

WE CLAIM:

1. A compound selected from the group consisting of the 4-chloro-3-(trifluoromethyl)phenyl ureas:

N-(4-chloro-3-(trifluoromethyl)phenyl)-N'-(3-(2-carbamoyl-4-pyridyloxy)phenyl)urea,
N-(4-chloro-3-(trifluoromethyl)phenyl)-N'-(3-(2-(N-methylcarbamoyl)-4-pyridyloxy)phenyl)urea,
N-(4-chloro-3-(trifluoromethyl)phenyl)-N'-(4-(2-carbamoyl)-4-pyridyloxy)phenyl)urea,
N-(4-chloro-3-(trifluoromethyl)phenyl)-N'-(4-(2-(N-methylcarbamoyl)-4-pyridyloxy)phenyl)urea and
N-(4-chloro-3-(trifluoromethyl)phenyl)-N'-(2-chloro-4-(2-N-methylcarbamoyl)(4-pyridyloxy)phenyl)urea,

the 4-bromo-3-(trifluoromethyl)phenyl ureas:

N-(4-bromo-3-(trifluoromethyl)phenyl)-N'-(3-(2-(N-methylcarbamoyl)-4-pyridyloxy)phenyl)urea,
N-(4-bromo-3-(trifluoromethyl)phenyl)-N'-(4-(2-(N-methylcarbamoyl)-4-pyridyloxy)phenyl)urea,
N-(4-bromo-3-(trifluoromethyl)phenyl)-N'-(3-(2-(N-methylcarbamoyl)-4-pyridylthio)phenyl)urea,
N-(4-bromo-3-(trifluoromethyl)phenyl)-N'-(2-chloro-4-(2-(N-methylcarbamoyl)(4-pyridyloxy))phenyl)urea, and
N-(4-bromo-3-(trifluoromethyl)phenyl)-N'-(3-chloro-4-(2-(N-methylcarbamoyl)(4-pyridyloxy)phenyl)urea.

the 2-methoxy-4-chloro-5-(trifluoromethyl)phenyl ureas:

N-(2-methoxy-4-chloro-5-(trifluoromethyl)phenyl)-N'-(4-(2-(N-methylcarbamoyl)-4-pyridyloxy)phenyl)urea.

N-(2-methoxy-4-chloro-5-(trifluoromethyl)phenyl)-N'-(2-chloro-4-(2-(N-methylcarbamoyl)(4-pyridyloxy))phenyl)urea.

or a pharmaceutically acceptable salt thereof.

2. A compound as claimed in claim 1, wherein a pharmaceutically acceptable salt thereof selected from the group consisting of:

a) basic salts of organic acids and inorganic acids selected from the group consisting of hydrochloric acid hydrobromic acid, sulphuric acid, phosphoric acid, methanesulphonic acid, trifluorosulphonic acid, benzenesulfonic acid, p-toluene sulphonic acid (tosylate salt), 1-naphthalene sulfonic acid, 2-napthalne sulfonic acid, acetic acid, trifluoroacetic acid, malic acid, tartaric acid, citric acid, lactic ^{acid} add, oxalic acid, succinic acid, fumaric acid, maleic acid, benzoic acid, salicylic acid, phenylacetic acid, and mandelic acid; and

b) acid salts of organic and inorganic bases containing cations selected from the group consisting of alkaline cations, alkaline earth cations, the ammonium cation, aliphatic substituted ammonium cations and aromatic substituted ammonium cations.

3. A pharmaceutical composition comprising a compound as claimed in claim 1 or a pharmaceutically acceptable salt thereof and a physiologically acceptable carrier.

4. A compound as claimed in claim 1 selected from the group consisting of:

N-(4-chloro-3-(trifluoromethyl)phenyl)-N'-(4-(2-(N-methylcarbamoyl-pyridyloxy)phenyl) urea,

N-(4-chloro-3-(trifluoromethyl)phenyl)-N'-(4-(2-carbamoyl-4-pyridyloxy)phenyl) urea,

N-(4-chloro-3-(trifluoromethyl)phenyl)-N'-(2-chloro-4-(2-(N-methylcarbamoyl)(4-pyridyloxy))phenyl) urea,

N-(4-bromo-3-(trifluoromethyl)phenyl)-N'-(4-(2-(N-methylcarbamoyl)-4-pyridyloxy) phenyl) urea,

N-(2-methoxy-4-chloro-5-(trifluoromethyl)phenyl)-N'-(4-(2-(N-methylcarbamoyl)-4-pyridyloxy)phenyl) urea,

N-(2-methoxy-4-chloro-5-(trifluoromethyl)phenyl)-N'-(2-chloro-4-(2-(N-methylcarbamoyl) (4-pyridyloxy)) phenyl) urea,

or a pharmaceutically acceptable salt thereof.

5. A compound as claimed in claim 4 which is a pharmaceutically acceptable salt thereof selected from the group consisting of:

a) basic salts of organic acids and inorganic acids selected from the group consisting of hydrochloric acid, hydrobromic acid, sulphuric acid, phosphoric acid, methanesulphonic acid, trifluorosulphonic acid, benzenesulfonic acid, p-toluene sulphonic acid (tosylate salt), 1-naphthalene sulfonic acid, 2-naphthalene sulfonic acid, acetic acid, trifluoroacetic acid, malic acid, tartaric acid, citric acid, lactic acid, oxalic acid, succinic acid, fumaric acid, maleic acid, benzoic acid, salicylic acid,

phenylacetic acid, and mandelic acid; and

b) acid salts of organic and inorganic bases containing cations selected from the group consisting of alkaline cations, alkaline earth cations, the ammonium cation, aliphatic substituted ammonium cations and aromatic substituted ammonium cations.

6. A pharmaceutical composition comprising a compound as claimed in claim 4 or a pharmaceutically acceptable salt thereof and a physiologically acceptable carrier.

7. A compound as claimed in claim 1 selected from the group consisting of:

the 4-chloro-3-(trifluoromethyl)phenyl ureas:

N-(4-chloro-3-(trifluoromethyl)phenyl)-N'-(3-(2-carbamoyl-4-pyridyloxy)phenyl) urea,
 N-(4-chloro-3-(trifluoromethyl)phenyl)-N'-(3-(2-(N-methylcarbamoyl)-4-pyridyloxy) phenyl) urea,
 N-(4-chloro-3-(trifluoromethyl)phenyl)-N'-(4-(2-carbamoyl-4-pyridyloxy)phenyl) urea,
 N-(4-chloro-3-(trifluoromethyl)phenyl)-N'-(4-(2-(N-methylcarbamoyl)-4-pyridyloxy) phenyl) urea and
 N-(4-chloro-3-(trifluoromethyl)phenyl)-N-(2-chloro-4-(2-(N-methylcarbamoyl)(4-pyridyloxy))phenyl) urea,

the 4-bromo-3(trifluoromethyl)phenyl ureas:

N-(4-bromo-3-(trifluoromethyl)phenyl)-N'-(3-(2-(N-methylcarbamoyl)-4-pyridyloxy) phenyl) urea,
 N-(4-bromo-3-(trifluoromethyl)phenyl)-N'-(4-(2-(N-methylcarbamoyl)-4-pyridyloxy) phenyl) urea.
 N-(4-bromo-3-(trifluoromethyl)phenyl)-N'-(3-(2-(N-methylcarbamoyl)-4-pyridylthio) phenyl) urea,
 N-(4-bromo-3-(trifluoromethyl)phenyl)-N'-(2-chloro-4-(2-(N-methylcarbamoyl)(4-pyridyloxy))phenyl) urea and
 N-(4-bromo-3-(trifluoromethyl)phenyl)-N'-(3-chloro-4-(2-(N-methylcarbamoyl)(4-pyridyloxy))phenyl) urea;

the 2-methoxy-4-chloro-5-(trifluoromethyl)phenyl ureas:

N-(2-methoxy-4-chloro-5-(trifluoromethyl)phenyl)-N'-(4-(2-(N-methylcarbamoyl)-4-pyridyloxy)phenyl) urea,
 N-(2-methoxy-4-chloro-5-(trifluoromethyl) phenyl)-N'-(2-chloro-4-(2-(N-methylcarbamoyl) (4-pyridyloxy)) phenyl) urea

or a pharmaceutically acceptable salt thereof for the manufacture of a medicament for the treatment of a cancerous cell growth mediated by raf kinase.

8. A compound as claimed in claim 1 selected from the group consisting of

the 4-chloro-3-(trifluoromethyl)phenyl ureas:

N-(4-chloro-3-(trifluoromethyl)phenyl)-N'-(3-(2-carbamoyl-4-pyridyloxy)phenyl) urea,

N-(4-chloro-3-(trifluoromethyl)phenyl)-N'-(3-(2-(N-methylcarbamoyl)-4-pyridyloxy) phenyl) urea,

N-(4-chloro-3-(trifluoromethyl)phenyl)-N'-(4-(2-carbamoyl-4-pyridyloxy)phenyl) urea,

N-(4-chloro-3-(trifluoromethyl)phenyl)-N'-(4-(2-(N-methylcarbamoyl)-4-pyridyloxy) phenyl) urea and

N-(4-chloro-3-(trifluoromethyl)phenyl)-N'-(2-chloro-4-(2-(N-methylcarbamoyl)(4-pyridyloxy))phenyl) urea,

the 4-bromo-3(trifluoromethyl)phenyl ureas:

N-(4-bromo-3-(trifluoromethyl)phenyl)-N'-(3-(2-(N-methylcarbamoyl)4-pyridyloxy) phenyl) urea,

N-(4-bromo-3-(trifluoromethyl)phenyl)-N'-(4-(2-(N-methylcarbamoyl)-4-pyridyloxy) phenyl) urea,

N-(4-bromo-3-(trifluoromethyl)phenyl)-N'-(3-(2-(N-methylcarbamoyl)-4-pyridylthio) phenyl) urea,

N-(4-bromo-3-(trifluoromethyl)phenyl)-N'-(2-chloro-4-(2-(N-methylcarbamoyl)(4-pyridyloxy))phenyl) urea and

N-(4-bromo-3-(trifluoromethyl)phenyl)-N'-(3-chloro-4-(2-(N-methylcarbamoyl)(4-pyridyloxy))phenyl) urea;

the 2-methoxy-4-chloro-5-(trifluoromethyl)phenyl ureas:

N-(2-methoxy-4-chloro-5-(trifluoromethyl)phenyl)-N'-(4-(2-(N-methylcarbamoyl)-4-pyridyloxy)phenyl) urea,

N-(2-methoxy-4-chloro-5-(trifluoromethyl) phenyl)-N'-(2-chloro-4-(2-(N-methylcarbamoyl) (4-pyridyloxy)) phenyl) urea

or a pharmaceutically acceptable salt thereof for the manufacture of a medicament for the treatment of:

- i) carcinoma of the lungs, pancreas, thyroid, bladder, colon,
- ii) myeloid leukemia or
- iii) villous colon adenoma.

9. A compound as claimed in claim 1 selected from the group consisting of:

the 4-chloro-3-(trifluoromethyl)phenyl ureas:

N-(4-chloro-3-(trifluoromethyl)phenyl)-N'-(3-(2-carbamoyl-4-pyridyloxy)phenyl) urea,

N-(4-chloro-3-(trifluoromethyl)phenyl)-N'-(3-(2-(N-methylcarbamoyl)-4-pyridyloxy) phenyl) urea,

N-(4-chloro-3-(trifluoromethyl)phenyl)-N'-(4-(2-carbamoyl-4-pyridyloxy)phenyl) urea,

N-(4-chloro-3-(trifluoromethyl)phenyl)-N'-(4-(2-(N-methylcarbamoyl)-4-pyridyloxy) phenyl) urea and

N-(4-chloro-3-(trifluoromethyl)phenyl)-N'-(2-chloro-4-(2-(N-methylcarbamoyl)(4-pyridyloxy))phenyl) urea,

the 4-bromo-3(trifluoromethyl)phenyl ureas:

N-(4-bromo-3-(trifluoromethyl)phenyl)-N'-(3-(2-(N-methylcarbamoyl)4-pyridyloxy) phenyl) urea,

N-(4-bromo-3-(trifluoromethyl)phenyl)-N'-(4-(2-(N-methylcarbamoyl)-4-pyridyloxy) phenyl urea,

N-(4-bromo-3-(trifluoromethyl)phenyl)-N-(3-(2-(N-methylcarbamoyl)-4-pyridylthio) phenyl) urea,

N-(4-bromo-3-(trifluoromethyl)phenyl)-N'-(2-chloro-4-(2-(N-methylcarbamoyl)(4-pyridyloxy))phenyl) urea and

N-(4-bromo-3-(trifluoromethyl)phenyl)-N'-(3-chloro-4-(2-(N-methylcarbamoyl)(4-pyridyloxy))phenyl) urea;

the 2-methoxy-4-chloro-5-(trifluoromethyl)phenyl ureas:

N-(2-methoxy-4-chloro-5-(trifluoromethyl)phenyl)-N'-(4-(2-(N-methylcarbamoyl)-4-pyridyloxy)phenyl) urea,

N-(2-methoxy-4-chloro-5-(trifluoromethyl)phenyl)-N'-(2-chloro-4-(2-(N-methylcarbamoyl)(4-pyridyloxy)phenyl) urea,

or a pharmaceutically acceptable salt thereof for the manufacture of a medicament for the treatment of tumors.

10. A compound as claimed in claim 4 selected from the group consisting of:

N-(4-chloro-3-(trifluoromethyl)phenyl)-N'-(4-(2-N-methylcarbamoyl)-4-pyridyloxy)phenyl) urea,

N-(4-chloro-3-(trifluoromethyl)phenyl)-N'-(4-(2-carbamoyl-4-pyridyloxy)phenyl) urea,

N-(4-chloro-3-(trifluoromethyl)phenyl)-N'-(2-chloro-4-(2-(N-methylcarbamoyl)(4-pyridyloxy))phenyl) urea,

N-(4-bromo-3-(trifluoromethyl)phenyl)-N'-(4-(2-(N-methylcarbamoyl)-4-pyridyloxy) phenyl) urea,

N-(2-methoxy-4-chloro-5-(trifluoromethyl)phenyl)-N'-(4-(2-(N-methylcarbamoyl)-4-pyridyloxy)phenyl) urea,

N-(2-methoxy-4-chloro-5-(trifluoromethyl)phenyl)-N'-(2-chloro-4-(2-(N-methylcarbamoyl) (4-pyridyloxy))phenyl) urea.

or a pharmaceutically acceptable salt hereof for the manufacture of a medicament for the treatment of a cancerous cell growth mediated by raf kinase.

11. A compound as claimed in claim 4 selected from the group consisting of

N-(4-chloro-3-(trifluoromethyl)phenyl)-N'-(4-(2-N-methylcarbamoyl)-4-pyridyloxy)phenyl) urea,

N-(4-chloro-3-(trifluoromethyl)phenyl)-N'-(4-(2-carbamoyl-4-pyridyloxy)phenyl) urea,

N-(4-chloro-3-(trifluoromethyl)phenyl)-N'-(2-chloro-4-(2-(N-methylcarbamoyl)(4-pyridyloxy))phenyl) urea,

N-(4-bromo-3-(trifluoromethyl)phenyl)-N'-(4-(2-(N-methylcarbamoyl)-4-pyridyloxy)phenyl)urea,

N-(2-methoxy-4-chloro-5-(trifluoromethyl)phenyl)-N'-(4-(2-(N-methylcarbamoyl)-4-pyridyloxy)phenyl) urea,

N-(2-methoxy-4-chloro-5-(trifluoromethyl)phenyl)-N'-(2-chloro-4-(2-(N-methylcarbamoyl)(4-pyridyloxy))phenyl) urea

or a pharmaceutically acceptable salt hereof for the manufacture of a medicament for the treatment of:

- i) carcinoma of the lungs, pancreas, thyroid, bladder, colon,
- ii) myeloid leukemia or
- iii) villous colon adenoma.

12. A compound as claimed in claim 4 selected from the group consisting of:

N-(4-chloro-3-(trifluoromethyl)phenyl)-N'-(4-(2-N-methylcarbamoyl)-4-pyridyloxy)phenyl)urea,

N-(4-chloro-3-(trifluoromethyl)phenyl)-N'-(4-(2-carbamoyl-4-pyridyloxy)phenyl) urea,

N-(4-chloro-3-(trifluoromethyl)phenyl)-N'-(2-chloro-4-(2-(N-methylcarbamoyl)(4-pyridyloxy))phenyl) urea,

N-(4-bromo-3-(trifluoromethyl)phenyl)-N'-(4-(2-(N-methylcarbamoyl)-4-pyridyloxy)phenyl)urea,

N-(2-methoxy-4-chloro-5-(trifluoromethyl)phenyl)-N'-(4-(2-(N-methylcarbamoyl)-4-pyridyloxy)phenyl)urea,

N-(2-methoxy-4-chloro-5-(trifluoromethyl)phenyl)-N'-(2-chloro-4-(2-(N-methylcarbamoyl)(4-pyridyloxy))phenyl) urea

or a pharmaceutically acceptable salt hereof for the manufacture of a medicament for the treatment of tumors.

13. A compound as claimed in claim 1 which is N-(4-chloro-3-(trifluoromethyl)phenyl)-N'-(4-(2-carbamoyl-4-pyridyloxy)phenyl) urea.

14. A compound as claimed in claim 1 which is N-(4-chloro-3-(trifluoromethyl)phenyl)-N'-(4-(2-(N-methylcarbamoyl)-4-pyridyloxy)phenyl) urea

15. A pharmaceutical composition comprising N-(4-chloro-3-(trifluoromethyl)phenyl)-N'-(4-(2-carbamoyl-4-pyridyloxy)phenyl) urea or a pharmaceutically acceptable salt thereof and a physiologically acceptable carrier.

16. A pharmaceutical composition comprising N-(4-chloro-3-(trifluoromethyl)phenyl)-N'-(4-(2-(N-methylcarbamoyl)-4-pyridyloxy) phenyl) urea or a pharmaceutically acceptable salt thereof and a physiologically acceptable carrier.

17. N-(4-chloro-3-(trifluoromethyl)phenyl)-N'-(4-(2-carbamoyl-4-pyridyloxy) phenyl) urea,

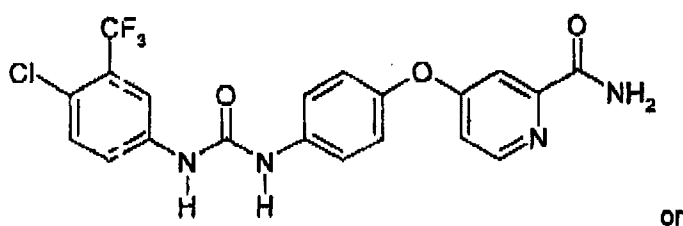
or a pharmaceutically acceptable salt thereof for the manufacture of a medicament for the treatment of a cancerous cell growth mediated by raf kinase.

18. N-(4-chloro-3-(trifluoromethyl)phenyl)-N'-(4-(2-(N-methylcarbamoyl)-4-

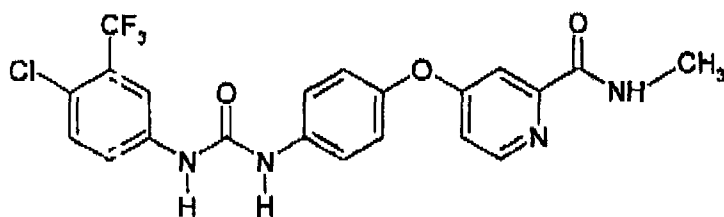
pyridyloxy)phenyl) urea or a pharmaceutical acceptable salt thereof for the manufacture of a medicament for the treatment of a cancerous cell growth mediated by raf kinase.

19. A pharmaceutically acceptable salt of a compound which is:

N-(4-chloro-3-(trifluoromethyl)phenyl)-N'-(4-(2-carbamoyl-4-pyridyloxy)phenyl) urea of the formula:



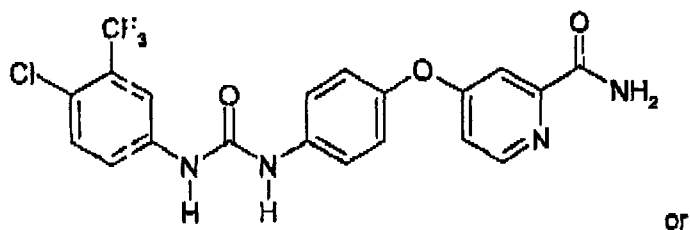
N-(4-chloro-3-(trifluoromethyl)phenyl)-N'-(4-(2-(N-methylcarbamoyl)-4-pyridyloxy)phenyl) urea of the formula:



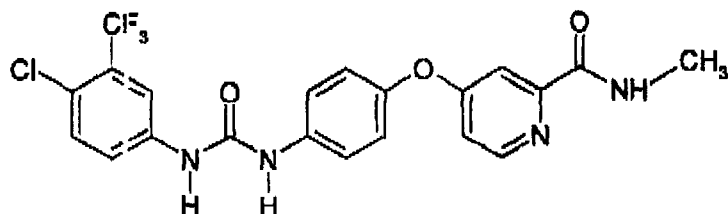
20. A pharmaceutically acceptable salt as claimed in claim 19 which is a basic salt of an organic acid or an inorganic acid which is hydrochloric acid, hydrobromic acid, sulfuric acid, phosphoric acid, methanesulfonic acid, trifluoromethanesulfonic acid, benzenesulfonic acid, p-toluene sulfonic acid (tosylate salt), 1-napthalene sulfonic acid, 2-napthalene sulfonic acid, acetic acid, trifluoroacetic acid, malic acid, tartaric acid, citric acid, lactic acid, oxalic acid, succinic acid, fumaric acid, maleic acid, benzoic acid, salicylic acid, phenylacetic acid, or mandelic acid.

21. A pharmaceutically acceptable salt which is the tosylate salt of:

N-(4-chloro-3-(trifluoromethyl)phenyl)-N'-(4-(2-carbamoyl-4-pyridyloxy)phenyl) urea of the formula:



N-(4-chloro-3-(trifluoromethyl)phenyl)-N'-(4-(2-N-methylcarbamoyl-4-pyridyloxy)phenyl) urea of the formula:



22. A pharmaceutical composition comprising a pharmaceutically acceptable salt of claim 19, 20 or 21 and pharmaceutically acceptable carrier.

Dated this 5th day of July, 2001.

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