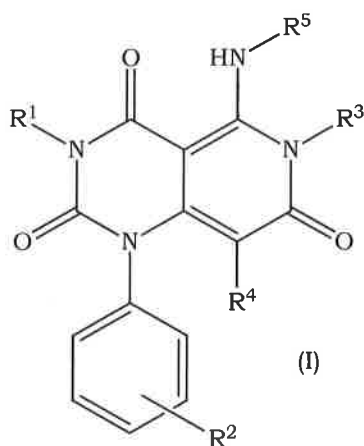


CLAIMS

1. A compound of the general formula I, its tautomeric forms, its pharmaceutically acceptable salts, their combinations with suitable medicament and pharmaceutical compositions containing them,



wherein,

R¹ is selected from the group consisting of hydrogen, substituted- or unsubstituted-alkyl, substituted- or unsubstituted- cycloalkyl, and substituted- or unsubstituted- heterocyclyl;

R² is selected from the group consisting of -R⁶-E, -SO₂R⁷, and -C(O)R⁸;

R³ is selected from the group consisting of hydrogen, substituted- or unsubstituted- alkyl, and substituted- or unsubstituted- cycloalkyl;

R⁴ is selected from the group consisting of hydrogen, halogen, substituted- or unsubstituted-alkyl, and substituted- or unsubstituted- cycloalkyl;

R⁵ is substituted- or unsubstituted- aryl, wherein the substituents are selected from with R^a and R^b;

R^a and R^b are selected from the group consisting of hydrogen, halogen and haloalkyl;

R^6 is selected from the group consisting of direct bond, $-[C(R^c)R^d]_nNR^9-$, $-[C(R^c)R^d]_nO-$, $-NHC(=O)[C(R^c)R^d]_p-$, $-S(O)_2NH-$, $-NHC(=O)[C(R^c)R^d]NR^9-$, $-NHC(=O)[C(R^c)R^d]O-$, and $-NHS(O)_2-$;

R^c and R^d are each independently selected from the group consisting of hydrogen and substituted- or unsubstituted- alkyl;

E is substituted- or unsubstituted-four membered heterocyclic ring, wherein the substituents are selected from the group consisting of alkyl, halogen, $-C(=O)OR^e$, and $-OR^e$;

R^e is selected from the group consisting of hydrogen, substituted- or unsubstituted-alkyl, and substituted or unsubstituted cycloalkyl;

R^7 is selected from the group consisting of substituted- or unsubstituted-cycloalkyl, and substituted- or unsubstituted- cycloalkenyl;

R^8 is selected from the group consisting of substituted- or unsubstituted-alkyl, substituted- or unsubstituted- alkenyl, substituted- or unsubstituted-alkynyl, substituted- or unsubstituted- cycloalkyl, and substituted- or unsubstituted- cycloalkenyl;

R^9 is selected from the group consisting of hydrogen, substituted- or unsubstituted- alkyl, substituted- or unsubstituted- alkenyl, substituted- or unsubstituted- alkynyl, substituted- or unsubstituted- cycloalkyl and substituted or unsubstituted- cycloalkenyl;

n is an integer selected from the group consisting of 0, 1 and 2;

p is an integer selected from the group consisting of 0 and 1.

when the alkyl group and alkenyl group is substituted, the alkyl group and alkenyl group is substituted with 1 to 4 substituents independently selected from the group consisting of oxo, halogen, nitro, cyano, perhaloalkyl, cycloalkyl, aryl, heteroaryl, heterocyclyl, $-OR^{10b}$, $-SO_2R^{10a}$, $-C(=O)OR^{10a}$, $-OC(=O)R^{10a}$, $-C(=O)N(H)R^{10}$, $-OR^{10a}$, $-C(=O)N(alkyl)R^{10}$, $-N(H)C(=O)R^{10a}$, $-N(H)R^{10}$, $-N(alkyl)R^{10}$, $-N(H)C(=O)N(H)R^{10}$, $-N(H)C(=O)N(alkyl)R^{10}$, $-NH-SO_2-alkyl$ and $-NH-SO_2-cycloalkyl$;

when the cycloalkyl group and cycloalkenyl group is a substituted, the cycloalkyl group and cycloalkenyl group is substituted with 1 to 3 substituents independently selected from the group consisting of oxo, halogen, nitro, cyano, alkyl, alkenyl, perhaloalkyl, aryl, heteroaryl, heterocyclyl, $-OR^{10b}$, $-SO_2R^{10a}$, $-C(=O)R^{10a}$, $-C(=O)OR^{10a}$, $-OC(=O)R^{10a}$, $-C(=O)N(H)R^{10}$, $-C(=O)N(alkyl)R^{10}$, $-N(H)C(=O)R^{10a}$, $-N(H)R^{10}$, $-N(alkyl)R^{10}$, $-N(H)C(=O)N(H)R^{10}$, and $-N(H)C(=O)N(alkyl)R^{10}$, $-NH-SO_2-alkyl$ and $-NH-SO_2-cycloalkyl$;

when the aryl group is a substituted, the aryl group is substituted with 1 to 3 substituents independently selected from the group consisting of halogen, nitro, cyano, hydroxy, alkyl, alkenyl, perhaloalkyl, cycloalkyl, cycloalkenyl, heterocycle, $-O-alkyl$, $-O-perhaloalkyl$, $-N(alkyl)alkyl$, $-N(H)alkyl$, $-NH_2$, $-SO_2-alkyl$, $-SO_2-perhaloalkyl$, $-N(alkyl)C(=O)alkyl$, $-N(H)C(=O)alkyl$, $-C(=O)N(alkyl)alkyl$, $-C(=O)N(H)alkyl$, $-C(=O)NH_2$, $-SO_2N(alkyl)alkyl$, $-SO_2N(H)alkyl$, $-SO_2NH_2$, $-NH-SO_2-alkyl$ and $-NH-SO_2-cycloalkyl$;

when the heteroaryl group is a substituted, the heteroaryl group is substituted with 1 to 3 substituents independently selected from the group consisting of halogen, nitro, cyano, hydroxy, alkyl, alkenyl, perhaloalkyl, cycloalkyl, cycloalkenyl, heterocycle, $-O-alkyl$, $O-perhaloalkyl$, $-N(alkyl)alkyl$, $-N(H)alkyl$, $-NH_2$, $-SO_2-alkyl$, $-SO_2-perhaloalkyl$, $-N(alkyl)C(=O)alkyl$, $-N(H)C(=O)alkyl$, $-C(=O)N(alkyl)alkyl$, $-C(=O)N(H)alkyl$, $-C(=O)NH_2$, $-SO_2N(alkyl)alkyl$, $-SO_2N(H)alkyl$, $-SO_2NH_2$, $-NH-SO_2-alkyl$ and $-NH-SO_2-cycloalkyl$;

when the heterocyclyl group is a substituted, the heterocyclyl group is substituted with 1 to 3 substituents, when the heterocyclic group is substituted on a ring

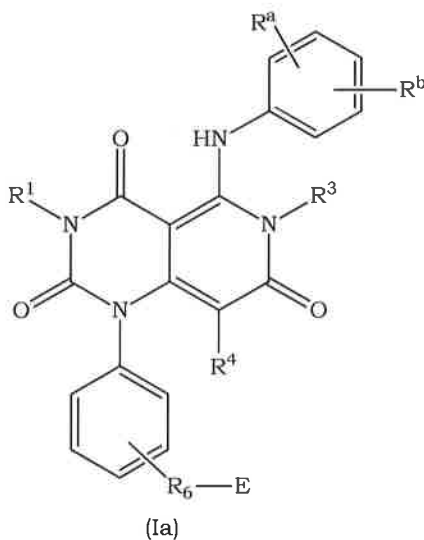
carbon of the 'heterocycle', the substituents are independently selected from the group consisting of halogen, nitro, cyano, oxo, alkyl, alkenyl, perhaloalkyl, cycloalkyl, cycloalkenyl, aryl, heteroaryl, heterocyclyl, $-OR^{10b}$, $-C(=O)OR^{10a}$, $-OC(=O)R^{10a}$, $-C(=O)N(H)R^{10}$, $-C(=O)N(alkyl)R^{10}$, $-N(H)C(=O)R^{10a}$, $-N(H)R^{10}$, $-N(alkyl)R^{10}$, $-N(H)C(=O)N(H)R^{10}$, $-N(H)C(=O)N(alkyl)R^{10}$; the substituents on ring nitrogen of the 'heterocycle'; substituents are independently selected from the group consisting of alkyl, alkenyl, cycloalkyl, cycloalkenyl, aryl, heteroaryl, $-SO_2R^{10a}$, $-C(=O)R^{10a}$, $C(=O)OR^{10a}$, $-C(=O)N(H)R^{10}$, $-C(=O)N(alkyl)R^{10}$, $-NH-SO_2-alkyl$ and $-NH-SO_2-cycloalkyl$;

R^{10} is selected from the group consisting of hydrogen, alkyl, alkenyl, cycloalkyl, cycloalkenyl, aryl, heteroaryl, and heterocyclyl;

R^{10a} is selected from the group consisting of alkyl, alkenyl, perhaloalkyl, cycloalkyl, cycloalkenyl, aryl, heteroaryl, and heterocyclyl; and

R^{10b} is selected from the group consisting of hydrogen, alkyl, alkenyl, perhaloalkyl, cycloalkyl, cycloalkenyl, aryl, heteroaryl, and heterocyclyl.

2. A compound of the general formula Ia, its tautomeric forms, its pharmaceutically acceptable salts, their combinations with suitable medicament and pharmaceutical compositions containing them,



wherein,

R^1 is selected from the group consisting of hydrogen, substituted- or unsubstituted-alkyl, substituted- or unsubstituted- cycloalkyl, and substituted- or unsubstituted- heterocyclyl;

R^3 is selected from the group consisting of hydrogen, substituted- or unsubstituted- alkyl, and substituted- or unsubstituted- cycloalkyl;

R^4 is selected from the group consisting of hydrogen, halogen, substituted- or unsubstituted-alkyl, and substituted- or unsubstituted- cycloalkyl;

R^a and R^b are selected from the group consisting of hydrogen, halogen and haloalkyl;

R^6 is selected from the group consisting of direct bond, $-[C(R^c)R^d]_nNR^9-$, $-[C(R^c)R^d]_nO-$, $-NHC(=O)[C(R^c)R^d]_p-$, $-S(O)_2NH-$, $-NHC(=O)[C(R^c)R^d]NR^9-$, $-NHC(=O)[C(R^c)R^d]O-$, and $-NHS(O)_2-$;

R^c and R^d are each independently selected from the group consisting of hydrogen and substituted- or unsubstituted- alkyl;

E is substituted- or unsubstituted-four membered heterocyclic ring, wherein the substituents are selected from the group consisting of alkyl, halogen, $-C(=O)OR^e$, and $-OR^e$;

R^e is selected from the group consisting of hydrogen, substituted- or unsubstituted-alkyl, and substituted or unsubstituted cycloalkyl;

R^9 is selected from the group consisting of hydrogen, substituted- or unsubstituted- alkyl, substituted- or unsubstituted- alkenyl, substituted- or unsubstituted- alkynyl, substituted- or unsubstituted- cycloalkyl and substituted or unsubstituted- cycloalkenyl;

n is an integer selected from the group consisting of 0, 1 and 2;

p is an integer selected from the group consisting of 0 and 1.

when the alkyl group and alkenyl group is substituted, the alkyl group and alkenyl group is substituted with 1 to 4 substituents independently selected from the group consisting of oxo, halogen, nitro, cyano, perhaloalkyl, cycloalkyl, aryl, heteroaryl, heterocyclyl, $-OR^{10b}$, $-SO_2R^{10a}$, $-C(=O)OR^{10a}$, $-OC(=O)R^{10a}$, $-C(=O)N(H)R^{10}$, $-OR^{10a}$, $-C(=O)N(alkyl)R^{10}$, $-N(H)C(=O)R^{10a}$, $-N(H)R^{10}$, $-N(alkyl)R^{10}$, $-N(H)C(=O)N(H)R^{10}$, $-N(H)C(=O)N(alkyl)R^{10}$, $-NH-SO_2-alkyl$ and $-NH-SO_2-cycloalkyl$;

when the cycloalkyl group and cycloalkenyl group is a substituted, the cycloalkyl group and cycloalkenyl group is substituted with 1 to 3 substituents independently selected from the group consisting of oxo, halogen, nitro, cyano, alkyl, alkenyl, perhaloalkyl, aryl, heteroaryl, heterocyclyl, $-OR^{10b}$, $-SO_2R^{10a}$, $-C(=O)R^{10a}$, $-C(=O)OR^{10a}$, $-OC(=O)R^{10a}$, $-C(=O)N(H)R^{10}$, $-C(=O)N(alkyl)R^{10}$, $-N(H)C(=O)R^{10a}$, $-N(H)R^{10}$, $-N(alkyl)R^{10}$, $-N(H)C(=O)N(H)R^{10}$, and $-N(H)C(=O)N(alkyl)R^{10}$, $-NH-SO_2-alkyl$ and $-NH-SO_2-cycloalkyl$;

when the aryl group is a substituted, the aryl group is substituted with 1 to 3 substituents independently selected from the group consisting of halogen, nitro, cyano, hydroxy, alkyl, alkenyl, perhaloalkyl, cycloalkyl, cycloalkenyl, heterocycle, $-O-alkyl$, $-O-perhaloalkyl$, $-N(alkyl)alkyl$, $-N(H)alkyl$, $-NH_2$, $-SO_2-alkyl$, $-SO_2-perhaloalkyl$, $-N(alkyl)C(=O)alkyl$, $-N(H)C(=O)alkyl$, $-C(=O)N(alkyl)alkyl$, $-C(=O)N(H)alkyl$, $-C(=O)NH_2$, $-SO_2N(alkyl)alkyl$, $-SO_2N(H)alkyl$, $-SO_2NH_2$, $-NH-SO_2-alkyl$ and $-NH-SO_2-cycloalkyl$;

when the heteroaryl group is a substituted, the heteroaryl group is substituted with 1 to 3 substituents independently selected from the group consisting of halogen, nitro, cyano, hydroxy, alkyl, alkenyl, perhaloalkyl, cycloalkyl, cycloalkenyl, heterocycle, $-O-alkyl$, $O-perhaloalkyl$, $-N(alkyl)alkyl$, $-N(H)alkyl$, $-NH_2$, $-SO_2-alkyl$, $-SO_2-perhaloalkyl$, $-N(alkyl)C(=O)alkyl$, $-N(H)C(=O)alkyl$, $-C(=O)N(alkyl)alkyl$, $-C(=O)N(H)alkyl$, $-C(=O)NH_2$, $-SO_2N(alkyl)alkyl$, $-SO_2N(H)alkyl$, $-SO_2NH_2$, $-NH-SO_2-alkyl$ and $-NH-SO_2-cycloalkyl$;

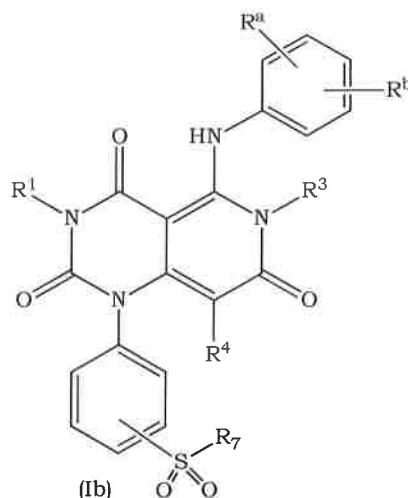
when the heterocyclyl group is a substituted, the heterocyclyl group is substituted with 1 to 3 substituents, when the heterocyclic group is substituted on a ring carbon of the 'heterocycle', the substituents are independently selected from the group consisting of halogen, nitro, cyano, oxo, alkyl, alkenyl, perhaloalkyl, cycloalkyl, cycloalkenyl, aryl, heteroaryl, heterocyclyl, $-OR^{10b}$, $-C(=O)OR^{10a}$, $-OC(=O)R^{10a}$, $-C(=O)N(H)R^{10}$, $-C(=O)N(alkyl)R^{10}$, $-N(H)C(=O)R^{10a}$, $-N(H)R^{10}$, $-N(alkyl)R^{10}$, $-N(H)C(=O)N(H)R^{10}$, $-N(H)C(=O)N(alkyl)R^{10}$; the substituents on ring nitrogen of the 'heterocycle'; substituents are independently selected from the group consisting of alkyl, alkenyl, cycloalkyl, cycloalkenyl, aryl, heteroaryl, $-SO_2R^{10a}$, $-C(=O)R^{10a}$, $-C(=O)OR^{10a}$, $-C(=O)N(H)R^{10}$, $-C(=O)N(alkyl)R^{10}$, $-NH-SO_2-alkyl$ and $-NH-SO_2-cycloalkyl$;

R^{10} is selected from the group consisting of hydrogen, alkyl, alkenyl, cycloalkyl, cycloalkenyl, aryl, heteroaryl, and heterocyclyl;

R^{10a} is selected from the group consisting of alkyl, alkenyl, perhaloalkyl, cycloalkyl, cycloalkenyl, aryl, heteroaryl, and heterocyclyl; and

R^{10b} is selected from the group consisting of hydrogen, alkyl, alkenyl, perhaloalkyl, cycloalkyl, cycloalkenyl, aryl, heteroaryl, and heterocyclyl.

3. A compound of the general formula Ib, its tautomeric forms, its pharmaceutically acceptable salts, their combinations with suitable medicament and pharmaceutical compositions containing them,



wherein,

R¹ is selected from the group consisting of hydrogen, substituted- or unsubstituted-alkyl, substituted- or unsubstituted- cycloalkyl, and substituted- or unsubstituted- heterocyclyl;

R³ is selected from the group consisting of hydrogen, substituted- or unsubstituted- alkyl, and substituted- or unsubstituted- cycloalkyl;

R⁴ is selected from the group consisting of hydrogen, halogen, substituted- or unsubstituted-alkyl, and substituted- or unsubstituted- cycloalkyl;

R^a and R^b are selected from the group consisting of hydrogen, halogen and haloalkyl;

R⁷ is selected from the group consisting of substituted- or unsubstituted- cycloalkyl, and substituted- or unsubstituted- cycloalkenyl;

when the alkyl group and alkenyl group is substituted, the alkyl group and alkenyl group is substituted with 1 to 4 substituents independently selected from the group consisting of oxo, halogen, nitro, cyano, perhaloalkyl, cycloalkyl, aryl, heteroaryl, heterocyclyl, -OR^{10b}, -SO₂R^{10a}, -C(=O)OR^{10a}, -OC(=O)R^{10a}, -C(=O)N(H)R¹⁰, -OR^{10a}, -C(=O)N(alkyl)R¹⁰, -N(H)C(=O)R^{10a}, -N(H)R¹⁰, -N(alkyl)R¹⁰ - N(H)C(=O)N(H)R¹⁰, -N(H)C(=O)N(alkyl)R¹⁰, -NH-SO₂-alkyl and -NH-SO₂-cycloalkyl;

when the cycloalkyl group and cycloalkenyl group is a substituted, the cycloalkyl group and cycloalkenyl group is substituted with 1 to 3 substituents independently selected from the group consisting of oxo, halogen, nitro, cyano, alkyl, alkenyl, perhaloalkyl, aryl, heteroaryl, heterocyclyl, $-OR^{10b}$, $-SO_2R^{10a}$, $-C(=O)R^{10a}$, $-C(=O)OR^{10a}$, $-OC(=O)R^{10a}$, $-C(=O)N(H)R^{10}$, $-C(=O)N(alkyl)R^{10}$, $-N(H)C(=O)R^{10a}$, $-N(H)R^{10}$, $-N(alkyl)R^{10}$, $-N(H)C(=O)N(H)R^{10}$, and $-N(H)C(=O)N(alkyl)R^{10}$, $-NH-SO_2-alkyl$ and $-NH-SO_2-cycloalkyl$;

when the aryl group is a substituted, the aryl group is substituted with 1 to 3 substituents independently selected from the group consisting of halogen, nitro, cyano, hydroxy, alkyl, alkenyl, perhaloalkyl, cycloalkyl, cycloalkenyl, heterocycle, $-O-alkyl$, $-O-perhaloalkyl$, $-N(alkyl)alkyl$, $-N(H)alkyl$, $-NH_2$, $-SO_2-alkyl$, $-SO_2-perhaloalkyl$, $-N(alkyl)C(=O)alkyl$, $-N(H)C(=O)alkyl$, $-C(=O)N(alkyl)alkyl$, $-C(=O)N(H)alkyl$, $-C(=O)NH_2$, $-SO_2N(alkyl)alkyl$, $-SO_2N(H)alkyl$, $-SO_2NH_2$, $-NH-SO_2-alkyl$ and $-NH-SO_2-cycloalkyl$;

when the heteroaryl group is a substituted, the heteroaryl group is substituted with 1 to 3 substituents independently selected from the group consisting of halogen, nitro, cyano, hydroxy, alkyl, alkenyl, perhaloalkyl, cycloalkyl, cycloalkenyl, heterocycle, $-O-alkyl$, $O-perhaloalkyl$, $-N(alkyl)alkyl$, $-N(H)alkyl$, $-NH_2$, $-SO_2-alkyl$, $-SO_2-perhaloalkyl$, $-N(alkyl)C(=O)alkyl$, $-N(H)C(=O)alkyl$, $-C(=O)N(alkyl)alkyl$, $-C(=O)N(H)alkyl$, $-C(=O)NH_2$, $-SO_2N(alkyl)alkyl$, $-SO_2N(H)alkyl$, $-SO_2NH_2$, $-NH-SO_2-alkyl$ and $-NH-SO_2-cycloalkyl$;

when the heterocyclyl group is a substituted, the heterocyclyl group is substituted with 1 to 3 substituents, when the heterocyclic group is substituted on a ring carbon of the 'heterocycle', the substituents are independently selected from the group consisting of halogen, nitro, cyano, oxo, alkyl, alkenyl, perhaloalkyl, cycloalkyl, cycloalkenyl, aryl, heteroaryl, heterocyclyl, $-OR^{10b}$, $-C(=O)OR^{10a}$, $-OC(=O)R^{10a}$, $-C(=O)N(H)R^{10}$, $-C(=O)N(alkyl)R^{10}$, $-N(H)C(=O)R^{10a}$, $-N(H)R^{10}$, $-N(alkyl)R^{10}$, $-N(H)C(=O)N(H)R^{10}$, $-N(H)C(=O)N(alkyl)R^{10}$; the substituents on ring nitrogen of the 'heterocycle'; substituents are independently selected from the group consisting of alkyl, alkenyl, cycloalkyl, cycloalkenyl, aryl, heteroaryl, $-SO_2R^{10a}$, $-C(=O)R^{10a}$,

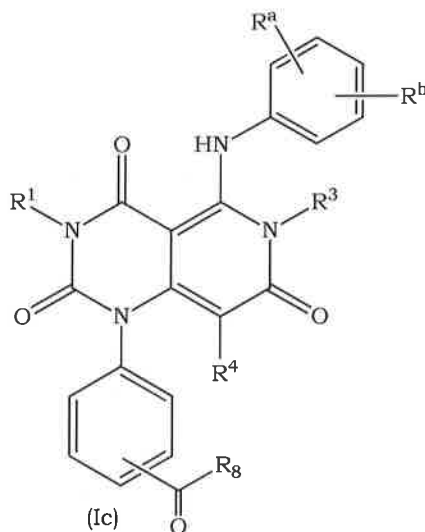
$C(=O)OR^{10a}$, $-C(=O)N(H)R^{10}$, $-C(=O)N(alkyl)R^{10}$, $-NH-SO_2-alkyl$ and $-NH-SO_2-$ cycloalkyl;

R^{10} is selected from the group consisting of hydrogen, alkyl, alkenyl, cycloalkyl, cycloalkenyl, aryl, heteroaryl, and heterocyclyl;

R^{10a} is selected from the group consisting of alkyl, alkenyl, perhaloalkyl, cycloalkyl, cycloalkenyl, aryl, heteroaryl, and heterocyclyl; and

R^{10b} is selected from the group consisting of hydrogen, alkyl, alkenyl, perhaloalkyl, cycloalkyl, cycloalkenyl, aryl, heteroaryl, and heterocyclyl.

4. A compound of the general formula Ic, its tautomeric forms, its pharmaceutically acceptable salts, their combinations with suitable medicament and pharmaceutical compositions containing them,



wherein,

R^1 is selected from the group consisting of hydrogen, substituted- or unsubstituted-alkyl, substituted- or unsubstituted- cycloalkyl, and substituted- or unsubstituted- heterocyclyl;

R^3 is selected from the group consisting of hydrogen, substituted- or unsubstituted- alkyl, and substituted- or unsubstituted- cycloalkyl;

R^4 is selected from the group consisting of hydrogen, halogen, substituted- or unsubstituted-alkyl, and substituted- or unsubstituted- cycloalkyl;

R^a and R^b are selected from the group consisting of hydrogen, halogen and haloalkyl;

R^8 is selected from the group consisting of substituted- or unsubstituted- alkyl, substituted- or unsubstituted- alkenyl, substituted- or unsubstituted- alkynyl, substituted- or unsubstituted- cycloalkyl, and substituted- or unsubstituted- cycloalkenyl;

when the alkyl group and alkenyl group is substituted, the alkyl group and alkenyl group is substituted with 1 to 4 substituents independently selected from the group consisting of oxo, halogen, nitro, cyano, perhaloalkyl, cycloalkyl, aryl, heteroaryl, heterocyclyl, $-OR^{10b}$, $-SO_2R^{10a}$, $-C(=O)OR^{10a}$, $-OC(=O)R^{10a}$, $-C(=O)N(H)R^{10}$, $-OR^{10a}$, $-C(=O)N(alkyl)R^{10}$, $-N(H)C(=O)R^{10a}$, $-N(H)R^{10}$, $-N(alkyl)R^{10}$, $-N(H)C(=O)N(H)R^{10}$, $-N(H)C(=O)N(alkyl)R^{10}$, $-NH-SO_2-alkyl$ and $-NH-SO_2-cycloalkyl$;

when the cycloalkyl group and cycloalkenyl group is a substituted, the cycloalkyl group and cycloalkenyl group is substituted with 1 to 3 substituents independently selected from the group consisting of oxo, halogen, nitro, cyano, alkyl, alkenyl, perhaloalkyl, aryl, heteroaryl, heterocyclyl, $-OR^{10b}$, $-SO_2R^{10a}$, $-C(=O)R^{10a}$, $-C(=O)OR^{10a}$, $-OC(=O)R^{10a}$, $-C(=O)N(H)R^{10}$, $-C(=O)N(alkyl)R^{10}$, $-N(H)C(=O)R^{10a}$, $-N(H)R^{10}$, $-N(alkyl)R^{10}$, $-N(H)C(=O)N(H)R^{10}$, and $-N(H)C(=O)N(alkyl)R^{10}$, $-NH-SO_2-alkyl$ and $-NH-SO_2-cycloalkyl$;

when the aryl group is a substituted, the aryl group is substituted with 1 to 3 substituents independently selected from the group consisting of halogen, nitro, cyano, hydroxy, alkyl, alkenyl, perhaloalkyl, cycloalkyl, cycloalkenyl, heterocycle, $-O-alkyl$, $-O-perhaloalkyl$, $-N(alkyl)alkyl$, $-N(H)alkyl$, $-NH_2$, $-SO_2-alkyl$, $-SO_2-perhaloalkyl$, $-N(alkyl)C(=O)alkyl$, $-N(H)C(=O)alkyl$, $-C(=O)N(alkyl)alkyl$, -

$C(=O)N(H)alkyl$, $-C(=O)NH_2$, $-SO_2N(alkyl)alkyl$, $-SO_2N(H)alkyl$, $-SO_2NH_2$, $-NH-SO_2-alkyl$ and $-NH-SO_2-cycloalkyl$;

when the heteroaryl group is a substituted, the heteroaryl group is substituted with 1 to 3 substituents independently selected from the group consisting of halogen, nitro, cyano, hydroxy, alkyl, alkenyl, perhaloalkyl, cycloalkyl, cycloalkenyl, heterocycle, $-O-alkyl$, $O-perhaloalkyl$, $-N(alkyl)alkyl$, $-N(H)alkyl$, $-NH_2$, $-SO_2-alkyl$, $-SO_2-perhaloalkyl$, $-N(alkyl)C(=O)alkyl$, $-N(H)C(=O)alkyl$, $-C(=O)N(alkyl)alkyl$, $-C(=O)N(H)alkyl$, $-C(=O)NH_2$, $-SO_2N(alkyl)alkyl$, $-SO_2N(H)alkyl$, $-SO_2NH_2$, $-NH-SO_2-alkyl$ and $-NH-SO_2-cycloalkyl$;

when the heterocyclyl group is a substituted, the heterocyclyl group is substituted with 1 to 3 substituents, when the heterocyclic group is substituted on a ring carbon of the 'heterocycle', the substituents are independently selected from the group consisting of halogen, nitro, cyano, oxo, alkyl, alkenyl, perhaloalkyl, cycloalkyl, cycloalkenyl, aryl, heteroaryl, heterocyclyl, $-OR^{10b}$, $-C(=O)OR^{10a}$, $-OC(=O)R^{10a}$, $-C(=O)N(H)R^{10}$, $-C(=O)N(alkyl)R^{10}$, $-N(H)C(=O)R^{10a}$, $-N(H)R^{10}$, $-N(alkyl)R^{10}$, $-N(H)C(=O)N(H)R^{10}$, $-N(H)C(=O)N(alkyl)R^{10}$; the substituents on ring nitrogen of the 'heterocycle'; substituents are independently selected from the group consisting of alkyl, alkenyl, cycloalkyl, cycloalkenyl, aryl, heteroaryl, $-SO_2R^{10a}$, $-C(=O)R^{10a}$, $C(=O)OR^{10a}$, $-C(=O)N(H)R^{10}$, $-C(=O)N(alkyl)R^{10}$, $-NH-SO_2-alkyl$ and $-NH-SO_2-cycloalkyl$;

R^{10} is selected from the group consisting of hydrogen, alkyl, alkenyl, cycloalkyl, cycloalkenyl, aryl, heteroaryl, and heterocyclyl;

R^{10a} is selected from the group consisting of alkyl, alkenyl, perhaloalkyl, cycloalkyl, cycloalkenyl, aryl, heteroaryl, and heterocyclyl; and

R^{10b} is selected from the group consisting of hydrogen, alkyl, alkenyl, perhaloalkyl, cycloalkyl, cycloalkenyl, aryl, heteroaryl, and heterocyclyl.

5. The compound of any one of claims 1-4, wherein R^1 is selected from the group consisting of hydrogen, alkyl, and cycloalkyl.

6. The compound of any one of claims 1-5, wherein R^1 is selected from the group consisting of hydrogen, methyl and cyclopropyl.
7. The compound of any one of claims 1-6, wherein R^3 is methyl.
8. The compound of any one of claims 1-7, wherein R^4 is selected as methyl.
9. The compound of any one of claims 1-8, wherein R^a and R^b are halogen.
10. The compound of any one of claims 1-9, wherein R^a and R^b are independently fluorine and iodine.
11. The compound of any one of claims 1-10, wherein R^6 is selected from the group consisting of direct bond, $-[C(R^c)R^d]_nNR^9-$, $-[C(R^c)R^d]_nO-$, and $-NHC(=O)[C(R^c)R^d]_p-$.
12. The compound of any one of claims 1-11, wherein R^6 is selected from the group selected from direct bond, $-NH-$, $-O-$, $-CH_2O-$, and $-NHC(=O)-$.
13. The compound of any one of claims 1-12, wherein E is substituted- or unsubstituted- four membered heterocyclic ring.
14. The compound of any one of claims 1-13, wherein E is selected from the group consisting of 3-oxetane, 1-azetidine, 1-azetidine-2-one and 3-azetidine substituted- or unsubstituted- with methyl, fluoro, $-C(=O)OR^e$ and $-OR^e$; wherein R^e is hydrogen, tert-butyl, and $-CH_2C(=O)NH_2$.
15. The compound of any one of claims 1-14, wherein R^7 is cyclopropyl.
16. The compound of any one of claims 1-15, wherein R^8 is cyclopropyl.
17. The compound of any one of claims 1-16, wherein R^1 is selected from the group consisting of hydrogen, alkyl, cycloalkyl; R^3 is alkyl; R^4 is alkyl; R^a and R^b are halogen; R^6 is selected from the group consisting of direct bond, $-[C(R^c)R^d]_nNR^9-$, $-[C(R^c)R^d]_nO-$ and $-NHC(=O)[C(R^c)R^d]_p-$; E is substituted- or unsubstituted- four

membered heterocyclic ring; R⁷ is substituted- or unsubstituted- cycloalkyl; R⁸ is substituted- or unsubstituted- cycloalkyl.

18. The compound of any one of claims 1-17, wherein R¹ is selected from the group consisting of hydrogen, methyl, cyclopropyl; R³ is methyl; R⁴ is methyl; R^a and R^b are fluoro and iodo; R⁶ is direct bond, -NH-, -O-, -CH₂O- and -NHC(=O)-; E is 3-oxetane, 1-azetidine, 1-azetidine-2-one and 3-azetidine substituted- or unsubstituted- with methyl, fluoro, tert-butoxy carbonyl, -OH and -OCH₂C(=O)NH₂; R⁷ is cyclopropyl and R⁸ is cyclopropyl.

19. The compound of any one of claims 1-18, wherein the compound is selected from the group consisting of –

1-(3-(cyclopropylsulfonyl)phenyl)-5-((2-fluoro-4-iodophenyl)amino)-6,8-dimethyl pyrido [4,3-d]pyrimidine-2,4,7(1H,3H,6H)-trione (Compound 1)

3-cyclopropyl-1-(2-fluoro-4-iodophenyl)-5-((3-(3-hydroxyazetidin-1-yl)phenyl)amino) -6,8-dimethylpyrido[2,3-d]pyrimidine-2,4,7(1H,3H,8H)-trione (Compound 2)

3-cyclopropyl-1-(3-(cyclopropylsulfonyl)phenyl)-5-((2-fluoro-4-iodophenyl)amino)-6,8-dimethylpyrido[4,3-d]pyrimidine-2,4,7(1H,3H,6H)-trione (Compound 3)

3-cyclopropyl-5-((2-fluoro-4-iodophenyl)amino)-6,8-dimethyl-1-(3-(2-oxoazetidin-1-yl)phenyl)pyrido[4,3-d]pyrimidine-2,4,7(1H,3H,6H)-trione (Compound 4)

3-cyclopropyl-5-((2-fluoro-4-iodophenyl)amino)-6,8-dimethyl-1-(3-(oxetan-3-ylamino) phenyl)pyrido[4,3-d]pyrimidine-2,4,7(1H,3H,6H)-trione (Compound 5)

3-cyclopropyl-5-((2-fluoro-4-iodophenyl)amino)-6,8-dimethyl-1-(3-(oxetan-3-yloxy) phenyl)pyrido[4,3-d]pyrimidine-2,4,7(1H,3H,6H)-trione (Compound 7)

1-(3-(azetidin-1-yl)phenyl)-3-cyclopropyl-5-((2-fluoro-4-iodophenyl)amino)-6,8-dimethyl pyrido[4,3-d]pyrimidine-2,4,7(1H,3H,6H)-trione (Compound 8)

3-cyclopropyl-5-((2-fluoro-4-iodophenyl)amino)-1-(3-(3-hydroxyoxetan-3-yl)phenyl)-6,8-dimethylpyrido[4,3-d]pyrimidine-2,4,7(1H,3H,6H)-trione (Compound 9)

N-(3-(3-cyclopropyl-5-((2-fluoro-4-iodophenyl)amino)-6,8-dimethyl-2,4,7-trioxo-3,4,6,7-tetrahydropyrido[4,3-d]pyrimidin-1(2H)-yl)phenyl)-3-methyloxetane-3-carboxamide (Compound 10)

1-(3-(cyclopropanecarbonyl)phenyl)-3-cyclopropyl-5-((2-fluoro-4-iodophenyl)amino)-6,8-dimethylpyrido[4,3-d]pyrimidine-2,4,7(1H,3H,6H)-trione (Compound 11)

1-(3-(cyclopropylsulfonyl)phenyl)-5-((2-fluoro-4-iodophenyl)amino)-3,6,8-trimethyl pyrido[4,3-d]pyrimidine-2,4,7(1H,3H,6H)-trione (Compound 12)

5-((2-fluoro-4-iodophenyl)amino)-3,6,8-trimethyl-1-(3-((oxetan-3-yloxy)methyl)phenyl)pyrido[4,3-d]pyrimidine-2,4,7(1H,3H,6H)-trione (Compound 13)

5-((2-fluoro-4-iodophenyl)amino)-1-(3-(3-hydroxyoxetan-3-yl)phenyl)-3,6,8-trimethylpyrido[4,3-d]pyrimidine-2,4,7(1H,3H,6H)-trione (Compound 14)

5-((2-fluoro-4-iodophenyl)amino)-3,6,8-trimethyl-1-(3-(oxetan-3-yloxy)phenyl)pyrido[4,3-d]pyrimidine-2,4,7(1H,3H,6H)-trione (Compound 15)

1-(3-(azetidin-1-yl)phenyl)-5-((2-fluoro-4-iodophenyl)amino)-3,6,8-trimethylpyrido[4,3-d]pyrimidine-2,4,7(1H,3H,6H)-trione (Compound 16)

5-((2-fluoro-4-iodophenyl)amino)-3,6,8-trimethyl-1-(3-(oxetan-3-ylamino)phenyl) pyrido[4,3-d]pyrimidine-2,4,7(1H,3H,6H)-trione (Compound 17)

N-(3-(5-((2-fluoro-4-iodophenyl)amino)-3,6,8-trimethyl-2,4,7-trioxo-3,4,6,7-tetrahydro pyrido[4,3-d]pyrimidin-1(2H)-yl)phenyl)-3-methyloxetane-3-carboxamide (Compound 18)

2-((1-(3-(5-((2-fluoro-4-iodophenyl)amino)-3,6,8-trimethyl-2,4,7-trioxo-3,4,6,7-tetra hydro pyrido[4,3-d]pyrimidin-1(2H)-yl)phenyl)azetidin-3-yl)oxy)acetamide (Compound 19)

5-((2-fluoro-4-iodophenyl)amino)-1-(3-(3-fluorooxetan-3-yl)phenyl)-3,6,8-trimethyl pyrido[4,3-d]pyrimidine-2,4,7(1H,3H,6H)-trione (Compound 20)

N-(3-(3-cyclopropyl-5-((2-fluoro-4-iodophenyl)amino)-6,8-dimethyl-2,4,7-trioxo-3,4,6,7-tetrahydropyrido[4,3-d]pyrimidin-1(2H)-yl)phenyl)azetidine-3-carboxamide (Compound 21)

20. A pharmaceutical composition comprising a compound or apharmaceutically acceptable salt of any one of claims 1-19 and one or more pharmaceutically acceptable carriers, diluents, or excipients.
21. Use of a compound of formula I, Ia, Ib, Ic, its tautomeric form, or its pharmaceutically acceptable salt as claimed in any one of claims 1-19, in the preparation of medicament ~~A method~~ for inhibiting MEK enzymes comprising contacting said MEK enzyme with a composition comprising a said compound of formula I, Ia, Ib, Ic ~~their tautomeric forms, their pharmaceutically acceptable salts as claimed in any one of claims 1-19~~, in an amount sufficient to inhibit said enzyme, wherein said enzyme is inhibited.
22. ~~The method of~~ use as claimed in claim 21, wherein said MEK enzyme is MEK kinase.
23. ~~The use as claimed in~~ method of claim 21 wherein said contacting occurs within a cell.
24. Use of a compound of formula I, Ia, Ib, Ic, its tautomeric form, or its pharmaceutically acceptable salt as claimed in any one of claims 1-19, in the preparation of medicament for the ~~A method of~~ treatment of a MEK mediated disorder in an individual suffering from said disorder, comprising administering to said individual an effective amount of a composition

comprising a said compound of formula I, Ia, Ib, Ic their tautomeric forms, or their pharmaceutically acceptable salts as claimed in any one of claims 1-19.

25. The ~~method of use~~ as claimed in claim 24, further ~~comprising~~ comprises administering an additional therapy.
26. The ~~use as claimed method of~~ claim 25, wherein said additional therapy is radiation therapy, chemotherapy or a combination of both.
27. The ~~use as claimed method of~~ claim 24, further ~~comprising~~ comprises administering at least one additional therapeutic agent.
28. The ~~use as claimed method of~~ claim 24, wherein said MEK mediated disorder is selected from the group consisting of inflammatory diseases, infections, autoimmune disorders. Stroke, ischemia, cardiac disorder, neurological disorders, fibrogenetic disorders, proliferative disorders, hyperproliferative disorders, tumors, leukemias, neoplasms, cancers, carcinomas, metabolic diseases and malignant diseases.
29. The ~~use as claimed in method of~~ claim 24, wherein said MEK mediated disorder is a hyperproliferative disease.
30. The ~~use as claimed in method of~~ claim 24, wherein said MEK mediated disorder is cancer, tumors, leukemias, neoplasms, or carcinomas.
31. The ~~use as claimed in method of~~ claim 24, wherein said MEK mediated disorder is an inflammatory disease.
32. The ~~use as claimed in method of~~ claim 24, wherein said individual is a mammal.
33. Use of a compound of formula I, Ia, Ib, Ic, its tautomeric form, or its pharmaceutically acceptable salt as claimed in any one of claims 1-19, in the preparation of medicament A ~~method~~ for the treatment or prophylaxis of a proliferative disease in an individual in need thereof comprising administering to said individual an effective amount of a composition comprising a ~~said~~ compound of formula I, Ia, Ib, Ic their tautomeric forms, their pharmaceutically acceptable salts as claimed in claim 1-19.
34. The ~~use as claimed in method of~~ claim 33, wherein said proliferative disease is cancer, psoriasis, restenosis, autoimmune disease, or atherosclerosis.

35. Use of a compound of formula I, Ia, Ib, Ic, its tautomeric form, or its pharmaceutically acceptable salt as claimed in any one of claims 1-19, in the preparation of medicament A ~~method~~ for the treatment or prophylaxis of an inflammatory disease in an individual in need thereof comprising administering to said individual an effective amount of a composition comprising a said compound of formula I, Ia, Ib, Ic their tautomeric forms, or their pharmaceutically acceptable salts as claimed in claim 1-19.
36. The ~~method of~~ use as claimed in claim 35, wherein said inflammatory disease is rheumatoid arthritis or multiple sclerosis.
37. Use of a compound of formula I, Ia, Ib, Ic, its tautomeric form, or its pharmaceutically acceptable salt as claimed in any one of claims 1-19, in the preparation of medicament A ~~method~~ for degrading, inhibiting the growth of or killing cancer cells comprising contacting the cells with an effective amount of a composition to degrade, inhibit the growth of or kill cancer cells, wherein the composition comprises a said compound of formula I, Ia, Ib, Ic their tautomeric forms, or their pharmaceutically acceptable salts as claimed in claims 1-19.
38. Use of a compound of formula I, Ia, Ib, Ic, its tautomeric form, or its pharmaceutically acceptable salt as claimed in any one of claims 1-19, in the preparation of medicament A ~~method~~ of inhibiting tumor size increase, reducing the size of a tumor, reducing tumor proliferation or preventing tumor proliferation in an individual thereof comprising administering to said individual an effective amount of a composition to inhibit tumor size increase, reduce the size of a tumor, reduce tumor proliferation or prevent tumor proliferation, wherein the composition comprises a said compound of formula I, Ia, Ib, Ic their tautomeric forms, or their pharmaceutically acceptable salts, as claimed in claims 1-19.