

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Patent Application of:
Guoxian Wu et al.

Application No.: Not Yet Assigned

Confirmation No.: N/A

Filed: Concurrently Herewith

Art Unit: N/A

For: COMPOUNDS AND METHODS FOR KINASE
MODULATION, AND INDICATIONS
THEREFOR

Examiner: Not Yet Assigned

PRELIMINARY AMENDMENT UNDER 37 CFR 1.115

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

Commissioner:

Prior to examination of the present Application, Applicant respectfully requests that the application be amended as follows:

Amendments to the Specification begin on page 2 of this document.

Amendments to the Claims are reflected in the listing of claims that begin on page 3 of this document.

Remarks/Arguments begin on page 5 of this document.

Please amend the application as follows:

Amendments to the Specification:

Please amend the specification as follows:

Please replace the first paragraph, paragraph [0001], with the following amended paragraph:

--This application is a continuation of U.S. Application No. 13/926,959, filed June 25, 2013, which is a continuation application of U.S. Application No. 13/866,353, filed April 19, 2013, which is a continuation application of 12/669,450, filed January 15, 2010, which application is a National Phase application under 35 U.S.C. § 371 of PCT/US2008/070124, filed July 16, 2008, which claims the benefit under 35 U.S.C. § 119(e) from U.S. Application No. 60/959,907, filed July 17, 2007, which applications are hereby incorporated by reference in their entirety.--

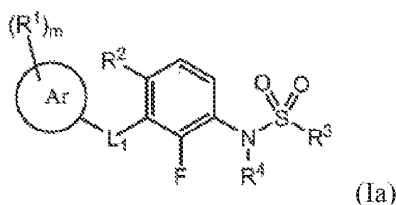
Amendments to the Claims:

This listing of claims will replace all prior versions, and listings, of claims in the application:

Listing of Claims:

1-20. (Canceled).

21. (New) A compound of formula (Ia):



or a pharmaceutically acceptable salt thereof,

wherein:

L_1 is a bond, $-N(H)C(O)-$, $-N(H)-$, $-N(H)-S(O)_2-$, or $-N(H)-C(NH)-$;

each R^1 is optionally substituted lower alkyl or optionally substituted heteroaryl;

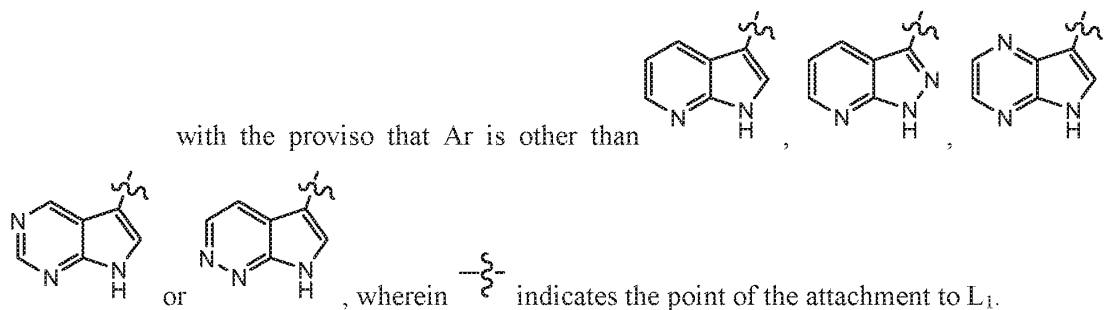
R^2 is hydrogen or halogen;

R^4 is hydrogen;

R^3 is optionally substituted lower alkyl or optionally substituted aryl;

m is 0, 1, 2, 3, 4, or 5; and

Ar is a monocyclic heteroaryl containing 5 to 6 atoms or a bicyclic heteroaryl containing 8 to 10 atoms wherein at least one atom is nitrogen,



22. (New) The compound of claim 21, wherein R^2 is hydrogen.

23. (New) The compound of claim 21, wherein R² is halogen.
24. (New) The compound of claim 21, wherein R³ is optionally substituted phenyl.
25. (New) The compound of claim 21, wherein R³ is phenyl substituted with one or more substituents selected from the group consisting of fluoro, lower alkyl, fluoro substituted lower alkyl, lower alkoxy, fluoro substituted lower alkoxy, lower alkylthio, and fluoro substituted lower alkylthio.
26. (New) The compound of claim 21, wherein R³ is phenyl substituted with one or more fluoro.
27. (New) The compound of claim 21, wherein each R¹ is optionally substituted lower alkyl.
28. (New) The compound of claim 21, wherein each R¹ is optionally substituted heteroaryl.
29. (New) The compound of claim 21, wherein Ar is a monocyclic heteroaryl containing 5 to 6 atoms.
30. (New) A pharmaceutical composition comprising a compound of claim 21 and a pharmaceutically acceptable carrier or excipient.
31. (New) A pharmaceutical composition comprising a compound of claim 21 and another therapeutic agent.
32. (New) A method for treating a subject suffering from melanoma, thyroid cancer or colorectal cancer, said method comprising administering to the subject an effective amount of a compound of claim 21.
33. (New) The method of claim 32, wherein the melanoma is melanoma having a mutation encoding a V600E amino acid substitution.

REMARKS

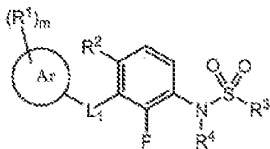
Applicant respectfully requests that the foregoing amendments be made prior to examination of the present application.

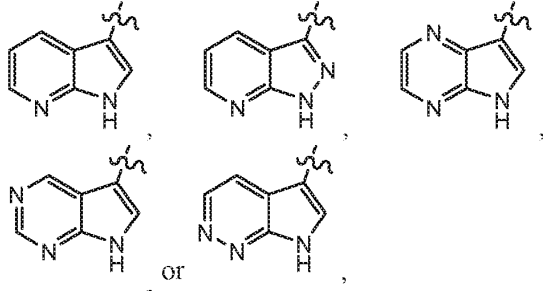


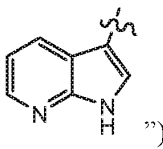
Amendments to the Specification

In the specification, paragraph [0001] has been amended to update the priority claim. No new matter is added by the amendment, and its entry is respectfully requested.

Claim Amendments

Claims 1-20 are canceled, and claims 21-33 are newly added. Support for these claims can be found throughout the original specification and priority application as summarized in the Table below.

Claim(s)	Claim Limitation	Exemplary Support in Present Application	Exemplary Support in Priority Application
21	Compounds of Formula (Ia) 	Para. [0006]	Para. [0008]
21	L ₁ is a bond, -N(H)C(O)-, -N(H)-, -N(H)-S(O) ₂ -, or -N(H)-C(NH)-	Para. [0005], [0007], [0009],	Para. [0007], [0009], and [0010]
21, 27, 28	each R ¹ is optionally substituted lower alkyl or optionally substituted heteroaryl	Para. [0005]	Para. [0007]
21, 22, 23	R ² is hydrogen or halogen	Para. [0009]	Para. [0010]
21	R ³ is optionally substituted lower alkyl or optionally substituted aryl	Para. [0005]	Para. [0007]

21	R ⁴ is hydrogen	Para. [0007]-[0009]	Para. [0009]-[0010]
21	m is 0, 1, 2, 3, 4, or 5	Para. [0005]	Para. [0007]
21, 29	Ar is a monocyclic heteroaryl containing 5 to 6 atoms or a bicyclic heteroaryl containing 8 to 10 atoms wherein at least one atom is nitrogen	Para. [0005], [0043]-[0044], and [0091]	Para. [0007], [0025], [0027], and [0074]
21	<p>with the proviso that Ar is other than</p>  <p>or</p>  <p>wherein  indicates the point of the attachment to L₁</p>	Para. [0005]	<p>Para. [0007]</p> <p>(Ar is not “7-azaindol-3-yl, i.e. is not</p>  <p>”)</p>
24	R ³ is optionally substituted phenyl	Para. [0048]	Para. [0029]
25, 26	R ³ is phenyl substituted with one or more substituents selected from the group consisting of fluoro, lower alkyl, fluoro substituted lower alkyl, lower alkoxy, fluoro substituted lower alkoxy, lower alkylthio, and fluoro substituted lower alkylthio.	Para. [0048]	Para. [0029]
30, 31	Pharmaceutical compositions comprising compounds of formula (Ia)	Para. [0143]-[0151]	Para. [0362]-[0372]
32, 33	Methods of treatment comprising administering compounds of formula (Ia)	Para. [0053] and [0077]	Para. [0035] and [0058]-[0061]

No new matter is added by this amendment, and as such, Applicant respectfully requests its entry. Further, Applicant reserves the right to pursue canceled subject matter in a continuing application.

Applicant respectfully requests the Office review the Interview Summary of parent application, U.S. App. No. 13/926,959 (“the ‘959 application”), filed on even date herewith. Additionally, as noted in an Applicant-Initiated Interview Summaries dated January 22, 2016, and February 4, 2016, of the ‘959 application, the Office agreed that the application has support for L1 as amide or a bond, and Ar as nitrogen-containing bicyclic heteroaryl and monocyclic heteroaryl. Further, the Applicant-Initiated Interview Summary dated January 22, 2016, provides that “[t]he examiner further indicate that compounds with L1 is –NH-C(O)– and Ar is nitrogen containing bicyclic heteroaryl, with the proviso therein, are allowable.”

Early examination of the application as amended is respectfully requested, and the Examiner is invited to contact the undersigned by telephone if it is felt that a telephone interview would advance the prosecution of the present application.

Dated: February 19, 2016

Respectfully submitted,

By /Joy Lynn Nemirow Reg. No. 67,163/ for
Lorna L. Tanner
Registration No.: 50,782
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Attorney For Applicant

Electronic Patent Application Fee Transmittal				
Application Number:				
Filing Date:				
Title of Invention:		COMPOUNDS AND METHODS FOR KINASE MODULATION, AND INDICATIONS THEREFOR		
First Named Inventor/Applicant Name:		Guoxian Wu		
Filer:		Joy Lynn Bala Nemirow/Aubrett Baker		
Attorney Docket Number:		37JF-193349-US5		
Filed as Large Entity				
Filing Fees for Track I Prioritized Examination - Nonprovisional Application under 35 USC 111(a)				
Description	Fee Code	Quantity	Amount	Sub-Total in USD(\$)
Basic Filing:				
Utility application filing	1011	1	280	280
Utility Search Fee	1111	1	600	600
Utility Examination Fee	1311	1	720	720
Request for Prioritized Examination	1817	1	4000	4000
Pages:				
Utility Appl Size fee per 50 sheets >100	1081	1	400	400
Claims:				
Miscellaneous-Filing:				

Description	Fee Code	Quantity	Amount	Sub-Total in USD(\$)
PROCESSING FEE, EXCEPT PROV. APPLS.	1830	1	140	140
Petition:				
Patent-Appeals-and-Interference:				
Post-Allowance-and-Post-Issuance:				
Extension-of-Time:				
Miscellaneous:				
Total in USD (\$)				6140

Electronic Acknowledgement Receipt	
EFS ID:	24971303
Application Number:	15048851
International Application Number:	
Confirmation Number:	5501
Title of Invention:	COMPOUNDS AND METHODS FOR KINASE MODULATION, AND INDICATIONS THEREFOR
First Named Inventor/Applicant Name:	Guoxian Wu
Customer Number:	117868
Filer:	Joy Lynn Bala Nemirow/Aubrett Baker
Filer Authorized By:	Joy Lynn Bala Nemirow
Attorney Docket Number:	37JF-193349-US5
Receipt Date:	19-FEB-2016
Filing Date:	
Time Stamp:	19:12:20
Application Type:	Utility under 35 USC 111(a)

Payment information:

Submitted with Payment	yes
Payment Type	Deposit Account
Payment was successfully received in RAM	\$6140
RAM confirmation Number	5940
Deposit Account	506219
Authorized User	NEMIROW, JOY LYNN B
<p>The Director of the USPTO is hereby authorized to charge indicated fees and credit any overpayment as follows:</p> <p>Charge any Additional Fees required under 37 CFR 1.16 (National application filing, search, and examination fees)</p> <p>Charge any Additional Fees required under 37 CFR 1.17 (Patent application and reexamination processing fees)</p>	

Charge any Additional Fees required under 37 CFR 1.19 (Document supply fees)					
Charge any Additional Fees required under 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 of New Application	193349-US5_UtilityTransmittal.pdf	93502 918abb86a027bb750dddada08fed9d967b890ee50	no	1
Warnings:					
Information:					
2		193349-US5_Application.pdf	6604508 7626572b697eaba0c443d35087ff3c2535723483	yes	143
	Multipart Description/PDF files in .zip description				
	Document Description		Start	End	
	Specification		1	139	
	Claims		140	142	
	Abstract		143	143	
Warnings:					
Information:					
3	TrackOne Request	193449-US5_Track1Request.pdf	105816 9a78af77aa515bfd3819276078e9f20c45128cf8	no	1
Warnings:					
Information:					
4	Application Data Sheet	193349-US5_ADS.pdf	76317 393ba3e7cd890fc850ea0ff7c5fd9ad7b11458de	no	10
Warnings:					
Information:					
This is not an USPTO supplied ADS fillable form					
5	Transmittal Letter	193349-US5_IDS.pdf	79658 9f8ce64914f754387575a89eead17a15259cd4d0	no	2
Warnings:					
Information:					

6	Information Disclosure Statement (IDS) Form (SB08)	193449-US5_SB08Form.pdf	451308 2cf4a9b503c11a55027d7dbb7f3643ca343898dccc	no	54
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7	Oath or Declaration filed	193349-US5-ExecutedDecls.pdf	418970 02f271c841caf3e7aed6721934d2bedf4b54f3a8	no	9
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Information:					
8		193349-US5_PAM.pdf	123856 1397bfc4d84aa9ea263483357acc33ff05cb a9d5	yes	7
	Multipart Description/PDF files in .zip description				
	Document Description		Start	End	
	Preliminary Amendment		1	1	
	Specification		2	2	
	Claims		3	4	
	Applicant Arguments/Remarks Made in an Amendment		5	7	
Warnings:					
Information:					
9	Fee Worksheet (SB06)	fee-info.pdf	41076 7f2cced287377a8a6eb13145c07ab4bb7ed534ff	no	2
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Information:					
Total Files Size (in bytes):			7995011		

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 15/048,851		Filing Date 02/19/2016		<input type="checkbox"/> To be Mailed			
ENTITY: <input checked="" type="checkbox"/> LARGE <input type="checkbox"/> SMALL <input type="checkbox"/> MICRO											
APPLICATION AS FILED – PART I											
(Column 1)		(Column 2)									
FOR		NUMBER FILED		NUMBER EXTRA		RATE (\$)		FEE (\$)			
<input type="checkbox"/> BASIC FEE (37 CFR 1.16(a), (b), or (c))		N/A		N/A		N/A					
<input type="checkbox"/> SEARCH FEE (37 CFR 1.16(k), (j), or (m))		N/A		N/A		N/A					
<input type="checkbox"/> 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 \$ =					
INDEPENDENT CLAIMS (37 CFR 1.16(h))		minus 3 =		*		X \$ =					
<input type="checkbox"/> 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).									
<input type="checkbox"/> 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	02/19/2016	CLAIMS REMAINING AFTER AMENDMENT		HIGHEST NUMBER PREVIOUSLY PAID FOR		PRESENT EXTRA		RATE (\$)		ADDITIONAL FEE (\$)	
	Total (37 CFR 1.16(i))	* 13	Minus	** 20	= 0		X \$80 =		0		
	Independent (37 CFR 1.16(h))	* 1	Minus	***3	= 0		X \$420 =		0		
	<input type="checkbox"/> Application Size Fee (37 CFR 1.16(s))										
	<input type="checkbox"/> FIRST PRESENTATION OF MULTIPLE DEPENDENT CLAIM (37 CFR 1.16(j))										
						TOTAL ADD'L FEE		0			
(Column 1)		(Column 2)		(Column 3)							
AMENDMENT		CLAIMS REMAINING AFTER AMENDMENT		HIGHEST NUMBER PREVIOUSLY PAID FOR		PRESENT EXTRA		RATE (\$)		ADDITIONAL FEE (\$)	
	Total (37 CFR 1.16(i))	*	Minus	**	=		X \$ =				
	Independent (37 CFR 1.16(h))	*	Minus	***	=		X \$ =				
	<input type="checkbox"/> Application Size Fee (37 CFR 1.16(s))										
	<input type="checkbox"/> FIRST PRESENTATION OF MULTIPLE DEPENDENT CLAIM (37 CFR 1.16(j))										
						TOTAL ADD'L FEE					
<p>* If the entry in column 1 is less than the entry in column 2, write "0" in column 3.</p> <p>** If the "Highest Number Previously Paid For" IN THIS SPACE is less than 20, enter "20".</p> <p>*** If the "Highest Number Previously Paid For" IN THIS SPACE is less than 3, enter "3".</p> <p>The "Highest Number Previously Paid For" (Total or Independent) is the highest number found in the appropriate box in column 1.</p>											

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.