - the modified PH20 polypeptide exhibits increased hyaluronidase activity compared to the unmodified PH20 polypeptide not containing the amino acid replacement(s);
 - the amino acid replacement(s) confer(s) the increased hyaluronidase activity;
 - an amino acid replacement that confers the increased hyaluronidase activity ~~and~~ is at a position corresponding to residue 309, with reference to amino acid positions of SEQ ID NO:3;
 - corresponding amino acid positions are identified by alignment of the PH20 polypeptide with the polypeptide having the amino acid sequence of SEQ ID NO:3; and
 - the modified PH20 polypeptide has at least 91% sequence identity to the amino acid sequence selected from the group consisting of SEQ ID NOs: 3, 7 and 32-66.
2. (Previously Presented) The modified PH20 polypeptide of claim 1, wherein the modified PH20 polypeptide has at least 95% sequence identity to the amino acid sequence selected from the group consisting of SEQ ID NOs: 3, 7, and 32-66.
3. (Original) The modified PH20 polypeptide of claim 2 that is a soluble PH20 polypeptide.
4. (Previously Presented) The modified PH20 polypeptide of claim 1, wherein the replacement is selected from among L at a position corresponding to position 309; N at a position corresponding to position 309; E at a position corresponding to position 309; G at a position corresponding to position 309; H at a position corresponding to position 309; and M at a position corresponding to position 309.
5. (Previously Presented) The modified PH20 polypeptide of claim 4, wherein the replacement at the position corresponding to position 309 is N.
6. (Previously Presented) The modified PH20 polypeptide of claim 1, wherein the unmodified PH20 polypeptide consists of the amino acid sequence selected from the group consisting of SEQ ID NOs: 3 and 32-66.

7. (Previously Presented) The modified PH20 polypeptide of claim 2, wherein the unmodified PH20 polypeptide consists of the amino acid sequence selected from the group consisting of SEQ ID NOs: 3 and 32-66.

8. (Previously Presented) The modified PH20 polypeptide of claim 5, wherein the unmodified PH20 polypeptide consists of the amino acid sequence selected from the group consisting of SEQ ID NOs: 3 and 32-66.

9. (Previously Presented) The modified PH20 polypeptide of claim 1, wherein the unmodified PH20 polypeptide consists of the amino acid sequence of SEQ ID NO:35.

10. (Previously Presented) The modified PH20 polypeptide of claim 1, wherein the unmodified PH20 polypeptide consists of the amino acid sequence of SEQ ID NO:32.

11. (Previously Presented) The modified PH20 polypeptide of claim 5, wherein the unmodified PH20 polypeptide consists of the amino acid sequence of SEQ ID NO:35.

12. (Original) The modified PH20 polypeptide of claim 1, wherein the modified PH20 polypeptide exhibits increased hyaluronidase activity that is at least 120% of the hyaluronidase activity compared to the unmodified PH20 polypeptide not containing the amino acid replacement or replacements.

13. (Currently Amended) The modified PH20 polypeptide of claim 1, comprising the amino acid sequence selected from the group consisting of SEQ ID NOs:576-586, or an amino acid sequence that exhibits at least 91% sequence identity to the amino acid sequence selected from the group consisting of SEQ ID NOs:3 and 32-66 and that contains the amino acid replacement L, N, E, G, H, M, Q, R, S, T or V at a position corresponding to residue 309.

14. (Currently Amended) The modified PH20 polypeptide of claim 1, comprising the amino acid sequence of SEQ ID NO:581, or an amino acid sequence that ~~has~~exhibits at least 91% sequence identity to the amino acid sequence selected from the group consisting of SEQ ID NOs: 3 and 32-66 and that contains the amino acid replacement N at a position corresponding to residue 309.

15. (Currently Amended) The modified PH20 polypeptide of claim 1 that further comprises one or more modifications selected from among glycosylation, ~~sialylation~~sialination, albumination, farnesylation, carboxylation, hydroxylation, and phosphorylation.

16. (Previously Presented) The modified PH20 polypeptide of claim 1 that further comprises an N-acetylglucosamine moiety linked to each of at least three asparagine (N) residues.

17. (Original) The modified PH20 polypeptide of claim 1 that is conjugated to a polymer.
18. (Previously Presented) The modified PH20 polypeptide of claim 17, wherein the polymer is dextran or polyethylene glycol (PEG).
19. (Currently Amended) The modified PH20 polypeptide of claim 1, further comprising a heterologous signal sequence, wherein the unmodified PH20 polypeptide consists of the amino acid sequence selected from the group consisting of SEQ ID NOs: 3 and 32-66.
20. (Original) A chimeric polypeptide, comprising the modified PH20 polypeptide of claim 1.
21. (Original) A pharmaceutical composition, comprising the modified PH20 polypeptide of claim 1.
22. (Cancelled)
23. (Currently Amended) The modified PH20 polypeptide of claim 1, comprising the amino acid sequence of SEQ ID NO:581, or an amino acid sequence that exhibits at least 95% sequence identity to the amino acid sequence of SEQ ID NO:581 and that contains the amino acid replacement N at a position corresponding to residue 309.
24. (Previously Presented) The modified PH20 polypeptide of claim 5, wherein:
the unmodified PH20 polypeptide consists of the amino acid sequence set forth in SEQ ID NO:32; and
the amino acid sequence of the modified PH20 polypeptide has at least 95% sequence identity to SEQ ID NO:32.
25. (Previously Presented) The modified PH20 polypeptide of claim 5, wherein:
the unmodified PH20 polypeptide consists of the amino acid sequence set forth in SEQ ID NO:35; and
the amino acid sequence of the modified PH20 polypeptide has at least 95% sequence identity to SEQ ID NO:35.
26. (Previously Presented) The modified PH20 polypeptide of claim 1, further comprising a signal sequence, wherein the unmodified PH20 polypeptide consists of the amino acid sequence selected from the group consisting of SEQ ID NOs: 3 and 32-66.



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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
16/912,590	06/25/2020	GE WEI	33320.03087.US27/3087D	9651
13565	7590	06/03/2021	EXAMINER	
Dentons US LLP 4655 Executive Drive Suite 700 San Diego, CA 92121			LIU, SAMUEL W	
			ART UNIT	PAPER NUMBER
			1656	
			NOTIFICATION DATE	DELIVERY MODE
			06/03/2021	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

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MLAIPSD@Dentons.com
lucy.begalla@dentons.com
rosalind.smith@dentons.com

Response to Rule 312 Communication	Application No. 16/912,590	Applicant(s) WEI et al.	
	Examiner SAMUEL W LIU	Art Unit 1656	AIA (FITF) Status No
-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address -- 1. ☒ The amendment filed on <u>21 May 2021</u> under 37 CFR 1.312 has been considered, and has been: a) ☒ entered. b) ☐ entered as directed to matters of form not affecting the scope of the invention. c) ☐ disapproved because the amendment was filed after the payment of the issue fee. Any amendment filed after the date the issue fee is paid must be accompanied by a petition under 37 CFR 1.313(c)(1) and the required fee to withdraw the application from issue. d) ☐ disapproved. See explanation below. e) ☐ entered in part. See explanation below. _____			
/SAMUEL W LIU/ Examiner, Art Unit 1656		/SCARLETT Y GOON/ QAS, Art Unit 1600	

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Inventor	: Ge WEI <i>et al.</i>	Art Unit	: 1656
Serial No.	: 16/912,590	Examiner	: Samuel W. LIU
Filed	: June 25, 2020	Conf. No.	: 9651
		Cust. No.	: 13565
Title	: PH20 POLYPEPTIDE VARIANTS, FORMULATIONS AND USES THEREOF		

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Respectfully submitted,

/Stephanie Seidman/
Stephanie Seidman
Reg. No. 33,779

Attorney Docket No. 33320.03087.US27/3087D
Address all correspondence to: 13565
Stephanie Seidman
Dentons US LLP
4655 Executive Drive, Ste. 700
San Diego, California 92121
Telephone: (619) 595-8010
Facsimile: (619) 595-8135
email: stephanie.seidman@dentons.com

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Rosalind E. Smith

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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
16/912,590	06/25/2020	GE WEI	33320.03087.US27/3087D	9651

TITLE OF INVENTION: PH20 POLYPEPTIDE VARIANTS, FORMULATIONS AND USES THEREOF

APPLN. TYPE	ENTITY STATUS	ISSUE FEE	PUBLICATION FEE	PREV. PAID ISSUE FEE	TOTAL FEE(S) DUE	DATE DUE
NONPROVISIONAL	UNDISCOUNTED	\$1200	\$0	\$0	\$1200	07/14/2021

EXAMINER	ART UNIT	CLASS-SUBCLASS
LIU, SAMUEL W.	1656	424-094620

1. Change of correspondence address or indication of "Fee Address" (37 CFR 1.363).

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1. **Dentons US LLP**
2. **Stephanie Seidman**
- 3.

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(B) RESIDENCE (CITY AND STATE OR COUNTRY)

Halozyyme, Inc.

San Diego, California

Please check the appropriate assignee category or categories (will not be printed on the patent): ☐ individual ☒ corporation or other private group entity ☐ government

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- ☐ a. Applicant claims MICRO ENTITY status. See 37 CFR 1.29.
☐ b. Applicant claims SMALL ENTITY status. See 37 CFR 1.27.
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(Authorized Signature) **/Stephanie Seidman/**
Typed or Printed Name **Stephanie Seidman**

(Date) **June 4, 2021**
Registration No. **33,779**

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APPLICATION NO. 16/912,590	FILING DATE 06/25/2020	FIRST NAMED INVENTOR GE WEI	ATTORNEY DOCKET NO. 33320.03087.US27/3087D	CONFIRMATION NO. 9651
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TITLE OF INVENTION: PH20 POLYPEPTIDE VARIANTS, FORMULATIONS AND USES THEREOF

APPLN. TYPE NONPROVISIONAL	ENTITY STATUS UNDISCOUNTED	ISSUE FEE \$1200	PUBLICATION FEE \$0	PREV. PAID ISSUE FEE \$0	TOTAL FEE(S) DUE \$1200	DATE DUE 07/14/2021
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EXAMINER LIU, SAMUEL W.	ART UNIT 1656	CLASS-SUBCLASS 424-094620
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2. **Stephanie Seidman**

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(B) RESIDENCE (CITY AND STATE OR COUNTRY)

Halozyyme, Inc.

San Diego, California

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☐ a. Applicant claims MICRO ENTITY status. See 37 CFR 1.29.

☐ b. Applicant claims SMALL ENTITY status. See 37 CFR 1.27.

☐ c. Applicant changing to regular UNDISCOUNTED fee status.

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(Authorized Signature) **/Stephanie Seidman/**

(Date) **June 4, 2021**

Typed or Printed Name **Stephanie Seidman**

Registration No. **33,779**

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Inventors	: Wei <i>et al.</i>	Art Unit	: 1656
Serial No.	: 16/912,590	Examiner	: Liu, Samuel W.
Filed	: June 25, 2020	Conf. No.	: 9651
		Cust. No.	: 13565
Title	: PH20 POLYPEPTIDE VARIANTS, FORMULATIONS AND USES THEREOF		

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COMMENTS ON EXAMINER'S REASONS FOR ALLOWANCE

Dear Sir:

Entry of the following amendment and consideration of the following remarks respectfully are requested. This amendment is filed concurrently with the payment of the issue fee.

Responsive to the Examiner's Reasons for Allowance, set forth with the *Notice of Allowance*, mailed April 14, 2021, entry of the following comments into the file history of the above-captioned application respectfully is requested.

Remarks begin on page 2 of this paper.

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/Rosalind E. Smith/

Rosalind E. Smith

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Comments on Statement of Reasons for Allowance:

The closest prior art is US20130071394 ('394) which discloses variant PH20 polypeptides (from human or non-human species) or truncated mutant forms thereof wherein the variant PH20 polypeptide ([0026]-[0028], '394) contains amino acid substitutions ([0150], '394). However, '394 does not teach or suggest that the modified PH20 polypeptide comprises the substitution at position 309 wherein the resultant modified PH20 has increased hyaluronidase activity and has at least 91% sequence identity to the unmodified PH20 polypeptide of SEQ ID NO:3 (a mature human PH20 polypeptide) or to the unmodified PH20 polypeptide of SEQ ID NO: 7 (a full-length human PH20 polypeptide) or to one of unmodified PH20 polypeptides of SEQ ID NOs: 32-66 (mature human PH20 polypeptides with amino acid truncation at C-terminal region) as set forth in claim 1. While '394 has taught that the PH20 polypeptide can comprise substitution mutations, '394 does not teach or suggest which amino acid residues are substituted to achieve the increased hyaluronidase activity as recited in the claimed "modified PH20 polypeptide" comprising the amino acid substitution at residue 309 which confers the increased hyaluronidase activity recited in the claim 1. It is noted that all of the unmodified PH20 polypeptides of SEQ ID NOs:3, 7 and 32-66 have the identical sequences at residues 1-465; and thus, the sequence of the modified PH20 comprising the substitution at residue 309 can be determined as compared to the unmodified PH20 polypeptide sequences. Thus, the claimed modified PH20 polypeptide (claim 1) is free from prior art. Therefore, claims 1-21 and 23-26 are allowed.

In accord with MPEP §1302.14, the Examiner's reasons for allowance need not set forth all of the details why the claims are allowed. Applicant does not concede that the Examiner's stated reasons for allowance are the only reasons for which the claims are allowable. As discussed below, the claims may be patentable for additional reasons.

The claims are directed to modified PH20 polypeptides, comprising one or more amino acid modifications, where one modification is an amino acid replacement at position 309, where the replacement confers increased hyaluronidase activity compared to a corresponding unmodified PH20 polypeptide not containing the amino acid replacement. The claims also are directed to chimeric polypeptides and pharmaceutical compositions comprising the modified PH20 polypeptides. The modified PH20 polypeptides are not found in nature. The modified PH20 polypeptides have at least 91% sequence identity to the amino acid sequence selected from among SEQ ID NOs: 3, 7, and 32-66; SEQ ID NO:7 corresponds to the full-length sequence of the unmodified, mature human PH20 polypeptide, and SEQ ID NOS: 3 and 32-66 correspond to C-terminally truncated soluble forms of the full-length polypeptide whose sequence is set forth in SEQ ID NO:7.

Applicant agrees with the Examiner that no art of any record, including U.S. Patent Publication No. 2013/0071394 ('394), which was not raised in a rejection under 35 U.S.C. § 102 or 35 U.S.C. § 103 during prosecution of the instant application, teaches or suggests a modification in PH20 polypeptide that is an amino acid modification at a position corresponding to position 309, and nor does any art of record disclose, teach or suggest the instantly claimed modified PH20 polypeptides, nor the properties thereof.

The '394 publication teaches the various soluble forms of the PH20 hyaluronidase in a co-formulation compositions that contains a soluble PH20 and an organophosphorus bioscavenger. Paragraph 150 of the '394 publication recites that the soluble PH20 in general can include variants thereof; there is no teaching or suggestion of a replacement at position 309. The '394 publication allows for some modification of the soluble hyaluronidases; it does not teach particular modifications nor modifications of the residue at the position corresponding to residue 309. Hence, the '394 publication is of no relevance to the allowed claims.

The instantly claimed modified PH20 polypeptides comprise one or more amino acid modifications, where one of the modifications is an amino acid replacement at a position corresponding to position 309; have at least 91% sequence identity to any of SEQ ID NOs: 3, 7, and 32-66; and include modifications at a position corresponding to residue 309 that increase hyaluronidase activity of a soluble form of the PH20. The extensive working examples provided in the instant application provide a structure/function survey of PH20, and identify the effects of about 7000 modifications. For example, Example 4 provides the results of testing about 6,700 modifications on activities and properties of the resulting PH20 polypeptides (see, *e.g.*, Table 8). The Example shows amino acid replacements at residue 309 that increase hyaluronidase activity compared to PH20 polypeptide that does contain such modification. There is no disclosure, teaching or suggestion in the '394 publication to replace the residue at position 309, nor does it teach or suggest the effect of any such modification.

Inventor(s): Wei *et al.*
Serial No. : 16/912,590
Filed : June 25, 2020

Attorney Docket No.: 33320.03087.US27/3087D
Comments on Reasons for Allowance

Entry of the remarks into the file history of the above-captioned application
respectfully is requested.

Respectfully submitted,

/Stephanie Seidman/

Stephanie Seidman

Reg. No. 33,779

Attorney Docket No.: 33320.03087.US27/3087D

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Electronic Patent Application Fee Transmittal				
Application Number:		16912590		
Filing Date:		25-Jun-2020		
Title of Invention:		PH20 POLYPEPTIDE VARIANTS, FORMULATIONS AND USES THEREOF		
First Named Inventor/Applicant Name:		GE WEI		
Filer:		Stephanie L. Seidman/Rosalind Smith		
Attorney Docket Number:		33320.03087.US27/3087D		
Filed as Large Entity				
Filing Fees for Utility under 35 USC 111(a)				
Description	Fee Code	Quantity	Amount	Sub-Total in USD(\$)
Basic Filing:				
Pages:				
Claims:				
Miscellaneous-Filing:				
Petition:				
Patent-Appeals-and-Interference:				
Post-Allowance-and-Post-Issuance:				

Description	Fee Code	Quantity	Amount	Sub-Total in USD(\$)
PUBL. FEE- EARLY, VOLUNTARY, OR NORMAL	1504	1	0	0
UTILITY APPL ISSUE FEE	1501	1	1200	1200
Extension-of-Time:				
Miscellaneous:				
PRINTED COPY OF PATENT - NO COLOR	8001	14	3	42
Total in USD (\$)				1242

Electronic Acknowledgement Receipt	
EFS ID:	42893031
Application Number:	16912590
International Application Number:	
Confirmation Number:	9651
Title of Invention:	PH20 POLYPEPTIDE VARIANTS, FORMULATIONS AND USES THEREOF
First Named Inventor/Applicant Name:	GE WEI
Customer Number:	13565
Filer:	Stephanie L. Seidman/Rosalind Smith
Filer Authorized By:	Stephanie L. Seidman
Attorney Docket Number:	33320.03087.US27/3087D
Receipt Date:	04-JUN-2021
Filing Date:	25-JUN-2020
Time Stamp:	14:25:00
Application Type:	Utility under 35 USC 111(a)

Payment information:

Submitted with Payment	yes
Payment Type	DA
Payment was successfully received in RAM	\$1242
RAM confirmation Number	E202164E25553229
Deposit Account	500911
Authorized User	Rosalind Smith
The Director of the USPTO is hereby authorized to charge indicated fees and credit any overpayment as follows: 37 CFR 1.16 (National application filing, search, and examination fees) 37 CFR 1.17 (Patent application and reexamination processing fees)	

37 CFR 1.19 (Document supply fees)					
37 CFR 1.20 (Post Issuance fees)					
37 CFR 1.21 (Miscellaneous fees and charges)					
File Listing:					
Document Number	Document Description	File Name	File Size(Bytes)/ Message Digest	Multi Part /.zip	Pages (if appl.)
1	Transmittal Letter	3087Dtra_06-04-21.pdf	165071	no	1
			7c0088e4fea46a6f78a995872497b13036f8b400		
Warnings:					
Information:					
2	Issue Fee Payment (PTO-85B)	3087Difp_06-04-21.pdf	318682	no	2
			006e14a177eeaf85a8ae12de99d6807897c9b0c9		
Warnings:					
Information:					
3	Post Allowance Communication - Incoming	3087Dcra_06-04-21.pdf	149235	no	4
			4ec516feb0d427e49cba27651f25d171e78760c4		
Warnings:					
Information:					
4	Fee Worksheet (SB06)	fee-info.pdf	33822	no	2
			d9c6212d2365a0a1f52dcc2a53995718c80f3eb0		
Warnings:					
Information:					
Total Files Size (in bytes):			666810		

This Acknowledgement Receipt evidences receipt on the noted date by the USPTO of the indicated documents, characterized by the applicant, and including page counts, where applicable. It serves as evidence of receipt similar to a Post Card, as described in MPEP 503.

New Applications Under 35 U.S.C. 111

If a new application is being filed and the application includes the necessary components for a filing date (see 37 CFR 1.53(b)-(d) and MPEP 506), a Filing Receipt (37 CFR 1.54) will be issued in due course and the date shown on this Acknowledgement Receipt will establish the filing date of the application.

National Stage of an International Application under 35 U.S.C. 371

If a timely submission to enter the national stage of an international application is compliant with the conditions of 35 U.S.C. 371 and other applicable requirements a Form PCT/DO/EO/903 indicating acceptance of the application as a national stage submission under 35 U.S.C. 371 will be issued in addition to the Filing Receipt, in due course.

New International Application Filed with the USPTO as a Receiving Office

If a new international application is being filed and the international application includes the necessary components for an international filing date (see PCT Article 11 and MPEP 1810), a Notification of the International Application Number and of the International Filing Date (Form PCT/RO/105) will be issued in due course, subject to prescriptions concerning national security, and the date shown on this Acknowledgement Receipt will establish the international filing date of the application.



UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	ISSUE DATE	PATENT NO.	ATTORNEY DOCKET NO.	CONFIRMATION NO.
16/912,590	07/20/2021	11066656	33320.03087.US27/3087D	9651

13565 7590 06/30/2021
Dentons US LLP
4655 Executive Drive
Suite 700
San Diego, CA 92121

ISSUE NOTIFICATION

The projected patent number and issue date are specified above.

Determination of Patent Term Adjustment under 35 U.S.C. 154 (b) (application filed on or after May 29, 2000)

The Patent Term Adjustment is 0 day(s). Any patent to issue from the above-identified application will include an indication of the adjustment on the front page.

If a Continued Prosecution Application (CPA) was filed in the above-identified application, the filing date that determines Patent Term Adjustment is the filing date of the most recent CPA.

Applicant will be able to obtain more detailed information by accessing the Patent Application Information Retrieval (PAIR) WEB site (<http://pair.uspto.gov>).

Any questions regarding the Patent Term Extension or Adjustment determination should be directed to the Office of Patent Legal Administration at (571)-272-7702. Questions relating to issue and publication fee payments should be directed to the Application Assistance Unit (AAU) of the Office of Data Management (ODM) at (571)-272-4200.

APPLICANT(s) (Please see PAIR WEB site <http://pair.uspto.gov> for additional applicants):

HALOZYME, INC., SAN DIEGO, CA;
GE WEI, SAN DIEGO, CA;
H. MICHAEL SHEPARD, Springfield, OR;
QIPING ZHAO, SAN DIEGO, CA;
ROBERT JAMES CONNOR, OCEANSIDE, CA;

The United States represents the largest, most dynamic marketplace in the world and is an unparalleled location for business investment, innovation, and commercialization of new technologies. The USA offers tremendous resources and advantages for those who invest and manufacture goods here. Through SelectUSA, our nation works to encourage and facilitate business investment. To learn more about why the USA is the best country in the world to develop technology, manufacture products, and grow your business, visit SelectUSA.gov.

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Inventor(s):	Wei <i>et al.</i>	Art Unit	: 1656
Patent No.:	11,066,656	Examiner	: Liu, Samuel W.
Issue Date:	July 20, 2021	Conf. No.	: 9651
Serial No.:	16/912,590	Cust. No.	: 13565
Filed	: June 25, 2020		
Title	: PH20 POLYPEPTIDE VARIANTS, FORMULATIONS AND USES THEREOF		

Attn.: Certificate of Correction Branch

Commissioner for Patents

P.O. Box 1450

Alexandria, VA 22313-1450

REQUEST FOR CERTIFICATE OF CORRECTION

Dear Sir:

Pursuant to 37 C.F.R. § 1.322, the patentee respectfully requests that a Certificate of Correction be issued for the above referenced patent to correct the following errors:

IN THE TITLE PAGES:

In Item (56) References Cited, in OTHER PUBLICATIONS, at page 3, 2nd column, line 71, please replace “lip” with —trp—;

IN THE SPECIFICATION:

At column 20, line 46, please replace "Rat a position" with —R at a position—;

At column 33, line 48, please replace "Tales" with —Talcs—;

At column 34, line 60, please replace "Antithrombin II 1s" with —Antithrombin
IIIs—;

At column 84, line 61, please replace "1271" with —I271—;

At column 88, line 13, please replace "Rat a position" with —R at a position—;

At column 136, line 4, please replace "W138" with —WI38—;

At column 140, line 55, please replace "GALS" with —GAL5—;

At column 176, line 20, please replace "Tales" with —Talcs—;

At column 177, line 39, please replace "Tales" with —Talcs—;

At column 179, line 53, please replace "Tales" with —Talcs—;

CERTIFICATE OF TRANSMISSION VIA EFS-WEB

I hereby certify that this paper is being transmitted via the Electronic Filing System (EFS-WEB) to the United States Patent and Trademark Office On **July 11, 2022**.

/Jimmy Schaub/
Jimmy Schaub

Inventor(s): Wei *et al.*
Patent No. : 11,066,656
Issue Date : July 20, 2021
Serial No. : 16/912,590
Filed : June 25, 2020

Attorney Docket No.: 33320.03087.US27/3087D
Request for Certificate of Correction Pursuant to
37 C.F.R. § 1.322

At column 180, line 65, please replace "Antithrombin I11s" with —Antithrombin I11s—;

At column 269, Table 10, please replace "R1161" with —R116I—;

At column 269, Table 10, please replace "D0591" with —D059I—;

At column 301, line 20, please replace "PH2P" with —PH20—;

At column 301, line 21, please replace "V8R" with —V58R—;

At column 305, Table 24, please replace "W/h" with —ft3/h—;

At column 309, line 29, please replace "PH2" with —PH20—;

At column 309, line 34, please replace "mg/min" with —mg/mL in—; and

At column 309, line 35, please replace "mL" with —5 mL—;

IN THE CLAIMS:

Please replace claim 1 with the following amended claim:

1. A modified PH20 polypeptide, comprising one or more amino acid replacements in an unmodified PH20 polypeptide, wherein:
 - the unmodified PH20 polypeptide consists of the amino acid sequence selected from the group consisting of SEQ ID NOs: 3, 7 and 32-66;
 - the modified PH20 polypeptide exhibits increased hyaluronidase activity compared to the unmodified PH20 polypeptide not containing the amino acid replacement(s);
 - the amino acid replacement(s) confer(s) the increased hyaluronidase activity;
 - an amino acid replacement that confers the increased hyaluronidase activity is at a position corresponding to residue 309, with reference to amino acid positions of SEQ ID NO:3;
 - corresponding amino acid positions are identified by alignment of the PH20 polypeptide with the polypeptide having the amino acid sequence of ~~amino acids~~ of SEQ ID NO:3; and

the modified PH20 polypeptide has at least 91% sequence identity to the amino acid sequence selected from the group consisting of SEQ ID NOs: 3, 7 and 32-66.

Please replace claim 10 with the following amended claim:

10. The modified PH20 polypeptide of claim 6, wherein:

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the unmodified PH20 polypeptide consists of the amino acid sequence set forth in SEQ ID NO:35; and

the amino acid sequence of the modified PH20 polypeptide has at least 95% sequence identity to SEQ ID NO:35~~SEQ ID NO:32~~.

Please replace claim 12 with the following amended claim:

12. The modified PH20 polypeptide of claim 1, wherein the unmodified PH20 polypeptide consists of the amino acid ~~sequence~~sequence of SEQ ID NO:35.

Please replace claim 21 with the following amended claim:

21. The modified PH20 polypeptide of claim 1, further comprising a heterologous signal sequence, wherein the unmodified PH20 polypeptide consists of the amino acid sequence~~an amino acid sequence~~ selected from the group consisting of SEQ ID NOs: 3 and 32-66.

Please replace claim 25 with the following amended claim:

25. The modified PH20 polypeptide of claim 1, further comprising a signal sequence, wherein the unmodified PH20 polypeptide consists of the amino acid sequence~~an amino acid sequence~~ selected from the group consisting of SEQ ID NOs: 3 and 32-66.

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Filed : June 25, 2020

Attorney Docket No.: 33320.03087.US27/3087D
Request for Certificate of Correction Pursuant to
37 C.F.R. § 1.322

REMARKS

A Certificate of Correction (Form PTO/SB/44) incorporating the above changes is included with this Request. Any fees that may be due can be charged to Deposit Account No. 50-0911.

IN THE TITLE PAGES

This Certificate of Correction also seeks to correct a typographical error introduced by the PTO in Item (56) References Cited, in OTHER PUBLICATIONS. At page 3, 2nd column, line 71, the error in the title is corrected by replacing the recitation "lip" with "trp." The citation was listed on the Form PTO-1449 as Item HW and provided to the Patent Office with an Information Disclosure Statement on July 08, 2020. A copy of page 8 of the Examiner-initialed Forms PTO-1449, considered by the Examiner on September 30, 2020, and mailed to the Applicant on May 03, 2021, is provided as evidence.

IN THE SPECIFICATION

This Certificate of Correction seeks to correct a typographical error introduced by the PTO in the specification at column 20, line 46. The error is corrected by replacing "Rat" with "R at," to render clearly the arginine (R) amino acid replacement corresponding to position 141 in a modified PH20 polypeptide. Basis for this correction can be found at page 24, line 23 of the specification as originally filed on June 25, 2020. A copy of page 24 of the specification as originally filed on June 25, 2020 is attached.

This Certificate of Correction seeks to correct a typographical error introduced by the PTO in the specification at column 33, line 48. The error is corrected by replacing "Tales" with "Talcs," to render clearly a pharmaceutical composition with Talcs. Basis for this correction can be found at page 39, line 27 of the specification as originally filed on June 25, 2020. A copy of page 39 of the specification as originally filed on June 25, 2020 is attached.

This Certificate of Correction seeks to correct a typographical error introduced by the PTO in the specification at column 34, line 60. The error is corrected by replacing "Antithrombin II Is" with "Antithrombin IIIs," to correct the spelling error. Basis for this correction can be found at page 41, line 5 of the specification as originally filed on June 25, 2020. A copy of page 41 of the specification as originally filed on June 25, 2020 is attached.

This Certificate of Correction seeks to correct a typographical error introduced by the PTO in the specification at column 84, line 61. The error is corrected by replacing "I271" with "I271," to render clearly the isoleucine (I) amino acid replacement corresponding to

Inventor(s): Wei *et al.*
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Request for Certificate of Correction Pursuant to
37 C.F.R. § 1.322

position 271 in a modified PH20 polypeptide. Basis for this correction can be found at page 98, line 11 of the specification as originally filed on June 25, 2020. A copy of page 98 of the specification as originally filed on June 25, 2020 is attached.

This Certificate of Correction seeks to correct a typographical error introduced by the PTO in the specification at column 88, line 13. The error is corrected by replacing "Rat" with "R at," to render clearly the arginine (R) amino acid replacement corresponding to position 141 in a modified PH20 polypeptide. Basis for this correction can be found at page 102, line 7 of the specification as originally filed on June 25, 2020. A copy of page 102 of the specification as originally filed on June 25, 2020 is attached.

This Certificate of Correction seeks to correct a typographical error introduced by the PTO in the specification at column 136, line 4. The error is corrected by replacing "W138" with "WI38," to render clearly the WI38 cell line. Basis for this correction can be found at page 155, line 2 of the specification as originally filed on June 25, 2020. A copy of page 155 of the specification as originally filed on June 25, 2020 is attached.

This Certificate of Correction seeks to correct a typographical error introduced by the PTO in the specification at column 140, line 55. The error is corrected by replacing "GALS" with "GAL5," to render clearly the GAL5 promoter in yeast. Basis for this correction can be found at page 160, line 29 of the specification as originally filed on June 25, 2020. A copy of page 160 of the specification as originally filed on June 25, 2020 is attached.

This Certificate of Correction seeks to correct a typographical error introduced by the PTO in the specification at column 176, line 20. The error is corrected by replacing "Tales" with "Talcs," to render clearly a pharmaceutical composition with Talcs. Basis for this correction can be found at page 203, line 8 of the specification as originally filed on June 25, 2020. A copy of page 203 of the specification as originally filed on June 25, 2020 is attached.

This Certificate of Correction seeks to correct a typographical error introduced by the PTO in the specification at column 177, line 39. The error is corrected by replacing "Tales" with "Talcs," to render clearly a pharmaceutical composition with Talcs. Basis for this correction can be found at page 204, line 27 of the specification as originally filed on June 25, 2020. A copy of page 204 of the specification as originally filed on June 25, 2020 is attached.

This Certificate of Correction seeks to correct a typographical error introduced by the PTO in the specification at column 179, line 53. The error is corrected by replacing "Tales"

Inventor(s): Wei *et al.*
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Request for Certificate of Correction Pursuant to
37 C.F.R. § 1.322

with "Tales," to render clearly a pharmaceutical composition with Talcs. Basis for this correction can be found at page 207, line 15 of the specification as originally filed on June 25, 2020. A copy of page 207 of the specification as originally filed on June 25, 2020 is attached.

This Certificate of Correction seeks to correct a typographical error introduced by the PTO in the specification at column 180, line 65. The error is corrected by replacing "Antithrombin I11s" with "Antithrombin IIIs," to correct the spelling error. Basis for this correction can be found at page 208, line 26 of the specification as originally filed on June 25, 2020. A copy of page 208 of the specification as originally filed on June 25, 2020 is attached.

This Certificate of Correction seeks to correct a typographical error introduced by the PTO in the specification at column 269, Table 10. The error is corrected by replacing "R1161" with "R116I," to render clearly the amino acid replacement at position 116 of PH20. Basis for this correction can be found at page 283, Table 10 of the specification as originally filed on June 25, 2020. A copy of page 283 of the specification as originally filed on June 25, 2020 is attached.

This Certificate of Correction seeks to correct a typographical error introduced by the PTO in the specification at column 269, Table 10. The error is corrected by replacing "D0591" with "D059I," to render clearly the amino acid replacement at position 059 of PH20. Basis for this correction can be found at page 283, Table 10 of the specification as originally filed on June 25, 2020. A copy of page 283 of the specification as originally filed on June 25, 2020 is attached.

This Certificate of Correction seeks to correct a typographical error introduced by the PTO in the specification at column 301, line 20. The error is corrected by replacing "PH2P" with "PH20," to correct the spelling error. Basis for this correction can be found at page 312, line 5 of the specification as originally filed on June 25, 2020. A copy of page 312 of the specification as originally filed on June 25, 2020 is attached.

This Certificate of Correction seeks to correct a typographical error introduced by the PTO in the specification at column 301, line 21. The error is corrected by replacing "V8R" with "V58R," to render clearly the V58R variant of PH20. Basis for this correction can be found at page 312, line 6 of the specification as originally filed on June 25, 2020. A copy of page 312 of the specification as originally filed on June 25, 2020 is attached.

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Issue Date : July 20, 2021
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Filed : June 25, 2020

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This Certificate of Correction seeks to correct a typographical error introduced by the PTO in the specification at column 305, Table 24. The error is corrected by replacing "W/h" with "ft³/h," to render clearly the unit for Nitrogen flow rate as specified in Example 13. Basis for this correction can be found at page 316, Table 24 of the specification as originally filed on June 25, 2020. A copy of page 316 of the specification as originally filed on June 25, 2020 is attached.

This Certificate of Correction seeks to correct a typographical error introduced by the PTO in the specification at column 309, line 29. The error is corrected by replacing "PH2" with "PH20," to correct the spelling error. Basis for this correction can be found at page 320, line 10 of the specification as originally filed on June 25, 2020. A copy of page 320 of the specification as originally filed on June 25, 2020 is attached.

This Certificate of Correction seeks to correct a typographical error introduced by the PTO in the specification at column 309, line 34. The error is corrected by replacing "mg/min" with "mg/mL in," to render clearly the concentration of the F204P-PH20 variant as specified in Example 16. Basis for this correction can be found at page 320, line 14 of the specification as originally filed on June 25, 2020. A copy of page 320 of the specification as originally filed on June 25, 2020 is attached.

This Certificate of Correction seeks to correct a typographical error introduced by the PTO in the specification at column 309, line 35. The error is corrected by replacing "mL" with "5 mL," to render clearly the dosing volume of a solution containing the F204P-PH20 variant as specified in Example 16. Basis for this correction can be found at page 320, line 14 of the specification as originally filed on June 25, 2020. A copy of page 320 of the specification as originally filed on June 25, 2020 is attached.

IN THE CLAIMS

This Certificate of Correction also seeks to correct a typographical error introduced by the PTO in claim 1, at column 311, line 38. This error is corrected by adding the recitation "amino acid" immediately preceding the recitation sequence and deleting the recitation "amino acids of " immediately preceding SEQ ID NO:3. Basis for this correction can be found in claim 1 as filed in the Amendment Pursuant to 37 C.F.R. § 1.312, on May 21, 2021. A copy of the claims from the Amendment Pursuant to 37 C.F.R. § 1.312, filed May 21, 2021, and entered by the Examiner on June 03, 2021 is attached.

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Issue Date : July 20, 2021
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This Certificate of Correction also seeks to correct a typographical error introduced by the PTO in claim 10, at column 312, line 29. This error is corrected by replacing the recitation "SEQ ID NO:32" with "SEQ ID NO:35." Basis for this correction can be found in claim 25 as filed in the Amendment Pursuant to 37 C.F.R. § 1.312, on May 21, 2021, in which claim 25 recites "the modified PH20 polypeptide has at least 95% sequence identity to SEQ ID NO:35." In the issued patent, claim 25 is renumbered as claim 10. A copy of the claims from the Amendment Pursuant to 37 C.F.R. § 1.312, filed May 21, 2021, and entered by the Examiner on June 03, 2021 is attached.

This Certificate of Correction also seeks to correct a typographical error introduced by the PTO in claim 12, at column 312, line 36. This error is corrected by replacing "sequence" with "sequence of" immediately following the recitation "amino acid." Basis for this correction can be found in claim 9 as filed in the Amendment Pursuant to 37 C.F.R. § 1.312, on May 21, 2021. In the issued patent, claim 9 is renumbered as claim 12. A copy of the claims from the Amendment Pursuant to 37 C.F.R. § 1.312, filed May 21, 2021, and entered by the Examiner on June 03, 2021 is attached.

This Certificate of Correction also seeks to correct a typographical error introduced by the PTO in claim 21, at column 313, line 7. This error is corrected by replacing the recitation "an amino acid sequence" with "the amino acid sequence" immediately following the recitation "PH20 polypeptide consists of." Basis for this correction can be found in claim 19 as filed in the Amendment Pursuant to 37 C.F.R. § 1.312, on May 21, 2021. In the issued patent, claim 19 is renumbered as claim 21. A copy of the claims from the Amendment Pursuant to 37 C.F.R. § 1.312, filed May 21, 2021, and entered by the Examiner on June 03, 2021 is attached.

This Certificate of Correction also seeks to correct a typographical error introduced by the PTO in claim 25, at column 313, line 22. This error is corrected by replacing the recitation "an amino acid sequence" with "the amino acid sequence" immediately following the recitation "PH20 polypeptide consists of." Basis for this correction can be found in claim 26 as filed in the Amendment Pursuant to 37 C.F.R. § 1.312, on May 21, 2021. In the issued patent, claim 26 is renumbered as claim 25. A copy of the claims from the Amendment Pursuant to 37 C.F.R. § 1.312, filed May 21, 2021, and entered by the Examiner on June 03, 2021 is attached.

Inventor(s): Wei *et al.*
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Issue Date : July 20, 2021
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Filed : June 25, 2020

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37 C.F.R. § 1.322

* * *

These changes do not constitute new matter. Patentee respectfully requests correction of these errors by issuance of a Certificate of Correction.

Respectfully submitted,

/Stephanie Seidman/

Stephanie Seidman

Reg. No. 33,779

Attorney Docket No.: 33320.03087.US27/3087D

Address all correspondence to: 13565

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Patent No. : 11,066,656
Issue Date : July 20, 2021
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CERTIFICATE OF CORRECTION

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Here
Only

UNITED STATES PATENT AND TRADEMARK OFFICE

CERTIFICATE OF CORRECTION

Page 1 of 4

PATENT NO. : 11,066,656
 APPLICATION NO. : 16/912,590
 DATED : JULY 20, 2021
 INVENTOR(S) : WEI ET AL.

It is certified that errors appear in the above-identified patent and that said Letters Patent is hereby corrected as shown below:

IN THE TITLE PAGES:

In Item (56) References Cited, in OTHER PUBLICATIONS, at page 3, 2nd column, line 71, please replace "lip" with —trp—;

IN THE SPECIFICATION:

At column 20, line 46, please replace "Rat a position" with —R at a position—;
 At column 33, line 48, please replace "Tales" with —Talcs—;
 At column 34, line 60, please replace "Antithrombin I11s" with —Antithrombin IIIs—;
 At column 84, line 61, please replace "1271" with —I271—;
 At column 88, line 13, please replace "Rat a position" with —R at a position—;
 At column 136, line 4, please replace "W138" with —WI38—;
 At column 140, line 55, please replace "GALS" with —GAL5—;
 At column 176, line 20, please replace "Tales" with —Talcs—;
 At column 177, line 39, please replace "Tales" with —Talcs—;
 At column 179, line 53, please replace "Tales" with —Talcs—;
 At column 180, line 65, please replace "Antithrombin I11s" with —Antithrombin IIIs—;

MAILING ADDRESS OF SENDER:

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UNITED STATES PATENT AND TRADEMARK OFFICE

CERTIFICATE OF CORRECTION

Page 2 of 4

PATENT NO. : 11,066,656
 APPLICATION NO. : 16/912,590
 DATED : JULY 20, 2021
 INVENTOR(S) : WEI ET AL.

It is certified that errors appear in the above-identified patent and that said Letters Patent is hereby corrected as shown below:

At column 269, Table 10, please replace "R1161" with —R116I—;
 At column 269, Table 10, please replace "D0591" with —D059I—;
 At column 301, line 20, please replace "PH2P" with —PH20—;
 At column 301, line 21, please replace "V8R" with —V58R—;
 At column 305, Table 24, please replace "W/h" with —ft³/h—;
 At column 309, line 29, please replace "PH2P" with —PH20—;
 At column 309, line 34, please replace "mg/min" with —mg/mL in—;
 Column 309, line 35, please replace "mL" with —5 mL—;

IN THE Claims:

Please replace claim 1 with the following amended claim:

1. A modified PH20 polypeptide, comprising one or more amino acid replacements in an unmodified PH20 polypeptide, wherein:
 the unmodified PH20 polypeptide consists of the amino acid sequence selected from the group consisting of SEQ ID NOs: 3, 7 and 32-66;

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CERTIFICATE OF CORRECTION

Page 3 of 4

PATENT NO. : 11,066,656
 APPLICATION NO. : 16/912,590
 DATED : JULY 20, 2021
 INVENTOR(S) : WEI ET AL.

It is certified that errors appear in the above-identified patent and that said Letters Patent is hereby corrected as shown below:

the modified PH20 polypeptide exhibits increased hyaluronidase activity compared to the unmodified PH20 polypeptide not containing the amino acid replacement(s);
 the amino acid replacement(s) confer(s) the increased hyaluronidase activity;
 an amino acid replacement that confers the increased hyaluronidase activity is at a position corresponding to residue 309, with reference to amino acid positions of SEQ ID NO:3;

corresponding amino acid positions are identified by alignment of the PH20 polypeptide with the polypeptide having the amino acid sequence of ~~amino acids~~ of SEQ ID NO:3; and the modified PH20 polypeptide has at least 91% sequence identity to the amino acid sequence selected from the group consisting of SEQ ID NOs: 3, 7 and 32-66.

Please replace claim 10 with the following amended claim:

10. The modified PH20 polypeptide of claim 6, wherein:
 the unmodified PH20 polypeptide consists of the amino acid sequence set forth in SEQ ID NO:35; and

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UNITED STATES PATENT AND TRADEMARK OFFICE CERTIFICATE OF CORRECTION

Page 4 of 4

PATENT NO. : 11,066,656
 APPLICATION NO. : 16/912,590
 DATED : JULY 20, 2021
 INVENTOR(S) : WEI ET AL.

It is certified that errors appear in the above-identified patent and that said Letters Patent is hereby corrected as shown below:

the amino acid sequence of the modified PH20 polypeptide has at least 95% sequence identity to SEQ ID NO:35~~SEQ ID NO:32~~.

Please replace claim 12 with the following amended claim:

12. The modified PH20 polypeptide of claim 1, wherein the unmodified PH20 polypeptide consists of the amino acid ~~sequence~~sequence of SEQ ID NO:35.

Please replace claim 21 with the following amended claim:

21. The modified PH20 polypeptide of claim 1, further comprising a heterologous signal sequence, wherein the unmodified PH20 polypeptide consists of ~~the amino acid sequence~~an amino acid sequence selected from the group consisting of SEQ ID NOs: 3 and 32-66.

Please replace claim 25 with the following amended claim:

25. The modified PH20 polypeptide of claim 1, further comprising a signal sequence, wherein the unmodified PH20 polypeptide consists of ~~the amino acid sequence~~an amino acid sequence selected from the group consisting of SEQ ID NOs: 3 and 32-66.

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Inventor(s): Wei *et al.*
Patent No. : 11,066,656
Issue Date : July 20, 2021
Serial No. : 16/912,590
Filed : June 25, 2020

Attorney Docket No.: 33320.03087.US27/3087D
Request for Certificate of Correction Pursuant to
37 C.F.R. § 1.322

COPY OF PAGE 8 OF THE EXAMINER-INITIALED FORM

PTO-1449 AS FILED ON JULY 08, 2020

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Sheet 8 of 24

Substitute Form PTO-1449 (Modified)		U.S. Department of Commerce Patent and Trademark Office		Attorney Docket No. 33320.03087.US27/3087D	Application No. 16/912,590
List of Patents and Publications for Applicant's Information Disclosure Statement				Inventors Wei <i>et al.</i>	
				Filing Date June 25, 2020	Group Art Unit 1652
(37 CFR §1.98(b))					
Other Documents (include Author, Title, Date, and Place of Publication)					
Examiner Initial	Desig. ID	Document			
	HK**	Cherr et al., "The dual functions of GPI-anchored PH-20: hyaluronidase and intracellular signaling," <i>Matrix Biol.</i> 20:515-525 (2001).			
	HL**	Cherr et al., "The PH-20 protein in cynomolgus macaque spermatozoa: identification of two different forms exhibiting hyaluronidase activity," <i>Dev. Biol.</i> 175:142-153 (1996).			
	HM**	Cho et al., "Construction of hepatitis C-SIN virus recombinants with replicative dependency on hepatitis C virus serine protease activity," <i>J. Virol. Meth.</i> (65):201-207 (1997).			
	HN**	Chowpongpan et al., "Cloning and characterization of the bovine testicular PH-20 hyaluronidase core domain," <i>Biotechnol. Lett.</i> 26(15):1247-1252 (2004).			
	HO**	Colbere-Garapin et al., "A new dominant hybrid selective marker for higher eukaryotic cells," <i>J. Mol. Biol.</i> 150:1-14 (1981).			
	HP**	Conserved domain search from US Application No. 10/795,095 of SEQ ID NO:6, Primakoff et al. US 5,721,348, performed on the NCBI website on August 5, 2008.			
	HQ**	Csoka et al., "Hyaluronidases in tissue invasion," <i>Invasion Metastasis</i> 17:297-311 (1997).			
	HR**	Csoka et al., "Purification and microsequencing of hyaluronidase isozymes from human urine," <i>FEBS Lett.</i> 417(3):307-310 (1997).			
	HS**	Csoka et al., "The six hyaluronidase-like genes in the human and mouse genomes," <i>Matrix Biol.</i> 20:499-508 (2001).			
	HT**	Czejka et al., "Influence of hyaluronidase on the blood plasma levels of 5-fluorouracil in patients," <i>Pharmazie</i> 45:H.9 (1990).			
	HU**	De Maeyer et al., "The growth rate of two transplantable murine tumors, 3LL lung carcinoma and B16F10 melanoma, is influenced by Hyal-1, a locus determining hyaluronidase levels and polymorphism," <i>Int. J. Cancer</i> 51:657-660 (1992).			
	HV**	De Saegui et al., "A comparison of serum and testicular hyaluronidase," <i>Arch. Biochem. Biophys.</i> 121:548-554 (1967).			
	HW**	DeBoer et al., "The tac promoter: a functional hybrid derived from the trp and lac promoters," <i>Proc. Natl. Acad. Sci. USA</i> 80:21-25 (1983).			
	HX**	Delpach et al., "Enzyme-linked hyaluronectin: a unique reagent for hyaluronan assay and tissue location and for hyaluronidase activity detection," <i>Anal. Biochem.</i> 229:35-41 (1995).			
	HY**	Derwent English abstract for Japanese Publication No. JP 2007-153797, published Jun. 21, 2007, entitled "Therapeutic Agent And Preventive Agent Of Autoimmune Disease, Inflammation, And Nervous Disease," 3 pages.			
	HZ**	Dorfman, A. and M. Ott, "A turbidimetric method for the assay of hyaluronidase," <i>J. Biol. Chem.</i> 172:367-375 (1948).			
	IA**	D'Souza et al., "In vitro cleavage of hepatitis C virus polyprotein substrates by purified recombinant NS3 protease," <i>J. Gen. Virol.</i> 76:1729-1736 (1995).			
	IB**	Duttaroy et al., "Development of a long-acting insulin analog using albumin fusion technology," <i>Diabetes</i> 54(1):251-258 (2005).			
	IC**	Elder et al., "Intra-arterial hyaluronidase in severe peripheral arterial disease," <i>Lancet</i> 648-649 (1980).			
	ID**	Ernst et al., "Enzymatic degradation of glycosaminoglycans," <i>Critical Reviews in Biochemistry and Molecular Biology</i> 30(5):387-444 (1995).			
	IE**	Eskens et al., "Enzymatic glycocalyx treatment impairs insulin-mediated recruitment of microvascular blood volume and decreases insulin sensitivity in rats," <i>FASEB Journal</i> 25: 1023.13 (2011) (Abstract).			
	IF**	European Pharmacopoeia, Chapter 5.1.3, "Efficacy of antimicrobial preservation," pages 447-449 (2005).			

Examiner Signature /SAMUEL W LIU/	Date Considered 09/30/2020
EXAMINER: Initial if citation considered, whether or not citation is in conformance with MPEP 609; Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.	

Inventor(s): Wei *et al.*
Patent No. : 11,066,656
Issue Date : July 20, 2021
Serial No. : 16/912,590
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Attorney Docket No.: 33320.03087.US27/3087D
Request for Certificate of Correction Pursuant to
37 C.F.R. § 1.322

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OF THE SPECIFICATION AS ORIGINALLY FILED ON JUNE 25, 2020

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position 93; T at a position corresponding to position 93; D at a position corresponding to position 94; Q at a position corresponding to position 94; R at a position corresponding to position 94; A at a position corresponding to position 97; C at an amino acid residue corresponding to position 97; D at a position corresponding to position 97; E at a position
5 corresponding to position 97; G at a position corresponding to position 97; L at a position corresponding to position 97; S at a position corresponding to position 97; S at a position corresponding to position 102; T at a position corresponding to position 102; R at a position corresponding to position 104; L at a position corresponding to position 107; A at a position corresponding to position 114; Q at a position corresponding to position 118; H at a position
10 corresponding to position 120; F at a position corresponding to position 120; I at a position corresponding to position 120; S at a position corresponding to position 120; V at a position corresponding to position 120; Y at a position corresponding to position 120; E at a position corresponding to position 127; H at a position corresponding to position 127; N at a position corresponding to position 127; Q at a position corresponding to position 127; R at a position
15 corresponding to position 127; I at a position corresponding to position 128; R at a position corresponding to position 130; G at a position corresponding to position 131; I at a position corresponding to position 131; M at a position corresponding to position 131; Q at a position corresponding to position 131; R at a position corresponding to position 131; V at a position corresponding to position 131; N at a position corresponding to position 132; L at a position
20 corresponding to position 132; D at a position corresponding to position 135; G at a position corresponding to position 135; R at a position corresponding to position 135, with L at a position corresponding to position 138; T at a position corresponding to position 139; K at a position corresponding to position 140; H at a position corresponding to position 141; R at a position corresponding to position 141; S at a position corresponding to position 141; W at a
25 position corresponding to position 141; Y at a position corresponding to position 141; D at a position corresponding to position 142; G at a position corresponding to position 142; K at a position corresponding to position 142; N at a position corresponding to position 142; P at a position corresponding to position 142; Q at a position corresponding to position 142; R at a position corresponding to position 142; S at a position corresponding to position 142; T at a
30 position corresponding to position 142; G at a position corresponding to position 143; K at a position corresponding to position 143; R at a position corresponding to position 144; T at a position corresponding to position 144; P at a position corresponding to position 146; R at a position corresponding to position 146; A at a position corresponding to position 147; F at a position corresponding to position 147; L at a position corresponding to position 147; R at a
35 position corresponding to position 147; S at a position corresponding to position 147; V at a position corresponding to position 147; H at a position corresponding to position 148; K at a position corresponding to position 148; Q at a position corresponding to position 148; T at a

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- Virus Vaccines, Rubella vaccines, Medroxyprogesterones, Meropenems,
Methylprednisolones, Midazolams, Morphines, Octreotides, Omalizumabs, Ondansetrons,
Palivizumabs, Pantoprazoles, Pegaspargases, Pegfilgrastims, Peg-Interferon Alpha-2a's, Peg-
Interferon Alpha-2b's, Pegvisomants, Pertussis vaccines, Piperacillins, Pneumococcal
5 Vaccines and Pneumococcal Conjugate Vaccines, Promethazines, Reteplases, Somatropins,
Sulbactams, Sumatriptans, Tazobactams, Tenecteplases, Tetanus Purified Toxoids,
Ticarcillins, Tositumomabs, Triamcinolones, Triamcinolone Acetonides, Triamcinolone
hexacetonides, Vancomycins, Varicella Zoster immunoglobulins, Varicella vaccines, other
vaccines, Alemtuzumabs, Alitretinoids, Allopurinols, Altretamines, Amifostines,
10 Anastrozoles, Arsenics, Arsenic Trioxides, Asparaginases, Bacillus Calmette-Guerin (BCG)
vaccines, BCG Live, Bexarotenes, Bleomycins, Busulfans, Busulfan intravenous, Busulfan
orals, Calusterones, Capecitabines, Carboplatins, Carmustines, Carmustines with
Polifeprosans, Celecoxibs, Chlorambucils, Cisplatins, Cladribines, Cyclophosphamides,
Cytarabines, Cytarabine liposomals, Dacarbazines, Dactinomycins, Daunorubicin liposomals,
15 Daunorubicins, Daunomycins, Denileukin Diftitoxes, Dexrazoxanes, Docetaxels,
Doxorubicins, Doxorubicin liposomals, Dromostanolone propionates, Elliott's B Solutions,
Epirubicins, Epoetin alfas, Estramustines, Etoposides, Etoposide phosphates, Etoposide VP-
16s, Exemestanes, Floxuridines, Fludarabines, Fluorouracils, 5-Fluorouracils, Fulvestrants,
Gemcitabines, Gemtuzumabs, Ozogamicins, Gemtuzumab ozogamicins, Hydroxyureas,
20 Idarubicins, Ifosfamides, Imatinib mesylates, Irinotecans, Letrozoles, Leucovorins,
Levamisoles, Lomustines, CCNUs, Mechlorethamines, Nitrogen mustards, Megestrols,
Megestrol acetates, Melfhalans, L-PAMs, Mercaptopurines, 6-Mercaptopurines, Mesnas,
Methotrexates, Methoxsalens, Mitomycins, Mitomycin C's, Mitotanes, Mitoxantrones,
Nandrolones, Nandrolone Phenpropionates, Nofetumomabs, Oprelvekins, Oxaliplatin,
25 Paclitaxels, Pamidronates, Pegademases, Pentostatins, Pipobromans, Plicamycins,
Mithramycins, Porfimers, Porfimer sodiums, Procarbazines, Quinacrine, Rasburicase,
Rituximabs, Sargramostims, Streptozocins, Talcs, Tamoxifens, Temozolomides, Teniposides,
Testolactones, Thioguanines, 6-Thioguanines, Triethylenethiophosphoramides (Thiotepas),
Topotecans, Toremifenes, Trastuzumabs, Tretinoids, Uracil Mustards, Valrubicins,
30 Vinblastines, Vincristines, Vinorelbines, Zoledronates, Acivicins, Aclarubicins, Acodazoles,
Acronines, Adozelesins, Aldesleukins, Retinoic Acids, Alitretinoids, 9-Cis-Retinoic Acids,
Alvocidibs, Ambazones, Ambomycins, Ametantrones, Aminoglutethimides, Amsacrine,
Anaxirones, Ancitabines, Anthramycins, Apaziquones, Argimesnas, Asperlins, Atrimustines,
Azacitidines, Azetepas, Azotomycins, Banoxantrones, Batabulins, Batimastats, Benaxibines,
35 Bendamustines, Benzodepas, Bicalutamides, Bietaserpines, Biricodars, Bisantrenes, Bisnafide
Dimesylates, Bizelesins, Bortezomibs, Brequinars, Bropirimines, Budotitanes,
Cactinomycins, Canertinibs, Caracemides, Carbetimers, Carboquones, Carmofurs,

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5 Zinostatins, Zorubicins, Zosuquidars, Acetazolamides, Acyclovirs, Adipiodones,
Alatrofloxacin, Alfentanils, Allergenic extracts, Alpha 1-proteinase inhibitors, Alprostadils,
Amikacins, Amino acids, Aminocaproic acids, Aminophyllines, Amitriptylines,
Amobarbitals, Amrinones, Analgesics, Anti-poliomyelitic vaccines, Anti-rabic serums, Anti-
10 tetanus immunoglobulins, tetanus vaccines, Antithrombin IIIs, Antivenom serums,
Argatrobans, Arginines, Ascorbic acids, Atenolols, Atracuriums, Atropines,
Aurothioglucoses, Azathioprine, Aztreonams, Bacitracins, Baclofens, Basiliximabs, Benzoic
acids, Benzotropines, Betamethasones, Biotins, Bivalirudins, Botulism antitoxins, Bretyliums,
Bumetanides, Bupivacaines, Buprenorphines, Butorphanols, Calcitonins, Calcitriols,
15 Calciums, Capreomycins, Carboprost, Carnitines, Cefamandoles, Cefoperazones,
Cefotaximes, Cefoxitins, Ceftizoximes, Cefuroximes, Chloramphenicols, Chloroprocaines,
Chloroquines, Chlorothiazides, Chlorpromazines, Chondroitinsulfuric acids,
Choriogonadotropin alfas, Chromiums, Cidofovir, Cimetidines, Ciprofloxacin,
Cisatracuriums, Clonidines, Codeines, Colchicines, Colistins, Collagens, Corticorelin ovine
20 triflutates, Corticotrophins, Cosyntropins, Cyanocobalamins, Cyclosporines, Cysteines,
Dacliximabs, Dalfopristins, Dalteparins, Danaparoids, Dantrolenes, Deferoxamines,
Desmopressins, Dexamethasones, Dexmedetomidines, Dexpanthenols, Dextran, Iron
dextran, Diatrizoic acids, Diazepam, Diazoxides, Dicyclomines, Digibinds, Digoxins,
Dihydroergotamines, Diltiazem, Diphenhydramines, Dipyrindamoles, Dobutamines,
25 Dopamines, Doxacuriums, Doxapram, Doxercalciferols, Doxycyclines, Droperidols,
Dyphyllines, Edetic acids, Edrophoniums, Enalaprilat, Ephedrine, Epoprostenols,
Ergocalciferols, Ergonovines, Ertapenem, Erythromycins, Esmolols, Estradiols, Estrogenics,
Ethacrynic acids, Ethanolamines, Ethanol, Ethiodized oils, Etidronic acids, Etomidate,
Famotidines, Fenoldopam, Fentanyl, Flumazenil, Fluoresceins, Fluphenazines, Folic acids,
25 Fomepizoles, Fomivirsen, Fondaparinux, Foscarnet, Fosphenytoin, Furosemide,
Gadoteridol, Gadoversetamide, Ganciclovir, Gentamicin, Glucagon, Glucose, Glycine,
Glycopyrrolate, Gonadorelin, Gonadotropin chorionic, Haemophilus B polysaccharides,
Hemins, Herbals, Histamines, Hydralazine, Hydrocortisone, Hydromorphone,
Hydroxocobalamins, Hydroxyzine, Hyoscyamine, Ibutilide, Imiglucerase, Indigo
30 carmine, Indomethacin, Iodides, Iopromides, Iothalamic acids, Ioxaglic acids, Ioxilan,
Isoniazid, Isoproterenol, Japanese encephalitis vaccine, Kanamycin, Ketamine,
Labetalol, Lepirudin, Levobupivacaine, Levothyroxine, Lincomycin, Liothyronine,
Luteinizing hormones, Lyme disease vaccine, Mangafodipir, Mantitol, Meningococcal
polysaccharide vaccine, Meperidine, Mepivacaine, Mesoridazine, Metaraminol,
35 Methadone, Methocarbamol, Methohexital, Methyldopate, Methylergonovine,
Metoclopramide, Metoprolol, Metronidazole, Minocycline, Mivacurium, Morrhua acid,
Moxifloxacin, Muromonab-CD3s, Mycophenolate mofetil, Nafcillin, Nalbuphine,

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acid positions can be replacements at positions corresponding to replacement of Leucine (L) at position 1 (L1), P6, V8, I9, P10, N11, V12, F14, L15, A20, S22, F24, L26, G27, K28, F29, D30, E31, P32, L33, D34, M35, S36, L37, F38, S39, F40, I41, I46, N47, A48, T49, G50, G52, V58, D59, Y63, I67, D68, S69, I70, T71, G72, V73, T74, V75, I79, K82, I83, S84, G86, D87, L89, D90, A92, K93, K94, T97, V102, N104, M107, E114, T118, A120, D127, V128, K130, N131, R132, E135, Q138, Q139, Q140, N141, V142, Q143, L144, L146, T147, E148, A149, T150, E151, K152, Q155, E156, E158, A160, K162, D163, F164, L165, V166, E167, I169, K170, G172, K173, L174, L175, N178, H179, H193, K195, K196, G198, F204, N205, V206, K209, D212, D213, S215, N219, E220, S221, T222, T232, Q233, Q234, S235, P236, V237, A238, T240, V247, R248, E249, P257, D258, A259, K260, S261, L263, A267, T269, I271, V272, F273, T274, Q276, V277, L278, K279, S282, Q283, E285, V287, T289, G291, E292, T293, A298, G305, L307, S308, I309, M310, M313, K314, S315, L317, L318, D320, N321, E324, T325, I326, N328, T335, Q347, Q349, V351, I353, N356, S359, P367, D368, N369, A371, Q373, L374, E375, K376, G377, F380, T381, R383, K385, E389, E392, Q393, S395, E396, Y399, S401, S404, T405, L406, S407, K409, E410, A412, D416, D418, A419, D421, A425, G427, A428, D431, F433, P436, P437, M438, E439, T440, E441, E442, P443, Q444, I445, F446 or Y447 with reference to amino acid positions set forth in SEQ ID NO:3.

Exemplary amino acid replacements in the modified PH20 polypeptides provided herein include, but are not limited, replacement with: histidine (H) at a position corresponding to position 1; A at a position corresponding to position 1; E at a position corresponding to position 1; G at a position corresponding to position 1; K at a position corresponding to position 1; Q at a position corresponding to position 1; R at a position corresponding to position 1; A at a position corresponding to position 6; M at a position corresponding to position 8; Q at a position corresponding to position 9; G at a position corresponding to position 10; H at a position corresponding to position 10; S at a position corresponding to position 11; E at a position corresponding to position 12; I at a position corresponding to position 12; K at a position corresponding to position 12; T at a position corresponding to position 12; V at a position corresponding to position 14; V at a position corresponding to position 15; M at a position corresponding to position 15; S at a position corresponding to position 20; T at a position corresponding to position 22; E at a position corresponding to position 24; H at a position corresponding to position 24; R at a position corresponding to position 24; A at a position corresponding to position 26; E at a position corresponding to position 26; K at a position corresponding to position 26; M at a position corresponding to position 26; Q at a position corresponding to position 26; R at a position corresponding to position 26; D at a position corresponding to position 27; K at a position corresponding to position 27; R at a position corresponding to position 27; R at a position corresponding to position 28; E at a position corresponding to position 29; I at a position corresponding to

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corresponding to position 131; M at a position corresponding to position 131; Q at a position
corresponding to position 131; R at a position corresponding to position 131; V at a position
corresponding to position 131; N at a position corresponding to position 132; L at a position
corresponding to position 132; D at a position corresponding to position 135; G at a position
5 corresponding to position 135; R at a position corresponding to position 135, with L at a
position corresponding to position 138; T at a position corresponding to position 139; K at a
position corresponding to position 140; H at a position corresponding to position 141; R at a
position corresponding to position 141; S at a position corresponding to position 141; W at a
position corresponding to position 141; Y at a position corresponding to position 141; D at a
10 position corresponding to position 142; G at a position corresponding to position 142; K at a
position corresponding to position 142; N at a position corresponding to position 142; P at a
position corresponding to position 142; Q at a position corresponding to position 142; R at a
position corresponding to position 142; S at a position corresponding to position 142; T at a
position corresponding to position 142; G at a position corresponding to position 143; K at a
15 position corresponding to position 143; R at a position corresponding to position 144; T at a
position corresponding to position 144; P at a position corresponding to position 146; R at a
position corresponding to position 146; A at a position corresponding to position 147; F at a
position corresponding to position 147; L at a position corresponding to position 147; R at a
position corresponding to position 147; S at a position corresponding to position 147; V at a
20 position corresponding to position 147; H at a position corresponding to position 148; K at a
position corresponding to position 148; Q at a position corresponding to position 148; T at a
position corresponding to position 149; V at a position corresponding to position 149; A at a
position corresponding to position 150; D at a position corresponding to position 150; G at a
position corresponding to position 150; N at a position corresponding to position 150; S at a
25 position corresponding to position 150; W at a position corresponding to position 150; Y at a
position corresponding to position 150; A at a position corresponding to position 151; H at a
position corresponding to position 151; K at a position corresponding to position 151; L at a
position corresponding to position 151; M at a position corresponding to position 151; Q at a
position corresponding to position 151; R at a position corresponding to position 151; S at a
30 position corresponding to position 151; T at a position corresponding to position 151; V at a
position corresponding to position 151; W at a position corresponding to position 151; Y at a
position corresponding to position 151; R at a position corresponding to position 152; T at a
position corresponding to position 152; W at a position corresponding to position 152; D at a
position corresponding to position 155; G at a position corresponding to position 155; K at a
35 position corresponding to position 155; R at a position corresponding to position 155; D at a
position corresponding to position 156; Q at a position corresponding to position 158; S at a
position corresponding to position 158; S at a position corresponding to position 160; E at a

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impact the folding and/or function of the polypeptide. Different host cells, such as, but not limited to, CHO (DG44, DXB11, CHO-K1), HeLa, MCDK, 293 and WI38 have specific cellular machinery and characteristic mechanisms for such post-translational activities and can be chosen to ensure the correct modification and processing of the introduced protein.

5 Generally, the choice of cell is one that is capable of introducing N-linked glycosylation into the expressed polypeptide. Hence, eukaryotic cells containing the vectors are provided. Exemplary eukaryotic cells are mammalian Chinese Hamster Ovary (CHO) cells. For example, CHO cells deficient in dihydrofolate reductase (*e.g.*, DG44 cells) are used to produce polypeptides provided herein. Note that bacterial expression of an PH20
10 polypeptide provided herein will not result in a catalytically active polypeptide, but when combined with proper glycosylation machinery, the PH20 can be artificially glycosylated.

Provided are vectors that contain a sequence of nucleotides that encodes the modified PH20 polypeptide, coupled to the native or heterologous signal sequence, as well as multiple copies thereof. The vectors can be selected for expression of the enzyme protein in the cell or
15 such that the enzyme protein is expressed as a secreted protein.

A variety of host-vector systems can be used to express the protein encoding sequence. These include but are not limited to mammalian cell systems infected with virus (*e.g.*, vaccinia virus, adenovirus and other viruses); insect cell systems infected with virus (*e.g.*, baculovirus); microorganisms such as yeast containing yeast vectors; or bacteria
20 transformed with bacteriophage, DNA, plasmid DNA, or cosmid DNA. The expression elements of vectors vary in their strengths and specificities. Depending on the host-vector system used, any one of a number of suitable transcription and translation elements can be used.

Any methods known to those of skill in the art for the insertion of DNA fragments
25 into a vector can be used to construct expression vectors containing a chimeric gene containing appropriate transcriptional/translational control signals and protein coding sequences. These methods can include *in vitro* recombinant DNA and synthetic techniques and *in vivo* recombinants (genetic recombination). Expression of nucleic acid sequences encoding protein, or domains, derivatives, fragments or homologs thereof, can be regulated
30 by a second nucleic acid sequence so that the genes or fragments thereof are expressed in a host transformed with the recombinant DNA molecule(s). For example, expression of the proteins can be controlled by any promoter/enhancer known in the art. In a specific embodiment, the promoter is not native to the genes for a desired protein. Promoters which can be used include, but are not limited to, the SV40 early promoter (Bernoist and Chambon,
35 *Nature* 290:304-310 (1981)), the promoter contained in the 3' long terminal repeat of Rous sarcoma virus (Yamamoto *et al.* *Cell* 22:787-797 (1980)), the herpes thymidine kinase promoter (Wagner *et al.*, *Proc. Natl. Acad. Sci. USA* 78:1441-1445 (1981)), the regulatory

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the lac promoter, the trp promoter, the hybrid tac promoter, the T7 and SP6 RNA promoters and the temperature regulated λ PL promoter.

Proteins, such as any provided herein, can be expressed in the cytoplasmic environment of *E. coli*. The cytoplasm is a reducing environment, and for some molecules, this can result in the formation of insoluble inclusion bodies. Reducing agents such as dithiothreitol and β -mercaptoethanol and denaturants, such as guanidine-HCl and urea can be used to resolubilize the proteins. An alternative approach effects protein expression in the periplasmic space of bacteria which provides an oxidizing environment and chaperonin-like and disulfide isomerases, which can aid in the production of soluble protein. Typically, a leader sequence is fused to the protein to be expressed which directs the protein to the periplasm. The leader is then removed by signal peptidases inside the periplasm. Examples of periplasmic-targeting leader sequences include the pelB leader from the pectate lyase gene and the leader derived from the alkaline phosphatase gene. In some cases, periplasmic expression allows leakage of the expressed protein into the culture medium. The secretion of proteins allows quick and simple purification from the culture supernatant. Proteins that are not secreted can be obtained from the periplasm by osmotic lysis. Similar to cytoplasmic expression, in some cases proteins can become insoluble and denaturants and reducing agents can be used to facilitate solubilization and refolding. Temperature of induction and growth also can influence expression levels and solubility, typically temperatures between 25 °C and 37 °C are used. Typically, bacteria produce aglycosylated proteins. Thus, if proteins require glycosylation for function, glycosylation can be added *in vitro* after purification from host cells.

b. Yeast Cells

Yeasts such as *Saccharomyces cerevisiae*, *Schizosaccharomyces pombe*, *Yarrowia lipolytica*, *Kluyveromyces lactis* and *Pichia pastoris* are well known yeast expression hosts that can be used for production of proteins, such as any described herein. Yeast can be transformed with episomal replicating vectors or by stable chromosomal integration by homologous recombination. Typically, inducible promoters are used to regulate gene expression. Examples of such promoters include GAL1, GAL7 and GAL5 and metallothionein promoters, such as CUP1, AOX1 or other *Pichia* or other yeast promoters. Expression vectors often include a selectable marker such as LEU2, TRP1, HIS3 and URA3 for selection and maintenance of the transformed DNA. Proteins expressed in yeast are often soluble. Co-expression with chaperonins such as Bip and protein disulfide isomerase can improve expression levels and solubility. Additionally, proteins expressed in yeast can be directed for secretion using secretion signal peptide fusions such as the yeast mating type alpha-factor secretion signal from *Saccharomyces cerevisiae* and fusions with yeast cell surface proteins such as the Aga2p mating adhesion receptor or the *Arxula adeninivorans*

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- Plomestanes; Porfimer sodiums; Porfimers; Porfiromycins; Prednimustines; Procarbazines;
Propamidines; Prospidiiums; Pumitepas; Puromycins; Pyrazofurins; Quinacrine;
Ranimustines; Rasburicases; Riboprines; Ritrosulfans; Rituximabs; Rogletimides;
Roquinimexs; Rufocromomycins; Sabarubicins; Safingols; Sargramostims; Satraplatins;
5 Sebriplatins; Semustines; Simtrazenes; Sizofirans; Sobuzoxanes; Sorafenibs; Sparfosates;
Sparfosic Acids; Sparsomycins; Spirogermaniums; Spiromustines; Spiroplatins; Spiroplatins;
Squalamines; Streptonigrins; Streptovarycins; Streptozocins; Sufosfamides; Sulofenurs;
Sunitinib Malate; 6-TG; Tacedinalines; Talcs; Talisomycins; Tallimustines; Tamoxifens;
Tariquidars; Tauromustines; Tecogalans; Tegafurs; Teloxantrones; Temoporfin;
10 Temozolomides; Teniposides/VM-26s; Teniposides; Teroxirones; Testolactones;
Thiamiprines; Thioguanines; Thiotepas; Tiamiprines; Tiazofurins; Tilomisoles; Tilorones;
Timcodars; Timonacics; Tirapazamines; Topixantrones; Topotecans; Toremifenes;
Tositumomabs; Trabectedins (Ecteinascidin 743); Trastuzumabs; Trestolones;
Tretinoin/ATRA; Triciribines; Trilostanes; Trimetrexates; Triplatin Tetranitrates;
15 Triptorelins; Trofosfamides; Tubulozoles; Ubenimexs; Uracil Mustards; Uredepas;
Valrubicins; Valspodars; Vapreotides; Verteporfin; Vinblastines; Vincristines; Vindesines;
Vinepidines; Vinflunines; Vinformides; Vinglycinates; Vinleucinols; Vinleurosines;
Vinorelbines; Vinrosidines; Vintriptols; Vinzolidines; Vorozoles; Xanthomycin A's
(Guamecyclines); Zeniplatins; Zilascorbs [2-H]; Zinostatins; Zoledronate; Zorubicins; and
20 Zosuquidars, for example:
Aldesleukins (*e.g.*, PROLEUKIN®); Alemtuzumabs (*e.g.*, CAMPATH®);
Alitretinoin (*e.g.*, PANRETIN®); Allopurinols (*e.g.*, ZYLOPRIM®); Altretamines (*e.g.*,
HEXALEN®); Amifostines (*e.g.*, ETHYOL®); Anastrozoles (*e.g.*, ARIMIDEX®); Arsenic
Trioxides (*e.g.*, TRISENOX®); Asparaginases (*e.g.*, ELSPAR®); BCG Live (*e.g.*, TICE®
25 BCG); Bexarotenes (*e.g.*, TARGRETIN®); Bevacizumab (AVASTIN®); Bleomycins (*e.g.*,
BLENOXANE®); Busulfan intravenous (*e.g.*, BUSULFEX®); Busulfan orals (*e.g.*,
MYLERAN™); Calusterones (*e.g.*, METHOSARB®); Capecitabines (*e.g.*, XELODA®);
Carboplatins (*e.g.*, PARAPLATIN®); Carmustines (*e.g.*, BCNU®, BiCNU®); Carmustines
with Polifeprosans (*e.g.*, GLIADEL® Wafer); Celecoxibs (*e.g.*, CELEBREX®);
30 Chlorambucils (*e.g.*, LEUKERAN®); Cisplatins (*e.g.*, PLATINOL®); Cladribines (*e.g.*,
LEUSTATIN®, 2-CdA®); Cyclophosphamides (*e.g.*, CYTOXAN®, NEOSAR®);
Cytarabines (*e.g.*, CYTOSAR-U®); Cytarabine liposomals (*e.g.*, DepoCyt®); Dacarbazines
(*e.g.*, DTIC-Domev); Dactinomycins (*e.g.*, COSMEGEN®); Darbepoetin Alfas (*e.g.*,
ARANESP®); Daunorubicin liposomals (*e.g.*, DAUNOXOME®);
35 Daunorubicins/Daunomycins (*e.g.*, CERUBIDINE®); Denileukin Diftitoxes (*e.g.*,
ONTAK®); Dexrazoxanes (*e.g.*, ZINECARD®); Docetaxels (*e.g.*, TAXOTERE®);
Doxorubicins (*e.g.*, ADRIAMYCIN®, RUBEX®); Doxorubicin liposomals, including

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Doxorubicin HCL liposome injections (*e.g.*, DOXIL®); Dromostanolone propionates (*e.g.*, DROMOSTANOLONE® and MASTERONE® Injection); Elliott's B Solutions (*e.g.*, Elliott's B Solution®); Epirubicins (*e.g.*, ELLENCE®); Epoetin alfas (*e.g.*, EPOGEN®); Estramustines (*e.g.*, EMCYT®); Etoposide phosphates (*e.g.*, ETOPOPHOS®); Etoposide VP-16s (*e.g.*, VEPESID®); Exemestanes (*e.g.*, AROMASIN®); Filgrastims (*e.g.*, NEUPOGEN®); Floxuridines (*e.g.*, FUDR®); Fludarabines (*e.g.*, FLUDARA®); Fluorouracils incl. 5-FUs (*e.g.*, ADRUCIL®); Fulvestrants (*e.g.*, FASLODEX®); Gemcitabines (*e.g.*, GEMZAR®); Gemtuzumabs/Ozogamicins (*e.g.*, MYLOTARG®); Goserelin acetates (*e.g.*, ZOLADEX®); Hydroxyureas (*e.g.*, HYDREA®); Ibritumomabs/Tiuxetans (*e.g.*, ZEVALIN®); Idarubicins (*e.g.*, IDAMYCIN®); Ifosfamides (*e.g.*, IFEX®); Imatinib mesylates (*e.g.*, GLEEVEC®); Interferon alfa-2as (*e.g.*, ROFERON-A®); Interferon alfa-2bs (*e.g.*, INTRON A®); Irinotecans (*e.g.*, CAMPTOSAR®); Letrozoles (*e.g.*, FEMARA®); Leucovorins (*e.g.*, WELLCOVORIN®, LEUCOVORIN®); Levamisoles (*e.g.*, ERGAMISOL®); Lomustines/CCNUs (*e.g.*, CeeNU®); Mechlorethamines/Nitrogen mustards (*e.g.*, MUSTARGEN®); Megestrol acetates (*e.g.*, MEGACE®); Melphalans/L-PAMs (*e.g.*, ALKERAN®); Mercaptopurine incl. 6-MPs (*e.g.*, PURINETHOL®); Mesnas (*e.g.*, MESNEX®); Methotrexates; Methoxsalens (*e.g.*, UVADEX®); Mitomycin Cs (*e.g.*, MUTAMYCIN®, MITOZYTREX®); Mitotanes (*e.g.*, LYSODREN®); Mitoxantrones (*e.g.*, NOVANTRONE®); Nandrolone Phenpropionates (*e.g.*, DURABOLIN-50®); Nofetumomabs (*e.g.*, VERLUMA®); Oprelvekins (*e.g.*, NEUMEGA®); Oxaliplatins (*e.g.*, ELOXATIN®); Paclitaxels (*e.g.*, PAXENE®, TAXOL®); Pamidronates (*e.g.*, AREDIA®); Pegademases (*e.g.*, ADAGEN®); Pegaspargases (*e.g.*, ONCASPAR®); Pegfilgrastims (*e.g.*, NEULASTA®); Pentostatin (*e.g.*, NIPENT®); Pipobromans (*e.g.*, VERCYTE®); Plicamycin/Mithramycins (*e.g.*, MITHRACIN®); Porfimer sodiums (*e.g.*, PHOTOFRIN®); Procarbazines (*e.g.*, MATULANE®); Quinacrine (*e.g.*, ATABRINE®); Rasburicase (*e.g.*, ELITEK®); Rituximabs (*e.g.*, RITUXAN®); Sargramostim (*e.g.*, PROKINE®); Streptozocin (*e.g.*, ZANOSAR®); Sunitinib Malate (*e.g.*, SUTENT®); Talcs (*e.g.*, SCLEROSOL®); Tamoxifen (*e.g.*, NOLVADEX®); Temozolomide (*e.g.*, TEMODAR®); Teniposides/VM-26s (*e.g.*, VUMON®); Testolactones (*e.g.*, TESLAC®); Thioguanines incl. 6-TG; Thiotepa (*e.g.*, THIOPLEX®); Topotecans (*e.g.*, Hycamtin®); Toremifene (*e.g.*, FARESTON®); Tositumomabs (*e.g.*, BEXXAR®); Trastuzumab (*e.g.*, HERCEPTIN®); Tretinoin/ATRA (*e.g.*, VESANOID®); Uracil Mustards; Valrubicin (*e.g.*, VALSTAR®); Vinblastine (*e.g.*, VELBAN®); Vincristine (*e.g.*, ONCOVIN®); Vinorelbine (*e.g.*, NAVELBINE®); and Zoledronate (*e.g.*, ZOMETA®).

For example, exemplary antibiotic agents include, but are not limited to, Aminoglycosides; Amphenicols; Ansamycins; Carbacephem; Carbapenem; Cephalosporin or Cephem; Cephamycin; Clavam; Cyclic lipopeptides; Diaminopyrimidines; Ketolides;

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Estramustines, Etoposides, Etoposide phosphates, Etoposide VP-16s, Exemestanes,
Floxuridines, Fludarabines, Fluorouracils, 5-Fluorouracils, Fulvestrants, Gemcitabines,
Gemtuzumabs, Ozogamicins, Gemtuzumab ozogamicins, Hydroxyureas, Idarubicins,
Ifosfamidates, Imatinib mesylates, Irinotecans, Letrozoles, Leucovorins, Levamisoles,
5 Lomustines, CCNUs, Mechlorethamines, Nitrogen mustards, Megestrols, Megestrol acetates,
Melphalans, L-PAMs, Mercaptopurines, 6-Mercaptopurines, Mesnas, Methotrexates,
Methoxsalens, Mitomycins, Mitomycin C's, Mitotanes, Mitoxantrones, Nandrolones,
Nandrolone Phenpropionates, Nofetumomabs, Oprelvekins, Oxaliplatin, Paclitaxel,
Pamidronates, Pegademases, Pentostatin, Pipobromans, Plicamycins, Mithramycin,
10 Porfimers, Porfimer sodiums, Procarbazine, Quinacrine, Rasburicase, Rituximab,
Sargramostim, Streptozocin, Talcs, Tamoxifen, Temozolomide, Teniposide,
Testolactones, Thioguanines, 6-Thioguanines, Triethylenethiophosphoramide (Thiotepa),
Topotecan, Toremifene, Trastuzumab, Treinoin, Uracil Mustards, Valrubicin,
Vinblastine, Vincristine, Vinorelbine, Zoledronate, Acivicin, Aclarubicin, Acodazole,
15 Acronine, Adozelesin, Aldesleukin, Retinoic Acids, Alitretinoin, 9-Cis-Retinoic Acids,
Alvocidib, Ambazone, Ambomycin, Ametantrone, Aminoglutethimide, Amsacrine,
Anaxirone, Ancitabine, Anthramycin, Apaziquone, Argimesna, Asperlin, Atrimustine,
Azacitidine, Azetepa, Azotomycin, Banoxantrone, Batabulin, Batimastat, Benaxibine,
Bendamustine, Benzodepa, Bicalutamides, Bietaserpine, Biricodar, Bisantrene, Bisnafide
20 Dimesylate, Bizelesin, Bortezomib, Brequinar, Bropirimine, Budotitan,
Cactinomycin, Canertinib, Caracemide, Carbetimer, Carboquone, Carmofur,
Carubicin, Carzelesin, Cedefingol, Cemadotin, Chlorambucil, Cioteronel, Cirolemycin,
Clanfenur, Clofarabine, Crisnatol, Decitabine, Dexniguldipine, Dexormaplatin,
Dezaguanine, Diaziquone, Dibrospidium, Dienogest, Dinalin, Disermolide,
25 Dofequidar, Doxifluridine, Droloxifen, Duazomycin, Ecomustine, Edatrexate,
Edotecarin, Eflomithine, Elacridar, Elinafide, Elsamitracin, Emitefur, Enloplatin,
Enpromate, Enzastaurin, Epiropidine, Eptaloprost, Erbulazole, Esorubicin,
Etanidazole, Etoglucid, Etoprine, Exisulind, Fadrozole, Fazarabine, Fenretinide,
Fluoxymesterone, Flurocitabine, Fosquidone, Fostriecin, Fotretamine, Galarubicin,
30 Galocitabine, Geroquinol, Gimatecan, Gimeracil, Gloxazone, Glufosfamide,
Ilmofofine, Ilomastat, Imexon, Improsulfan, Indisulam, Inproquone, Interleukin,
Interleukin-2s, recombinant Interleukins, Intoplicin, Iobenguane, Iproplatin, Irsogladine,
Ixabepilone, Ketotrexate, L-Alanosine, Lanreotide, Lapatinib, Ledoxantrone,
Leuprolide, Leuprorelin, Lexacalcitol, Liarazole, Lobaplatin, Lometrexol, Lonafarnib,
35 Losoxantrone, Lurtotecan, Mafosfamide, Mannosulfan, Marimastat, Masoprocol,
Maytansine, Mechlorethamine, Melengestrol, Melphalan, Menogaril, Mepitiostane,
Metesind, Metomidate, Metoprine, Meturedopa, Miboplatin, Miproxifen,

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Misonidazoles, Mitindomides, Mitocarcins, Mitocromins, Mitoflaxones, Mitogillins,
Mitoguazones, Mitomalcins, Mitonafides, Mitoquidones, Mitospers, Mitozolomides,
Mivobulins, Mizoribines, Mofarotenes, Mopidamols, Mubritinibs, Mycophenolic Acids,
Nedaplatins, Neizarabines, Nemorubicins, Nitracrine, Nocodazoles, Nogalamycins,
5 Nolatrexeds, Nortopixantrones, Ormaplatins, Ortataxels, Oteracils, Oxisurans,
Oxophenarsines, Patupilones, Peldesines, Peliomycins, Pelitrexols, Pemetrexeds,
Pentamustines, Peplomycins, Perfosfamides, Perifosines, Picoplatins, Pinafides, Pipo sulfans,
Pirfenidones, Piroxantrones, Pixantrones, Plevitrexeds, Plomestanes, Porfiromycins,
Prednimustines, Propamidines, Prospidium, Pumitepas, Puromycins, Pyrazofurins,
10 Ranimustines, Riboprines, Ritrosulfans, Rogletimides, Roquinimexs, Rufocromomycins,
Sabarubicins, Safingols, Satraplatins, Sebriplatins, Semustines, Simtrazenes, Sizofirans,
Sobuzoxanes, Sorafenibs, Sparfosates, Sparfosic Acids, Sparsomycins, Spirogermaniums,
Spiromustines, Spiroplatins, Squalamines, Streptonigrins, Streptovarycins, Sufosfamides,
Sulofenurs, Tacedinalines, Talisomycins, Tallimustines, Tariquidars, Tauromustines,
15 Tecogalans, Tegafurs, Teloxantrones, Temoporfins, Teroxirones, Thiamiprines, Tiamiprines,
Tiazofurins, Tilomisoles, Tilorones, Timcodars, Timonacics, Tirapazamines, Topixantrones,
Trabectedins, Ecteinascidin 743, Trestolones, Triciribines, Trilostanes, Trimetrexates,
Triplatin Tetranitrates, Triptorelins, Trofosfamides, Tubulozoles, Ubenimexs, Uredepas,
Valspodars, Vapreotides, Verteporfins, Vinblastines, Vindesines, Vinepidines, Vinflunines,
20 Vinformides, Vinglycinates, Vinleucinols, Vinleurosines, Vinrosidines, Vintriptols,
Vinzolidines, Vorozoles, Xanthomycin A's, Guamecyclines, Zeniplatins, Zilascorbs [2-H],
Zinostatin, Zorubicins, Zosuquidars, Acetazolamides, Acyclovirs, Adipiodones,
Alatrofloxacin, Alfentanils, Allergenic extracts, Alpha 1-proteinase inhibitors, Alprostadils,
Amikacins, Amino acids, Aminocaproic acids, Aminophyllines, Amitriptylines,
25 Amobarbitals, Amrinones, Analgesics, Anti-poliomyelitic vaccines, Anti-rabic serums, Anti-
tetanus immunoglobulins, tetanus vaccines, Antithrombin IIIs, Antivenom serums,
Argatroban, Arginines, Ascorbic acids, Atenolols, Atracurium, Atropines,
Aurothioglucoses, Azathioprine, Aztreonams, Bacitracins, Baclofen, Basiliximabs, Benzoic
acids, Benzotropines, Betamethasone, Biotins, Bivalirudins, Botulism antitoxins, Bretylium,
30 Bumetanides, Bupivacaine, Buprenorphine, Butorphanol, Calcitonin, Calcitriol,
Calcium, Capreomycin, Carboprost, Carnitine, Cefamandole, Cefoperazone,
Cefotaxime, Cefoxitin, Ceftizoxime, Cefuroxime, Chloramphenicol, Chloroprocaine,
Chloroquine, Chlorothiazide, Chlorpromazine, Chondroitin sulfuric acid,
Choriogonadotropin alfa, Chromium, Cidofovir, Cimetidine, Ciprofloxacin,
35 Cisatracurium, Clonidine, Codeine, Colchicine, Colistin, Collagen, Corticorelin ovine
triflutate, Corticotrophin, Cosyntropin, Cyanocobalamin, Cyclosporine, Cysteine,
Daclizumab, Dalfopristin, Dalteparin, Danaparoid, Dantrolene, Deferoxamine,

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TABLE 10: Inactive Mutants							
Y057I	W115R	P187M	T232P	S282W	V334G	A371W	I430E
Y057L	W115S	P187N	T232Q	S282Y	V334M	I372A	I430L
Y057M	W115V	P187Q	T232V	Q283A	V334N	I372D	I430M
Y057P	W115Y	P187R	T232Y	Q283C	V334R	I372E	I430N
Y057Q	R116A	P187S	Q233D	Q283D	V334S	I372F	I430S
Y057R	R116C	P187T	Q233I	Q283F	T335F	I372G	I430T
Y057V	R116D	P187V	Q233P	Q283W	T335G	I372H	I430V
Y057W	R116E	P187W	Q233S	D284C	T335H	I372K	D431P
V058A	R116G	P187Y	Q233T	D284I	T335I	I372L	A432C
D059A	R116H	D188A	Q234A	D284P	T335K	I372N	A432F
D059E	R116I	D188C	Q234D	E285K	T335L	I372P	A432I
D059I	R116L	D188F	Q234E	E285P	T335P	I372R	A432K
D059L	R116N	D188G	Q234G	E285R	T335V	I372S	A432L
D059M	R116P	D188H	Q234H	E285T	T335W	I372T	A432M
D059P	R116Q	D188L	Q234N	E285V	T335Y	I372V	A432P
D059R	R116S	D188M	Q234P	L286A	L336A	I372W	A432Y
D059T	R116V	D188N	Q234S	L286C	L336E	Q373C	L434H
D059V	R116W	D188P	Q234T	L286D	L336F	Q373P	L434K
D059W	P117D	D188Q	Q234V	L286F	L336G	Q373W	L434P
D059Y	P117G	D188R	Q234W	L286H	L336K	L374D	L434Q
R060A	P117I	D188S	S235F	L286K	L336N	L374E	L434R
R060D	P117K	D188T	S235L	L286M	L336P	E375C	L434W
R060F	P117N	D188V	S235M	L286P	L336R	E375F	P437T
R060G	P117Q	D188W	S235R	L286T	L336S	E375P	M438Y
R060H	P117R	C189A	S235W	L286Y	L336T	E375V	E439N
R060I	P117S	C189E	S235Y	V287A	L336V	E375Y	E439R
R060L	P117V	C189G	P236C	V287C	R121G	K376I	T440Q
R060N	P117W	C189H	W119L	V287D	R121H	K376P	E441R
R060P	T118C	C189K	W119N	V287E	R121K	K376W	E442M
R060Q	T118D	C189L	W119P	V287G	R121L	G377C	E442N
R060S	T118E	C189M	W119R	V287K	R121M	G377I	E442S
R060T	T118G	C189N	R121A	V287L	R121P	G377L	P443D
T118R	T118P	T118W	R121C	R121F	G378D	G377V	G378E
T118Y	W119I	W119A	W119K	R121E	G378F	G378I	

EXAMPLE 5**ASSAY FOR HYALURONIDASE ACTIVITY UNDER TEMPERATURE AND PHENOPHILIC CONDITIONS**

5 Supernatants from PH20 activity variants set forth in Table 9, as identified in Example 4, were tested for stability under thermophilic and/or phenophilic conditions. The assay to measure hyaluronidase activity under temperature and phenophile conditions using biotinylated-HA (bHA) as substrate for measuring hyaluronidase activity was modified from

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Table 18. Enzymatic activity of rHuPH20 wild type and F204P mutant incubated at 30°C				
ID	PH20 activity U/mL, (% of remaining activity)			
	Initial Activity	6d	2w	4w
F1.Humalog + F204P	583 (100%)	345 (59%)	250 (43%)	111 (19%)
F2.Humalog + wt	439 (100%)	1 (0%)	16 (4%)	-1
F3.Aspart + F204P	625 (100%)	601(96%)	650(104%)	579 (93%)
F4.Aspart + wt	566 (100%)	428 (76%)	390 (69%)	277 (49%)
F5.Aspart + F204P	657 (100%)	632 (96%)	655 (100%)	561 (85%)
F6.Aspart+ wt	596 (100%)	145 (24%)	65 (11%)	9 (1.5%)

TABLE 19: Enzymatic Activity at 5 °C			
ID	PH20 activity (U/mL) at 5 °C		
	Initial Activity	2w	4w
F1.Humalog + F204P	583	544	565
F2.Humalog + wt	439	428	404
F3.Aspart + F204P	625	647	607
F4.Aspart + wt	566	580	496
F5.Aspart + F204P	657	695	574
F6.Aspart+ wt	596	583	519

EXAMPLE 11

STABILITY OF V58R-PH20 IN INSULIN COFORMULATION

5 A. Stability of V58R-PH20

The PH20 variant V58R was expressed in CHO-S cells as described in Example 2 or Example 6. The transfected plasmid DNA had a sequence of nucleotides set forth in SEQ ID NO:4 containing a codon change of GTG to CGG at nucleotide positions 1295-1297, thereby encoding the V58R mutant. The V58R mutant was tested for its stability in a coformulation containing insulin aspart (insulin aspart analog prepared as described in Example 10) and under EPA or EPB preservative levels. Briefly, four (4) formulations were generated each containing 600 Units (U) of PH20-V58R or wildtype rHuPH20 (generated as described in Example 1) as set forth in Table 20. Formulations F1 and F2 represent the EPB preservative levels while formulations F3 and F4 represent the EPA preservative levels.

TABLE 20: Summary of Insulin Formulations											
ID	pH	Buffer		Tonicity modifier	Anti-Ox		Metal	Surfactant	Preservatives		
		NaPO ₄	Tris/HCl	NaCl	Methionine	Glycerin	Zn	F68	Phenol	m-Cresol	API PH20 (U/mL) Analog (mg/mL)
F1.Aspart + V58R	7.3		30 mM	100 mM	5 mM			0.010%	0.100%	0.150%	600 3.5
F2.Aspart + rHuPH20 wt	7.3		30 mM	100 mM	5 mM			0.010%	0.100%	0.150%	600 3.5
F3.Aspart + V58R	7.3		30 mM	100 mM	5 mM			0.010%		0.315%	600 3.5
F4.Aspart+ rHuPH20 wt	7.3		30 mM	100 mM	5 mM			0.010%		0.315%	600 3.5

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concentration of 1 µg/mL. The medium was changed regularly at 3-4 day intervals, and the cells were transferred to a T75 flask for expansion. Two weeks after the initial infection, the cells were expanded to shaker flasks and maintained in culture using medium containing 1 µg/mL blasticidin. F204P-PH20 protein secreted into the CHO-S medium was collected and purified by affinity chromatography using an anti-rHuPH20 affinity column as described in Example 6. The protein was prepared in standard API buffer (10 mM Histidine, 130 mM NaCl, pH 6.5).

EXAMPLE 13

ANALYSIS OF SECONDARY STRUCTURE AND MELTING TEMPERATURE

The secondary structure and melting temperature of the PH20 variant F204P was tested and compared to wild-type rHuPH20 (generated as described in Example 1) to further assess stability of the variant. The secondary structure was tested by circular dichroism. A Jasco J-810-150S equipped with PTC-424S was employed for the CD spectral measurement and the CD spectra were collected by Spectra Manager (Version 1.5, Jasco). Procedures for instrumental set up and data collection are described in Table 24.

Table 24: CD Spectroscopy Operation Conditions	
Parameters	Conditions
Nitrogen flow rate	25 ft ³ /h
Sample temperature	30-75 °C
Sample concentration	Approx. 0.1 mg/mL
Cell pathlength	1 mm
Wavelength	220 nm
Data pitch	1 °C
Delay time	60 seconds
Temperature slope	1 °C/min
Sensitivity	standard
Response	4 seconds
Band width	1 nm

I. Sample Preparation and Measurement

Two hundred (200) µL of a 0.1 mg/mL protein sample diluted in McIlvaine's buffer (McIlvaine (1921) JBC 49:183) adjusted to pH 6.5 were prepared. A series of samples of the F204P variant were also generated that varied in pH by adjustment using McIlvaine's buffer to a pH range from 5.0 to 7.5 as set forth in Table 25. In addition, samples also were generated by adjusting the NaCl concentration to 17.5 mM to 140 mM as set forth in Table 26. Samples were filtered using a 0.2 µm syringe filter prior to measurement. Similar samples were generated for rHuPH20. Then, 200 µL samples were transferred to a rectangular cuvetted having a 1 mm width and seated on Jasco J-810 spectropolarimeter. CD spectra of the samples were collected under the conditions described in Table 20. The melting temperature (T_m) was calculated using Spectra Manager (v 1.5, Jasco) from the CD spectral intensity measured at the temperature range from 30 °C to 75 °C. The cuvettes were

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- enzymes, however, there was not a statistically significant increase in the area of dye dispersion compared to control. In addition, no statistically significant differences in the area of dye dispersion was observed between the rHuPH20 and F204P-PH20 treatment groups. Therefore, the duration of the spreading activity of rHuPH20 and F204P were similar and
- 5 show that rHuPH20 and F204P-PH20 have comparable *in vivo* performance.

TABLE 30: Dermal Reconstitution				
time Point	min post-injection	Vehicle	rHuPH20	F204P-PH20
30	5	49.96 ± 2.05	80.84 ± 8.03	80.76 ± 4.46
	20	64.42 ± 2.49	94.55 ± 7.09	95.75 ± 5.18
1 hour	5	58.01 ± 3.21	82.56 ± 6.40	77.11 ± 3.18
	20	65.19 ± 6.21	96.19 ± 6.39	91.45 ± 1.73
4 hour	5	52.10 ± 3.47	67.19 ± 2.39	67.33 ± 3.93
	20	57.69 ± 3.92	81.15 ± 4.45	82.21 ± 4.14
24 hour	5	49.87 ± 3.25	59.01 ± 2.15	54.91 ± 3.54
	20	57.15 ± 3.47	67.65 ± 2.27	62.91 ± 3.30
48 hour	5	53.64 ± 2.99	53.53 ± 4.88	55.64 ± 7.19
	20	61.57 ± 4.02	66.33 ± 4.12	63.11 ± 5.97

Example 16

In Vivo Pharmacokinetics of F204P-PH20 Compared to rHuPH20

- The pharmacokinetics (PK) of rHuPH20 and F204P-PH20 were compared following intravenous tail-vein administration by measuring the plasma hyaluronidase levels over time
- 10 after administration. The proteins used in the study were purified PH20 variant F204P (prepared as described in Example 12; batch concentration 1.02 mg/mL) and wild-type rHuPH20 (prepared as described in Example 1; batch concentration 0.95 mg/mL) formulated in API buffer (10 mM Histidine, 130 mM NaCl, pH 6.5). The proteins were prepared at a concentration of 0.087 mg/mL in API buffer for a dose volume of about 5 mL. An animal
- 15 that was not administered with protein was used as a control (pre-dose control). Forty two (42) male CD-1 mice (~ 20-30 grams) were used in the study with six animals per treatment group as set forth in Table 31.

TABLE 31: Pharmacokinetics of Single Intravenous Dose of rHuPH20 or F204P-PH20					
Group	number of animals (No.)	Test Article	Dose (mg/kg)	Dose Volume (mL/kg)	Euthanasia
1	6 (Nos. 1-6)	no treatment	N/A	N/A	pre-dose
2	6 (Nos. 7-12)	rHuPH20	0.433	5	1 min
3	6 (Nos. 13-18)	rHuPH20	0.433	5	5 ± 1 min
4	6 (Nos. 19-24)	rHuPH20	0.433	5	10 ± 2 min

Inventor(s): Wei *et al.*
Patent No. : 11,066,656
Issue Date : July 20, 2021
Serial No. : 16/912,590
Filed : June 25, 2020

Attorney Docket No.: 33320.03087.US27/3087D
Request for Certificate of Correction Pursuant to
37 C.F.R. § 1.322

A COPY OF THE CLAIMS IN THE AMENDMENT PURSUANT TO 37 C.F.R. § 1.312 AS
FILED ON MAY 21, 2021

COPY

Inventor(s): Wei *et al.*
Serial No. : 16/912,590
Filed : June 25, 2020

Attorney Docket No.: 33320.03087.US27/3087D
Amendment Pursuant to 37 C.F.R. §1.312

AMENDMENTS TO THE CLAIMS:

Please amend claims 1, 13-15, 19 and 23, as indicated below. This listing of claims replaces all prior versions and listing of claims in the application.

LISTING OF CLAIMS:

1. (Currently Amended) A modified PH20 polypeptide, comprising one or more amino acid replacements in an unmodified PH20 polypeptide, wherein:

the unmodified PH20 polypeptide consists of the amino acid sequence selected from the group consisting of SEQ ID NOs~~SEP ID NOs~~: 3, 7 and 32-66;

the modified PH20 polypeptide exhibits increased hyaluronidase activity compared to the unmodified PH20 polypeptide not containing the amino acid replacement(s);

the amino acid replacement(s) confer(s) the increased hyaluronidase activity;

an amino acid replacement that confers the increased hyaluronidase activity ~~and~~ is at a position corresponding to residue 309, with reference to amino acid positions of SEQ ID NO:3;

corresponding amino acid positions are identified by alignment of the PH20 polypeptide with the polypeptide having the amino acid sequence of SEQ ID NO:3; and

the modified PH20 polypeptide has at least 91% sequence identity to the amino acid sequence selected from the group consisting of SEQ ID NOs: 3, 7 and 32-66.

2. (Previously Presented) The modified PH20 polypeptide of claim 1, wherein the modified PH20 polypeptide has at least 95% sequence identity to the amino acid sequence selected from the group consisting of SEQ ID NOs: 3, 7, and 32-66.

3. (Original) The modified PH20 polypeptide of claim 2 that is a soluble PH20 polypeptide.

4. (Previously Presented) The modified PH20 polypeptide of claim 1, wherein the replacement is selected from among L at a position corresponding to position 309; N at a position corresponding to position 309; E at a position corresponding to position 309; G at a position corresponding to position 309; H at a position corresponding to position 309; and M at a position corresponding to position 309.

5. (Previously Presented) The modified PH20 polypeptide of claim 4, wherein the replacement at the position corresponding to position 309 is N.

6. (Previously Presented) The modified PH20 polypeptide of claim 1, wherein the unmodified PH20 polypeptide consists of the amino acid sequence selected from the group consisting of SEQ ID NOs: 3 and 32-66.

COPY

Inventor(s): Wei *et al.*
Serial No.: 16/912,590
Filed: June 25, 2020

Attorney Docket No.: 33320.03087.US27/3087D
Amendment Pursuant to 37 C.F.R. §1.312

7. (Previously Presented) The modified PH20 polypeptide of claim 2, wherein the unmodified PH20 polypeptide consists of the amino acid sequence selected from the group consisting of SEQ ID NOs: 3 and 32-66.
8. (Previously Presented) The modified PH20 polypeptide of claim 5, wherein the unmodified PH20 polypeptide consists of the amino acid sequence selected from the group consisting of SEQ ID NOs: 3 and 32-66.
9. (Previously Presented) The modified PH20 polypeptide of claim 1, wherein the unmodified PH20 polypeptide consists of the amino acid sequence of SEQ ID NO:35.
10. (Previously Presented) The modified PH20 polypeptide of claim 1, wherein the unmodified PH20 polypeptide consists of the amino acid sequence of SEQ ID NO:32.
11. (Previously Presented) The modified PH20 polypeptide of claim 5, wherein the unmodified PH20 polypeptide consists of the amino acid sequence of SEQ ID NO:35.
12. (Original) The modified PH20 polypeptide of claim 1, wherein the modified PH20 polypeptide exhibits increased hyaluronidase activity that is at least 120% of the hyaluronidase activity compared to the unmodified PH20 polypeptide not containing the amino acid replacement or replacements.
13. (Currently Amended) The modified PH20 polypeptide of claim 1, comprising the amino acid sequence selected from the group consisting of SEQ ID NOs:576-586, or an amino acid sequence that exhibits at least 91% sequence identity to the amino acid sequence selected from the group consisting of SEQ ID NOs:3 and 32-66 and that contains the amino acid replacement L, N, E, G, H, M, Q, R, S, T or V at a position corresponding to residue 309.
14. (Currently Amended) The modified PH20 polypeptide of claim 1, comprising the amino acid sequence of SEQ ID NO:581, or an amino acid sequence that ~~has~~exhibits at least 91% sequence identity to the amino acid sequence selected from the group consisting of SEQ ID NOs: 3 and 32-66 and that contains the amino acid replacement N at a position corresponding to residue 309.
15. (Currently Amended) The modified PH20 polypeptide of claim 1 that further comprises one or more modifications selected from among glycosylation, ~~sialylation~~sialination, albumination, farnesylation, carboxylation, hydroxylation, and phosphorylation.
16. (Previously Presented) The modified PH20 polypeptide of claim 1 that further comprises an N-acetylglucosamine moiety linked to each of at least three asparagine (N) residues.

COPY

Inventor(s): Wei *et al.*
Serial No. : 16/912,590
Filed : June 25, 2020

Attorney Docket No.: 33320.03087.US27/3087D
Amendment Pursuant to 37 C.F.R. §1.312

17. (Original) The modified PH20 polypeptide of claim 1 that is conjugated to a polymer.
18. (Previously Presented) The modified PH20 polypeptide of claim 17, wherein the polymer is dextran or polyethylene glycol (PEG).
19. (Currently Amended) The modified PH20 polypeptide of claim 1, further comprising a heterologous signal sequence, wherein the unmodified PH20 polypeptide consists of the amino acid sequence selected from the group consisting of SEQ ID NOs: 3 and 32-66.
20. (Original) A chimeric polypeptide, comprising the modified PH20 polypeptide of claim 1.
21. (Original) A pharmaceutical composition, comprising the modified PH20 polypeptide of claim 1.
22. (Cancelled)
23. (Currently Amended) The modified PH20 polypeptide of claim 1, comprising the amino acid sequence of SEQ ID NO:581, or an amino acid sequence that exhibits at least 95% sequence identity to the amino acid sequence of SEQ ID NO:581 and that contains the amino acid replacement N at a position corresponding to residue 309.
24. (Previously Presented) The modified PH20 polypeptide of claim 5, wherein:
the unmodified PH20 polypeptide consists of the amino acid sequence set forth in SEQ ID NO:32; and
the amino acid sequence of the modified PH20 polypeptide has at least 95% sequence identity to SEQ ID NO:32.
25. (Previously Presented) The modified PH20 polypeptide of claim 5, wherein:
the unmodified PH20 polypeptide consists of the amino acid sequence set forth in SEQ ID NO:35; and
the amino acid sequence of the modified PH20 polypeptide has at least 95% sequence identity to SEQ ID NO:35.
26. (Previously Presented) The modified PH20 polypeptide of claim 1, further comprising a signal sequence, wherein the unmodified PH20 polypeptide consists of the amino acid sequence selected from the group consisting of SEQ ID NOs: 3 and 32-66.

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Inventor(s):	Wei <i>et al.</i>	Art Unit	: 1656
Patent No. :	11,066,656	Examiner	: Liu, Samuel W.
Issue Date :	July 20, 2021	Conf. No.	: 9651
Serial No. :	16/912,590	Cust. No.	: 13565
Filed	: June 25, 2020		
Title	: PH20 POLYPEPTIDE VARIANTS, FORMULATIONS AND USES THEREOF		

Attn: Certificate of Correction Branch

Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

TRANSMITTAL LETTER

Dear Sir:

Transmitted herewith are a Request for Certificate of Correction (9 pages); a Certificate of Correction (4 pages); a copy of page 8 of the Form PTO-1449 as filed on July 08, 2020, as initialed by the Examiner on September 30, 2020, and mailed to the Applicant on May 03, 2021 (1 page); copies of pages 24, 39, 41, 98, 102, 155, 160, 203, 204, 207, 208, 283, 312, 316 and 320 of the Specification as originally filed on June 25, 2020 (15 pages); and a copy of the claims from the Amendment Pursuant to 37 C.F.R. § 1.312, filed May 21, 2021 entered by the Examiner on June 03, 2021 (3 pages).



The Commissioner is hereby authorized to charge any fees that may be due in connection with this and the attached papers or with this application during its entire pendency to Deposit Account No. 50-0911.

Respectfully submitted,

/Stephanie Seidman/

Stephanie Seidman

Reg. No. 33,779

Attorney Docket No.: 33320.03087.US27/3087D

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CERTIFICATE OF TRANSMISSION VIA EFS-WEB

I hereby certify that this paper is being transmitted via the Electronic Filing System (EFS-WEB) to the United States Patent and Trademark Office On **July 11, 2022**.

/Jimmy Schaub/

Jimmy Schaub

Electronic Acknowledgement Receipt	
EFS ID:	46156219
Application Number:	16912590
International Application Number:	
Confirmation Number:	9651
Title of Invention:	PH20 POLYPEPTIDE VARIANTS, FORMULATIONS AND USES THEREOF
First Named Inventor/Applicant Name:	GE WEI
Customer Number:	13565
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File Listing:					
Document Number	Document Description	File Name	File Size(Bytes)/ Message Digest	Multi Part /.zip	Pages (if appl.)
1	Request for Certificate of Correction	3087Drcc_000.pdf	162958	no	9
			05ceb996b01cd1137e720a697e3403033c33b841		
Warnings:					

Information:					
2	Request for Certificate of Correction	3087D_COC.pdf	1649841	no	27
			fb1dcad74550a93b1864985706642561cbe8154c		
Warnings:					
Information:					
3	Transmittal Letter	3087Dtra_000.pdf	136740	no	1
			80d26c2ab859d2fa31f947dcd23f8cdd9a2e393f		
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UNITED STATES PATENT AND TRADEMARK OFFICE
CERTIFICATE OF CORRECTION

PATENT NO. : 11,066,656 B2
APPLICATION NO. : 16/912590
DATED : July 20, 2021
INVENTOR(S) : Wei et al.

Page 1 of 3

It is certified that error appears in the above-identified patent and that said Letters Patent is hereby corrected as shown below:

On the Title Page

In Item (56) References Cited, in OTHER PUBLICATIONS, at page 3, 2nd Column, Line 71, please replace “lip” with —trp—;

In the Specification

At Column 20, Line 46, please replace “Rat a position” with —R at a position—;

At Column 33, Line 48, please replace “Tales” with —Tals—;

At Column 34, Line 60, please replace “Antithrombin I11s” with —Antithrombin IIIs—;

At Column 84, Line 61, please replace “1271” with —I271—;

At Column 88, Line 13, please replace “Rat a position” with —R at a position—;

At Column 136, Line 4, please replace “W138” with —WI38—;

At Column 140, Line 55, please replace “GALS” with —GAL5—;

At Column 176, Line 20, please replace “Tales” with —Tals—;

At Column 177, Line 39, please replace “Tales” with —Tals—;

At Column 179, Line 53, please replace “Tales” with —Tals—;

At Column 180, Line 65, please replace “Antithrombin I11s” with —Antithrombin IIIs—;

Signed and Sealed this
Ninth Day of August, 2022



Katherine Kelly Vidal
Director of the United States Patent and Trademark Office

CERTIFICATE OF CORRECTION (continued)
U.S. Pat. No. 11,066,656 B2

Page 2 of 3

At Column 269, Table 10, please replace “R1161” with —R116I—;

At Column 269, Table 10, please replace “D0591” with —D059I—;

At Column 301, Line 20, please replace “PH2P” with —PH20—;

At Column 301, Line 21, please replace “V8R” with —V58R—;

At Column 305, Table 24, please replace “W/h” with —ft3/h—;

At Column 309, Line 29, please replace “PH2P” with —PH20—;

At Column 309, Line 34, please replace “mg/min” with —mg/mL in—;

Column 309, Line 35, please replace “mL” with —5 mL—;

In the Claims

Please replace Claim 1 with the following amended claim:

—1. A modified PH20 polypeptide, comprising one or more amino acid replacements in an unmodified PH20 polypeptide, wherein:
the unmodified PH20 polypeptide consists of the amino acid sequence selected from the group consisting of SEQ ID NOs: 3, 7 and 32-66;
the modified PH20 polypeptide exhibits increased hyaluronidase activity compared to the unmodified PH20 polypeptide not containing the amino acid replacement(s);
the amino acid replacement(s) confer(s) the increased hyaluronidase activity;
an amino acid replacement that confers the increased hyaluronidase activity is at a position corresponding to residue 309, with reference to amino acid positions of SEQ ID NO:3;
corresponding amino acid positions are identified by alignment of the PH20 polypeptide with the polypeptide having the amino acid sequence of SEQ ID NO:3; and
the modified PH20 polypeptide has at least 91% sequence identity to the amino acid sequence selected from the group consisting of SEQ ID NOs: 3, 7 and 32-66.—;

Please replace Claim 10 with the following amended claim:

—10. The modified PH20 polypeptide of claim 6, wherein:
the unmodified PH20 polypeptide consists of the amino acid sequence set forth in SEQ ID NO:35; and
the amino acid sequence of the modified PH20 polypeptide has at least 95% sequence identity to SEQ ID NO:35.—;

Please replace Claim 12 with the following amended claim:

—12. The modified PH20 polypeptide of claim 1, wherein the unmodified PH20 polypeptide consists of the amino acid sequence of SEQ ID NO:35.—;

Please replace Claim 21 with the following amended claim:

—21. The modified PH20 polypeptide of claim 1, further comprising a heterologous signal sequence, wherein the unmodified PH20 polypeptide consists of the amino acid sequence selected from the group consisting of SEQ ID NOs: 3 and 32-66.—;

Please replace Claim 25 with the following amended claim:

—25. The modified PH20 polypeptide of claim 1, further comprising a signal sequence, wherein the unmodified PH20 polypeptide consists of the amino acid sequence selected from the group consisting of SEQ ID NOs: 3 and 32-66.—.