03-09-03

Docket No.: 62814-A/JPW/GJG

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicants: Timothy Norris et al.

Serial No.: 09/711,272 Examiner: T. McKenzie

Filed : November 9, 2000 Group Art Unit: 1624

For : STABLE POLYMORPH ON N-(3-ETHYNYLPHENYL)-6,7-BIS (2-METHOXYETHOXY)-4-QUINAZOLINAMINE HYDROCHLORIDE, METHODS OF PRODUCTION, AND PHARMACEUTICAL USES THEREOF

1185 Avenue of the Americas
New York, New York 10036
February 28, 2003

Assistant Commissioner for Patents
Washington, D.C. 20231

Box AF

SIR:

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Respectfully submitted,

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EXPEDITED PROCEDURE
RESPONSE UNDER 37 C.F.R. § 1.116
GROUP ART UNIT 1624

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SIR:

AMENDMENT IN RESPONSE TO AUGUST 30, 2002 FINAL OFFICE ACTION AND PETITION FOR A THREE-MONTH EXTENSION OF TIME

This Amendment is submitted in response to the Final Office Action issued August 30, 2002 by the U.S. Patent and Trademark Office in connection with the above-identified application. A response to the August 30, 2002 Final Office Action was due November 30, 2002. Applicants hereby request a three-month extension of time from November 30, 2002 to February 28, 2003 for responding to the August 30, 2002 Final Office Action. The required fee for the three-month extension of time is $930.00 and a check including this amount is enclosed. Therefore, a response to the August 30, 2002 Final Office Action is now due February 28, 2003 and this Amendment is being timely filed.

O.K. to enter MM

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Please amend the subject application as follows:

In the Claims

Please cancel claims 55-57 without prejudice to applicants rights to pursue the subject matter of these claims in this or a subsequent application.

Please amend claims 1, 3, 5, 14-16, 23-32, 50, 52-54, 58 and 61-64, and add new claims 73-91 under the provisions of 37 C.F.R. §1.121(c). The amended claims are presented below and the amendments to the claims are indicated in the marked-up set of claims attached hereto.

1. (Amended) A homogeneous crystalline polymorph of the hydrochloride salt of N-(3-ethynylphenyl)-6,7-bis(2-methoxyethoxy)-4-quinazolinamine designated the B polymorph that exhibits an X-ray powder diffraction pattern having characteristic peaks expressed in degrees 2-theta at approximately 6.26, 12.48, 13.39, 16.96, 20.20, 21.10, 22.98, 24.46, 25.14, and 26.91.

3. (Amended) A crystalline polymorph of the hydrochloride salt of N-(3-ethynylphenyl)-6,7-bis(2-methoxyethoxy)-4-quinazolinamine designated the B polymorph that exhibits an X-ray powder diffraction pattern having characteristic peaks expressed in degrees 2-theta at approximately 6.26, 12.48, 13.39, 16.96, 20.20, 21.10, 22.98, 24.46, 25.14 and, 26.91, which is free of the A polymorph.

5. (Amended) A composition comprising a crystalline polymorph of the hydrochloride salt of N-(3-ethynylphenyl)-6,7-bis(2-methoxyethoxy)-4-quinazolinamine

designated the B polymorph that exhibits an X-ray powder diffraction pattern having characteristic peaks expressed in degrees 2-theta at approximately 6.26, 12.48, 13.39, 16.96, 20.20, 21.10, 22.98, 24.46, 25.14 and, 26.91, and a carrier, wherein the composition is free of the A polymorph.

14. (Twice Amended) A method of treating abnormal cell growth of a cell expressing the epidermal growth factor receptor (EGFR) in a mammal which comprises administering to said mammal a therapeutically effective amount of the polymorph of claim 3.

16. (Amended) The method of claim 14, wherein the abnormal cell growth is brain, squamous cell, bladder, gastric, pancreatic, hepatic, glioblastoma multiforme breast, head, neck, esophageal, prostate, colorectal, lung, renal, kidney, ovarian, gynecological or thyroid cancer.

16. (Amended) The method of claim 14, wherein the abnormal cell growth is non-small cell lung cancer (NSCLC), refractory ovarian cancer, or head and neck cancer.

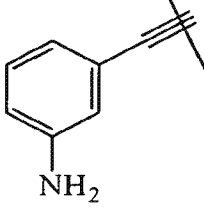
23. (Twice Amended) A method for the treatment of abnormal cell growth of a cell expressing the epidermal growth factor receptor (EGFR) in a mammal which comprises administering to said mammal a therapeutically effective amount of the polymorph of claim 3 in combination with an anti-tumor agent selected from the group consisting of a mitotic inhibitor, an alkylating agent, an anti-metabolite, an intercalating antibiotic, a growth factor inhibitor, a cell cycle inhibitor, an enzyme, a

topoisomerase inhibitor, a biological response modifier, an anti-hormone, and an anti-androgen.

24. (Amended) A process for preparing a crystalline polymorph of N-(3-ethynylphenyl)-6,7-bis(2-methoxyethoxy)-4-quinazolinamine hydrochloride designated the B polymorph, which is free of the A polymorph, which comprises the step of recrystallizing N-(3-ethynylphenyl)-6,7-bis(2-methoxyethoxy)-4-quinazolinamine hydrochloride in a solvent comprising alcohol.

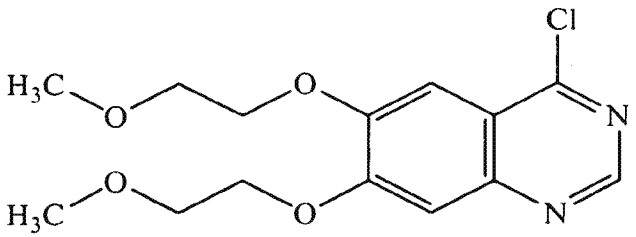
25. (Amended) The process of claim 24, wherein the solvent further comprises water.

26. (Amended) The process of claim 24, wherein N-(3-ethynylphenyl)-6,7-bis(2-methoxyethoxy)-4-quinazolinamine hydrochloride is prepared by coupling a compound of formula 6



6

with a compound of formula 4



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