

EXHIBIT A

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Request For Continued Examination (RCE) Transmittal

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Application Number	12/523,652; Conf. No.: 1432
Filing Date	June 15, 2010
First Named Inventor	Scott Wilhelm
Art Unit	1629
Examiner Name	Raymond J. Henley
Attorney Docket Number	BAYER-0143

This is a Request for Continued Examination (RCE) under 37 CFR 1.114 of the above-identified application.
 Request for Continued Examination (RCE) practice under 37 CFR 1.114 does not apply to any utility or plant application filed prior to June 8, 1995, or to any design application. See Instruction Sheet for RCEs (not to be submitted to the USPTO) on page 2.

1. **Submission required under 37 C.F.R. 1.114** Note: If the RCE is proper, any previously filed unentered amendments and amendments enclosed with the RCE will be entered in the order in which they were filed unless applicant instructs otherwise. If applicant does not wish to have any previously filed unentered amendment(s) entered, applicant must request non-entry of such amendment(s).

- a. Previously submitted. If a final Office action is outstanding, any amendments filed after the final Office action may be considered as a submission even if this box is not checked.
- i. Consider the arguments in the Reply previously filed on _____.
 - ii. Other _____
- b. Enclosed
- i. Amendment/Reply
 - ii. Affidavit(s)/Declaration(s)
 - iii. Information Disclosure Statement (IDS)
 - iv. Other _____

2. **Miscellaneous**

- a. Suspension of action on the above-identified application is requested under 37 C.F.R. 1.103(c) for a period of _____ months. (Period of suspension shall not exceed 3 months, Fee under 37 C.F.R. 1.17(i) required)
- b. Other _____

3. **Fees** The RCE fee under 37 C.F.R. 1.17(e) is required by 37 C.F.R. 1.114 when the RCE is filed.

- a. The Director is hereby authorized to charge the required fees, or credit any overpayments, to Deposit Account No. 13-3402.
- i. RCE fee required under 37 C.F.R. 1.17(e)
 - ii. Extension of time fee (37 C.F.R. 1.136 and 1.17)
 - iii. Other _____
- b. Check in the amount of \$ _____ enclosed
- c. Payment by credit card (Form PTO-2038 enclosed)

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SIGNATURE OF APPLICANT, ATTORNEY, OR AGENT REQUIRED

Signature	/Richard J. Traverso/	Date	November 5, 2013
Name (Print /Type)	Richard J. Traverso	Registration No.	30,595

CERTIFICATE OF MAILING OR TRANSMISSION

I hereby certify that this correspondence is being deposited with the United States Postal Service with sufficient postage as first class mail in an envelope addressed to: Mail Stop RCE, Commissioner for Patents, P. O. Box 1450, Alexandria, VA 22313-1450 or facsimile transmitted to the U.S. Patent and Trademark Office on the date shown below.

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This collection of information is required by 37 CFR 1.114. 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 1.11 and 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: Mail Stop RCE, Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.**

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IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of:

Scott WILHELM et al.

Examiner: Henley III, Raymond J

Serial No.: 12/523,652

Group Art Unit: 1629

Filed: June 16, 2010

Confirmation No.: 1432

Title: TREATMENT OF CANCERS WITH ACQUIRED
RESISTANCE TO KIT INHIBITORS

SUBMISSION WITH RCE

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Sir:

In response to the notice of Allowance dated August 9, 2013, Applicants submit the following amendments to accompany the Request for Continued Examination filed concurrently in the above application:

Amendments to the Claims are reflected in the listing of claims which begins on page 2 of this paper.

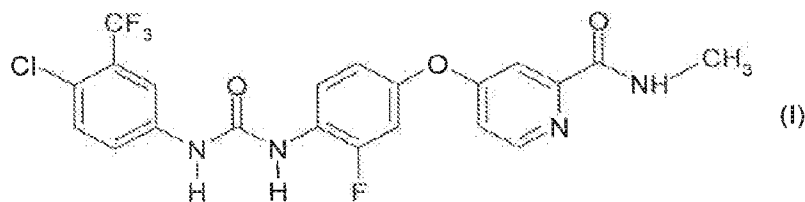
Remarks/Arguments begin on page 11 of this paper.

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

Listing of Claims:

1. (Original) A method of treating a cancer in a subject in need thereof, wherein said cancer was initially sensitive to KIT tyrosine kinase inhibitor and acquired resistance to said KIT tyrosine kinase inhibitor, said method comprising:

administering to said subject, an effective amount of 4{4-[3-(4-chloro-3-trifluoromethylphenyl)-ureido]-3-fluorophenoxy}-pyridine-2-carboxylic acid methylamide of the formula I below including all polymorphs, hydrates, pharmaceutically acceptable salts, metabolites, prodrugs, solvates or combinations thereof.



2. (Previously presented) A method as in claim 1 wherein the cancer has acquired resistance to one of the following KIT inhibitors:

imatinib mesylate, salts of imatinib mesylate; PPI(4-Amino-5-(4-methylphenyl)-7-(t-butyl)pyrazolo[3,4-d]pyrimidine); MLN518 (CT53518); PD180970; SU112481 SU5416; SU5414; SU6597; SU6663 or SU6561.

3. (Previously presented) A method as in claim 1 wherein said cancer is one or more of a malignant gastrointestinal stromal tumor (GIST), a benign gastrointestinal stromal tumor (GIST), a mesenchymal tumor of the intestinal tract, chronic myelogenous leukemia (CML), a mast cell tumor, SCLC, a germ cell tumors, breast cancer, and/or neuroblastoma.

4. (Previously presented) A method as in claim 1 wherein the cancer has acquired resistance to imatinib mesylate.

5. (Previously presented) A method of claim 1, wherein said acquired resistance of said cancer is associated with a secondary mutation in a KIT gene mutated in the primary tumor.
6. (Previously presented) A method of claim 5, wherein said secondary mutation is in the kinase catalytic domain.
7. (Previously presented) A method as in claim 5 wherein the mutation is in Exons 13, 14, and or 17.
8. (Previously presented) A method as in claim 5 wherein the mutation is at residues 654, 670, 716, 816, 820, 822, and 823.
9. (Previously presented) A method as in claim 5 wherein the mutation is at residues 650-654.
10. (Previously presented) A method as in claim 5 wherein the mutation is at residues 670-674.
11. (Previously presented) A method as in claim 5 wherein the mutation is at residues 816-824.
12. (Previously presented) A method as in claim 5 wherein the secondary mutation is one or more of V654A (Exon 13), T670I (Exon 14), T670E, D716N, S709F (Exon 14), D816G, D816E (Exon 17), D820E, D820Y, D820G N822K, Y823D (Exon 17), or deletions and other amino acid substitutions at such positions or adjacent positions.
13. (Previously presented) A method as in claim 5 wherein the secondary mutation is one or more of
 - i) deletion of amino acid residues 557-558;
 - ii) deletion of amino acid residues 551-555;

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