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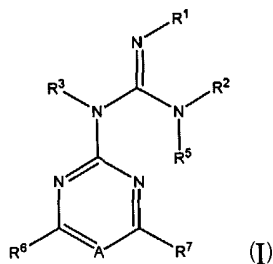
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(54) Title: THERAPEUTIC GUANIDINES



(57) Abstract: The present invention is directed, in part, to guanidine derivatives of formula (I), or pharmaceutically acceptable salt forms thereof, compositions thereof, and uses thereof related to, for example, the inhibition of IRES-mediated translation and the treatment of viral and other infections.

THERAPEUTIC GUANIDINES

FIELD OF THE INVENTION

[0001] The present invention is directed, in part, to guanidine derivatives and their use in the treatment of viral and other infections.

BACKGROUND OF THE INVENTION

[0002] The incidence of hepatitis C virus (HCV) infection is becoming an increasingly severe public health concern with up to 15% individuals infected worldwide. While primary infection with HCV is often asymptomatic, most HCV infections progress to a chronic state that can persist for decades. Of those with chronic HCV infections, it is believed that about up to half will eventually develop chronic liver disease (e.g. cirrhosis) and 20-30% of these cases will lead to liver failure or liver cancer. As the current HCV-infected population ages, the morbidity and mortality associated with HCV are expected to triple.

[0003] An approved treatment for HCV infection uses interferon (IFN) which indirectly effects HCV infection by stimulating the host antiviral response. IFN treatment is largely ineffective, however, as a sustained antiviral response is produced in less than 30% of treated patients. Further, IFN treatment induces an array of side effects of varying severity in upwards of 90% of patients (eg: acute pancreatitis, depression, retinopathy, thyroiditis). Therapy with a combination of IFN and ribavirin has provided a slightly higher sustained response rate, but has not alleviated the IFN-induced side effects.

[0004] HCV translation is believed to be mediated by an internal ribosome entry site (IRES) located within the 5' non-translated region. IRES elements were first reported in picornaviral mRNAs which are naturally uncapped but nonetheless efficiently translated (Jang *et al.*, *J. Virol.*, **1988**, 62, 2636). Recent studies have revealed that the HCV IRES recruits the cellular translation machinery in a distinct manner compared with cellular mRNA strategies which is generally mediated by a "cap" at the 5' end of mRNA upstream of the coding sequence. Picornaviruses, rhinovirus, HCV and others have been shown to possess an IRES which mediates translation in the absence of the cap structure at the 5' end of the messenger RNA. This IRES region is typically at least 450 nucleotides long when it occurs in viruses and possesses, at its 3' end, a conserved UUUC motif followed by a polypyrimidine tract, a G-poor spacer and an AUG triplet. Agol *et al.*, *Cell*, **1992**, 68,

119. The IRES is located within the 5' untranslated (5' UTR) region, but downstream from the cap.

[0005] Generally, the IRES is difficult to identify by sequence homology. Known IRES have been identified and defined functionally (Mountford *et al.*, *TIG*, **1995**, *11*(5), 179). It is believed that the conformation of the IRES sequence enables the binding on the ribosome. RNA secondary structure appears to play an important role in viral IRES-mediated translation. For example, maintenance of a phylogenetically conserved stem-loop structure was found to be important for the ability of the HCV IRES to mediate translation (Honda, *et al.*, *J. Virol.*, **1999**, *73*, 1165).

[0006] It has been hypothesized that interference with IRES can block translation and potentially viral replication. Antisense molecules and catalytic enzymes have been studied as HCV translation inhibitors that interfere with IRES function (Jubin, *Curr Opin Mol Ther.*, **2001**, *3*(3), 278).

[0007] While small molecule inhibitors of HCV translation are largely unknown, derivatives of guanidine have been reported as potential antiviral therapeutics. For example, Geluk *et al.*, *J. Med. Chem.*, **1969**, *12*, 712 report adamantyl disubstituted guanidines as possible antiviral agents and Eslager, *et al.*, *J. Med. Chem.*, **1974**, *17*, 75 report antimalarial guanidines. Guanidine derivatives as therapeutics are also reported in U.S. Pat. No. 3,270,054; 4,051,256; 4,721,785, 4,743,294, 4,772,609; 4,797,484, 4,851,423; 4,851,441, 4,880,932; and 6,156,758, as well as EP 806,205 and WO 90/04390.

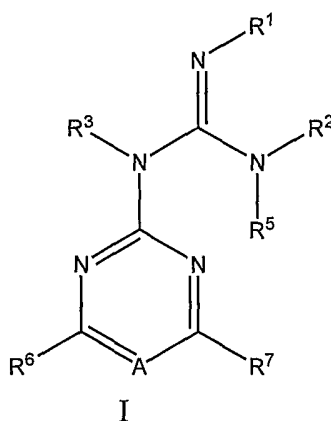
[0008] Other guanidine compounds are reported in the literature: HU 59567; U.S. Pat. No. 4,602,938; Shuto *et al.*, *Agricultural and Biological Chemistry*, **1979**, *43*, 2245; Shuto *et al.*, *Agricultural and Biological Chemistry*, **1979**, *43*, 771; Shuto *et al.*, *Agricultural and Biological Chemistry*, **1979**, *43*, 861; Shuto *et al.*, *Journal of the Faculty of Agriculture, Kyushu University*, **1979**, *23*, 125; Paul *et al.*, *Indian Journal of Chemistry, Section B: Organic Chemistry Including Medicinal Chemistry*, **1976**, *14B*, 887; Maekawa *et al.*, *Journal of the Faculty of Agriculture, Kyushu University*, **1977**, *21*, 99; Shuto *et al.*, *Journal of the Faculty of Agriculture, Kyushu University*, **1974**, *18*, 221; Furukawa *et al.*, *Chemical & Pharmaceutical Bulletin*, **1971**, *19*, 2284; Mamlis *et al.*, *J. Chem. Soc., Abstracts*, **1962**, 3915; Brus *et al.*, *Acta Parasitologica Polonica*, **1967**, *15*, 81; Urbanski *et al.*, *J. Med. Chem.*, **1967**, *10*, 521; and Serafin *et al.*, *Nitro Compounds, Proceedings of the International Symposium*, **1964**, Volume Date 1963, 469-73.

[0009] As evidenced above, current therapies for viral infections such as HCV are inadequate. Thus, there is an ongoing need for new and more effective treatments. The

guanidine compounds, compositions thereof, and methods of use thereof described herein help meet these and other needs.

SUMMARY OF THE INVENTION

[0010] The present invention provides, *inter alia*, guanidine derivatives of Formula I:



or pharmaceutically acceptable salt forms thereof, wherein:

R^1 is H or COOR^{1a} ;

R^{1a} is H or $\text{C}_1\text{-C}_{10}$ alkyl, aryl, cycloalkyl, or aralkyl;

R^2 and R^3 are each, independently, H, $\text{C}_1\text{-C}_{10}$ alkyl, or $\text{C}_3\text{-C}_7$ cycloalkyl;

A is N or CR^4 ;

R^4 is H, halo, $\text{C}_1\text{-C}_6$ alkyl, $\text{C}_1\text{-C}_6$ haloalkyl, $\text{C}_3\text{-C}_7$ cycloalkyl, $\text{C}_2\text{-C}_6$ alkenyl, $\text{C}_2\text{-C}_6$ alkynyl, OH, alkoxy, aryloxy, aralkoxy, cycloalkyloxy, cycloalkylalkyloxy, heterocycloalkyloxy, heterocycloalkylalkyloxy, heteroaryloxy, heteroarylalkyloxy, cyano, nitro, hydroxy, mercapto, or $\text{O}(\text{CR}^{4a}\text{R}^{4b})_a\text{NR}^{4c}\text{R}^{4d}$;

R^{4a} and R^{4b} are each, independently, H or $\text{C}_1\text{-C}_4$ alkyl;

R^{4c} and R^{4d} are each, independently, H, $\text{C}_1\text{-C}_4$ alkyl, $\text{C}_3\text{-C}_7$ cycloalkyl, $\text{C}_1\text{-C}_4$ haloalkyl, aryl, $\text{C}(\text{O})\text{-(C}_1\text{-C}_6\text{ alkyl)}$, $\text{C}(\text{O})\text{-aryl}$, $\text{C}(\text{O})\text{-(C}_3\text{-C}_7\text{ cycloalkyl)}$, $\text{C}(\text{O})\text{O-(C}_1\text{-C}_6\text{ alkyl)}$, $\text{C}(\text{O})\text{O-aryl}$, or $\text{C}(\text{O})\text{O-(C}_3\text{-C}_7\text{ cycloalkyl)}$, or R^{4c} and R^{4d} together with the N atom to which they are attached form a 5- or 6-membered heterocycle;

a is 1, 2, 3, 4, 5, or 6;

R^5 is $\text{N(R}^{5a}\text{)-Q}$;

R^{5a} is H or $\text{C}_1\text{-C}_6$ alkyl;

Q is aryl, heteroaryl, cycloalkyl, or heterocycloalkyl, wherein Q is optionally substituted by one or more $\text{C}_1\text{-C}_{10}$ alkyl, $\text{C}_2\text{-C}_{10}$ alkenyl, $\text{C}_2\text{-C}_{10}$ alkynyl, alkoxy,

aryloxy, aralkoxy, aralkyl, OH, SH, thioalkoxy, halo, C₁-C₁₀ haloalkyl, haloalkoxy, COOH, C(O)-(C₁-C₆ alkyl), C(O)-(C₃-C₇ cycloalkyl), C(O)-aryl, C(O)O-(C₁-C₆ alkyl), C(O)O-(C₃-C₇ cycloalkyl), C(O)O-aryl, C(O)NR^{Q1}R^{Q2}, NO₂, CN, or NR^{Q3}R^{Q4};

R^{Q1} and R^{Q2} are each, independently, H, C₁-C₆ alkyl, C₃-C₆ cycloalkyl, aryl, or R^{Q1} and R^{Q2} together with the N atom to which they are attached form a 5- or 6-membered heterocycle;

R^{Q3} and R^{Q4} are each, independently, H, C₁-C₆ alkyl, aryl, C(O)-C₁-C₆ alkyl, C(O)-(C₃-C₇ cycloalkyl), C(O)-aryl, C(O)O-(C₁-C₆ alkyl), C(O)O-(C₃-C₇ cycloalkyl), C(O)O-aryl, or R^{Q1} and R^{Q2} together with the N atom to which they are attached form a 5- or 6-membered heterocycle;

or R⁵ is phenyl, naphthyl, or heteroaryl, wherein said naphthyl or heteroaryl is substituted by one or more OH or O(CR⁸R⁹)_pY and wherein said phenyl is substituted by one or more O(CR⁸R⁹)_pY;

R⁸ and R⁹ are each, independently, H or C₁-C₄ alkyl;

p is 1, 2, 3, 4, 5, or 6;

Y is Y¹ or Y²;

Y¹ is NR¹⁰R¹¹, C₃-C₇ cycloalkyl, heterocycloalkyl, or heteroaryl, wherein Y¹ is optionally substituted by one or more halo, C₁-C₆ alkyl, C₁-C₆ haloalkyl, C₂-C₆ alkenyl, C₂-C₆ alkynyl, C₃-C₇ cycloalkyl, aryl, heteroaryl, heterocycloalkyl, OH, SH, CN, NO₂, COOH, C(O)-(C₁-C₆ alkyl), C(O)-(C₃-C₇ cycloalkyl), C(O)-aryl, C(O)O-(C₁-C₆ alkyl), C(O)O-(C₃-C₇ cycloalkyl), C(O)O-aryl, NH₂, NH(C₁-C₄ alkyl), N(C₁-C₄ alkyl)₂, NHC(O)O-(C₁-C₆ alkyl), NHC(O)O-aryl or (CH₂)_qOH;

R¹⁰ and R¹¹ are each, independently, H, (C₁-C₆)alkyl, C(O)-(C₁-C₆ alkyl), C(O)-(C₃-C₇ cycloalkyl), C(O)-aryl, C(O)O-(C₁-C₆ alkyl), C(O)O-(C₃-C₇ cycloalkyl), C(O)O-aryl, aryl, heteroaryl, cycloalkyl, or heterocycloalkyl, or R¹⁰ and R¹¹ together with the N atom to which they are attached form a 5- or 6- membered heterocycle;

q is 0, 1, 2, or 3;

Y² is OR^{12a} or OSO₂R^{12b};

R^{12a} is H, C₁-C₁₀ alkyl, C₁-C₁₀ alkenyl, C₁-C₁₀ alkynyl, aryl, heteroaryl, C₃-C₇ cycloalkyl, or heterocycloalkyl;

R^{12b} is H, C₁-C₆ alkyl, aryl, or NH₂;

or R⁵ is cycloalkyl or heterocycloalkyl, wherein said cycloalkyl or heterocycloalkyl is optionally substituted by one or more halo, C₁-C₁₀ alkyl, C₁-C₁₀ haloalkyl, C₂-C₁₀

alkenyl, C₂-C₁₀ alkynyl, aryl, heteroaryl, cycloalkyl, heterocycloalkyl, alkoxy, aryloxy, aralkoxy, aralkyl, OH, SH, thioalkoxy, haloalkoxy, COOH, C(O)-(C₁-C₆ alkyl), C(O)-(C₃-C₇ cycloalkyl), C(O)-aryl, C(O)O-(C₁-C₆ alkyl), C(O)O-(C₃-C₇ cycloalkyl), C(O)O-aryl, CONR^{5b}R^{5c}, NO₂, CN, NR^{5d}R^{5e}, or O(CR⁸R⁹)_pY;

R^{5b} and R^{5c} are each, independently, H, C₁-C₆ alkyl, C₃-C₆ cycloalkyl, aryl, or R^{5b} and R^{5c} together with the N atom to which they are attached form a 5- or 6-membered heterocycle;

R^{5d} and R^{5e} are each, independently, H, C₁-C₆ alkyl, aryl, C(O)-C₁-C₆ alkyl, C(O)-(C₃-C₇ cycloalkyl), C(O)-aryl, C(O)O-(C₁-C₆ alkyl), C(O)O-(C₃-C₇ cycloalkyl), C(O)O-aryl, or R^{5d} and R^{5e} together with the N atom to which they are attached form a 5- or 6-membered heterocycle;

or R⁵ is -(CR¹³R¹⁴)_n-Z;

n is 1, 2, 3, 4, 5, 6, 7, or 8;

R¹³ and R¹⁴ are each, independently, H or C₁-C₆ alkyl, C₂-C₆ alkenyl, C₂-C₆ alkynyl, OH, SH, aryl, or aralkyl, or R¹³ and R¹⁴ together form C₃-C₇ cycloalkyl, oxo, or sulfido;

Z is naphthyl, anthracenyl, heteroaryl, cycloalkyl, heterocycloalkyl, biaryl, biheteroaryl, arylheteroaryl, or heteroarylaryl, each of which is optionally substituted by one or more R¹⁵, wherein when Z is morpholino, Z is substituted by at least one R¹⁵;

or Z is phenyl optionally substituted by at least one R¹⁶;

R¹⁵ is halo, C₁-C₁₀ alkyl, C₁-C₁₀ haloalkyl, C₂-C₁₀ alkenyl, C₂-C₁₀ alkynyl, alkoxy, aryloxy, aralkoxy, aralkyl, OH, SH, guanidiny, thioalkoxy, haloalkoxy, COOH, C(O)-(C₁-C₆ alkyl), C(O)-(C₃-C₇ cycloalkyl), C(O)-aryl, C(O)O-(C₁-C₆ alkyl), C(O)O-(C₃-C₇ cycloalkyl), C(O)O-aryl, CONR^{18a}R^{19a}, NO₂, CN, (CH₂)_tNR^{18b}R^{19b}, heteroaryl, heterocycloalkyl, aryl, C₃-C₇ cycloalkyl, or O(CR²⁰R²¹)_tX;

R¹⁶ is halo, C₁-C₁₀ alkyl, C₁-C₁₀ haloalkyl, C₂-C₁₀ alkenyl, C₂-C₁₀ alkynyl, alkoxy, aryloxy, aralkoxy, aralkyl, OH, SH, guanidiny, thioalkoxy, haloalkoxy, COOH, C(O)-(C₁-C₆ alkyl), C(O)-(C₃-C₇ cycloalkyl), C(O)-aryl, C(O)O-(C₁-C₆ alkyl), C(O)O-(C₃-C₇ cycloalkyl), C(O)O-aryl, CONR^{18c}R^{19c}, NO₂, CN, (CH₂)_tNR^{18d}R^{19d}, heteroaryl, heterocycloalkyl, aryl, C₃-C₇ cycloalkyl, or O(CR²⁰R²¹)_tX;

R^{18a} and R^{19a} are each, independently, H or C₁-C₆ alkyl, or R^{18a} and R^{19a} together with the N atom to which they are attached form a 5- or 6-membered heterocycle;

R^{18b} and R^{19b} are each, independently, H, C₁-C₆ alkyl, aryl, C(O)-C₁-C₆ alkyl, C(O)-(C₃-C₇ cycloalkyl), C(O)-aryl, C(O)O-(C₁-C₆ alkyl), C(O)O-(C₃-C₇ cycloalkyl), C(O)O-aryl, or R^{18b} and R^{19b} together with the N atom to which they are attached form a 5- or 6-membered heterocycle;

R^{18c} and R^{19c} are each, independently, H or C₁-C₆ alkyl, or R^{18c} and R^{19c} together with the N atom to which they are attached form a heterocycle;

R^{18d} and R^{19d} are each, independently, H, C₁-C₆ alkyl, aryl, C(O)-C₁-C₆ alkyl, C(O)-(C₃-C₇ cycloalkyl), C(O)-aryl, C(O)O-(C₁-C₆ alkyl), C(O)O-(C₃-C₇ cycloalkyl), C(O)O-aryl, or R^{18d} and R^{19d} together with the N atom to which they are attached form a 5- or 6-membered heterocycle;

R^{20} and R^{21} are each, independently, H or C₁-C₆ alkyl;

r is 0, 1, 2, 3, 4, 5, or 6;

t is 0, 1, or 2;

X is X¹ or X²;

X¹ is NR²²R²³, C₃-C₇ cycloalkyl, aryl, heteroaryl, or heterocycloalkyl, wherein X¹ is optionally substituted by one or more halo, C₁-C₆ alkyl, C₃-C₇ cycloalkyl, C₁-C₆ haloalkyl, aryl, heteroaryl, heterocycloalkyl, CN, NO₂, OH, COOH, C(O)-C₁-C₆ alkyl, C(O)-(C₃-C₇ cycloalkyl), C(O)-aryl, C(O)O-(C₁-C₆ alkyl), C(O)O-(C₃-C₇ cycloalkyl), C(O)O-aryl, NH₂, NH(C₁-C₄ alkyl), N(C₁-C₄ alkyl)₂, NHC(O)O-(C₁-C₆ alkyl), NHC(O)O-aryl or (CH₂)₈OH;

R^{22} and R^{23} are each, independently, H, C₁-C₆ alkyl, aryl, heteroaryl, heterocycloalkyl, cycloalkyl, C(O)-C₁-C₆ alkyl, C(O)-(C₃-C₇ cycloalkyl), C(O)-aryl, C(O)O-(C₁-C₆ alkyl), C(O)O-(C₃-C₇ cycloalkyl), C(O)O-aryl, or R^{22} and R^{23} together with the N atom to which they are attached form a 5- or 6-membered heterocycle;

s is 0, 1, 2, or 3;

X² is OH or OSO₂R²⁴;

R²⁴ is H, C₁-C₆ alkyl, aryl, or NH₂;

or R⁵ and R² together with the N atom to which they are attached form heterocycloalkyl optionally substituted by halo, C₁-C₄ alkyl, OH, SH, alkoxy or aryloxy; and

R⁶ and R⁷ are each, independently, H, halo, C₁-C₆ alkyl, C₁-C₆ haloalkyl, C₂-C₆ alkenyl, C₂-C₆ alkynyl, alkoxy, aryloxy, or aralkoxy, or R⁶ and R⁷ together with the atoms to which they are attached form a fused cycloalkyl, heterocycloalkyl, aryl, or heteroaryl group.

[0011] In other embodiments, the present invention provides compounds of Formula I,

or pharmaceutically acceptable salt forms thereof, wherein:

R^1 is H or COOR^{1a} ;

R^{1a} is H or $\text{C}_1\text{-C}_{10}$ alkyl, aryl, cycloalkyl, or aralkyl;

R^2 and R^3 are each, independently, H, $\text{C}_1\text{-C}_{10}$ alkyl, or $\text{C}_3\text{-C}_7$ cycloalkyl;

A is CR^4 ;

R^4 is OH, alkoxy, aryloxy, aralkoxy, cycloalkyloxy, cycloalkylalkyloxy, heterocycloalkyloxy, heterocycloalkylalkyloxy, heteroaryloxy, heteroarylalkyloxy, or $\text{O}(\text{CR}^{4a}\text{R}^{4b})_a\text{NR}^{4c}\text{R}^{4d}$;

R^{4a} and R^{4b} are each, independently, H or $\text{C}_1\text{-C}_4$ alkyl;

R^{4c} and R^{4d} are each, independently, H, $\text{C}_1\text{-C}_4$ alkyl, $\text{C}_3\text{-C}_7$ cycloalkyl, $\text{C}_1\text{-C}_4$ haloalkyl, aryl, $\text{C}(\text{O})\text{-(C}_1\text{-C}_6\text{ alkyl)}$, $\text{C}(\text{O})\text{-aryl}$, $\text{C}(\text{O})\text{-(C}_3\text{-C}_7\text{ cycloalkyl)}$, $\text{C}(\text{O})\text{O-(C}_1\text{-C}_6\text{ alkyl)}$, $\text{C}(\text{O})\text{O-aryl}$, or $\text{C}(\text{O})\text{O-(C}_3\text{-C}_7\text{ cycloalkyl)}$, or R^{4c} and R^{4d} together with the N atom to which they are attached form a 5- or 6-membered heterocycle;

a is 1, 2, 3, 4, 5, or 6;

R^5 is $\text{N(R}^{5a})\text{-Q}$;

R^{5a} is H or $\text{C}_1\text{-C}_6$ alkyl;

Q is aryl, heteroaryl, cycloalkyl, or heterocycloalkyl, wherein Q is optionally substituted by one or more $\text{C}_1\text{-C}_{10}$ alkyl, $\text{C}_2\text{-C}_{10}$ alkenyl, $\text{C}_2\text{-C}_{10}$ alkynyl, alkoxy, aryloxy, aralkoxy, aralkyl, OH, SH, thioalkoxy, halo, $\text{C}_1\text{-C}_{10}$ haloalkyl, haloalkoxy, COOH, $\text{C}(\text{O})\text{-(C}_1\text{-C}_6\text{ alkyl)}$, $\text{C}(\text{O})\text{-(C}_3\text{-C}_7\text{ cycloalkyl)}$, $\text{C}(\text{O})\text{-aryl}$, $\text{C}(\text{O})\text{O-(C}_1\text{-C}_6\text{ alkyl)}$, $\text{C}(\text{O})\text{O-(C}_3\text{-C}_7\text{ cycloalkyl)}$, $\text{C}(\text{O})\text{O-aryl}$, $\text{C}(\text{O})\text{NR}^{\text{Q1}}\text{R}^{\text{Q2}}$, NO_2 , CN, or $\text{NR}^{\text{Q3}}\text{R}^{\text{Q4}}$;

R^{Q1} and R^{Q2} are each, independently, H, $\text{C}_1\text{-C}_6$ alkyl, $\text{C}_3\text{-C}_6$ cycloalkyl, aryl, or R^{Q1} and R^{Q2} together with the N atom to which they are attached form a 5- or 6-membered heterocycle;

R^{Q3} and R^{Q4} are each, independently, H, $\text{C}_1\text{-C}_6$ alkyl, aryl, $\text{C}(\text{O})\text{-C}_1\text{-C}_6$ alkyl, $\text{C}(\text{O})\text{-(C}_3\text{-C}_7\text{ cycloalkyl)}$, $\text{C}(\text{O})\text{-aryl}$, $\text{C}(\text{O})\text{O-(C}_1\text{-C}_6\text{ alkyl)}$, $\text{C}(\text{O})\text{O-(C}_3\text{-C}_7\text{ cycloalkyl)}$, $\text{C}(\text{O})\text{O-aryl}$, or R^{Q1} and R^{Q2} together with the N atom to which they are attached form a 5- or 6-membered heterocycle;

or R^5 is aryl or heteroaryl, wherein said aryl or heteroaryl is optionally substituted by one or more OH or $\text{O}(\text{CR}^8\text{R}^9)_p\text{Y}$;

R^8 and R^9 are each, independently, H or $\text{C}_1\text{-C}_4$ alkyl;

p is 1, 2, 3, 4, 5, or 6;

Y is Y¹ or Y²;

Y¹ is NR¹⁰R¹¹, C₃-C₇ cycloalkyl, heterocycloalkyl, or heteroaryl,

wherein Y¹ is optionally substituted by one or more halo, C₁-C₆ alkyl, C₁-C₆ haloalkyl, C₂-C₆ alkenyl, C₂-C₆ alkynyl, C₃-C₇ cycloalkyl, aryl, heteroaryl, heterocycloalkyl, OH, SH, CN, NO₂, COOH, C(O)-(C₁-C₆ alkyl), C(O)-(C₃-C₇ cycloalkyl), C(O)-aryl, C(O)O-(C₁-C₆ alkyl), C(O)O-(C₃-C₇ cycloalkyl), C(O)O-aryl, NH₂, NH(C₁-C₄ alkyl), N(C₁-C₄ alkyl)₂, NHC(O)O-(C₁-C₆ alkyl), NHC(O)O-aryl or (CH₂)_qOH;

R¹⁰ and R¹¹ are each, independently, H, (C₁-C₆)alkyl, C(O)-(C₁-C₆ alkyl), C(O)-(C₃-C₇ cycloalkyl), C(O)-aryl, C(O)O-(C₁-C₆ alkyl), C(O)O-(C₃-C₇ cycloalkyl), C(O)O-aryl, aryl, heteroaryl, cycloalkyl, or heterocycloalkyl, or R¹⁰ and R¹¹ together with the N atom to which they are attached form a 5- or 6- membered heterocycle;

q is 0, 1, 2, or 3;

Y² is OR^{12a} or OSO₂R^{12b};

R^{12a} is H, C₁-C₁₀ alkyl, C₁-C₁₀ alkenyl, C₁-C₁₀ alkynyl, aryl, heteroaryl, C₃-C₇ cycloalkyl, or heterocycloalkyl;

R^{12b} is H, C₁-C₆ alkyl, aryl, or NH₂;

or R⁵ is cycloalkyl or heterocycloalkyl, wherein said cycloalkyl or heterocycloalkyl is optionally substituted by one or more halo, C₁-C₁₀ alkyl, C₁-C₁₀ haloalkyl, C₂-C₁₀ alkenyl, C₂-C₁₀ alkynyl, aryl, heteroaryl, cycloalkyl, heterocycloalkyl, alkoxy, aryloxy, aralkoxy, aralkyl, OH, SH, thioalkoxy, haloalkoxy, COOH, C(O)-(C₁-C₆ alkyl), C(O)-(C₃-C₇ cycloalkyl), C(O)-aryl, C(O)O-(C₁-C₆ alkyl), C(O)O-(C₃-C₇ cycloalkyl), C(O)O-aryl, CONR^{5b}R^{5c}, NO₂, CN, NR^{5d}R^{5e}, or O(CR⁸R⁹)_pY;

R^{5b} and R^{5c} are each, independently, H, C₁-C₆ alkyl, C₃-C₆ cycloalkyl, aryl, or R^{5b} and R^{5c} together with the N atom to which they are attached form a 5- or 6-membered heterocycle;

R^{5d} and R^{5e} are each, independently, H, C₁-C₆ alkyl, aryl, C(O)-C₁-C₆ alkyl, C(O)-(C₃-C₇ cycloalkyl), C(O)-aryl, C(O)O-(C₁-C₆ alkyl), C(O)O-(C₃-C₇ cycloalkyl), C(O)O-aryl, or R^{5d} and R^{5e} together with the N atom to which they are attached form a 5- or 6-membered heterocycle;

or R⁵ is -(CR¹³R¹⁴)_n-Z;

n is 1, 2, 3, 4, 5, 6, 7, or 8;

R^{13} and R^{14} are each, independently, H or C₁-C₆ alkyl, C₂-C₆ alkenyl, C₂-C₆ alkynyl, OH, SH, aryl, or aralkyl, or R^{13} and R^{14} together form C₃-C₇ cycloalkyl, oxo, or sulfido;

Z is aryl, heteroaryl, cycloalkyl, heterocycloalkyl, biaryl, biheteroaryl, arylheteroaryl, or heteroarylaryl, each of which is optionally substituted by one or more R^{15} ;

R^{15} is halo, C₁-C₁₀ alkyl, C₁-C₁₀ haloalkyl, C₂-C₁₀ alkenyl, C₂-C₁₀ alkynyl, alkoxy, aryloxy, aralkoxy, aralkyl, OH, SH, guanidiny, thioalkoxy, haloalkoxy, COOH, C(O)-(C₁-C₆ alkyl), C(O)-(C₃-C₇ cycloalkyl), C(O)-aryl, C(O)O-(C₁-C₆ alkyl), C(O)O-(C₃-C₇ cycloalkyl), C(O)O-aryl, CONR^{18a}R^{19a}, NO₂, CN, (CH₂)_tNR^{18b}R^{19b}, heteroaryl, heterocycloalkyl, aryl, C₃-C₇ cycloalkyl, or O(CR²⁰R²¹)_rX;

R^{18a} and R^{19a} are each, independently, H or C₁-C₆ alkyl, or R^{18a} and R^{19a} together with the N atom to which they are attached form a 5- or 6-membered heterocycle;

R^{18b} and R^{19b} are each, independently, H, C₁-C₆ alkyl, aryl, C(O)-C₁-C₆ alkyl, C(O)-(C₃-C₇ cycloalkyl), C(O)-aryl, C(O)O-(C₁-C₆ alkyl), C(O)O-(C₃-C₇ cycloalkyl), C(O)O-aryl, or R^{18b} and R^{19b} together with the N atom to which they are attached form a 5- or 6-membered heterocycle;

R^{18c} and R^{19c} are each, independently, H or C₁-C₆ alkyl, or R^{18c} and R^{19c} together with the N atom to which they are attached form a heterocycle;

R^{18d} and R^{19d} are each, independently, H, C₁-C₆ alkyl, aryl, C(O)-C₁-C₆ alkyl, C(O)-(C₃-C₇ cycloalkyl), C(O)-aryl, C(O)O-(C₁-C₆ alkyl), C(O)O-(C₃-C₇ cycloalkyl), C(O)O-aryl, or R^{18d} and R^{19d} together with the N atom to which they are attached form a 5- or 6-membered heterocycle;

R^{20} and R^{21} are each, independently, H or C₁-C₆ alkyl;

r is 0, 1, 2, 3, 4, 5, or 6;

t is 0, 1, or 2;

X is X¹ or X²;

X¹ is NR²²R²³, C₃-C₇ cycloalkyl, aryl, heteroaryl, or heterocycloalkyl, wherein X¹ is optionally substituted by one or more halo, C₁-C₆ alkyl, C₃-C₇ cycloalkyl, C₁-C₆ haloalkyl, aryl, heteroaryl, heterocycloalkyl, CN, NO₂, OH, COOH, C(O)-C₁-C₆ alkyl, C(O)-(C₃-C₇ cycloalkyl), C(O)-aryl, C(O)O-(C₁-C₆ alkyl), C(O)O-(C₃-C₇ cycloalkyl), C(O)O-aryl, NH₂, NH(C₁-C₄ alkyl), N(C₁-C₄ alkyl)₂, NHC(O)O-(C₁-C₆ alkyl), NHC(O)O-aryl or (CH₂)_sOH;

R^{22} and R^{23} are each, independently, H, C_1 - C_6 alkyl, aryl, heteroaryl, heterocycloalkyl, cycloalkyl, $C(O)$ - C_1 - C_6 alkyl, $C(O)$ -(C_3 - C_7 cycloalkyl), $C(O)$ -aryl, $C(O)O$ -(C_1 - C_6 alkyl), $C(O)O$ -(C_3 - C_7 cycloalkyl), $C(O)O$ -aryl, or R^{22} and R^{23} together with the N atom to which they are attached form a 5- or 6-membered heterocycle;

s is 0, 1, 2, or 3;

X^2 is OH or OSO_2R^{24} ;

R^{24} is H, C_1 - C_6 alkyl, aryl, or NH_2 ;

or R^5 and R^2 together with the N atom to which they are attached form heterocycloalkyl optionally substituted by halo, C_1 - C_4 alkyl, OH, SH, alkoxy or aryloxy; and

R^6 and R^7 are each, independently, H, halo, C_1 - C_6 alkyl, C_1 - C_6 haloalkyl, C_2 - C_6 alkenyl, C_2 - C_6 alkynyl, alkoxy, aryloxy, or aralkoxy, or R^6 and R^7 together with the atoms to which they are attached form a fused cycloalkyl, heterocycloalkyl, aryl, or heteroaryl group.

[0012] The present invention further provides methods of modulating activity of an infectious agent comprising contacting the infectious agent with a compound of Formula I, or pharmaceutically acceptable salt form thereof, wherein:

R^1 is H or $COOR^{1a}$;

R^{1a} is H or C_1 - C_{10} alkyl, aryl, cycloalkyl, or aralkyl;

R^2 and R^3 are each, independently, H, C_1 - C_{10} alkyl, or C_3 - C_7 cycloalkyl;

A is N or CR^4 ;

R^4 is H, halo, C_1 - C_6 alkyl, C_1 - C_6 haloalkyl, C_3 - C_7 cycloalkyl, C_2 - C_6 alkenyl, C_2 - C_6 alkynyl, OH, alkoxy, aryloxy, aralkoxy, cycloalkyloxy, cycloalkylalkyloxy, heterocycloalkyloxy, heterocycloalkylalkyloxy, heteroaryloxy, heteroarylalkyloxy, cyano, nitro, hydroxy, mercapto, or $O(CR^{4a}R^{4b})_aNR^{4c}R^{4d}$;

R^{4a} and R^{4b} are each, independently, H or C_1 - C_4 alkyl;

R^{4c} and R^{4d} are each, independently, H, C_1 - C_4 alkyl, C_3 - C_7 cycloalkyl, C_1 - C_4 haloalkyl, aryl, $C(O)$ -(C_1 - C_6 alkyl), $C(O)$ -aryl, $C(O)$ -(C_3 - C_7 cycloalkyl), $C(O)O$ -(C_1 - C_6 alkyl), $C(O)O$ -aryl, or $C(O)O$ -(C_3 - C_7 cycloalkyl), or R^{4c} and R^{4d} together with the N atom to which they are attached form a 5- or 6-membered heterocycle;

a is 1, 2, 3, 4, 5, or 6;

R^5 is $N(R^{5a})-Q$;

R^{5a} is H or C_1 - C_6 alkyl;

Q is aryl, heteroaryl, cycloalkyl, or heterocycloalkyl, wherein Q is optionally substituted by one or more C₁-C₁₀ alkyl, C₂-C₁₀ alkenyl, C₂-C₁₀ alkynyl, alkoxy, aryloxy, aralkoxy, aralkyl, OH, SH, thioalkoxy, halo, C₁-C₁₀ haloalkyl, haloalkoxy, COOH, C(O)-(C₁-C₆ alkyl), C(O)-(C₃-C₇ cycloalkyl), C(O)-aryl, C(O)O-(C₁-C₆ alkyl), C(O)O-(C₃-C₇ cycloalkyl), C(O)O-aryl, C(O)NR^{Q1}R^{Q2}, NO₂, CN, or NR^{Q3}R^{Q4};

R^{Q1} and R^{Q2} are each, independently, H, C₁-C₆ alkyl, C₃-C₆ cycloalkyl, aryl, or R^{Q1} and R^{Q2} together with the N atom to which they are attached form a 5- or 6-membered heterocycle;

R^{Q3} and R^{Q4} are each, independently, H, C₁-C₆ alkyl, aryl, C(O)-C₁-C₆ alkyl, C(O)-(C₃-C₇ cycloalkyl), C(O)-aryl, C(O)O-(C₁-C₆ alkyl), C(O)O-(C₃-C₇ cycloalkyl), C(O)O-aryl, or R^{Q1} and R^{Q2} together with the N atom to which they are attached form a 5- or 6-membered heterocycle;

or R⁵ is aryl, heteroaryl, cycloalkyl, or heterocycloalkyl, wherein said aryl, heteroaryl, cycloalkyl, or heterocycloalkyl is optionally substituted by one or more halo, C₁-C₁₀ alkyl, C₁-C₁₀ haloalkyl, C₂-C₁₀ alkenyl, C₂-C₁₀ alkynyl, aryl, heteroaryl, cycloalkyl, heterocycloalkyl, alkoxy, aryloxy, aralkoxy, aralkyl, CN, NO₂, OH, SH, thioalkoxy, haloalkoxy, COOH, C(O)-(C₁-C₆ alkyl), C(O)-aryl, C(O)-(C₃-C₇ cycloalkyl), C(O)O-(C₁-C₆ alkyl), C(O)O-aryl, or C(O)O-(C₃-C₇ cycloalkyl), CONR^{5b}R^{5c}, NR^{5d}R^{5e}, or O(CR⁸R⁹)_pY;

R^{5b} and R^{5c} are each, independently, H, C₁-C₆ alkyl, C₃-C₆ cycloalkyl, aryl, or R^{5b} and R^{5c} together with the N atom to which they are attached form a 5- or 6-membered heterocycle;

R^{5d} and R^{5e} are each, independently, H, C₁-C₆ alkyl, aryl, C(O)-C₁-C₆ alkyl, C(O)-(C₃-C₇ cycloalkyl), C(O)-aryl, C(O)O-(C₁-C₆ alkyl), C(O)O-(C₃-C₇ cycloalkyl), C(O)O-aryl, or R^{5d} and R^{5e} together with the N atom to which they are attached form a 5- or 6-membered heterocycle;

R⁸ and R⁹ are each, independently, H or C₁-C₆ alkyl;

p is 1, 2, 3, 4, 5, or 6;

Y is NR¹⁰R¹¹, OR^{12a}, OSO₂R^{12b}, C₃-C₇ cycloalkyl, heterocycloalkyl, or heteroaryl, wherein Y is optionally substituted by one or more halo, C₁-C₆ alkyl, C₁-C₆ haloalkyl, C₂-C₆ alkenyl, C₂-C₆ alkynyl, C₃-C₇ cycloalkyl, aryl, heteroaryl, heterocycloalkyl, OH, SH, CN, NO₂, COOH, C(O)-(C₁-C₆ alkyl), C(O)-(C₃-C₇ cycloalkyl), C(O)-aryl, C(O)O-(C₁-C₆ alkyl), C(O)O-(C₃-C₇ cycloalkyl), C(O)O-aryl,

NH₂, NH(C₁-C₄ alkyl), N(C₁-C₄ alkyl)₂, NHC(O)O-(C₁-C₆ alkyl), NHC(O)O-aryl or (CH₂)_qOH;

R¹⁰ and R¹¹ are each, independently, H, (C₁-C₆)alkyl, C(O)-(C₁-C₆ alkyl), C(O)-(C₃-C₇ cycloalkyl), C(O)-aryl, C(O)O-(C₁-C₆ alkyl), C(O)O-(C₃-C₇ cycloalkyl), C(O)O-aryl, aryl, heteroaryl, cycloalkyl, or heterocycloalkyl, or R¹⁰ and R¹¹ together with the N atom to which they are attached form a 5- or 6- membered heterocycle;

q is 0, 1, 2, or 3;

R^{12a} is H, C₁-C₁₀ alkyl, C₁-C₁₀ alkenyl, C₁-C₁₀ alkynyl, aryl, heteroaryl, C₃-C₇ cycloalkyl, or heterocycloalkyl;

R^{12b} is H, C₁-C₆ alkyl, aryl, or NH₂;

or R⁵ is -(CR¹³R¹⁴)_n-Z;

n is 1, 2, 3, 4, 5, 6, 7, or 8;

R¹³ and R¹⁴ are each, independently, H, C₁-C₆ alkyl, C₂-C₆ alkenyl, C₂-C₆ alkynyl, OH, aryl, or aralkyl, or R¹³ and R¹⁴ together form cycloalkyl, oxo, or sulfido;

Z is aryl, heteroaryl, cycloalkyl, heterocycloalkyl, biaryl, biheteroaryl, arylheteroaryl, heteroarylaryl, each of which is optionally substituted by one or more R¹⁵,

R¹⁵ is halo, C₁-C₁₀ alkyl, C₁-C₁₀ haloalkyl, C₂-C₁₀ alkenyl, C₂-C₁₀ alkynyl, alkoxy, aryloxy, aralkoxy, aralkyl, OH, SH, guanidiny, thioalkoxy, haloalkoxy, COOH, C(O)-(C₁-C₆ alkyl), C(O)-(C₃-C₇ cycloalkyl), C(O)-aryl, C(O)O-(C₁-C₆ alkyl), C(O)O-(C₃-C₇ cycloalkyl), C(O)O-aryl, CONR^{18a}R^{19a}, NO₂, CN, (CH₂)_tNR^{18b}R^{19b}, heteroaryl, heterocycloalkyl, aryl, C₃-C₇ cycloalkyl, or O(CR²⁰R²¹)_rX;

R^{18a} and R^{19a} are each, independently, H or C₁-C₆ alkyl, or R^{18a} and R^{19a} together with the N atom to which they are attached form a 5- or 6-membered heterocycle;

R^{18b} and R^{19b} are each, independently, H, C₁-C₆ alkyl, aryl, C(O)-C₁-C₆ alkyl, C(O)-(C₃-C₇ cycloalkyl), C(O)-aryl, C(O)O-(C₁-C₆ alkyl), C(O)O-(C₃-C₇ cycloalkyl), C(O)O-aryl, or R^{18b} and R^{19b} together with the N atom to which they are attached form a 5- or 6-membered heterocycle;

R²⁰ and R²¹ are each, independently, H or C₁-C₆ alkyl;

r is 0, 1, 2, 3, 4, 5, or 6;

t is 0, 1, or 2;

X is NR²²R²³, OH, NH₂, OSO₂R²⁴, C₃-C₇ cycloalkyl, aryl, heteroaryl, or heterocycloalkyl, wherein X is optionally substituted by one or more halo,

C₁-C₆ alkyl, C₃-C₇ cycloalkyl, C₁-C₆ haloalkyl, aryl, heteroaryl, heterocycloalkyl, CN, NO₂, OH, COOH, C(O)-C₁-C₆ alkyl, C(O)-(C₃-C₇ cycloalkyl), C(O)-aryl, C(O)O-(C₁-C₆ alkyl), C(O)O-(C₃-C₇ cycloalkyl), C(O)O-aryl, NH₂, NH(C₁-C₄ alkyl), N(C₁-C₄ alkyl)₂, NHC(O)O-(C₁-C₆ alkyl), NHC(O)O-aryl or (CH₂)_sOH;

R²² and R²³ are each, independently, H, C₁-C₆ alkyl, aryl, heteroaryl, heterocycloalkyl, cycloalkyl, C(O)-C₁-C₆ alkyl, C(O)-(C₃-C₇ cycloalkyl), C(O)-aryl, C(O)O-(C₁-C₆ alkyl), C(O)O-(C₃-C₇ cycloalkyl), C(O)O-aryl, or R²² and R²³ together with the N atom to which they are attached form a 5- or 6-membered heterocycle;

s is 0, 1, 2, or 3;

R²⁴ is H, C₁-C₆ alkyl, aryl, or NH₂;

or R⁵ and R² together with the N atom to which they are attached form heterocycloalkyl optionally substituted by one or more halo, C₁-C₄ alkyl, OH, SH, alkoxy or aryloxy; and

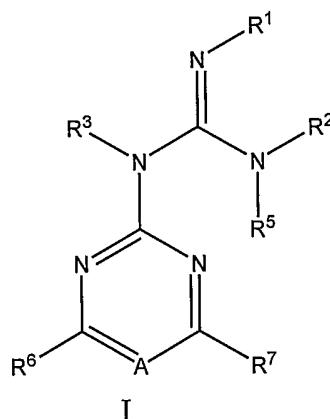
R⁶ and R⁷ are each, independently, H, halo, C₁-C₆ alkyl, C₁-C₆ haloalkyl, C₂-C₆ alkenyl, C₂-C₆ alkynyl, alkoxy, aryloxy, or aralkoxy, or R⁶ and R⁷ together with the atoms to which they are attached form a fused cycloalkyl, heterocycloalkyl, aryl, or heteroaryl group.

[0013] The present invention further provides a method of treating a viral infection in a patient by administering to the patient a therapeutically effective amount of a compound of Formula I, or pharmaceutically acceptable salt form thereof.

[0014] The present invention also provides a method of inhibiting translation of a nucleic acid wherein replication of the nucleic acid is mediated by an internal ribosome entry site (IRES), by contacting the nucleic acid with a compound of Formula I, or pharmaceutically acceptable salt form thereof.

DETAILED DESCRIPTION OF EMBODIMENTS OF THE INVENTION

[0010] The present invention provides, *inter alia*, guanidine derivatives of Formula I:



or pharmaceutically acceptable salt forms thereof, wherein:

R^1 is H or COOR^{1a} ;

R^{1a} is H or $\text{C}_1\text{-C}_{10}$ alkyl, aryl, cycloalkyl, or aralkyl;

R^2 and R^3 are each, independently, H, $\text{C}_1\text{-C}_{10}$ alkyl, or $\text{C}_3\text{-C}_7$ cycloalkyl;

A is N or CR^4 ;

R^4 is H, halo, $\text{C}_1\text{-C}_6$ alkyl, $\text{C}_1\text{-C}_6$ haloalkyl, $\text{C}_3\text{-C}_7$ cycloalkyl, $\text{C}_2\text{-C}_6$ alkenyl, $\text{C}_2\text{-C}_6$ alkynyl, OH, alkoxy, aryloxy, aralkoxy, cycloalkyloxy, cycloalkylalkyloxy, heterocycloalkyloxy, heterocycloalkylalkyloxy, heteroaryloxy, heteroarylalkyloxy, cyano, nitro, hydroxy, mercapto, or $\text{O}(\text{CR}^{4a}\text{R}^{4b})_a\text{NR}^{4c}\text{R}^{4d}$;

R^{4a} and R^{4b} are each, independently, H or $\text{C}_1\text{-C}_4$ alkyl;

R^{4c} and R^{4d} are each, independently, H, $\text{C}_1\text{-C}_4$ alkyl, $\text{C}_3\text{-C}_7$ cycloalkyl, $\text{C}_1\text{-C}_4$ haloalkyl, aryl, $\text{C}(\text{O})\text{-(C}_1\text{-C}_6\text{ alkyl)}$, $\text{C}(\text{O})\text{-aryl}$, $\text{C}(\text{O})\text{-(C}_3\text{-C}_7\text{ cycloalkyl)}$, $\text{C}(\text{O})\text{O-(C}_1\text{-C}_6\text{ alkyl)}$, $\text{C}(\text{O})\text{O-aryl}$, or $\text{C}(\text{O})\text{O-(C}_3\text{-C}_7\text{ cycloalkyl)}$, or R^{4c} and R^{4d} together with the N atom to which they are attached form a 5- or 6-membered heterocycle;

a is 1, 2, 3, 4, 5, or 6;

R^5 is $\text{N(R}^{5a}\text{)-Q}$;

R^{5a} is H or $\text{C}_1\text{-C}_6$ alkyl;

Q is aryl, heteroaryl, cycloalkyl, or heterocycloalkyl, wherein Q is optionally substituted by one or more $\text{C}_1\text{-C}_{10}$ alkyl, $\text{C}_2\text{-C}_{10}$ alkenyl, $\text{C}_2\text{-C}_{10}$ alkynyl, alkoxy, aryloxy, aralkoxy, aralkyl, OH, SH, thioalkoxy, halo, $\text{C}_1\text{-C}_{10}$ haloalkyl, haloalkoxy, COOH , $\text{C}(\text{O})\text{-(C}_1\text{-C}_6\text{ alkyl)}$, $\text{C}(\text{O})\text{-(C}_3\text{-C}_7\text{ cycloalkyl)}$, $\text{C}(\text{O})\text{-aryl}$, $\text{C}(\text{O})\text{O-(C}_1\text{-C}_6\text{ alkyl)}$, $\text{C}(\text{O})\text{O-(C}_3\text{-C}_7\text{ cycloalkyl)}$, $\text{C}(\text{O})\text{O-aryl}$, $\text{C}(\text{O})\text{NR}^{\text{Q1}}\text{R}^{\text{Q2}}$, NO_2 , CN, or $\text{NR}^{\text{Q3}}\text{R}^{\text{Q4}}$;

R^{Q1} and R^{Q2} are each, independently, H, $\text{C}_1\text{-C}_6$ alkyl, $\text{C}_3\text{-C}_6$ cycloalkyl, aryl, or R^{Q1} and R^{Q2} together with the N atom to which they are attached form a 5- or 6-membered heterocycle;

R^{Q3} and R^{Q4} are each, independently, H, C_1 - C_6 alkyl, aryl, $C(O)$ - C_1 - C_6 alkyl, $C(O)$ -(C_3 - C_7 cycloalkyl), $C(O)$ -aryl, $C(O)O$ -(C_1 - C_6 alkyl), $C(O)O$ -(C_3 - C_7 cycloalkyl), $C(O)O$ -aryl, or R^{Q1} and R^{Q2} together with the N atom to which they are attached form a 5- or 6-membered heterocycle;

or R^5 is phenyl, naphthyl, or heteroaryl, wherein said naphthyl or heteroaryl is substituted by one or more OH or $O(CR^8R^9)_pY$ and wherein said phenyl is substituted by one or more $O(CR^8R^9)_pY$;

R^8 and R^9 are each, independently, H or C_1 - C_4 alkyl;

p is 1, 2, 3, 4, 5, or 6;

Y is Y^1 or Y^2 ;

Y^1 is $NR^{10}R^{11}$, C_3 - C_7 cycloalkyl, heterocycloalkyl, or heteroaryl, wherein Y^1 is optionally substituted by one or more halo, C_1 - C_6 alkyl, C_1 - C_6 haloalkyl, C_2 - C_6 alkenyl, C_2 - C_6 alkynyl, C_3 - C_7 cycloalkyl, aryl, heteroaryl, heterocycloalkyl, OH, SH, CN, NO_2 , COOH, $C(O)$ -(C_1 - C_6 alkyl), $C(O)$ -(C_3 - C_7 cycloalkyl), $C(O)$ -aryl, $C(O)O$ -(C_1 - C_6 alkyl), $C(O)O$ -(C_3 - C_7 cycloalkyl), $C(O)O$ -aryl, NH_2 , $NH(C_1$ - C_4 alkyl), $N(C_1$ - C_4 alkyl) $_2$, $NHC(O)O$ -(C_1 - C_6 alkyl), $NHC(O)O$ -aryl or $(CH_2)_qOH$;

R^{10} and R^{11} are each, independently, H, (C_1 - C_6)alkyl, $C(O)$ -(C_1 - C_6 alkyl), $C(O)$ -(C_3 - C_7 cycloalkyl), $C(O)$ -aryl, $C(O)O$ -(C_1 - C_6 alkyl), $C(O)O$ -(C_3 - C_7 cycloalkyl), $C(O)O$ -aryl, aryl, heteroaryl, cycloalkyl, or heterocycloalkyl, or R^{10} and R^{11} together with the N atom to which they are attached form a 5- or 6- membered heterocycle;

q is 0, 1, 2, or 3;

Y^2 is OR^{12a} or OSO_2R^{12b} ;

R^{12a} is H, C_1 - C_{10} alkyl, C_1 - C_{10} alkenyl, C_1 - C_{10} alkynyl, aryl, heteroaryl, C_3 - C_7 cycloalkyl, or heterocycloalkyl;

R^{12b} is H, C_1 - C_6 alkyl, aryl, or NH_2 ;

or R^5 is cycloalkyl or heterocycloalkyl, wherein said cycloalkyl or heterocycloalkyl is optionally substituted by one or more halo, C_1 - C_{10} alkyl, C_1 - C_{10} haloalkyl, C_2 - C_{10} alkenyl, C_2 - C_{10} alkynyl, aryl, heteroaryl, cycloalkyl, heterocycloalkyl, alkoxy, aryloxy, aralkoxy, aralkyl, OH, SH, thioalkoxy, haloalkoxy, COOH, $C(O)$ -(C_1 - C_6 alkyl), $C(O)$ -(C_3 - C_7 cycloalkyl), $C(O)$ -aryl, $C(O)O$ -(C_1 - C_6 alkyl), $C(O)O$ -(C_3 - C_7 cycloalkyl), $C(O)O$ -aryl, $CONR^{5b}R^{5c}$, NO_2 , CN, $NR^{5d}R^{5e}$, or $O(CR^8R^9)_pY$;

R^{5b} and R^{5c} are each, independently, H, C_1 - C_6 alkyl, C_3 - C_6 cycloalkyl, aryl, or R^{5b} and R^{5c} together with the N atom to which they are attached form a 5- or 6-membered heterocycle;

R^{5d} and R^{5e} are each, independently, H, C_1 - C_6 alkyl, aryl, $C(O)$ - C_1 - C_6 alkyl, $C(O)$ -(C_3 - C_7 cycloalkyl), $C(O)$ -aryl, $C(O)O$ -(C_1 - C_6 alkyl), $C(O)O$ -(C_3 - C_7 cycloalkyl), $C(O)O$ -aryl, or R^{5d} and R^{5e} together with the N atom to which they are attached form a 5- or 6-membered heterocycle;

or R^5 is $-(CR^{13}R^{14})_n-Z$;

n is 1, 2, 3, 4, 5, 6, 7, or 8;

R^{13} and R^{14} are each, independently, H or C_1 - C_6 alkyl, C_2 - C_6 alkenyl, C_2 - C_6 alkynyl, OH, SH, aryl, or aralkyl, or R^{13} and R^{14} together form C_3 - C_7 cycloalkyl, oxo, or sulfido;

Z is naphthyl, anthracenyl, heteroaryl, cycloalkyl, heterocycloalkyl, biaryl, biheteroaryl, arylheteroaryl, or heteroarylaryl, each of which is optionally substituted by one or more R^{15} , wherein when Z is morpholino, Z is substituted by at least one R^{15} ;

or Z is phenyl optionally substituted by at least one R^{16} ;

R^{15} is halo, C_1 - C_{10} alkyl, C_1 - C_{10} haloalkyl, C_2 - C_{10} alkenyl, C_2 - C_{10} alkynyl, alkoxy, aryloxy, aralkoxy, aralkyl, OH, SH, guanidiny, thioalkoxy, haloalkoxy, $COOH$, $C(O)$ -(C_1 - C_6 alkyl), $C(O)$ -(C_3 - C_7 cycloalkyl), $C(O)$ -aryl, $C(O)O$ -(C_1 - C_6 alkyl), $C(O)O$ -(C_3 - C_7 cycloalkyl), $C(O)O$ -aryl, $CONR^{18a}R^{19a}$, NO_2 , CN , $(CH_2)_tNR^{18b}R^{19b}$, heteroaryl, heterocycloalkyl, aryl, C_3 - C_7 cycloalkyl, or $O(CR^{20}R^{21})_rX$;

R^{16} is halo, C_1 - C_{10} alkyl, C_1 - C_{10} haloalkyl, C_2 - C_{10} alkenyl, C_2 - C_{10} alkynyl, alkoxy, aryloxy, aralkoxy, aralkyl, OH, SH, guanidiny, thioalkoxy, haloalkoxy, $COOH$, $C(O)$ -(C_1 - C_6 alkyl), $C(O)$ -(C_3 - C_7 cycloalkyl), $C(O)$ -aryl, $C(O)O$ -(C_1 - C_6 alkyl), $C(O)O$ -(C_3 - C_7 cycloalkyl), $C(O)O$ -aryl, $CONR^{18c}R^{19c}$, NO_2 , CN , $(CH_2)_tNR^{18d}R^{19d}$, heteroaryl, heterocycloalkyl, aryl, C_3 - C_7 cycloalkyl, or $O(CR^{20}R^{21})_rX$;

R^{18a} and R^{19a} are each, independently, H or C_1 - C_6 alkyl, or R^{18a} and R^{19a} together with the N atom to which they are attached form a 5- or 6-membered heterocycle;

R^{18b} and R^{19b} are each, independently, H, C_1 - C_6 alkyl, aryl, $C(O)$ - C_1 - C_6 alkyl, $C(O)$ -(C_3 - C_7 cycloalkyl), $C(O)$ -aryl, $C(O)O$ -(C_1 - C_6 alkyl), $C(O)O$ -(C_3 - C_7 cycloalkyl), $C(O)O$ -aryl, or R^{18b} and R^{19b} together with the N atom to which they are attached form a 5- or 6-membered heterocycle;

R^{18c} and R^{19c} are each, independently, H or C₁-C₆ alkyl, or R^{18c} and R^{19c} together with the N atom to which they are attached form a heterocycle;

R^{18d} and R^{19d} are each, independently, H, C₁-C₆ alkyl, aryl, C(O)-C₁-C₆ alkyl, C(O)-(C₃-C₇ cycloalkyl), C(O)-aryl, C(O)O-(C₁-C₆ alkyl), C(O)O-(C₃-C₇ cycloalkyl), C(O)O-aryl, or R^{18d} and R^{19d} together with the N atom to which they are attached form a 5- or 6-membered heterocycle;

R^{20} and R^{21} are each, independently, H or C₁-C₆ alkyl;

r is 0, 1, 2, 3, 4, 5, or 6;

t is 0, 1, or 2;

X is X¹ or X²;

X¹ is NR²²R²³, C₃-C₇ cycloalkyl, aryl, heteroaryl, or heterocycloalkyl, wherein X¹ is optionally substituted by one or more halo, C₁-C₆ alkyl, C₃-C₇ cycloalkyl, C₁-C₆ haloalkyl, aryl, heteroaryl, heterocycloalkyl, CN, NO₂, OH, COOH, C(O)-C₁-C₆ alkyl, C(O)-(C₃-C₇ cycloalkyl), C(O)-aryl, C(O)O-(C₁-C₆ alkyl), C(O)O-(C₃-C₇ cycloalkyl), C(O)O-aryl, NH₂, NH(C₁-C₄ alkyl), N(C₁-C₄ alkyl)₂, NHC(O)O-(C₁-C₆ alkyl), NHC(O)O-aryl or (CH₂)_sOH;

R^{22} and R^{23} are each, independently, H, C₁-C₆ alkyl, aryl, heteroaryl, heterocycloalkyl, cycloalkyl, C(O)-C₁-C₆ alkyl, C(O)-(C₃-C₇ cycloalkyl), C(O)-aryl, C(O)O-(C₁-C₆ alkyl), C(O)O-(C₃-C₇ cycloalkyl), C(O)O-aryl, or R^{22} and R^{23} together with the N atom to which they are attached form a 5- or 6-membered heterocycle;

s is 0, 1, 2, or 3;

X² is OH or OSO₂R²⁴;

R²⁴ is H, C₁-C₆ alkyl, aryl, or NH₂;

or R⁵ and R² together with the N atom to which they are attached form heterocycloalkyl optionally substituted by halo, C₁-C₄ alkyl, OH, SH, alkoxy or aryloxy; and

R⁶ and R⁷ are each, independently, H, halo, C₁-C₆ alkyl, C₁-C₆ haloalkyl, C₂-C₆ alkenyl, C₂-C₆ alkynyl, alkoxy, aryloxy, or aralkoxy, or R⁶ and R⁷ together with the atoms to which they are attached form a fused cycloalkyl, heterocycloalkyl, aryl, or heteroaryl group.

[0011] In some embodiments, when R¹ is COOR^{1A}; R⁵ is not phenyl substituted by methyl;

[0012] In some embodiments, when R⁵ is cycloalkyl or heterocycloalkyl, R⁵ is not piperidinyl, tetrahydrothiophenyl, pyrazol-3-one, or oxo or dioxo derivatives thereof,

- [0013] In some embodiments, when R^4 is OH, R^6 and R^7 are not both C_4 alkyl;
- [0014] In some embodiments, when R^5 is $-(CR^{13}R^{14})_n-Z$ and Z is phenyl substituted by at least one halo, n is greater than 1;
- [0015] In some embodiments, when R^5 is $-(CR^{13}R^{14})_n-Z$ and Z is phenyl substituted by one C_1 - C_4 alkoxy, said C_1 - C_4 alkoxy is located at the 2- or 3- position of said phenyl;
- [0016] In some embodiments, when R^5 is $-(CR^{13}R^{14})_n-Z$ and Z is phenyl substituted by two C_1 - C_4 alkoxy, said two C_1 - C_4 alkoxy are located at the 2- and 4-, 2- and 5-, or 2- and 6-positions of said phenyl; and
- [0017] In some embodiments, when R^5 is $-(CR^{13}R^{14})_n-Z$ and Z is unsubstituted phenyl, R^4 is other than H and C_1 - C_6 alkyl or R^{13} is other than H.
- [0018] In further embodiments, R^1 is H.
- [0019] In further embodiments, R^2 and R^3 are each H.
- [0020] In further embodiments, A is CR^4 .
- [0021] In further embodiments, R^4 is H.
- [0022] In further embodiments, R^4 is C_1 - C_4 alkyl such as methyl.
- [0023] In further embodiments, R^4 is OH.
- [0024] In further embodiments, R^4 is or $O(CR^{4a}R^{4b})_aNR^{4c}R^{4d}$.
- [0025] In further embodiments, R^6 and R^7 are each C_1 - C_6 alkyl.
- [0026] In further embodiments, at least one of R^6 and R^7 is C_1 - C_6 alkyl such as methyl.
- [0027] In further embodiments, both R^6 and R^7 are methyl.
- [0028] In further embodiments, R^5 is $-(CR^{13}R^{14})_n-Z$.
- [0029] In further embodiments, Z is phenyl substituted by at least one $O(CR^{20}R^{21})_rX$.
- [0030] In further embodiments, n is 1 or 2.
- [0031] In further embodiments, n is 2.
- [0032] In further embodiments, R^5 is $-(CR^{13}R^{14})_n-Z$ and n is 1 or 2.
- [0033] In further embodiments, R^5 is phenyl substituted by at least one $O(CR^8R^9)_pY$.
- [0034] In further embodiments, R^5 is heteroaryl substituted by at least one $O(CR^8R^9)_pY$.
- [0035] In further embodiments, R^5 is substituted or unsubstituted cycloalkyl or heterocycloalkyl.

[0036] In further embodiments, R^{16} is C_2 - C_{10} alkyl, C_2 - C_{10} alkenyl, C_2 - C_{10} alkynyl, C_2 - C_{10} alkoxy, aryloxy, aralkoxy, aralkyl, OH, SH, thioalkoxy, haloalkyl, haloalkoxy, COOH, $C(O)$ -(C_1 - C_6 alkyl), $C(O)$ -(C_3 - C_7 cycloalkyl), $C(O)$ -aryl, $C(O)O$ -(C_1 - C_6 alkyl), $C(O)O$ -(C_3 - C_7 cycloalkyl), $C(O)O$ -aryl, $CONR^{18a}R^{19a}$, NO_2 , CN, $(CH_2)_tNR^{18b}R^{19b}$, heteroaryl, heterocycloalkyl, aryl, C_3 - C_7 cycloalkyl, or $O(CR^{20}R^{21})_rX$.

[0037] In further embodiments, R^{16} is C_2 - C_{10} alkenyl, C_2 - C_{10} alkynyl, C_2 - C_{10} alkoxy, aryloxy, aralkoxy, aralkyl, OH, SH, thioalkoxy, haloalkyl, haloalkoxy, COOH, $C(O)$ -(C_1 - C_6 alkyl), $C(O)$ -(C_3 - C_7 cycloalkyl), $C(O)$ -aryl, $C(O)O$ -(C_1 - C_6 alkyl), $C(O)O$ -(C_3 - C_7 cycloalkyl), $C(O)O$ -aryl, $CONR^{18a}R^{19a}$, NO_2 , CN, $(CH_2)_tNR^{18b}R^{19b}$, heteroaryl, heterocycloalkyl, aryl, C_3 - C_7 cycloalkyl, or $O(CR^{20}R^{21})_rX$.

[0038] In further embodiments, R^5 is $-(CR^{13}R^{14})_n-Z$ and Z is substituted or unsubstituted pyridinyl, pyrimidinyl, furanyl, thienyl, quinolinyl, isoquinolinyl, indolyl, benzo[1,3]dioxolyl, or benzoimidazolyl.

[0039] In further embodiments, R^5 is $-(CR^{13}R^{14})_n-Z$ and Z is furanyl, 2-methylfuranyl, 2,3-dimethylfuranyl, 2-phenylfuranyl, or benzofuranyl.

[0040] In further embodiments, R^5 is $-(CR^{13}R^{14})_n-Z$ and at least one of R^{13} and R^{14} is methyl or OH.

[0041] In further embodiments, R^5 is $-(CR^{13}R^{14})_n-Z$ and Z is phenyl substituted by at least one $O(CR^{20}R^{21})_rX$.

[0042] In further embodiments, R^5 is $-(CR^{13}R^{14})_n-Z$ and Z is substituted or unsubstituted biaryl, biheteroaryl, arylheteroaryl, or heteroarylaryl.

[0043] In further embodiments, the present invention provides compound of Formula I wherein:

R^5 is $N(R^{5a})-Q$;

or R^5 is phenyl, naphthyl, or heteroaryl, wherein said naphthyl or heteroaryl is substituted by one or more OH or $O(CR^8R^9)_pY$ and wherein said phenyl is substituted by one or more $O(CR^8R^9)_pY$;

or R^5 is cycloalkyl or heterocycloalkyl, wherein said cycloalkyl or heterocycloalkyl is optionally substituted by one or more halo, C_1 - C_{10} alkyl, C_1 - C_{10} haloalkyl, C_2 - C_{10} alkenyl, C_2 - C_{10} alkynyl, alkoxy, aryloxy, aralkoxy, aralkyl, OH, SH, thioalkoxy, haloalkoxy, COOH, $C(O)$ -(C_1 - C_6 alkyl), $C(O)$ -(C_3 - C_7 cycloalkyl), $C(O)$ -aryl, $C(O)O$ -(C_1 - C_6 alkyl), $C(O)O$ -(C_3 - C_7 cycloalkyl), $C(O)O$ -aryl, $CONR^{5b}R^{5c}$, NO_2 , CN, $NR^{5d}R^{5e}$, or $O(CR^8R^9)_pY$;

or R^5 is $-(CR^{13}R^{14})_n-Z$.

[0044] In further embodiments, the present invention provides compound of Formula I wherein:

R^5 is $N(R^{5a})-Q$;

or R^5 is phenyl, naphthyl, or heteroaryl, wherein said naphthyl or heteroaryl is substituted by one or more OH or $O(CR^8R^9)_pY$ and wherein said phenyl is substituted by one or more $O(CR^8R^9)_pY$;

or R^5 is $-(CR^{13}R^{14})_n-Z$.

[0045] In further embodiments, the present invention provides compound of Formula I wherein:

R^1 is H;

R^2 and R^3 are each, independently, H or C_1-C_6 alkyl;

A is CR^4 ;

R^4 is H, C_1-C_4 alkyl, C_1-C_4 haloalkyl, C_3-C_7 cycloalkyl, C_1-C_4 alkoxy, aryloxy, aralkoxy, hydroxy, or $O(CH_2)_aNR^{4c}R^{4d}$;

R^{4c} and R^{4d} are each, independently, H, C_1-C_4 alkyl, or R^{4c} and R^{4d} together with the N atom to which they are attached form a 5- or 6-membered heterocycle;

a is 1 or 2;

R^5 is $NH-Q$;

Q is aryl, heteroaryl, cycloalkyl, or heterocycloalkyl, wherein Q is optionally substituted by one or more C_1-C_{10} alkyl, C_2-C_{10} alkenyl, C_2-C_{10} alkynyl, alkoxy, aryloxy, aralkoxy, aralkyl, OH, SH, thioalkoxy, halo, C_1-C_{10} haloalkyl, haloalkoxy, COOH, $C(O)-(C_1-C_6 \text{ alkyl})$, $C(O)-(C_3-C_7 \text{ cycloalkyl})$, $C(O)\text{-aryl}$, $C(O)O-(C_1-C_6 \text{ alkyl})$, $C(O)O-(C_3-C_7 \text{ cycloalkyl})$, $C(O)O\text{-aryl}$, $C(O)NR^{Q1}R^{Q2}$, NO_2 , CN, or $NR^{Q3}R^{Q4}$;

R^{Q1} and R^{Q2} are each, independently, H, C_1-C_6 alkyl, C_3-C_6 cycloalkyl, aryl, or R^{Q1} and R^{Q2} together with the N atom to which they are attached form a 5- or 6-membered heterocycle;

R^{Q3} and R^{Q4} are each, independently, H, C_1-C_6 alkyl, aryl, $C(O)-C_1-C_6$ alkyl, $C(O)-(C_3-C_7 \text{ cycloalkyl})$, $C(O)\text{-aryl}$, $C(O)O-(C_1-C_6 \text{ alkyl})$, $C(O)O-(C_3-C_7 \text{ cycloalkyl})$, $C(O)O\text{-aryl}$, or R^{Q1} and R^{Q2} together with the N atom to which they are attached form a 5- or 6-membered heterocycle;

or R^5 is phenyl, naphthyl, or heteroaryl, wherein said naphthyl or heteroaryl is substituted by one or more OH or $O(CR^8R^9)_pY$ and wherein said phenyl is substituted by one or more $O(CR^8R^9)_pY$;

R^8 and R^9 are each, independently, H or C_1-C_4 alkyl;

p is 1, 2, or 3;

Y is Y¹ or Y²;

Y¹ is NR¹⁰R¹¹;

R¹⁰ and R¹¹ are each, independently, H, C₁-C₆ alkyl, C(O)-(C₁-C₆ alkyl), C(O)-(C₃-C₇ cycloalkyl), C(O)-aryl, C(O)O-(C₁-C₆ alkyl), C(O)O-(C₃-C₇ cycloalkyl), C(O)O-aryl, aryl, heteroaryl, cycloalkyl, or heterocycloalkyl, or R¹⁰ and R¹¹ together with the N atom to which they are attached form a 5- or 6- membered heterocycle;

Y² is OR^{12a} or OSO₂R^{12b};

R^{12a} is H, C₁-C₁₀ alkyl, C₁-C₁₀ alkenyl, C₁-C₁₀ alkynyl, aryl, heteroaryl, C₃-C₇ cycloalkyl, or heterocycloalkyl;

R^{12b} is H, C₁-C₆ alkyl, aryl, or NH₂;

or R⁵ is cycloalkyl optionally substituted by one or more halo, C₁-C₁₀ alkyl, C₁-C₁₀ haloalkyl, C₂-C₁₀ alkenyl, C₂-C₁₀ alkynyl, alkoxy, aryloxy, aralkoxy, aralkyl, OH, SH, thioalkoxy, haloalkoxy, COOH, C(O)-(C₁-C₆ alkyl), C(O)-(C₃-C₇ cycloalkyl), C(O)-aryl, C(O)O-(C₁-C₆ alkyl), C(O)O-(C₃-C₇ cycloalkyl), C(O)O-aryl, CONR^{5b}R^{5c}, NO₂, CN, NR^{5d}R^{5e}, or O(CR⁸R⁹)_pY;

R^{5b} and R^{5c} are each, independently, H, C₁-C₆ alkyl, C₃-C₆ cycloalkyl, aryl, or R^{5b} and R^{5c} together with the N atom to which they are attached form a 5- or 6-membered heterocycle;

R^{5d} and R^{5e} are each, independently, H, C₁-C₆ alkyl, aryl, C(O)-C₁-C₆ alkyl, C(O)-(C₃-C₇ cycloalkyl), C(O)-aryl, C(O)O-(C₁-C₆ alkyl), C(O)O-(C₃-C₇ cycloalkyl), C(O)O-aryl, or R^{5d} and R^{5e} together with the N atom to which they are attached form a 5- or 6-membered heterocycle;

or R⁵ is -(CR¹³R¹⁴)_n-Z;

n is 1, 2, or 3;

R¹³ and R¹⁴ are each, independently, H or C₁-C₄ alkyl;

Z is naphthyl, anthracenyl, or heteroaryl, wherein said naphthyl, anthracenyl, or heteroaryl, is optionally substituted by one or more R¹⁵;

or Z is phenyl optionally substituted by at least one R¹⁶;

R¹⁵ is halo, C₁-C₁₀ alkyl, C₁-C₁₀ haloalkyl, C₂-C₁₀ alkenyl, C₂-C₁₀ alkynyl, alkoxy, aryloxy, aralkoxy, aralkyl, OH, SH, thioalkoxy, haloalkoxy, COOH, C(O)-(C₁-C₆ alkyl), C(O)-(C₃-C₇ cycloalkyl), C(O)-aryl, C(O)O-(C₁-C₆ alkyl), C(O)O-

(C₃-C₇ cycloalkyl), C(O)O-aryl, CONR^{18a}R^{19a}, NO₂, CN, (CH₂)_tNR^{18b}R^{19b}, heteroaryl, heterocycloalkyl, aryl, C₃-C₇ cycloalkyl, or O(CR²⁰R²¹)_rX;

R¹⁶ is C₂-C₁₀ alkenyl, C₂-C₁₀ alkynyl, C₂-C₁₀ alkoxy, aryloxy, aralkoxy, aralkyl, OH, SH, thioalkoxy, haloalkyl, haloalkoxy, COOH, C(O)-(C₁-C₆ alkyl), C(O)-(C₃-C₇ cycloalkyl), C(O)-aryl, C(O)O-(C₁-C₆ alkyl), C(O)O-(C₃-C₇ cycloalkyl), C(O)O-aryl, CONR^{18a}R^{19a}, NO₂, CN, (CH₂)_tNR^{18b}R^{19b}, heteroaryl, heterocycloalkyl, aryl, C₃-C₇ cycloalkyl, or O(CR²⁰R²¹)_rX;

R^{18a} and R^{19a} are each, independently, H or C₁-C₆ alkyl, or R^{18a} and R^{19a} together with the N atom to which they are attached form a 5- or 6-membered heterocycle;

R^{18b} and R^{19b} are each, independently, H, C₁-C₆ alkyl, aryl, C(O)-C₁-C₆ alkyl, C(O)-(C₃-C₇ cycloalkyl), C(O)-aryl, C(O)O-(C₁-C₆ alkyl), C(O)O-(C₃-C₇ cycloalkyl), C(O)O-aryl, or R^{18b} and R^{19b} together with the N atom to which they are attached form a 5- or 6-membered heterocycle;

R²⁰ and R²¹ are each, independently, H or C₁-C₄ alkyl;

r is 0, 1, or 2;

t is 0, 1, or 2;

X is X¹ or X²;

X¹ is NR²²R²³, C₃-C₇ cycloalkyl, aryl, heteroaryl, or heterocycloalkyl, wherein X¹ is optionally substituted by one or more halo, C₁-C₆ alkyl, C₃-C₇ cycloalkyl, C₁-C₆ haloalkyl, aryl, heteroaryl, heterocycloalkyl, CN, NO₂, OH, COOH, C(O)-C₁-C₆ alkyl, C(O)-(C₃-C₇ cycloalkyl), C(O)-aryl, C(O)O-(C₁-C₆ alkyl), C(O)O-(C₃-C₇ cycloalkyl), C(O)O-aryl, NH₂, NH(C₁-C₄ alkyl), N(C₁-C₄ alkyl)₂, NHC(O)O-(C₁-C₆ alkyl), NHC(O)O-aryl or (CH₂)_sOH;

R²² and R²³ are each, independently, H, C₁-C₆ alkyl, aryl, heteroaryl, heterocycloalkyl, cycloalkyl, C(O)-C₁-C₆ alkyl, C(O)-(C₃-C₇ cycloalkyl), C(O)-aryl, C(O)O-(C₁-C₆ alkyl), C(O)O-(C₃-C₇ cycloalkyl), C(O)O-aryl, or R²² and R²³ together with the N atom to which they are attached form a 5- or 6-membered heterocycle;

s is 0, 1, 2, or 3;

X² is OH, NH₂, or OSO₂R²⁴;

R²⁴ is H, C₁-C₆ alkyl, aryl, or NH₂; and

R⁶ and R⁷ are each, independently, H or C₁-C₆ alkyl;

with the proviso that when R⁵ is -(CR¹³R¹⁴)_n-Z and Z is unsubstituted phenyl, R⁴ is other than H and C₁-C₆ alkyl.

[0046] In further embodiments, the present invention provides compound of Formula I wherein:

R^1 is H;
 R^2 and R^3 are each H;
 A is CH; and
 R^6 and R^7 are each methyl.

[0047] In further embodiments, the present invention provides compound of Formula I wherein:

R^1 is H;
 R^2 and R^3 are each H;
 A is CH;
 R^5 is $-(CR^{13}R^{14})_n-Z$;
 n is 1 or 2; and
 R^6 and R^7 are each methyl.

[0048] In further embodiments, the present invention provides compound of Formula I wherein:

A is CR^4 ;
 R^4 is hydroxy, alkoxy, cyloalkyloxy, aryloxy, heteroaryloxy, heterocycloalkyloxy, aralkoxy, cycloalkylalkyloxy, heteroarylalkyloxy, heterocycloalkylalkyloxy, or $O(CR^{4a}R^{4b})_aNR^{4c}R^{4d}$;
 R^{4a} and R^{4b} are each, independently, H or C_1 - C_4 alkyl;
 R^{4c} and R^{4d} are each, independently, H, C_1 - C_4 alkyl, C_3 - C_7 cycloalkyl, C_1 - C_4 haloalkyl, aryl, $C(O)$ -(C_1 - C_6 alkyl), $C(O)$ -aryl, $C(O)$ -(C_3 - C_7 cycloalkyl), $C(O)O$ -(C_1 - C_6 alkyl), $C(O)O$ -aryl, or $C(O)O$ -(C_3 - C_7 cycloalkyl), or R^{4c} and R^{4d} together with the N atom to which they are attached form a 5- or 6-membered heterocycle; and
 a is 1, 2, 3, 4, 5, or 6.

[0049] In further embodiments, the present invention provides compound of Formula I wherein:

A is CR^4 ;
 R^4 is hydroxy, alkoxy, cyloalkyloxy, aryloxy, aralkoxy, heterocycloalkyloxy, heterocycloalkylalkyloxy, or $O(CR^{4a}R^{4b})_aNR^{4c}R^{4d}$;
 R^{4a} and R^{4b} are each, independently, H or C_1 - C_4 alkyl;

R^{4c} and R^{4d} are each, independently, H, C_1 - C_4 alkyl, C_3 - C_7 cycloalkyl, C_1 - C_4 haloalkyl, aryl, $C(O)$ -(C_1 - C_6 alkyl), $C(O)$ -aryl, $C(O)$ -(C_3 - C_7 cycloalkyl), $C(O)O$ -(C_1 - C_6 alkyl), $C(O)O$ -aryl, or $C(O)O$ -(C_3 - C_7 cycloalkyl), or R^{4c} and R^{4d} together with the N atom to which they are attached form a 5- or 6-membered heterocycle;

a is 1, 2, 3, 4, 5, or 6; and

R^6 and R^7 are each, independently, H, halo, C_1 - C_3 alkyl, or C_1 - C_6 haloalkyl.

[0050] In further embodiments, the present invention provides compound of Formula I wherein:

R^1 , R^2 , and R^3 are each H;

A is CR^4 ;

R^4 is hydroxy, alkoxy, cyloalkyloxy, aryloxy, aralkoxy, heterocycloalkyloxy, heterocycloalkylalkyloxy, or $O(CR^{4a}R^{4b})_aNR^{4c}R^{4d}$;

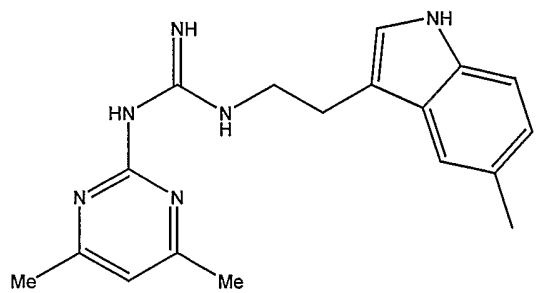
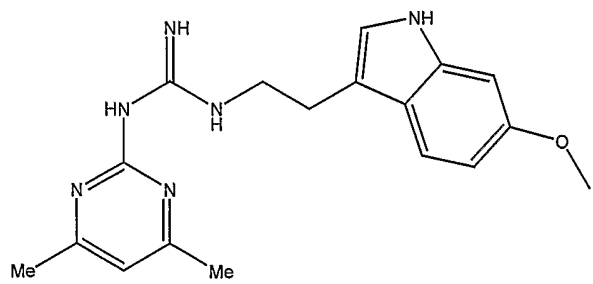
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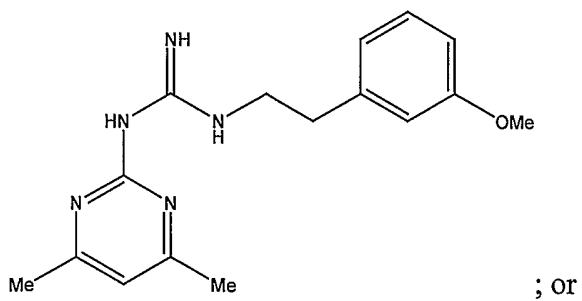
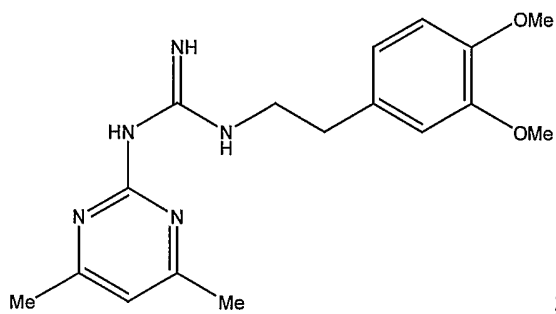
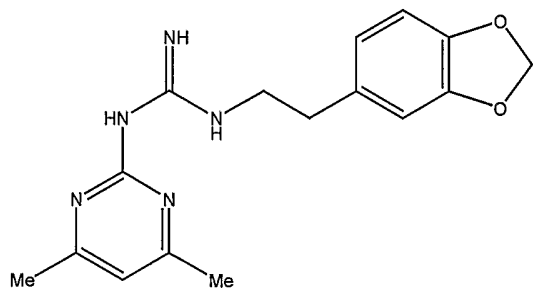
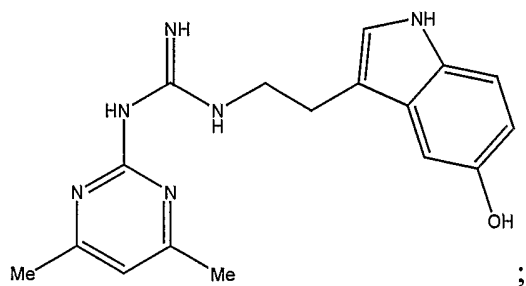
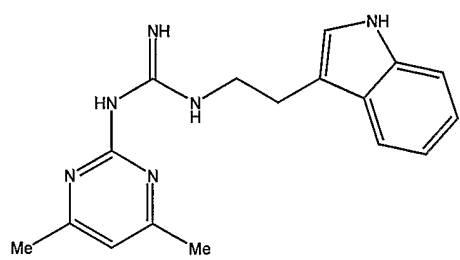
R^{4c} and R^{4d} are each, independently, H, C_1 - C_4 alkyl, C_3 - C_7 cycloalkyl, C_1 - C_4 haloalkyl, aryl, $C(O)$ -(C_1 - C_6 alkyl), $C(O)$ -aryl, $C(O)$ -(C_3 - C_7 cycloalkyl), $C(O)O$ -(C_1 - C_6 alkyl), $C(O)O$ -aryl, or $C(O)O$ -(C_3 - C_7 cycloalkyl), or R^{4c} and R^{4d} together with the N atom to which they are attached form a 5- or 6-membered heterocycle;

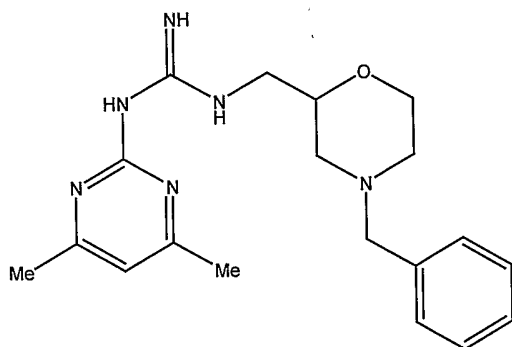
a is 1, 2, 3, 4, 5, or 6; and

R^6 and R^7 are each, independently, H, halo, C_1 - C_3 alkyl, or C_1 - C_6 haloalkyl.

[0051] In further embodiments, the present invention provides compound of Formula I having the Formula:

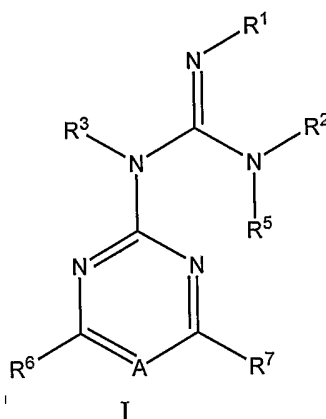






[0052]

The present invention further provides compounds of Formula I:



or pharmaceutically acceptable salt forms thereof, wherein:

R^1 is H or COOR^{1a} ;

R^{1a} is H or $\text{C}_1\text{-C}_{10}$ alkyl, aryl, cycloalkyl, or aralkyl;

R^2 and R^3 are each, independently, H, $\text{C}_1\text{-C}_{10}$ alkyl, or $\text{C}_3\text{-C}_7$ cycloalkyl;

A is CR^4 ;

R^4 is OH, alkoxy, aryloxy, aralkoxy, cycloalkyloxy, cycloalkylalkyloxy, heterocycloalkyloxy, heterocycloalkylalkyloxy, heteroaryloxy, heteroarylalkyloxy, or $\text{O}(\text{CR}^{4a}\text{R}^{4b})_a\text{NR}^{4c}\text{R}^{4d}$;

R^{4a} and R^{4b} are each, independently, H or $\text{C}_1\text{-C}_4$ alkyl;

R^{4c} and R^{4d} are each, independently, H, $\text{C}_1\text{-C}_4$ alkyl, $\text{C}_3\text{-C}_7$ cycloalkyl, $\text{C}_1\text{-C}_4$ haloalkyl, aryl, $\text{C}(\text{O})\text{-(C}_1\text{-C}_6\text{ alkyl)}$, $\text{C}(\text{O})\text{-aryl}$, $\text{C}(\text{O})\text{-(C}_3\text{-C}_7\text{ cycloalkyl)}$, $\text{C}(\text{O})\text{O-(C}_1\text{-C}_6\text{ alkyl)}$, $\text{C}(\text{O})\text{O-aryl}$, or $\text{C}(\text{O})\text{O-(C}_3\text{-C}_7\text{ cycloalkyl)}$, or R^{4c} and R^{4d} together with the N atom to which they are attached form a 5- or 6-membered heterocycle;

a is 1, 2, 3, 4, 5, or 6;

R^5 is $\text{N(R}^{5a})\text{-Q}$;

R^{5a} is H or $\text{C}_1\text{-C}_6$ alkyl;

Q is aryl, heteroaryl, cycloalkyl, or heterocycloalkyl, wherein Q is optionally substituted by one or more C₁-C₁₀ alkyl, C₂-C₁₀ alkenyl, C₂-C₁₀ alkynyl, alkoxy, aryloxy, aralkoxy, aralkyl, OH, SH, thioalkoxy, halo, C₁-C₁₀ haloalkyl, haloalkoxy, COOH, C(O)-(C₁-C₆ alkyl), C(O)-(C₃-C₇ cycloalkyl), C(O)-aryl, C(O)O-(C₁-C₆ alkyl), C(O)O-(C₃-C₇ cycloalkyl), C(O)O-aryl, C(O)NR^{Q1}R^{Q2}, NO₂, CN, or NR^{Q3}R^{Q4};

R^{Q1} and R^{Q2} are each, independently, H, C₁-C₆ alkyl, C₃-C₆ cycloalkyl, aryl, or R^{Q1} and R^{Q2} together with the N atom to which they are attached form a 5- or 6-membered heterocycle;

R^{Q3} and R^{Q4} are each, independently, H, C₁-C₆ alkyl, aryl, C(O)-C₁-C₆ alkyl, C(O)-(C₃-C₇ cycloalkyl), C(O)-aryl, C(O)O-(C₁-C₆ alkyl), C(O)O-(C₃-C₇ cycloalkyl), C(O)O-aryl, or R^{Q1} and R^{Q2} together with the N atom to which they are attached form a 5- or 6-membered heterocycle;

or R⁵ is aryl or heteroaryl, wherein said aryl or heteroaryl is optionally substituted by one or more OH or O(CR⁸R⁹)_pY;

R⁸ and R⁹ are each, independently, H or C₁-C₄ alkyl;

p is 1, 2, 3, 4, 5, or 6;

Y is Y¹ or Y²;

Y¹ is NR¹⁰R¹¹, C₃-C₇ cycloalkyl, heterocycloalkyl, or heteroaryl, wherein Y¹ is optionally substituted by one or more halo, C₁-C₆ alkyl, C₁-C₆ haloalkyl, C₂-C₆ alkenyl, C₂-C₆ alkynyl, C₃-C₇ cycloalkyl, aryl, heteroaryl, heterocycloalkyl, OH, SH, CN, NO₂, COOH, C(O)-(C₁-C₆ alkyl), C(O)-(C₃-C₇ cycloalkyl), C(O)-aryl, C(O)O-(C₁-C₆ alkyl), C(O)O-(C₃-C₇ cycloalkyl), C(O)O-aryl, NH₂, NH(C₁-C₄ alkyl), N(C₁-C₄ alkyl)₂, NHC(O)O-(C₁-C₆ alkyl), NHC(O)O-aryl or (CH₂)_qOH;

R¹⁰ and R¹¹ are each, independently, H, (C₁-C₆)alkyl, C(O)-(C₁-C₆ alkyl), C(O)-(C₃-C₇ cycloalkyl), C(O)-aryl, C(O)O-(C₁-C₆ alkyl), C(O)O-(C₃-C₇ cycloalkyl), C(O)O-aryl, aryl, heteroaryl, cycloalkyl, or heterocycloalkyl, or R¹⁰ and R¹¹ together with the N atom to which they are attached form a 5- or 6- membered heterocycle;

q is 0, 1, 2, or 3;

Y² is OR^{12a} or OSO₂R^{12b};

R^{12a} is H, C₁-C₁₀ alkyl, C₁-C₁₀ alkenyl, C₁-C₁₀ alkynyl, aryl, heteroaryl, C₃-C₇ cycloalkyl, or heterocycloalkyl;

R^{12b} is H, C₁-C₆ alkyl, aryl, or NH₂;

or R^5 is cycloalkyl or heterocycloalkyl, wherein said cycloalkyl or heterocycloalkyl is optionally substituted by one or more halo, C_1 - C_{10} alkyl, C_1 - C_{10} haloalkyl, C_2 - C_{10} alkenyl, C_2 - C_{10} alkynyl, aryl, heteroaryl, cycloalkyl, heterocycloalkyl, alkoxy, aryloxy, aralkoxy, aralkyl, OH, SH, thioalkoxy, haloalkoxy, COOH, $C(O)$ -(C_1 - C_6 alkyl), $C(O)$ -(C_3 - C_7 cycloalkyl), $C(O)$ -aryl, $C(O)O$ -(C_1 - C_6 alkyl), $C(O)O$ -(C_3 - C_7 cycloalkyl), $C(O)O$ -aryl, $CONR^{5b}R^{5c}$, NO_2 , CN, $NR^{5d}R^{5e}$, or $O(CR^8R^9)_pY$;

R^{5b} and R^{5c} are each, independently, H, C_1 - C_6 alkyl, C_3 - C_6 cycloalkyl, aryl, or R^{5b} and R^{5c} together with the N atom to which they are attached form a 5- or 6-membered heterocycle;

R^{5d} and R^{5e} are each, independently, H, C_1 - C_6 alkyl, aryl, $C(O)$ - C_1 - C_6 alkyl, $C(O)$ -(C_3 - C_7 cycloalkyl), $C(O)$ -aryl, $C(O)O$ -(C_1 - C_6 alkyl), $C(O)O$ -(C_3 - C_7 cycloalkyl), $C(O)O$ -aryl, or R^{5d} and R^{5e} together with the N atom to which they are attached form a 5- or 6-membered heterocycle;

or R^5 is $-(CR^{13}R^{14})_n-Z$;

n is 1, 2, 3, 4, 5, 6, 7, or 8;

R^{13} and R^{14} are each, independently, H or C_1 - C_6 alkyl, C_2 - C_6 alkenyl, C_2 - C_6 alkynyl, OH, SH, aryl, or aralkyl, or R^{13} and R^{14} together form C_3 - C_7 cycloalkyl, oxo, or sulfido;

Z is aryl, heteroaryl, cycloalkyl, heterocycloalkyl, biaryl, biheteroaryl, arylheteroaryl, or heteroarylaryl, each of which is optionally substituted by one or more R^{15} ;

R^{15} is halo, C_1 - C_{10} alkyl, C_1 - C_{10} haloalkyl, C_2 - C_{10} alkenyl, C_2 - C_{10} alkynyl, alkoxy, aryloxy, aralkoxy, aralkyl, OH, SH, guanidinyl, thioalkoxy, haloalkoxy, COOH, $C(O)$ -(C_1 - C_6 alkyl), $C(O)$ -(C_3 - C_7 cycloalkyl), $C(O)$ -aryl, $C(O)O$ -(C_1 - C_6 alkyl), $C(O)O$ -(C_3 - C_7 cycloalkyl), $C(O)O$ -aryl, $CONR^{18a}R^{19a}$, NO_2 , CN, $(CH_2)_tNR^{18b}R^{19b}$, heteroaryl, heterocycloalkyl, aryl, C_3 - C_7 cycloalkyl, or $O(CR^{20}R^{21})_rX$;

R^{18a} and R^{19a} are each, independently, H or C_1 - C_6 alkyl, or R^{18a} and R^{19a} together with the N atom to which they are attached form a 5- or 6-membered heterocycle;

R^{18b} and R^{19b} are each, independently, H, C_1 - C_6 alkyl, aryl, $C(O)$ - C_1 - C_6 alkyl, $C(O)$ -(C_3 - C_7 cycloalkyl), $C(O)$ -aryl, $C(O)O$ -(C_1 - C_6 alkyl), $C(O)O$ -(C_3 - C_7 cycloalkyl), $C(O)O$ -aryl, or R^{18b} and R^{19b} together with the N atom to which they are attached form a 5- or 6-membered heterocycle;

R^{18c} and R^{19c} are each, independently, H or C₁-C₆ alkyl, or R^{18c} and R^{19c} together with the N atom to which they are attached form a heterocycle;

R^{18d} and R^{19d} are each, independently, H, C₁-C₆ alkyl, aryl, C(O)-C₁-C₆ alkyl, C(O)-(C₃-C₇ cycloalkyl), C(O)-aryl, C(O)O-(C₁-C₆ alkyl), C(O)O-(C₃-C₇ cycloalkyl), C(O)O-aryl, or R^{18d} and R^{19d} together with the N atom to which they are attached form a 5- or 6-membered heterocycle;

R^{20} and R^{21} are each, independently, H or C₁-C₆ alkyl;

r is 0, 1, 2, 3, 4, 5, or 6;

t is 0, 1, or 2;

X is X^1 or X^2 ;

X^1 is $NR^{22}R^{23}$, C₃-C₇ cycloalkyl, aryl, heteroaryl, or heterocycloalkyl, wherein X^1 is optionally substituted by one or more halo, C₁-C₆ alkyl, C₃-C₇ cycloalkyl, C₁-C₆ haloalkyl, aryl, heteroaryl, heterocycloalkyl, CN, NO₂, OH, COOH, C(O)-C₁-C₆ alkyl, C(O)-(C₃-C₇ cycloalkyl), C(O)-aryl, C(O)O-(C₁-C₆ alkyl), C(O)O-(C₃-C₇ cycloalkyl), C(O)O-aryl, NH₂, NH(C₁-C₄ alkyl), N(C₁-C₄ alkyl)₂, NHC(O)O-(C₁-C₆ alkyl), NHC(O)O-aryl or (CH₂)_sOH;

R^{22} and R^{23} are each, independently, H, C₁-C₆ alkyl, aryl, heteroaryl, heterocycloalkyl, cycloalkyl, C(O)-C₁-C₆ alkyl, C(O)-(C₃-C₇ cycloalkyl), C(O)-aryl, C(O)O-(C₁-C₆ alkyl), C(O)O-(C₃-C₇ cycloalkyl), C(O)O-aryl, or R^{22} and R^{23} together with the N atom to which they are attached form a 5- or 6-membered heterocycle;

s is 0, 1, 2, or 3;

X^2 is OH or OSO₂R²⁴;

R^{24} is H, C₁-C₆ alkyl, aryl, or NH₂;

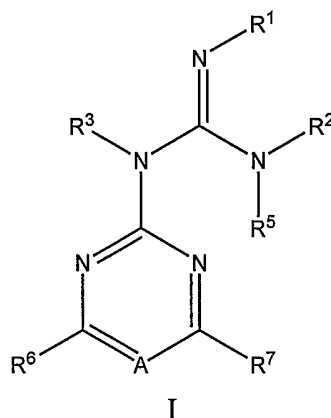
or R^5 and R^2 together with the N atom to which they are attached form heterocycloalkyl optionally substituted by halo, C₁-C₄ alkyl, OH, SH, alkoxy or aryloxy; and

R^6 and R^7 are each, independently, H, halo, C₁-C₆ alkyl, C₁-C₆ haloalkyl, C₂-C₆ alkenyl, C₂-C₆ alkynyl, alkoxy, aryloxy, or aralkoxy, or R^6 and R^7 together with the atoms to which they are attached form a fused cycloalkyl, heterocycloalkyl, aryl, or heteroaryl group.

[0053] In some embodiments, R^4 is OH, C₁-C₆ alkoxy, or O(CR^{4a}R^{4b})_aNR^{4c}R^{4d}.

[0054] In further embodiments, R^4 is OH or C₁-C₆ alkoxy.

[0055] The present invention further provides methods of modulating activity of an infectious agent comprising contacting the infectious agent with a compound of Formula I:



or pharmaceutically acceptable salt form thereof, wherein:

R^1 is H or COOR^{1a} ;

R^{1a} is H or $\text{C}_1\text{-C}_{10}$ alkyl, aryl, cycloalkyl, or aralkyl;

R^2 and R^3 are each, independently, H, $\text{C}_1\text{-C}_{10}$ alkyl, or $\text{C}_3\text{-C}_7$ cycloalkyl;

A is N or CR^4 ;

R^4 is H, halo, $\text{C}_1\text{-C}_6$ alkyl, $\text{C}_1\text{-C}_6$ haloalkyl, $\text{C}_3\text{-C}_7$ cycloalkyl, $\text{C}_2\text{-C}_6$ alkenyl, $\text{C}_2\text{-C}_6$ alkynyl, OH, alkoxy, aryloxy, aralkoxy, cycloalkyloxy, cycloalkylalkyloxy, heterocycloalkyloxy, heterocycloalkylalkyloxy, heteroaryloxy, heteroarylalkyloxy, cyano, nitro, hydroxy, mercapto, or $\text{O}(\text{CR}^{4a}\text{R}^{4b})_a\text{NR}^{4c}\text{R}^{4d}$;

R^{4a} and R^{4b} are each, independently, H or $\text{C}_1\text{-C}_4$ alkyl;

R^{4c} and R^{4d} are each, independently, H, $\text{C}_1\text{-C}_4$ alkyl, $\text{C}_3\text{-C}_7$ cycloalkyl, $\text{C}_1\text{-C}_4$ haloalkyl, aryl, $\text{C}(\text{O})\text{-(C}_1\text{-C}_6\text{ alkyl)}$, $\text{C}(\text{O})\text{-aryl}$, $\text{C}(\text{O})\text{-(C}_3\text{-C}_7\text{ cycloalkyl)}$, $\text{C}(\text{O})\text{O-(C}_1\text{-C}_6\text{ alkyl)}$, $\text{C}(\text{O})\text{O-aryl}$, or $\text{C}(\text{O})\text{O-(C}_3\text{-C}_7\text{ cycloalkyl)}$, or R^{4c} and R^{4d} together with the N atom to which they are attached form a 5- or 6-membered heterocycle;

a is 1, 2, 3, 4, 5, or 6;

R^5 is $\text{N(R}^{5a})\text{-Q}$;

R^{5a} is H or $\text{C}_1\text{-C}_6$ alkyl;

Q is aryl, heteroaryl, cycloalkyl, or heterocycloalkyl, wherein Q is optionally substituted by one or more $\text{C}_1\text{-C}_{10}$ alkyl, $\text{C}_2\text{-C}_{10}$ alkenyl, $\text{C}_2\text{-C}_{10}$ alkynyl, alkoxy, aryloxy, aralkoxy, aralkyl, OH, SH, thioalkoxy, halo, $\text{C}_1\text{-C}_{10}$ haloalkyl, haloalkoxy, COOH , $\text{C}(\text{O})\text{-(C}_1\text{-C}_6\text{ alkyl)}$, $\text{C}(\text{O})\text{-(C}_3\text{-C}_7\text{ cycloalkyl)}$, $\text{C}(\text{O})\text{-aryl}$, $\text{C}(\text{O})\text{O-(C}_1\text{-C}_6\text{ alkyl)}$, $\text{C}(\text{O})\text{O-(C}_3\text{-C}_7\text{ cycloalkyl)}$, $\text{C}(\text{O})\text{O-aryl}$, $\text{C}(\text{O})\text{NR}^{Q1}\text{R}^{Q2}$, NO_2 , CN, or $\text{NR}^{Q3}\text{R}^{Q4}$;

R^{Q1} and R^{Q2} are each, independently, H, C₁-C₆ alkyl, C₃-C₆ cycloalkyl, aryl, or R^{Q1} and R^{Q2} together with the N atom to which they are attached form a 5- or 6-membered heterocycle;

R^{Q3} and R^{Q4} are each, independently, H, C₁-C₆ alkyl, aryl, C(O)-C₁-C₆ alkyl, C(O)-(C₃-C₇ cycloalkyl), C(O)-aryl, C(O)O-(C₁-C₆ alkyl), C(O)O-(C₃-C₇ cycloalkyl), C(O)O-aryl, or R^{Q1} and R^{Q2} together with the N atom to which they are attached form a 5- or 6-membered heterocycle;

or R^5 is aryl, heteroaryl, cycloalkyl, or heterocycloalkyl, wherein said aryl, heteroaryl, cycloalkyl, or heterocycloalkyl is optionally substituted by one or more halo, C₁-C₁₀ alkyl, C₁-C₁₀ haloalkyl, C₂-C₁₀ alkenyl, C₂-C₁₀ alkynyl, aryl, heteroaryl, cycloalkyl, heterocycloalkyl, alkoxy, aryloxy, aralkoxy, aralkyl, CN, NO₂, OH, SH, thioalkoxy, haloalkoxy, COOH, C(O)-(C₁-C₆ alkyl), C(O)-aryl, C(O)-(C₃-C₇ cycloalkyl), C(O)O-(C₁-C₆ alkyl), C(O)O-aryl, or C(O)O-(C₃-C₇ cycloalkyl), CONR^{5b}R^{5c}, NR^{5d}R^{5e}, or O(CR⁸R⁹)_pY;

R^{5b} and R^{5c} are each, independently, H, C₁-C₆ alkyl, C₃-C₆ cycloalkyl, aryl, or R^{5b} and R^{5c} together with the N atom to which they are attached form a 5- or 6-membered heterocycle;

R^{5d} and R^{5e} are each, independently, H, C₁-C₆ alkyl, aryl, C(O)-C₁-C₆ alkyl, C(O)-(C₃-C₇ cycloalkyl), C(O)-aryl, C(O)O-(C₁-C₆ alkyl), C(O)O-(C₃-C₇ cycloalkyl), C(O)O-aryl, or R^{5d} and R^{5e} together with the N atom to which they are attached form a 5- or 6-membered heterocycle;

R^8 and R^9 are each, independently, H or C₁-C₆ alkyl;

p is 1, 2, 3, 4, 5, or 6;

Y is NR¹⁰R¹¹, OR^{12a}, OSO₂R^{12b}, C₃-C₇ cycloalkyl, heterocycloalkyl, or heteroaryl, wherein Y is optionally substituted by one or more halo, C₁-C₆ alkyl, C₁-C₆ haloalkyl, C₂-C₆ alkenyl, C₂-C₆ alkynyl, C₃-C₇ cycloalkyl, aryl, heteroaryl, heterocycloalkyl, OH, SH, CN, NO₂, COOH, C(O)-(C₁-C₆ alkyl), C(O)-(C₃-C₇ cycloalkyl), C(O)-aryl, C(O)O-(C₁-C₆ alkyl), C(O)O-(C₃-C₇ cycloalkyl), C(O)O-aryl, NH₂, NH(C₁-C₄ alkyl), N(C₁-C₄ alkyl)₂, NHC(O)O-(C₁-C₆ alkyl), NHC(O)O-aryl or (CH₂)_qOH;

R^{10} and R^{11} are each, independently, H, (C₁-C₆)alkyl, C(O)-(C₁-C₆ alkyl), C(O)-(C₃-C₇ cycloalkyl), C(O)-aryl, C(O)O-(C₁-C₆ alkyl), C(O)O-(C₃-C₇ cycloalkyl), C(O)O-aryl, aryl, heteroaryl, cycloalkyl, or heterocycloalkyl, or R^{10} and R^{11}

together with the N atom to which they are attached form a 5- or 6- membered heterocycle;

q is 0, 1, 2, or 3;

R^{12a} is H, C₁-C₁₀ alkyl, C₁-C₁₀ alkenyl, C₁-C₁₀ alkynyl, aryl, heteroaryl, C₃-C₇ cycloalkyl, or heterocycloalkyl;

R^{12b} is H, C₁-C₆ alkyl, aryl, or NH₂;

or R⁵ is $-(CR^{13}R^{14})_n-Z$;

n is 1, 2, 3, 4, 5, 6, 7, or 8;

R¹³ and R¹⁴ are each, independently, H, C₁-C₆ alkyl, C₂-C₆ alkenyl, C₂-C₆ alkynyl, OH, aryl, or aralkyl, or R¹³ and R¹⁴ together form cycloalkyl, oxo, or sulfido;

Z is aryl, heteroaryl, cycloalkyl, heterocycloalkyl, biaryl, biheteroaryl, arylheteroaryl, heteroarylaryl, each of which is optionally substituted by one or more R¹⁵,

R¹⁵ is halo, C₁-C₁₀ alkyl, C₁-C₁₀ haloalkyl, C₂-C₁₀ alkenyl, C₂-C₁₀ alkynyl, alkoxy, aryloxy, aralkoxy, aralkyl, OH, SH, guanidiny, thioalkoxy, haloalkoxy, COOH, C(O)-(C₁-C₆ alkyl), C(O)-(C₃-C₇ cycloalkyl), C(O)-aryl, C(O)O-(C₁-C₆ alkyl), C(O)O-(C₃-C₇ cycloalkyl), C(O)O-aryl, CONR^{18a}R^{19a}, NO₂, CN, (CH₂)_tNR^{18b}R^{19b}, heteroaryl, heterocycloalkyl, aryl, C₃-C₇ cycloalkyl, or O(CR²⁰R²¹)_rX;

R^{18a} and R^{19a} are each, independently, H or C₁-C₆ alkyl, or R^{18a} and R^{19a} together with the N atom to which they are attached form a 5- or 6-membered heterocycle;

R^{18b} and R^{19b} are each, independently, H, C₁-C₆ alkyl, aryl, C(O)-C₁-C₆ alkyl, C(O)-(C₃-C₇ cycloalkyl), C(O)-aryl, C(O)O-(C₁-C₆ alkyl), C(O)O-(C₃-C₇ cycloalkyl), C(O)O-aryl, or R^{18b} and R^{19b} together with the N atom to which they are attached form a 5- or 6-membered heterocycle;

R²⁰ and R²¹ are each, independently, H or C₁-C₆ alkyl;

r is 0, 1, 2, 3, 4, 5, or 6;

t is 0, 1, or 2;

X is NR²²R²³, OH, NH₂, OSO₂R²⁴, C₃-C₇ cycloalkyl, aryl, heteroaryl, or heterocycloalkyl, wherein X is optionally substituted by one or more halo, C₁-C₆ alkyl, C₃-C₇ cycloalkyl, C₁-C₆ haloalkyl, aryl, heteroaryl, heterocycloalkyl, CN, NO₂, OH, COOH, C(O)-C₁-C₆ alkyl, C(O)-(C₃-C₇ cycloalkyl), C(O)-aryl, C(O)O-(C₁-C₆ alkyl), C(O)O-(C₃-C₇ cycloalkyl), C(O)O-aryl, NH₂, NH(C₁-C₄ alkyl), N(C₁-C₄ alkyl)₂, NHC(O)O-(C₁-C₆ alkyl), NHC(O)O-aryl or (CH₂)_sOH;

R^{22} and R^{23} are each, independently, H, C_1 - C_6 alkyl, aryl, heteroaryl, heterocycloalkyl, cycloalkyl, $C(O)$ - C_1 - C_6 alkyl, $C(O)$ -(C_3 - C_7 cycloalkyl), $C(O)$ -aryl, $C(O)O$ -(C_1 - C_6 alkyl), $C(O)O$ -(C_3 - C_7 cycloalkyl), $C(O)O$ -aryl, or R^{22} and R^{23} together with the N atom to which they are attached form a 5- or 6-membered heterocycle;

s is 0, 1, 2, or 3;

R^{24} is H, C_1 - C_6 alkyl, aryl, or NH_2 ;

or R^5 and R^2 together with the N atom to which they are attached form heterocycloalkyl optionally substituted by one or more halo, C_1 - C_4 alkyl, OH, SH, alkoxy or aryloxy; and

R^6 and R^7 are each, independently, H, halo, C_1 - C_6 alkyl, C_1 - C_6 haloalkyl, C_2 - C_6 alkenyl, C_2 - C_6 alkynyl, alkoxy, aryloxy, or aralkoxy, or R^6 and R^7 together with the atoms to which they are attached form a fused cycloalkyl, heterocycloalkyl, aryl, or heteroaryl group.

[0056] In some embodiments, the infectious agent is a virus, such as a virus that can replicate by an IRES-mediated pathway. An example infectious agent is hepatitis C virus.

[0057] In some embodiments, modulating is inhibiting.

[0058] In further embodiments of methods of the present invention, R^1 is H.

[0059] In further embodiments of methods of the present invention, R^2 and R^3 are each H.

[0060] In further embodiments of methods of the present invention, A is CR^4 .

[0061] In further embodiments of methods of the present invention, R^4 is H.

[0062] In further embodiments of methods of the present invention, R^4 is C_1 - C_4 alkyl such as methyl.

[0063] In further embodiments of methods of the present invention, R^4 is OH, alkoxy, aryloxy, aralkoxy, cycloalkyloxy, cycloalkylalkyloxy, heterocycloalkyloxy, heterocycloalkylalkyloxy, heteroaryloxy, heteroarylalkyloxy, or $O(CR^{4a}R^{4b})_aNR^{4c}R^{4d}$.

[0064] In further embodiments of methods of the present invention, R^4 is OH, alkoxy, or $O(CR^{4a}R^{4b})_aNR^{4c}R^{4d}$.

[0065] In further embodiments of methods of the present invention, R^4 is or $O(CR^{4a}R^{4b})_aNR^{4c}R^{4d}$.

[0066] In further embodiments of methods of the present invention, R^6 and R^7 are each C_1 - C_6 alkyl.

[0067] In further embodiments of methods of the present invention, at least one of R^6 and R^7 is C_1 - C_6 alkyl.

[0068] In further embodiments of methods of the present invention, at least one of R^6 and R^7 is methyl.

[0069] In further embodiments of methods of the present invention, both R^6 and R^7 are methyl.

[0070] In further embodiments of methods of the present invention, R^5 is $-(CR^{13}R^{14})_n-Z$.

[0071] In further embodiments of methods of the present invention, Z is phenyl substituted by at least one $O(CR^{20}R^{21})_rX$.

[0072] In further embodiments of methods of the present invention, n is 1 or 2.

[0073] In further embodiments of methods of the present invention, n is 2.

[0074] In further embodiments of methods of the present invention, R^5 is $-(CR^{13}R^{14})_n-Z$ and n is 1 or 2.

[0075] In further embodiments of methods of the present invention, R^5 is phenyl substituted by at least one $O(CR^8R^9)_pY$.

[0076] In further embodiments of methods of the present invention, R^5 is heteroaryl substituted by at least one $O(CR^8R^9)_pY$.

[0077] In further embodiments of methods of the present invention, R^5 is substituted or unsubstituted cycloalkyl or heterocycloalkyl.

[0078] In further embodiments of methods of the present invention, R^5 is $-(CR^{13}R^{14})_n-Z$ and Z is substituted or unsubstituted pyridinyl, pyrimidinyl, furanyl, thienyl, quinolinyl, isoquinolinyl, indolyl, benzo[1,3]dioxolyl, or benzoimidazolyl.

[0079] In further embodiments of methods of the present invention, R^5 is $-(CR^{13}R^{14})_n-Z$ and Z is furanyl, 2-methylfuranyl, 2,3-dimethylfuranyl, 2-phenylfuranyl, or benzofuranyl.

[0080] In further embodiments of methods of the present invention, R^5 is $-(CR^{13}R^{14})_n-Z$ and at least one of R^{13} and R^{14} is methyl or OH.

[0081] In further embodiments of methods of the present invention, R^5 is $-(CR^{13}R^{14})_n-Z$ and Z is phenyl substituted by at least one $O(CR^{20}R^{21})_rX$.

[0082] In further embodiments of methods of the present invention, R^5 is $-(CR^{13}R^{14})_n-Z$ and Z is substituted or unsubstituted biaryl, biheteroaryl, arylheteroaryl, or heteroarylaryl.

[0083] In further embodiments of methods of the present invention, R^5 is $N(R^{5a})$ -Q.

[0084] In further embodiments of methods of the present invention, R^5 is substituted or unsubstituted aryl, heteroaryl, cycloalkyl, or heterocycloalkyl.

[0085] In further embodiments of methods of the present invention:

R^5 is $N(R^{5a})$ -Q;

or R^5 is aryl, heteroaryl, cycloalkyl, or heterocycloalkyl, wherein said aryl, heteroaryl, cycloalkyl, or heterocycloalkyl is optionally substituted by one or more halo, C_1 - C_{10} alkyl, C_1 - C_{10} haloalkyl, C_2 - C_{10} alkenyl, C_2 - C_{10} alkynyl, alkoxy, aryloxy, aralkoxy, aralkyl, CN, NO_2 , OH, SH, thioalkoxy, haloalkoxy, COOH, $C(O)$ -(C_1 - C_6 alkyl), $C(O)$ -aryl, $C(O)$ -(C_3 - C_7 cycloalkyl), $C(O)O$ -(C_1 - C_6 alkyl), $C(O)O$ -aryl, or $C(O)O$ -(C_3 - C_7 cycloalkyl), $CONR^{5b}R^{5c}$, $NR^{5d}R^{5e}$, or $O(CR^8R^9)_pY$;

or R^5 is $-(CR^{13}R^{14})_n-Z$.

[0086] In further embodiments of methods of the present invention:

R^1 is H;

R^2 and R^3 are each, independently, H, C_1 - C_6 alkyl;

A is CR^4 ;

R^4 is H, C_1 - C_6 alkyl, C_1 - C_6 haloalkyl, alkoxy, or $O(CR^{4a}R^{4b})_aNR^{4c}R^{4d}$;

R^{4a} and R^{4b} are each H;

R^{4c} and R^{4d} are each, independently, H, C_1 - C_4 alkyl, C_3 - C_7 cycloalkyl, C_1 - C_4 haloalkyl, aryl, $C(O)$ -(C_1 - C_6 alkyl), $C(O)$ -aryl, $C(O)$ -(C_3 - C_7 cycloalkyl), $C(O)O$ -(C_1 - C_6 alkyl), $C(O)O$ -aryl, or $C(O)O$ -(C_3 - C_7 cycloalkyl), or R^{4c} and R^{4d} together with the N atom to which they are attached form a 5- or 6-membered heterocycle;

a is 1, 2, or 3;

R^5 is NH -Q;

Q is aryl, heteroaryl, cycloalkyl, or heterocycloalkyl, wherein Q is optionally substituted by one or more C_1 - C_{10} alkyl, C_2 - C_{10} alkenyl, C_2 - C_{10} alkynyl, alkoxy, aryloxy, aralkoxy, aralkyl, OH, SH, thioalkoxy, halo, C_1 - C_{10} haloalkyl, haloalkoxy, COOH, $C(O)$ -(C_1 - C_6 alkyl), $C(O)$ -(C_3 - C_7 cycloalkyl), $C(O)$ -aryl, $C(O)O$ -(C_1 - C_6 alkyl), $C(O)O$ -(C_3 - C_7 cycloalkyl), $C(O)O$ -aryl, $C(O)NR^{Q1}R^{Q2}$, NO_2 , CN, or $NR^{Q3}R^{Q4}$;

R^{Q1} and R^{Q2} are each, independently, H, C_1 - C_6 alkyl, C_3 - C_6 cycloalkyl, aryl, or R^{Q1} and R^{Q2} together with the N atom to which they are attached form a 5- or 6-membered heterocycle;

R^{Q3} and R^{Q4} are each, independently, H, C_1 - C_6 alkyl, aryl, $C(O)$ - C_1 - C_6 alkyl, $C(O)$ -(C_3 - C_7 cycloalkyl), $C(O)$ -aryl, $C(O)O$ -(C_1 - C_6 alkyl), $C(O)O$ -(C_3 - C_7 cycloalkyl), $C(O)O$ -aryl, or R^{Q1} and R^{Q2} together with the N atom to which they are attached form a 5- or 6-membered heterocycle;

or R^5 is aryl, heteroaryl, cycloalkyl, or heterocycloalkyl, wherein said aryl, heteroaryl, cycloalkyl, or heterocycloalkyl is optionally substituted by one or more halo, C_1 - C_{10} alkyl, C_1 - C_{10} haloalkyl, C_2 - C_{10} alkenyl, C_2 - C_{10} alkynyl, alkoxy, aryloxy, aralkoxy, aralkyl, CN, NO_2 , OH, SH, thioalkoxy, haloalkoxy, COOH, $C(O)$ -(C_1 - C_6 alkyl), $C(O)$ -aryl, $C(O)$ -(C_3 - C_7 cycloalkyl), $C(O)O$ -(C_1 - C_6 alkyl), $C(O)O$ -aryl, or $C(O)O$ -(C_3 - C_7 cycloalkyl), $CONR^{5b}R^{5c}$, $NR^{5d}R^{5e}$, or $O(CR^8R^9)_pY$;

R^{5b} and R^{5c} are each, independently, H, C_1 - C_6 alkyl, C_3 - C_6 cycloalkyl, aryl, or R^{5b} and R^{5c} together with the N atom to which they are attached form a 5- or 6-membered heterocycle;

R^{5d} and R^{5e} are each, independently, H, C_1 - C_6 alkyl, aryl, $C(O)$ - C_1 - C_6 alkyl, $C(O)$ -(C_3 - C_7 cycloalkyl), $C(O)$ -aryl, $C(O)O$ -(C_1 - C_6 alkyl), $C(O)O$ -(C_3 - C_7 cycloalkyl), $C(O)O$ -aryl, or R^{5d} and R^{5e} together with the N atom to which they are attached form a 5- or 6-membered heterocycle;

R^8 and R^9 are each, independently, H or C_1 - C_6 alkyl;

p is 1 or 2;

Y is $NR^{10}R^{11}$, OR^{12a} , OSO_2R^{12b} , C_3 - C_7 cycloalkyl, heterocycloalkyl, or heteroaryl, wherein Y is optionally substituted by one or more halo, C_1 - C_6 alkyl, C_1 - C_6 haloalkyl, C_2 - C_6 alkenyl, C_2 - C_6 alkynyl, C_3 - C_7 cycloalkyl, aryl, heteroaryl, heterocycloalkyl, OH, SH, CN, NO_2 , COOH, $C(O)$ -(C_1 - C_6 alkyl), $C(O)$ -(C_3 - C_7 cycloalkyl), $C(O)$ -aryl, $C(O)O$ -(C_1 - C_6 alkyl), $C(O)O$ -(C_3 - C_7 cycloalkyl), $C(O)O$ -aryl, NH_2 , $NH(C_1$ - C_4 alkyl), $N(C_1$ - C_4 alkyl) $_2$, $NHC(O)O$ -(C_1 - C_6 alkyl), $NHC(O)O$ -aryl or $(CH_2)_qOH$;

R^{10} and R^{11} are each, independently, H, C_1 - C_6 alkyl, $C(O)$ -(C_1 - C_6 alkyl), $C(O)$ -(C_3 - C_7 cycloalkyl), $C(O)$ -aryl, $C(O)O$ -(C_1 - C_6 alkyl), $C(O)O$ -(C_3 - C_7 cycloalkyl), $C(O)O$ -aryl, aryl, heteroaryl, cycloalkyl, or heterocycloalkyl, or R^{10} and R^{11} together with the N atom to which they are attached form a 5- or 6- membered heterocycle;

q is 0, 1, 2, or 3;

R^{12a} is H, C_1 - C_{10} alkyl, C_1 - C_{10} alkenyl, C_1 - C_{10} alkynyl, aryl, heteroaryl, C_3 - C_7 cycloalkyl, or heterocycloalkyl;

R^{12b} is H, C_1 - C_6 alkyl, aryl, or NH_2 ;

or R^5 is $-(CR^{13}R^{14})_n-Z$;

n is 1, 2, or 3;

R^{13} and R^{14} are each, independently, H or C_1 - C_4 alkyl;

Z is aryl, heteroaryl, cycloalkyl, or heterocycloalkyl, wherein said aryl, heteroaryl, cycloalkyl, or heterocycloalkyl is optionally substituted by one or more R^{15} ,

R^{15} is halo, C_1 - C_6 alkyl, C_1 - C_6 haloalkyl, C_2 - C_6 alkenyl, C_2 - C_6 alkynyl, alkoxy, aryloxy, aralkoxy, aralkyl, OH, SH, thioalkoxy, haloalkoxy, COOH, $C(O)-(C_1-C_6 \text{ alkyl})$, $C(O)-(C_3-C_7 \text{ cycloalkyl})$, $C(O)\text{-aryl}$, $C(O)O-(C_1-C_6 \text{ alkyl})$, $C(O)O-(C_3-C_7 \text{ cycloalkyl})$, $C(O)O\text{-aryl}$, $CONR^{18a}R^{19a}$, NO_2 , CN, $(CH_2)_tNR^{18b}R^{19b}$, heteroaryl, heterocycloalkyl, aryl, C_3 - C_7 cycloalkyl, or $O(CR^{20}R^{21})_rX$;

R^{18a} and R^{19a} are each, independently, H or C_1 - C_6 alkyl, or R^{18a} and R^{19a} together with the N atom to which they are attached form a 5- or 6-membered heterocycle;

R^{18b} and R^{19b} are each, independently, H, C_1 - C_6 alkyl, aryl, $C(O)-C_1-C_6$ alkyl, $C(O)-(C_3-C_7 \text{ cycloalkyl})$, $C(O)\text{-aryl}$, $C(O)O-(C_1-C_6 \text{ alkyl})$, $C(O)O-(C_3-C_7 \text{ cycloalkyl})$, $C(O)O\text{-aryl}$, or R^{18b} and R^{19b} together with the N atom to which they are attached form a 5- or 6-membered heterocycle;

R^{20} and R^{21} are each, independently, H or C_1 - C_4 alkyl;

r is 0, 1, 2, or 3;

t is 0, 1, or 2;

X is $NR^{22}R^{23}$, OH, NH_2 , OSO_2R^{24} , C_3 - C_7 cycloalkyl, aryl, heteroaryl, or heterocycloalkyl, wherein X is optionally substituted by one or more halo, C_1 - C_6 alkyl, C_3 - C_7 cycloalkyl, C_1 - C_6 haloalkyl, aryl, heteroaryl, heterocycloalkyl, CN, NO_2 , OH, COOH, $C(O)-C_1-C_6$ alkyl, $C(O)-(C_3-C_7 \text{ cycloalkyl})$, $C(O)\text{-aryl}$, $C(O)O-(C_1-C_6 \text{ alkyl})$, $C(O)O-(C_3-C_7 \text{ cycloalkyl})$, $C(O)O\text{-aryl}$, NH_2 , $NH(C_1-C_4 \text{ alkyl})$, $N(C_1-C_4 \text{ alkyl})_2$, $NHC(O)O-(C_1-C_6 \text{ alkyl})$, $NHC(O)O\text{-aryl}$ or $(CH_2)_sOH$;

R^{22} and R^{23} are each, independently, H, C_1 - C_6 alkyl, aryl, heteroaryl, heterocycloalkyl, cycloalkyl, $C(O)-C_1-C_6$ alkyl, $C(O)-(C_3-C_7 \text{ cycloalkyl})$, $C(O)\text{-aryl}$, $C(O)O-(C_1-C_6 \text{ alkyl})$, $C(O)O-(C_3-C_7 \text{ cycloalkyl})$, $C(O)O\text{-aryl}$, or R^{22} and R^{23} together with the N atom to which they are attached form a 5- or 6-membered heterocycle;

s is 0 or 1;

R^{24} is H, C_1 - C_6 alkyl, aryl, or NH_2 ; and

R^6 and R^7 are each, independently, H, C_1 - C_4 alkyl, C_1 - C_4 alkoxy.

[0087] In further embodiments of methods of the present invention:

R^1 is H;

R^2 and R^3 are each H;

A is CH; and

R^6 and R^7 are each methyl.

[0088] In further embodiments of methods of the present invention:

R^1 is H;

R^2 and R^3 are each H;

A is CH;

R^5 is $-(CR^{13}R^{14})_n-Z$;

n is 1 or 2; and

R^6 and R^7 are each methyl.

[0089] In further embodiments of methods of the present invention:

A is CR^4 ; and

R^4 is alkoxy, aryloxy, aralkoxy, cycloalkyloxy, cycloalkylalkyloxy, heterocycloalkyloxy, heterocycloalkylalkyloxy, heteroaryloxy, heteroarylalkyloxy, hydroxy, or $O(CR^{4a}R^{4b})_aNR^{4c}R^{4d}$.

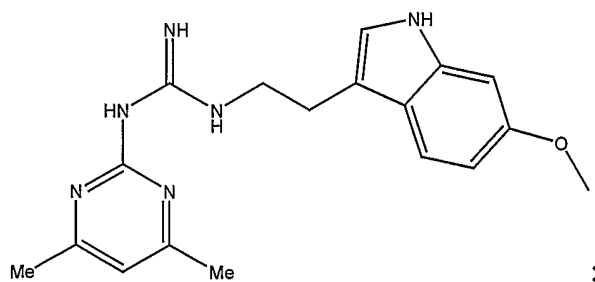
[0090] In further embodiments of methods of the present invention:

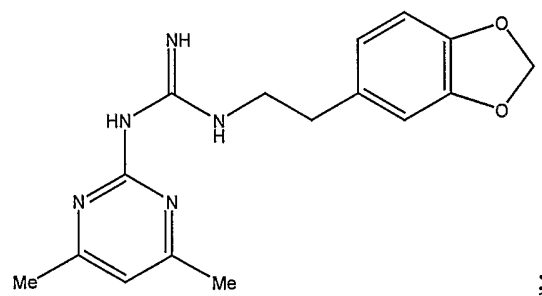
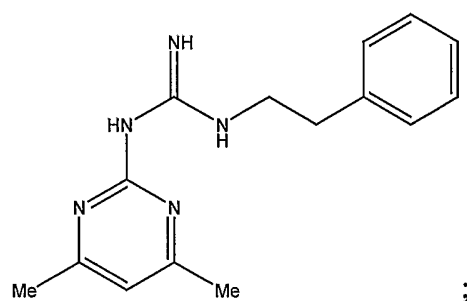
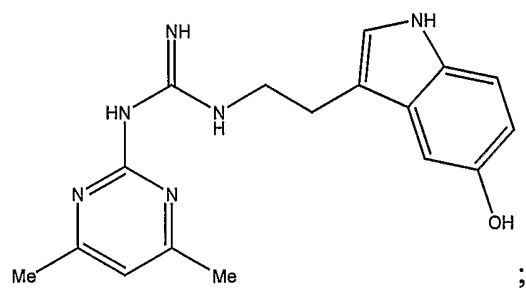
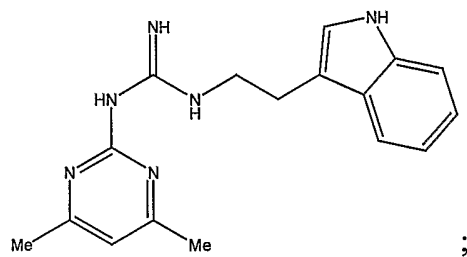
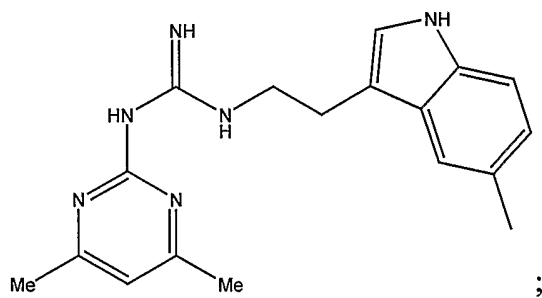
A is CR^4 ;

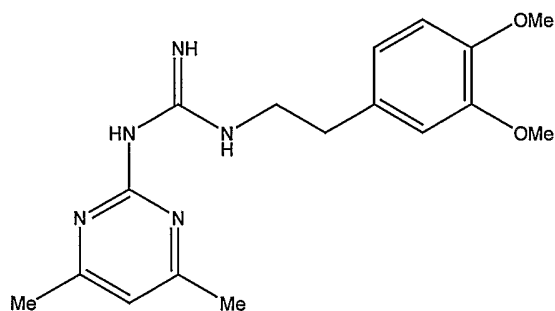
R^4 is alkoxy, aryloxy, aralkoxy, cycloalkyloxy, cycloalkylalkyloxy, heterocycloalkyloxy, heterocycloalkylalkyloxy, heteroaryloxy, heteroarylalkyloxy, hydroxy, or $O(CR^{4a}R^{4b})_aNR^{4c}R^{4d}$; and

R^6 and R^7 are each, independently, H, halo, C_1 - C_3 alkyl, or C_1 - C_6 haloalkyl.

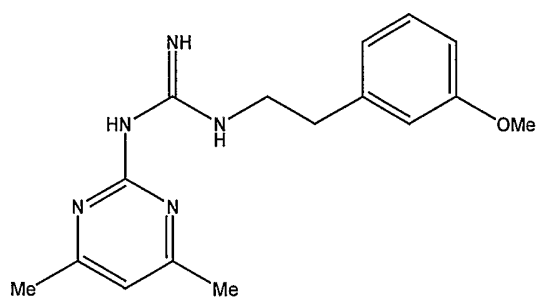
[0091] The present invention further provides methods of modulating activity of an infectious agent comprising contacting the infectious agent with any of the compounds listed in Tables I, II, or III, such as a compound of Formula:



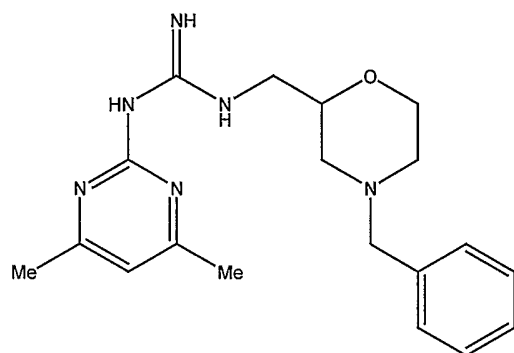




;



; or



[0092] The present invention further provides a method of treating a viral infection in a patient by administering to the patient a therapeutically effective amount of a compound of Formula I, or pharmaceutically acceptable salt form thereof, wherein:

R^1 is H or COOR^{1a} ;

R^{1a} is H or $\text{C}_1\text{-C}_{10}$ alkyl, aryl, cycloalkyl, or aralkyl;

R^2 and R^3 are each, independently, H, $\text{C}_1\text{-C}_{10}$ alkyl, or $\text{C}_3\text{-C}_7$ cycloalkyl;

A is N or CR^4 ;

R^4 is H, halo, $\text{C}_1\text{-C}_6$ alkyl, $\text{C}_1\text{-C}_6$ haloalkyl, $\text{C}_3\text{-C}_7$ cycloalkyl, $\text{C}_2\text{-C}_6$ alkenyl, $\text{C}_2\text{-C}_6$ alkynyl, OH, alkoxy, aryloxy, aralkoxy, cycloalkyloxy, cycloalkylalkyloxy, heterocycloalkyloxy, heterocycloalkylalkyloxy, heteroaryloxy, heteroarylalkyloxy, cyano, nitro, hydroxy, mercapto, or $\text{O}(\text{CR}^{4a}\text{R}^{4b})_a\text{NR}^{4c}\text{R}^{4d}$;

R^{4a} and R^{4b} are each, independently, H or $\text{C}_1\text{-C}_4$ alkyl;

R^{4c} and R^{4d} are each, independently, H, C₁-C₄ alkyl, C₃-C₇ cycloalkyl, C₁-C₄ haloalkyl, aryl, C(O)-(C₁-C₆ alkyl), C(O)-aryl, C(O)-(C₃-C₇ cycloalkyl), C(O)O-(C₁-C₆ alkyl), C(O)O-aryl, or C(O)O-(C₃-C₇ cycloalkyl), or R^{4c} and R^{4d} together with the N atom to which they are attached form a 5- or 6-membered heterocycle;

a is 1, 2, 3, 4, 5, or 6;

R^5 is N(R^{5a})-Q;

R^{5a} is H or C₁-C₆ alkyl;

Q is aryl, heteroaryl, cycloalkyl, or heterocycloalkyl, wherein Q is optionally substituted by one or more C₁-C₁₀ alkyl, C₂-C₁₀ alkenyl, C₂-C₁₀ alkynyl, alkoxy, aryloxy, aralkoxy, aralkyl, OH, SH, thioalkoxy, halo, C₁-C₁₀ haloalkyl, haloalkoxy, COOH, C(O)-(C₁-C₆ alkyl), C(O)-(C₃-C₇ cycloalkyl), C(O)-aryl, C(O)O-(C₁-C₆ alkyl), C(O)O-(C₃-C₇ cycloalkyl), C(O)O-aryl, C(O)NR^{Q1}R^{Q2}, NO₂, CN, or NR^{Q3}R^{Q4};

R^{Q1} and R^{Q2} are each, independently, H, C₁-C₆ alkyl, C₃-C₆ cycloalkyl, aryl, or R^{Q1} and R^{Q2} together with the N atom to which they are attached form a 5- or 6-membered heterocycle;

R^{Q3} and R^{Q4} are each, independently, H, C₁-C₆ alkyl, aryl, C(O)-C₁-C₆ alkyl, C(O)-(C₃-C₇ cycloalkyl), C(O)-aryl, C(O)O-(C₁-C₆ alkyl), C(O)O-(C₃-C₇ cycloalkyl), C(O)O-aryl, or R^{Q1} and R^{Q2} together with the N atom to which they are attached form a 5- or 6-membered heterocycle;

or R^5 is aryl, heteroaryl, cycloalkyl, or heterocycloalkyl, wherein said aryl, heteroaryl, cycloalkyl, or heterocycloalkyl is optionally substituted by one or more halo, C₁-C₁₀ alkyl, C₁-C₁₀ haloalkyl, C₂-C₁₀ alkenyl, C₂-C₁₀ alkynyl, aryl, heteroaryl, cycloalkyl, heterocycloalkyl, alkoxy, aryloxy, aralkoxy, aralkyl, CN, NO₂, OH, SH, thioalkoxy, haloalkoxy, COOH, C(O)-(C₁-C₆ alkyl), C(O)-aryl, C(O)-(C₃-C₇ cycloalkyl), C(O)O-(C₁-C₆ alkyl), C(O)O-aryl, or C(O)O-(C₃-C₇ cycloalkyl), CONR^{5b}R^{5c}, NR^{5d}R^{5e}, or O(CR⁸R⁹)_pY;

R^{5b} and R^{5c} are each, independently, H, C₁-C₆ alkyl, C₃-C₆ cycloalkyl, aryl, or R^{5b} and R^{5c} together with the N atom to which they are attached form a 5- or 6-membered heterocycle;

R^{5d} and R^{5e} are each, independently, H, C₁-C₆ alkyl, aryl, C(O)-C₁-C₆ alkyl, C(O)-(C₃-C₇ cycloalkyl), C(O)-aryl, C(O)O-(C₁-C₆ alkyl), C(O)O-(C₃-C₇ cycloalkyl), C(O)O-aryl, or R^{5d} and R^{5e} together with the N atom to which they are attached form a 5- or 6-membered heterocycle;

R^8 and R^9 are each, independently, H or C₁-C₆ alkyl;

p is 1, 2, 3, 4, 5, or 6;

Y is NR¹⁰R¹¹, OR^{12a}, OSO₂R^{12b}, C₃-C₇ cycloalkyl, heterocycloalkyl, or heteroaryl, wherein Y is optionally substituted by one or more halo, C₁-C₆ alkyl, C₁-C₆ haloalkyl, C₂-C₆ alkenyl, C₂-C₆ alkynyl, C₃-C₇ cycloalkyl, aryl, heteroaryl, heterocycloalkyl, OH, SH, CN, NO₂, COOH, C(O)-(C₁-C₆ alkyl), C(O)-(C₃-C₇ cycloalkyl), C(O)-aryl, C(O)O-(C₁-C₆ alkyl), C(O)O-(C₃-C₇ cycloalkyl), C(O)O-aryl, NH₂, NH(C₁-C₄ alkyl), N(C₁-C₄ alkyl)₂, NHC(O)O-(C₁-C₆ alkyl), NHC(O)O-aryl or (CH₂)_aOH;

R¹⁰ and R¹¹ are each, independently, H, (C₁-C₆)alkyl, C(O)-(C₁-C₆ alkyl), C(O)-(C₃-C₇ cycloalkyl), C(O)-aryl, C(O)O-(C₁-C₆ alkyl), C(O)O-(C₃-C₇ cycloalkyl), C(O)O-aryl, aryl, heteroaryl, cycloalkyl, or heterocycloalkyl, or R¹⁰ and R¹¹ together with the N atom to which they are attached form a 5- or 6- membered heterocycle;

q is 0, 1, 2, or 3;

R^{12a} is H, C₁-C₁₀ alkyl, C₁-C₁₀ alkenyl, C₁-C₁₀ alkynyl, aryl, heteroaryl, C₃-C₇ cycloalkyl, or heterocycloalkyl;

R^{12b} is H, C₁-C₆ alkyl, aryl, or NH₂;

or R^5 is $-(CR^{13}R^{14})_n-Z$;

n is 1, 2, 3, 4, 5, 6, 7, or 8;

R¹³ and R¹⁴ are each, independently, H, C₁-C₆ alkyl, C₂-C₆ alkenyl, C₂-C₆ alkynyl, OH, aryl, or aralkyl, or R¹³ and R¹⁴ together form cycloalkyl, oxo, or sulfido;

Z is aryl, heteroaryl, cycloalkyl, heterocycloalkyl, biaryl, biheteroaryl, arylheteroaryl, heteroarylaryl, each of which is optionally substituted by one or more R¹⁵,

R¹⁵ is halo, C₁-C₁₀ alkyl, C₁-C₁₀ haloalkyl, C₂-C₁₀ alkenyl, C₂-C₁₀ alkynyl, alkoxy, aryloxy, aralkoxy, aralkyl, OH, SH, guanidiny, thioalkoxy, haloalkoxy, COOH, C(O)-(C₁-C₆ alkyl), C(O)-(C₃-C₇ cycloalkyl), C(O)-aryl, C(O)O-(C₁-C₆ alkyl), C(O)O-(C₃-C₇ cycloalkyl), C(O)O-aryl, CONR^{18a}R^{19a}, NO₂, CN, (CH₂)_tNR^{18b}R^{19b}, heteroaryl, heterocycloalkyl, aryl, C₃-C₇ cycloalkyl, or O(CR²⁰R²¹)_rX;

R^{18a} and R^{19a} are each, independently, H or C₁-C₆ alkyl, or R^{18a} and R^{19a} together with the N atom to which they are attached form a 5- or 6-membered heterocycle;

R^{18b} and R^{19b} are each, independently, H, C₁-C₆ alkyl, aryl, C(O)-C₁-C₆ alkyl, C(O)-(C₃-C₇ cycloalkyl), C(O)-aryl, C(O)O-(C₁-C₆ alkyl), C(O)O-(C₃-

C₇ cycloalkyl), C(O)O-aryl, or R^{18b} and R^{19b} together with the N atom to which they are attached form a 5- or 6-membered heterocycle;

R²⁰ and R²¹ are each, independently, H or C₁-C₆ alkyl;

r is 0, 1, 2, 3, 4, 5, or 6;

t is 0, 1, or 2;

X is NR²²R²³, OH, NH₂, OSO₂R²⁴, C₃-C₇ cycloalkyl, aryl, heteroaryl, or heterocycloalkyl, wherein X is optionally substituted by one or more halo, C₁-C₆ alkyl, C₃-C₇ cycloalkyl, C₁-C₆ haloalkyl, aryl, heteroaryl, heterocycloalkyl, CN, NO₂, OH, COOH, C(O)-C₁-C₆ alkyl, C(O)-(C₃-C₇ cycloalkyl), C(O)-aryl, C(O)O-(C₁-C₆ alkyl), C(O)O-(C₃-C₇ cycloalkyl), C(O)O-aryl, NH₂, NH(C₁-C₄ alkyl), N(C₁-C₄ alkyl)₂, NHC(O)O-(C₁-C₆ alkyl), NHC(O)O-aryl or (CH₂)_sOH;

R²² and R²³ are each, independently, H, C₁-C₆ alkyl, aryl, heteroaryl, heterocycloalkyl, cycloalkyl, C(O)-C₁-C₆ alkyl, C(O)-(C₃-C₇ cycloalkyl), C(O)-aryl, C(O)O-(C₁-C₆ alkyl), C(O)O-(C₃-C₇ cycloalkyl), C(O)O-aryl, or R²² and R²³ together with the N atom to which they are attached form a 5- or 6-membered heterocycle;

s is 0, 1, 2, or 3;

R²⁴ is H, C₁-C₆ alkyl, aryl, or NH₂;

or R⁵ and R² together with the N atom to which they are attached form heterocycloalkyl optionally substituted by one or more halo, C₁-C₄ alkyl, OH, SH, alkoxy or aryloxy; and

R⁶ and R⁷ are each, independently, H, halo, C₁-C₆ alkyl, C₁-C₆ haloalkyl, C₂-C₆ alkenyl, C₂-C₆ alkynyl, alkoxy, aryloxy, or aralkoxy, or R⁶ and R⁷ together with the atoms to which they are attached form a fused cycloalkyl, heterocycloalkyl, aryl, or heteroaryl group.

[0093] In some embodiments, the viral infection is a hepatitis C viral infection.

[0094] The present invention also provides a method of inhibiting translation of a nucleic acid wherein replication of the nucleic acid is mediated by an internal ribosome entry site (IRES), by contacting the nucleic acid with a compound of Formula I, or pharmaceutically acceptable salt form thereof, wherein:

R¹ is H or COOR^{1a};

R^{1a} is H or C₁-C₁₀ alkyl, aryl, cycloalkyl, or aralkyl;

R² and R³ are each, independently, H, C₁-C₁₀ alkyl, or C₃-C₇ cycloalkyl;

A is N or CR⁴;

R^4 is H, halo, C_1 - C_6 alkyl, C_1 - C_6 haloalkyl, C_3 - C_7 cycloalkyl, C_2 - C_6 alkenyl, C_2 - C_6 alkynyl, OH, alkoxy, aryloxy, aralkoxy, cycloalkyloxy, cycloalkylalkyloxy, heterocycloalkyloxy, heterocycloalkylalkyloxy, heteroaryloxy, heteroarylalkyloxy, cyano, nitro, hydroxy, mercapto, or $O(CR^{4a}R^{4b})_aNR^{4c}R^{4d}$;

R^{4a} and R^{4b} are each, independently, H or C_1 - C_4 alkyl;

R^{4c} and R^{4d} are each, independently, H, C_1 - C_4 alkyl, C_3 - C_7 cycloalkyl, C_1 - C_4 haloalkyl, aryl, $C(O)$ -(C_1 - C_6 alkyl), $C(O)$ -aryl, $C(O)$ -(C_3 - C_7 cycloalkyl), $C(O)O$ -(C_1 - C_6 alkyl), $C(O)O$ -aryl, or $C(O)O$ -(C_3 - C_7 cycloalkyl), or R^{4c} and R^{4d} together with the N atom to which they are attached form a 5- or 6-membered heterocycle;

a is 1, 2, 3, 4, 5, or 6;

R^5 is $N(R^{5a})-Q$;

R^{5a} is H or C_1 - C_6 alkyl;

Q is aryl, heteroaryl, cycloalkyl, or heterocycloalkyl, wherein Q is optionally substituted by one or more C_1 - C_{10} alkyl, C_2 - C_{10} alkenyl, C_2 - C_{10} alkynyl, alkoxy, aryloxy, aralkoxy, aralkyl, OH, SH, thioalkoxy, halo, C_1 - C_{10} haloalkyl, haloalkoxy, COOH, $C(O)$ -(C_1 - C_6 alkyl), $C(O)$ -(C_3 - C_7 cycloalkyl), $C(O)$ -aryl, $C(O)O$ -(C_1 - C_6 alkyl), $C(O)O$ -(C_3 - C_7 cycloalkyl), $C(O)O$ -aryl, $C(O)NR^{Q1}R^{Q2}$, NO_2 , CN, or $NR^{Q3}R^{Q4}$;

R^{Q1} and R^{Q2} are each, independently, H, C_1 - C_6 alkyl, C_3 - C_6 cycloalkyl, aryl, or R^{Q1} and R^{Q2} together with the N atom to which they are attached form a 5- or 6-membered heterocycle;

R^{Q3} and R^{Q4} are each, independently, H, C_1 - C_6 alkyl, aryl, $C(O)$ - C_1 - C_6 alkyl, $C(O)$ -(C_3 - C_7 cycloalkyl), $C(O)$ -aryl, $C(O)O$ -(C_1 - C_6 alkyl), $C(O)O$ -(C_3 - C_7 cycloalkyl), $C(O)O$ -aryl, or R^{Q1} and R^{Q2} together with the N atom to which they are attached form a 5- or 6-membered heterocycle;

or R^5 is aryl, heteroaryl, cycloalkyl, or heterocycloalkyl, wherein said aryl, heteroaryl, cycloalkyl, or heterocycloalkyl is optionally substituted by one or more halo, C_1 - C_{10} alkyl, C_1 - C_{10} haloalkyl, C_2 - C_{10} alkenyl, C_2 - C_{10} alkynyl, aryl, heteroaryl, cycloalkyl, heterocycloalkyl, alkoxy, aryloxy, aralkoxy, aralkyl, CN, NO_2 , OH, SH, thioalkoxy, haloalkoxy, COOH, $C(O)$ -(C_1 - C_6 alkyl), $C(O)$ -aryl, $C(O)$ -(C_3 - C_7 cycloalkyl), $C(O)O$ -(C_1 - C_6 alkyl), $C(O)O$ -aryl, or $C(O)O$ -(C_3 - C_7 cycloalkyl), $CONR^{5b}R^{5c}$, $NR^{5d}R^{5e}$, or $O(CR^8R^9)_pY$;

R^{5b} and R^{5c} are each, independently, H, C_1 - C_6 alkyl, C_3 - C_6 cycloalkyl, aryl, or R^{5b} and R^{5c} together with the N atom to which they are attached form a 5- or 6-membered heterocycle;

R^{5d} and R^{5e} are each, independently, H, C_1 - C_6 alkyl, aryl, $C(O)$ - C_1 - C_6 alkyl, $C(O)$ -(C_3 - C_7 cycloalkyl), $C(O)$ -aryl, $C(O)O$ -(C_1 - C_6 alkyl), $C(O)O$ -(C_3 - C_7 cycloalkyl), $C(O)O$ -aryl, or R^{5d} and R^{5e} together with the N atom to which they are attached form a 5- or 6-membered heterocycle;

R^8 and R^9 are each, independently, H or C_1 - C_6 alkyl;

p is 1, 2, 3, 4, 5, or 6;

Y is $NR^{10}R^{11}$, OR^{12a} , OSO_2R^{12b} , C_3 - C_7 cycloalkyl, heterocycloalkyl, or heteroaryl, wherein Y is optionally substituted by one or more halo, C_1 - C_6 alkyl, C_1 - C_6 haloalkyl, C_2 - C_6 alkenyl, C_2 - C_6 alkynyl, C_3 - C_7 cycloalkyl, aryl, heteroaryl, heterocycloalkyl, OH, SH, CN, NO_2 , COOH, $C(O)$ -(C_1 - C_6 alkyl), $C(O)$ -(C_3 - C_7 cycloalkyl), $C(O)$ -aryl, $C(O)O$ -(C_1 - C_6 alkyl), $C(O)O$ -(C_3 - C_7 cycloalkyl), $C(O)O$ -aryl, NH_2 , NH (C_1 - C_4 alkyl), N (C_1 - C_4 alkyl) $_2$, $NHC(O)O$ -(C_1 - C_6 alkyl), $NHC(O)O$ -aryl or $(CH_2)_qOH$;

R^{10} and R^{11} are each, independently, H, (C_1 - C_6)alkyl, $C(O)$ -(C_1 - C_6 alkyl), $C(O)$ -(C_3 - C_7 cycloalkyl), $C(O)$ -aryl, $C(O)O$ -(C_1 - C_6 alkyl), $C(O)O$ -(C_3 - C_7 cycloalkyl), $C(O)O$ -aryl, aryl, heteroaryl, cycloalkyl, or heterocycloalkyl, or R^{10} and R^{11} together with the N atom to which they are attached form a 5- or 6- membered heterocycle;

q is 0, 1, 2, or 3;

R^{12a} is H, C_1 - C_{10} alkyl, C_1 - C_{10} alkenyl, C_1 - C_{10} alkynyl, aryl, heteroaryl, C_3 - C_7 cycloalkyl, or heterocycloalkyl;

R^{12b} is H, C_1 - C_6 alkyl, aryl, or NH_2 ;

or R^5 is $-(CR^{13}R^{14})_n-Z$;

n is 1, 2, 3, 4, 5, 6, 7, or 8;

R^{13} and R^{14} are each, independently, H, C_1 - C_6 alkyl, C_2 - C_6 alkenyl, C_2 - C_6 alkynyl, OH, aryl, or aralkyl, or R^{13} and R^{14} together form cycloalkyl, oxo, or sulfido;

Z is aryl, heteroaryl, cycloalkyl, heterocycloalkyl, biaryl, biheteroaryl, arylheteroaryl, heteroarylaryl, each of which is optionally substituted by one or more R^{15} ,

R^{15} is halo, C_1 - C_{10} alkyl, C_1 - C_{10} haloalkyl, C_2 - C_{10} alkenyl, C_2 - C_{10} alkynyl, alkoxy, aryloxy, aralkoxy, aralkyl, OH, SH, guanidiny, thioalkoxy, haloalkoxy, COOH, $C(O)$ -(C_1 - C_6 alkyl), $C(O)$ -(C_3 - C_7 cycloalkyl), $C(O)$ -aryl, $C(O)O$ -(C_1 - C_6 alkyl), $C(O)O$ -(C_3 - C_7 cycloalkyl), $C(O)O$ -aryl, $CONR^{18a}R^{19a}$, NO_2 , CN, $(CH_2)_tNR^{18b}R^{19b}$, heteroaryl, heterocycloalkyl, aryl, C_3 - C_7 cycloalkyl, or $O(CR^{20}R^{21})_rX$;

R^{18a} and R^{19a} are each, independently, H or C₁-C₆ alkyl, or R^{18a} and R^{19a} together with the N atom to which they are attached form a 5- or 6-membered heterocycle;

R^{18b} and R^{19b} are each, independently, H, C₁-C₆ alkyl, aryl, C(O)-C₁-C₆ alkyl, C(O)-(C₃-C₇ cycloalkyl), C(O)-aryl, C(O)O-(C₁-C₆ alkyl), C(O)O-(C₃-C₇ cycloalkyl), C(O)O-aryl, or R^{18b} and R^{19b} together with the N atom to which they are attached form a 5- or 6-membered heterocycle;

R^{20} and R^{21} are each, independently, H or C₁-C₆ alkyl;

r is 0, 1, 2, 3, 4, 5, or 6;

t is 0, 1, or 2;

X is $NR^{22}R^{23}$, OH, NH_2 , OSO_2R^{24} , C₃-C₇ cycloalkyl, aryl, heteroaryl, or heterocycloalkyl, wherein X is optionally substituted by one or more halo, C₁-C₆ alkyl, C₃-C₇ cycloalkyl, C₁-C₆ haloalkyl, aryl, heteroaryl, heterocycloalkyl, CN, NO_2 , OH, COOH, C(O)-C₁-C₆ alkyl, C(O)-(C₃-C₇ cycloalkyl), C(O)-aryl, C(O)O-(C₁-C₆ alkyl), C(O)O-(C₃-C₇ cycloalkyl), C(O)O-aryl, NH_2 , $NH(C_1-C_4 \text{ alkyl})$, $N(C_1-C_4 \text{ alkyl})_2$, $NHC(O)O-(C_1-C_6 \text{ alkyl})$, $NHC(O)O-aryl$ or $(CH_2)_sOH$;

R^{22} and R^{23} are each, independently, H, C₁-C₆ alkyl, aryl, heteroaryl, heterocycloalkyl, cycloalkyl, C(O)-C₁-C₆ alkyl, C(O)-(C₃-C₇ cycloalkyl), C(O)-aryl, C(O)O-(C₁-C₆ alkyl), C(O)O-(C₃-C₇ cycloalkyl), C(O)O-aryl, or R^{22} and R^{23} together with the N atom to which they are attached form a 5- or 6-membered heterocycle;

s is 0, 1, 2, or 3;

R^{24} is H, C₁-C₆ alkyl, aryl, or NH_2 ;

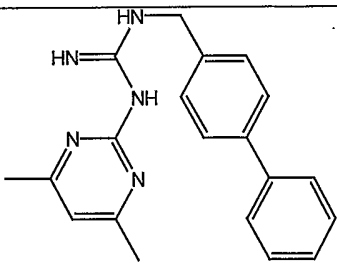
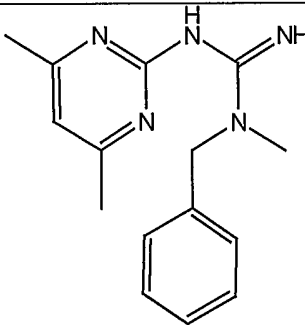
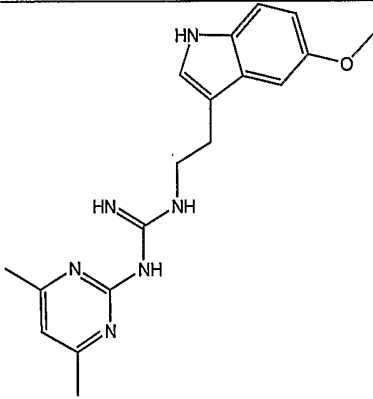
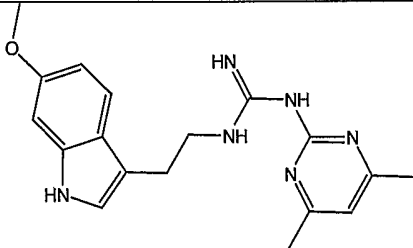
or R^5 and R^2 together with the N atom to which they are attached form heterocycloalkyl optionally substituted by one or more halo, C₁-C₄ alkyl, OH, SH, alkoxy or aryloxy; and

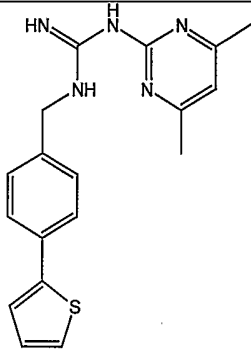
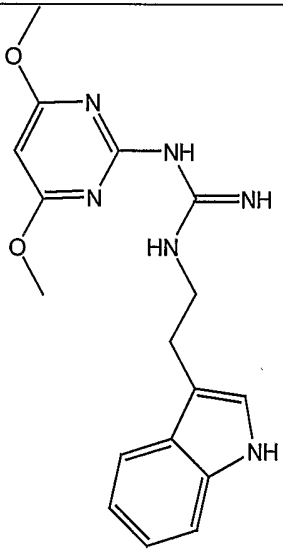
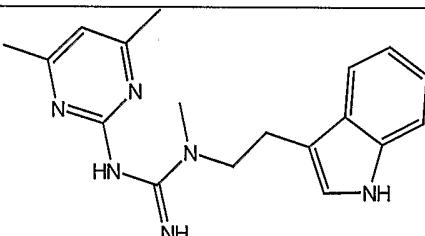
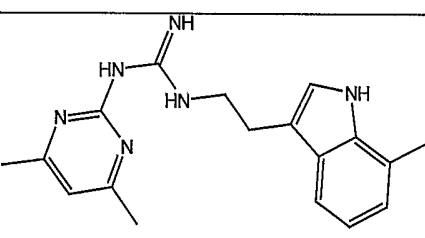
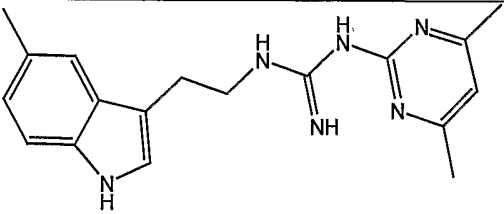
R^6 and R^7 are each, independently, H, halo, C₁-C₆ alkyl, C₁-C₆ haloalkyl, C₂-C₆ alkenyl, C₂-C₆ alkynyl, alkoxy, aryloxy, or aralkoxy, or R^6 and R^7 together with the atoms to which they are attached form a fused cycloalkyl, heterocycloalkyl, aryl, or heteroaryl group.

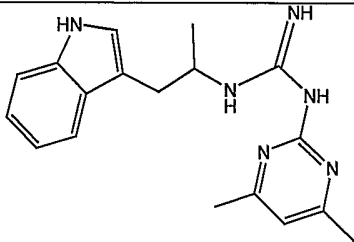
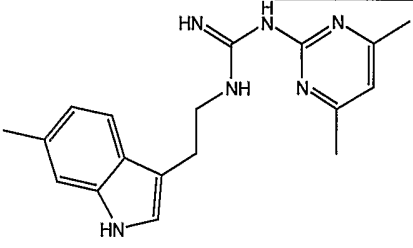
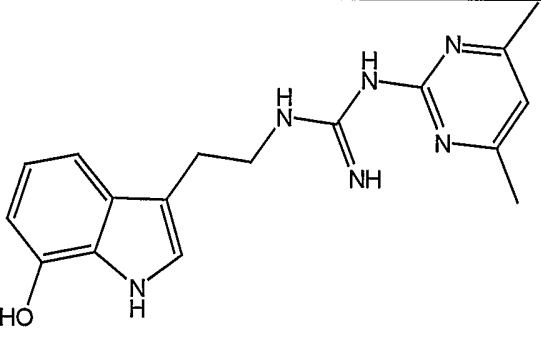
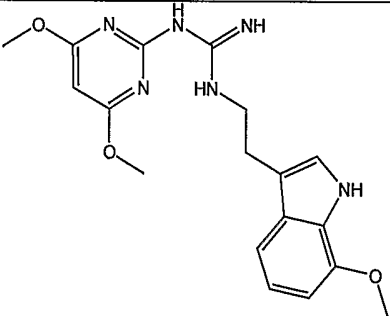
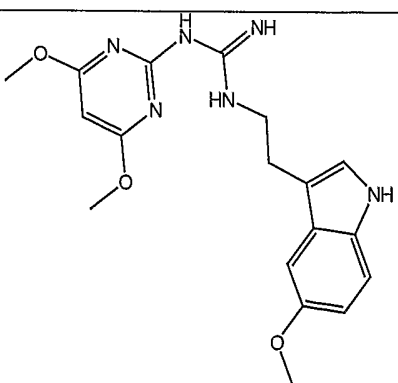
[0095] In some embodiments, the nucleic acid is derived from a virus such as hepatitis C virus.

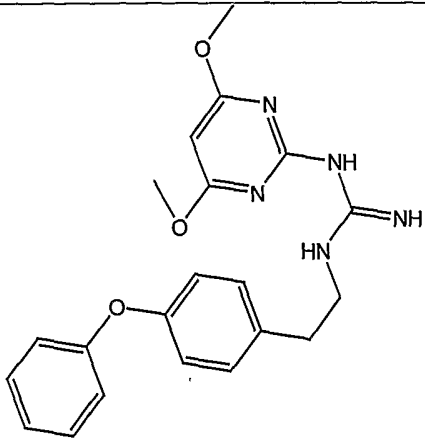
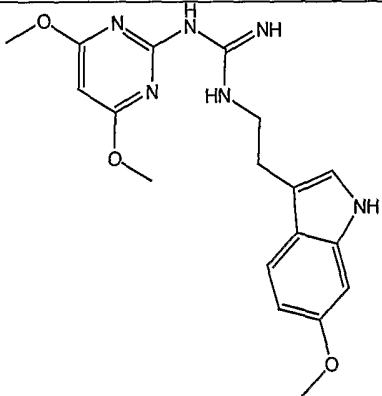
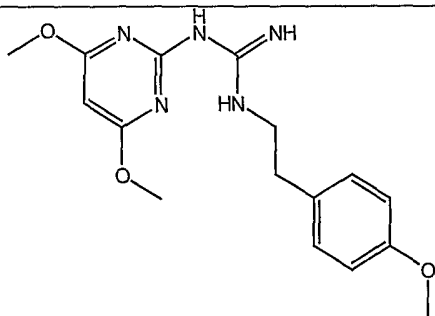
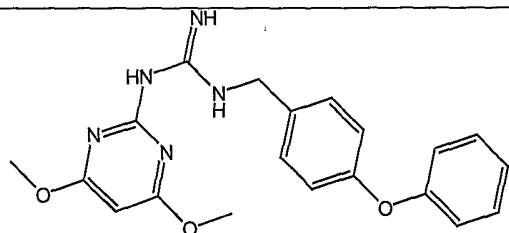
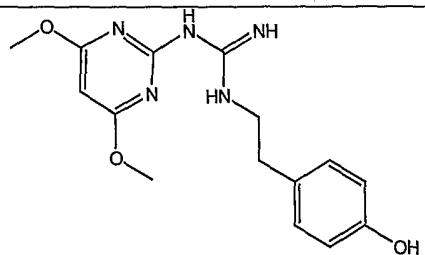
[0096] Example compounds of the present invention have been prepared and are provided in Table 1 below.

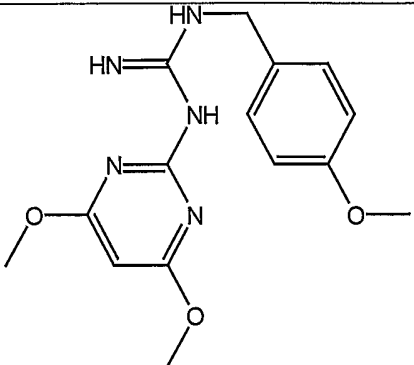
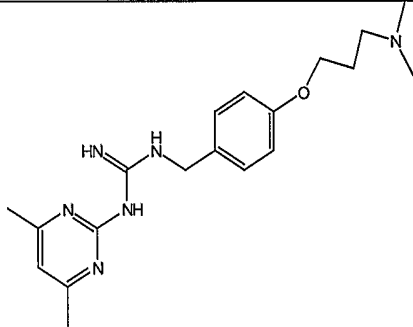
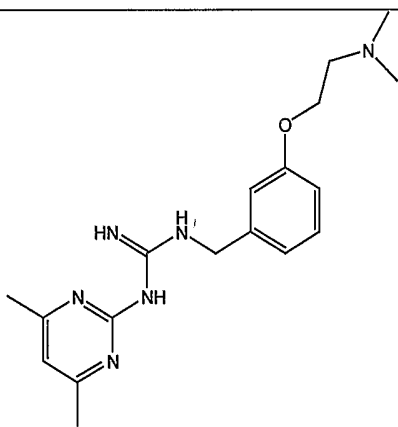
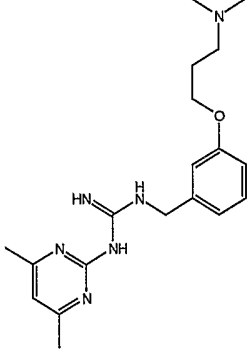
Table 1

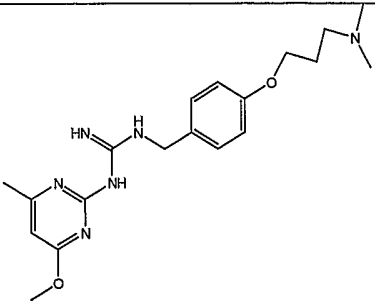
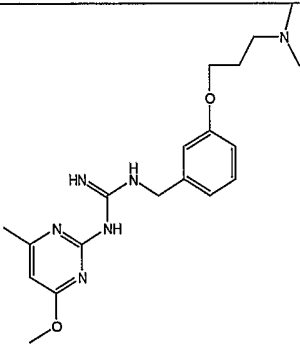
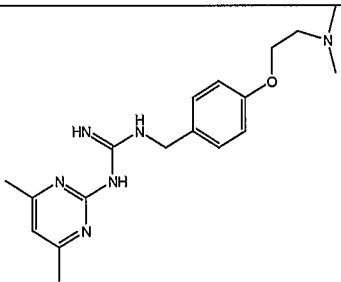
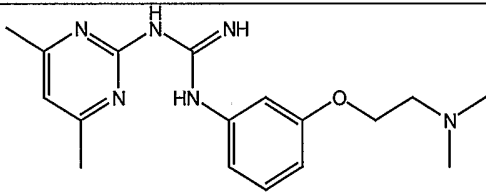
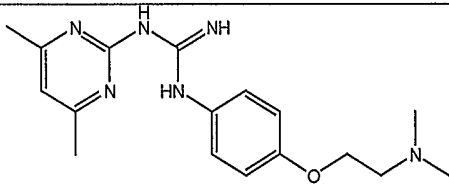
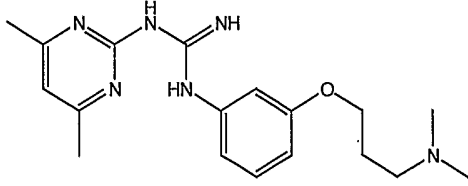
No.	Compound	Mass Calculated	Mass Found
1.1		331.179683	332.2
1.2		269.164033	270.2
1.3		338.185495	339.2
1.4		338.185495	339.2

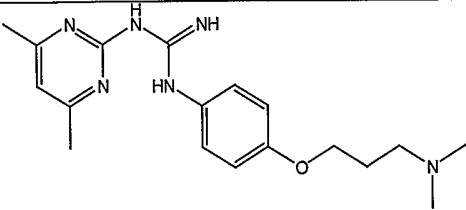
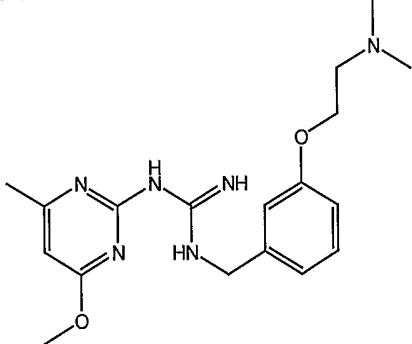
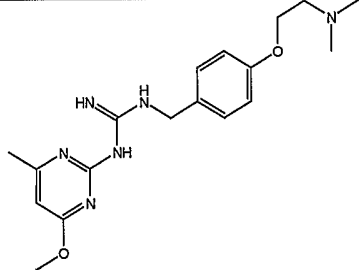
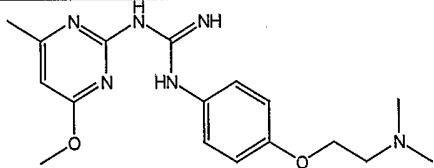
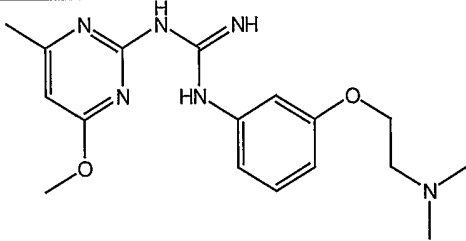
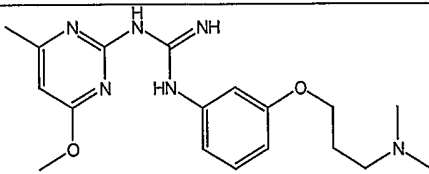
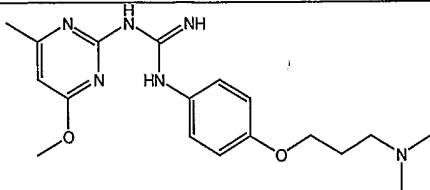
1.5		337.136103	338.1
1.6		340.164759	341.2
1.7		322.19058	323.2
1.8		322.19058	323.2
1.9		322.19058	323.2

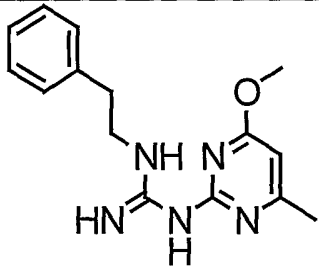
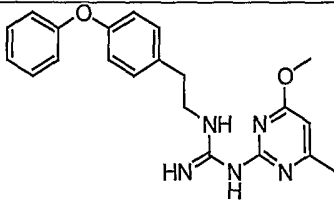
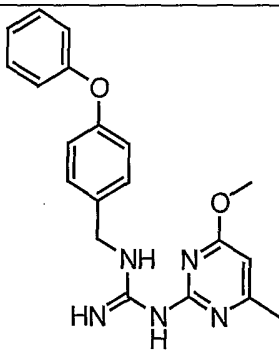
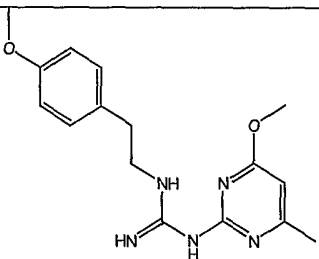
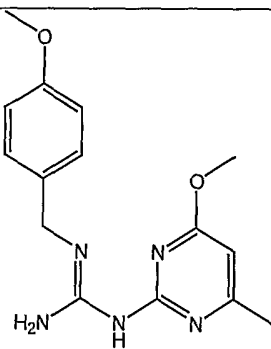
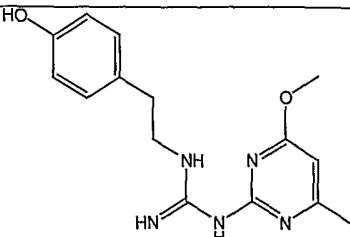
1.10		322.19058	323.2
1.11		322.19058	323.2
1.12		324.169845	325.2
1.13		370.175323	371.2
1.14		370.175323	371.2

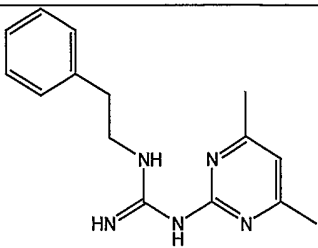
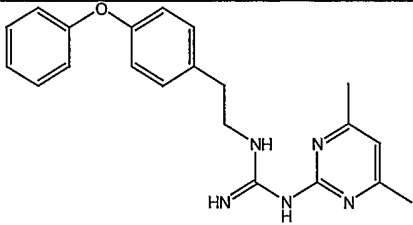
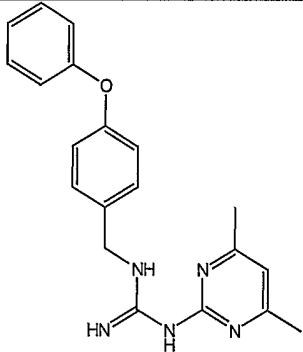
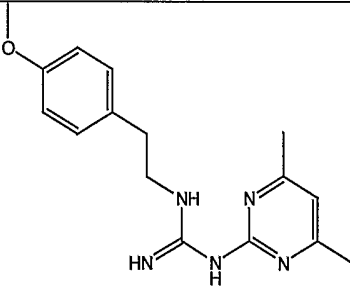
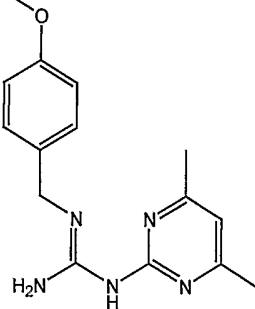
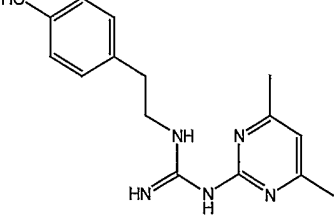
1.15		393.180074	394.2
1.16		370.175323	371.2
1.17		331.164425	332.2
1.18		379.164425	380.2
1.19		317.148776	318.1

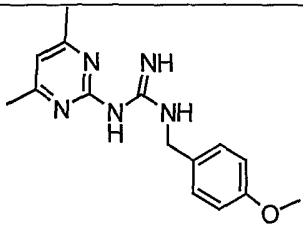
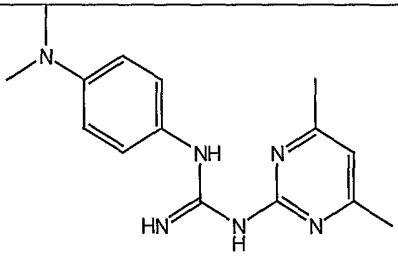
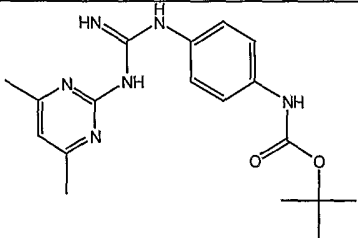
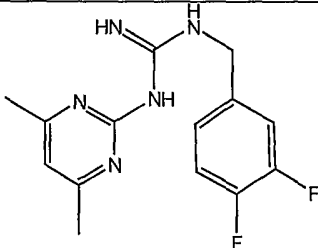
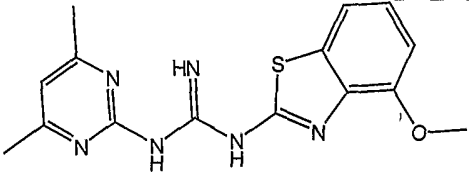
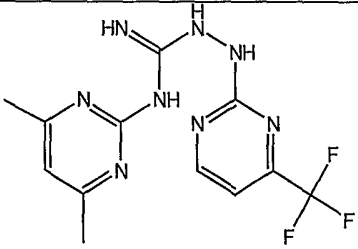
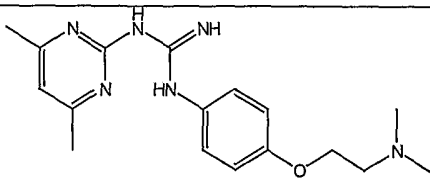
1.20		317.148776	318.1
1.21		356.232442	357.2
1.22		342.216793	343.2
1.23		356.232442	357.2

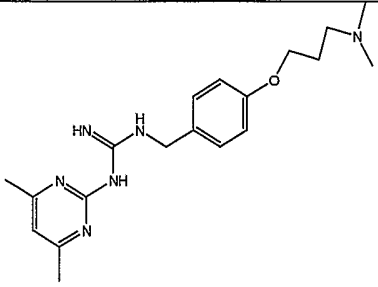
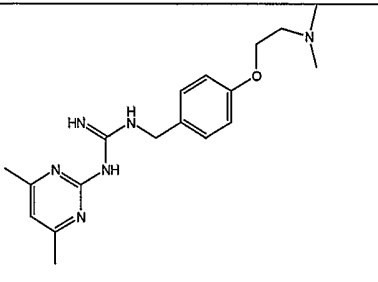
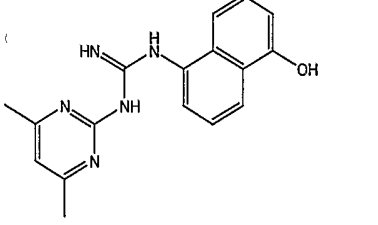
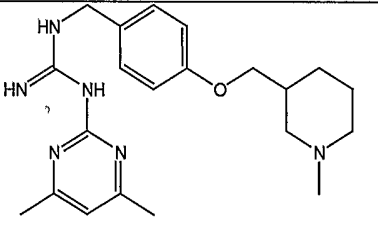
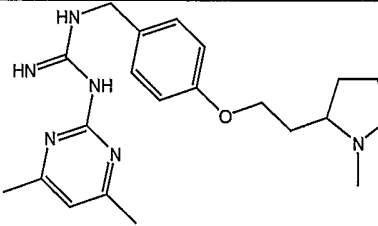
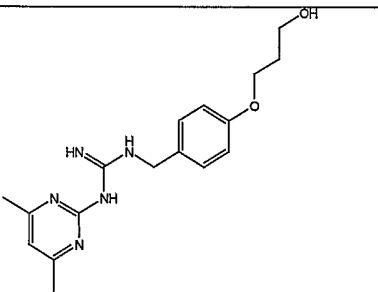
1.24		372.227356	373.2
1.25		372.227356	373.2
1.26		342.216793	343.2
1.27		328.201144	329.2
1.28		328.201144	329.2
1.29		342.216793	343.2

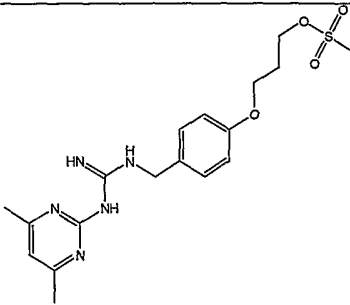
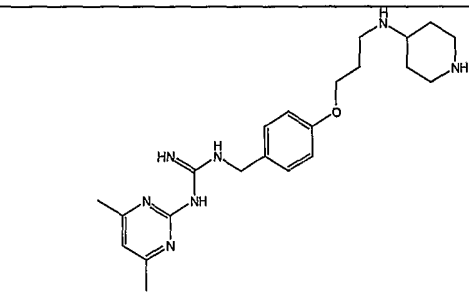
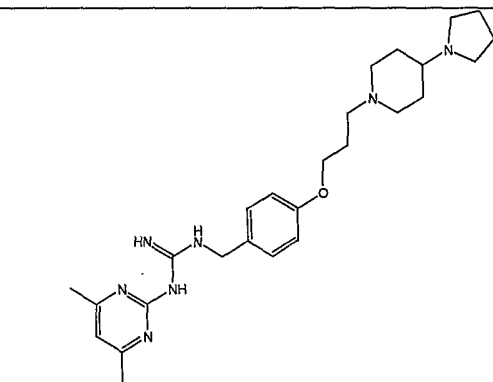
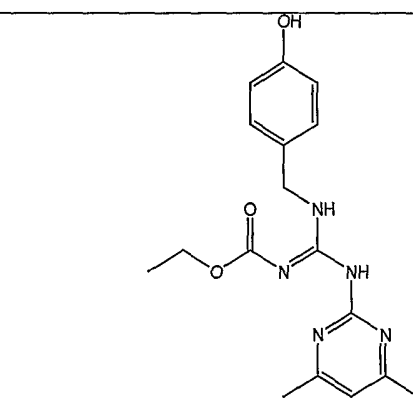
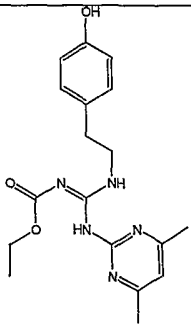
1.30		342.216793	343.2
1.31		358.211707	359.2
1.32		358.211707	359.2
1.33		344.196058	345.2
1.34		344.196058	345.2
1.35		358.211707	359.2
1.36		358.211707	359.2

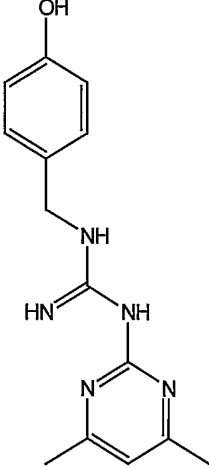
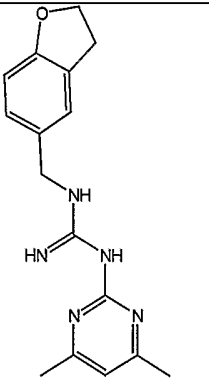
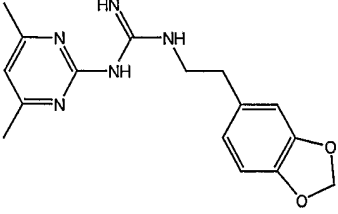
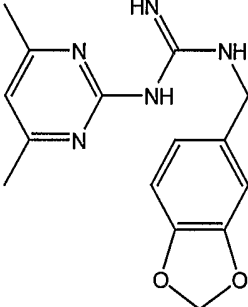
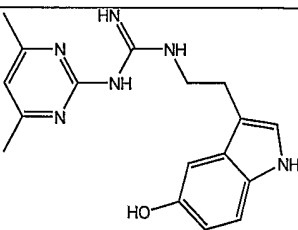
1.37		285.158948	286.2
1.38		377.18516	378.2
1.39		363.169511	364.2
1.40		315.169511	316.2
1.41		301.153862	302.2
1.42		301.153862	302.2

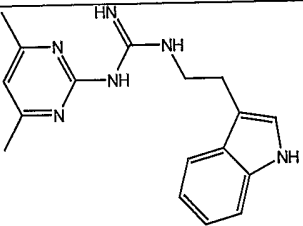
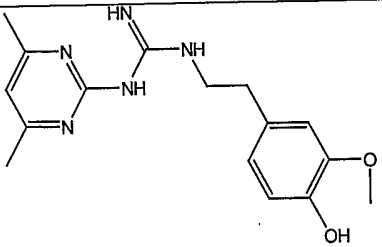
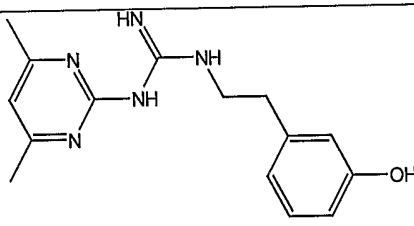
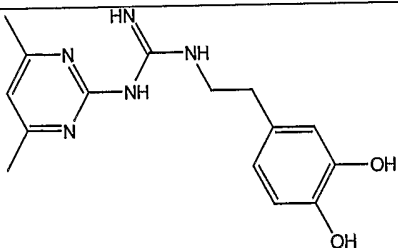
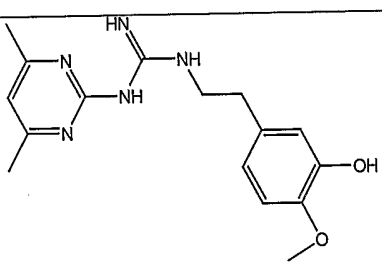
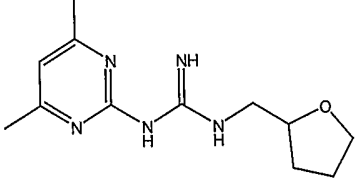
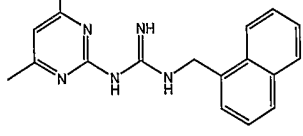
1.43		269.164033	270.2
1.44		361.190246	362.2
1.45		347.174597	348.2
1.46		299.174597	300.2
1.47		16.0312984	17.0
1.48		285.158948	286.2

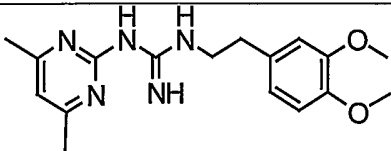
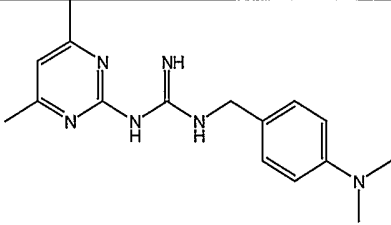
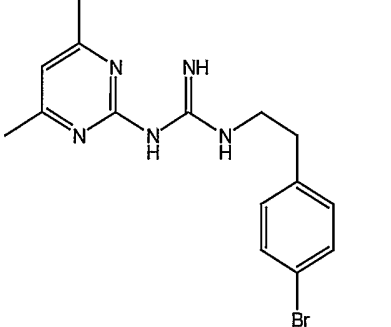
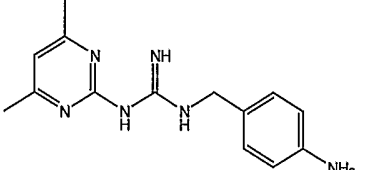
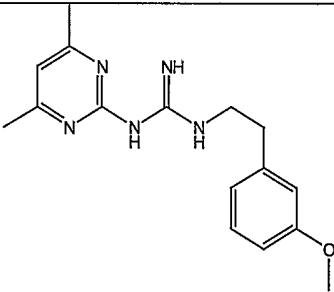
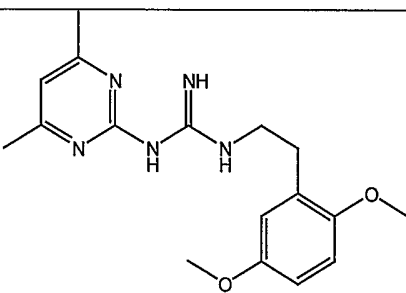
1.49		285.158948	286.2
1.50		284.174931	285.2
1.51		356.196058	357.2
1.52		291.129541	292.1
1.53		328.110617	329.1
1.54		326.121515	327.1
1.55		328.201144	329.2

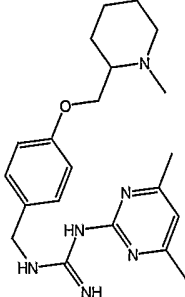
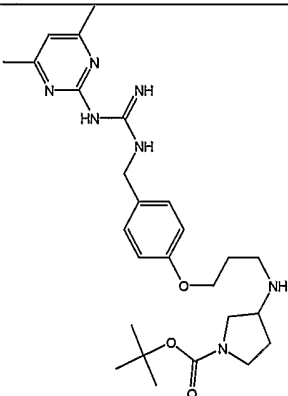
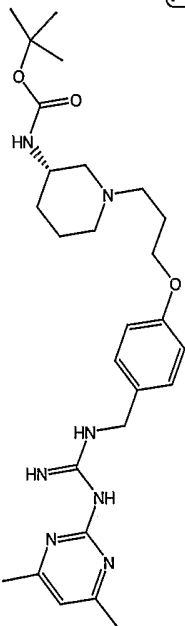
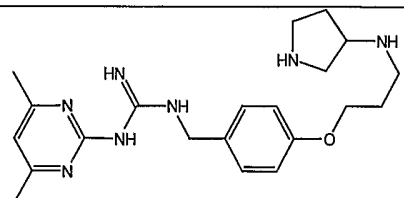
1.56		356.232442	357.2
1.57		342.216793	343.2
1.58		307.143298	308.1
1.59		382.248091	383.2
1.60		382.248091	383.2
1.61		329.18516	330.2

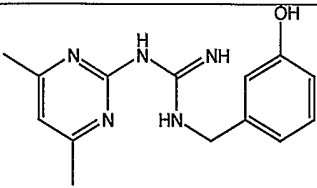
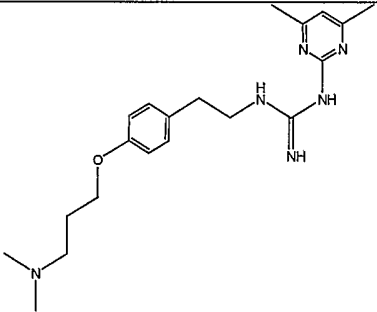
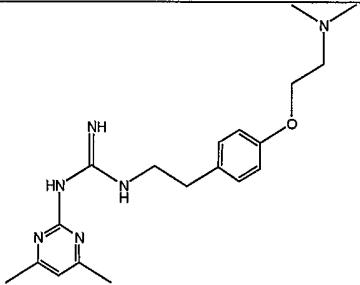
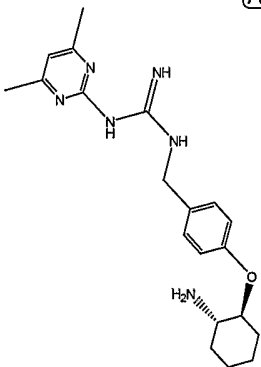
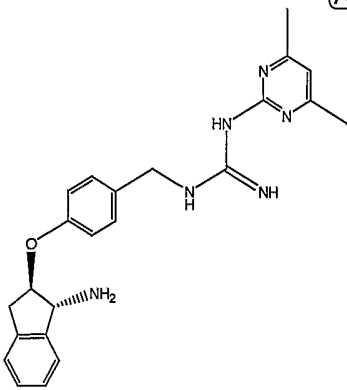
1.62		407.162707	408.2
1.63		411.274638	412.3
1.64		465.321586	466.3
1.65		343.164425	344.2
1.66		357.180074	358.2

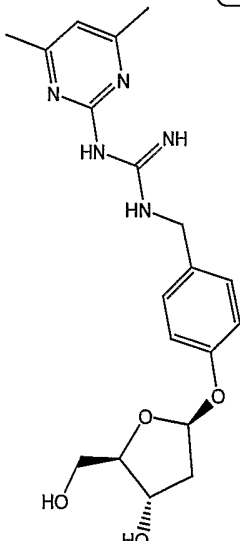
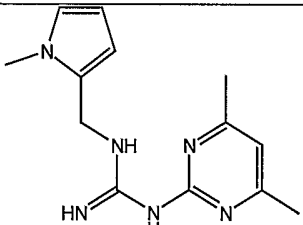
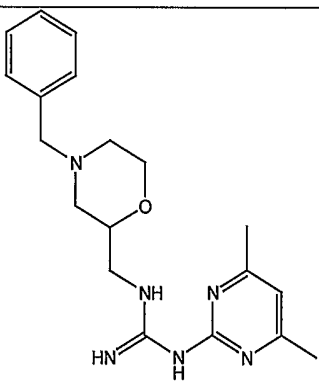
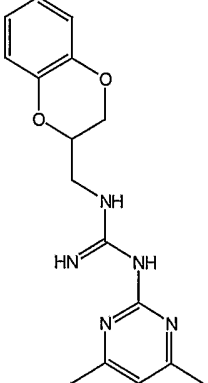
1.67		271.143298	272.1
1.68		297.158948	298.2
1.69		313.153862	314.2
1.70		299.138212	300.1
1.71		324.169845	325.2

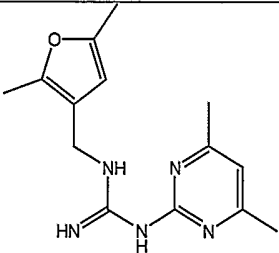
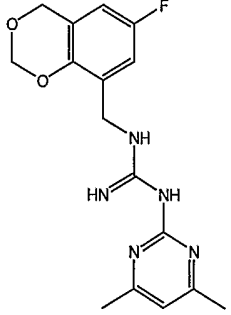
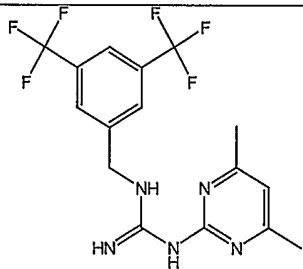
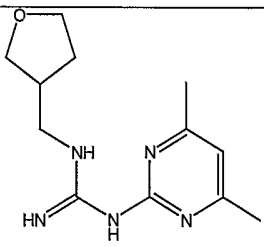
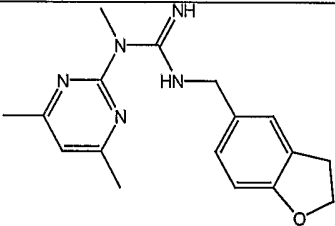
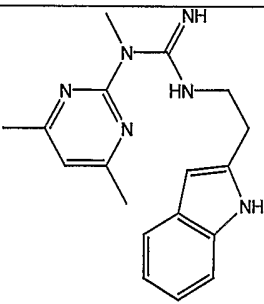
1.72		308.174931	309.2
1.73		315.169511	316.2
1.74		285.158948	286.2
1.75		301.153862	302.2
1.76		315.169511	316.2
1.77		249.158948	250.2
1.78		305.164033	306.2

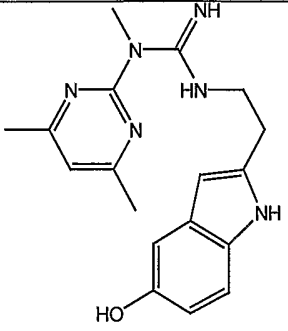
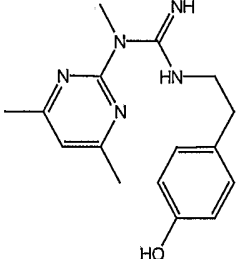
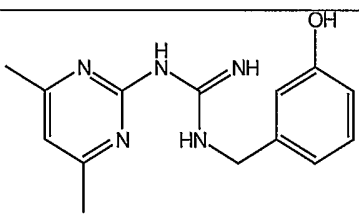
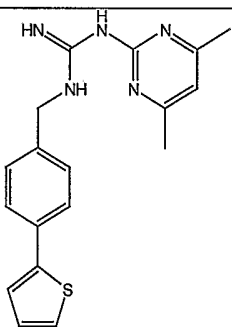
1.79	 <chem>Cc1nc(C)c(NC(=N)NCCc2cc(OC)c(OC)cc2)n1</chem>	329.18516	330.2
1.80	 <chem>Cc1nc(C)c(NC(=N)NCCc2ccc(N(C)C)cc2)n1</chem>	298.19058	299.2
1.81	 <chem>Cc1nc(C)c(NC(=N)NCCc2ccc(Br)cc2)n1</chem>	347.074545	348.1
1.82	 <chem>Cc1nc(C)c(NC(=N)NCCc2ccc(N)cc2)n1</chem>	270.159282	271.2
1.83	 <chem>Cc1nc(C)c(NC(=N)NCCc2cc(OC)ccc2)n1</chem>	299.174597	300.2
1.84	 <chem>Cc1nc(C)c(NC(=N)NCCc2cc(OC)cc(OC)c2)n1</chem>	329.18516	330.2

1.85		382.248091	383.2
1.86		497.311414	498.3
1.87	Abs 	511.327063	512.3
1.88		397.258989	398.3

1.89		271.143298	272.1
1.90		370.248091	371.2
1.91		356.232442	357.2
1.92	(Abs) 	368.232442	369.2
1.93	(Abs) 	402.216793	403.2

1.94	Abs 	387.190637	388.2
1.95		258.159282	259.2
1.96		354.216793	355.2
1.97		313.153862	314.2

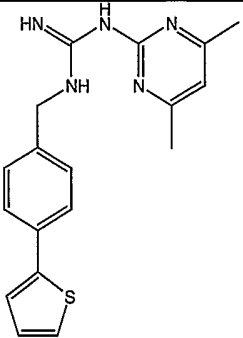
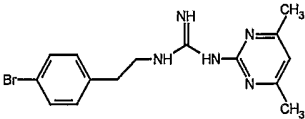
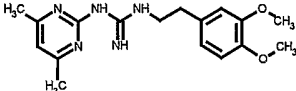
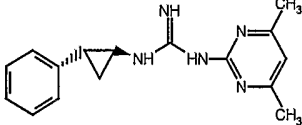
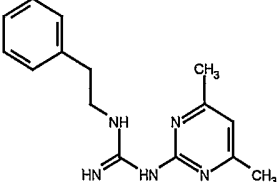
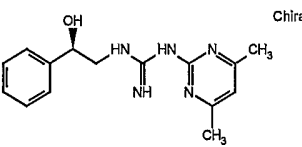
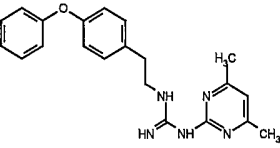
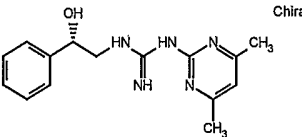
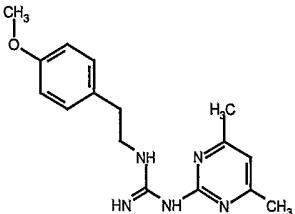
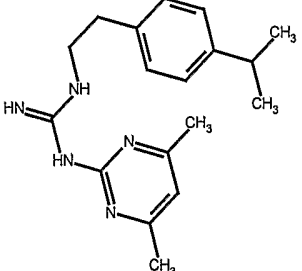
1.98		273.158948	274.2
1.99		331.14444	332.1
1.100		391.123154	392.1
1.101		249.158948	250.2
1.102		311.174597	312.2
1.103		322.19058	323.2

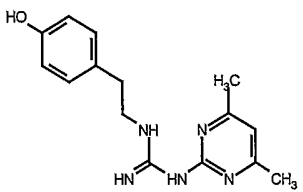
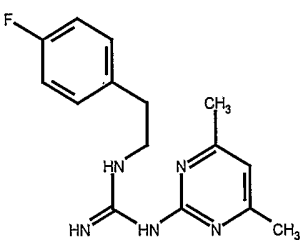
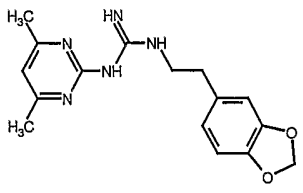
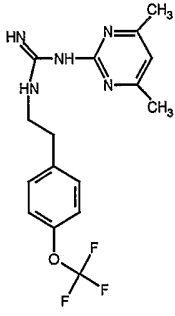
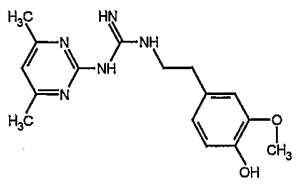
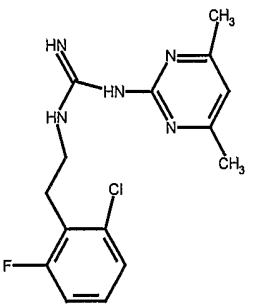
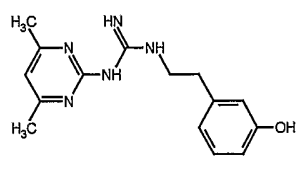
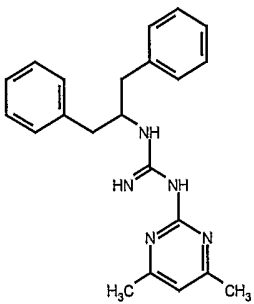
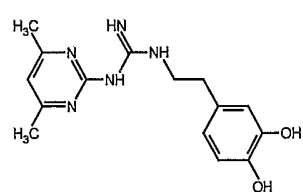
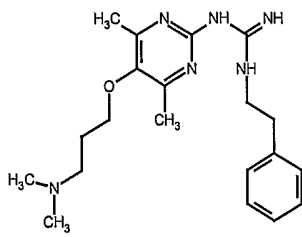
1.104		338.185495	339.2
1.105		299.174597	300.2
1.106		271.143298	272.1
1.107		337.136103	338.1

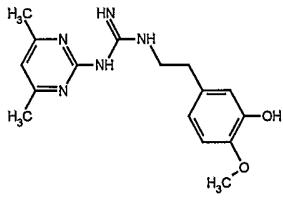
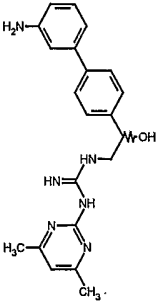
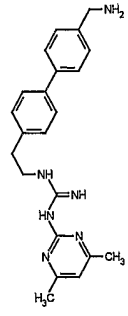
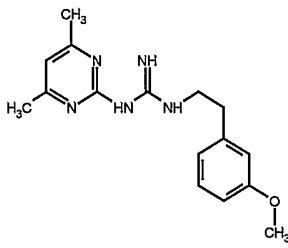
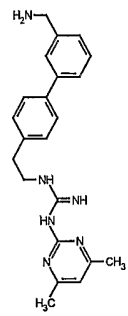
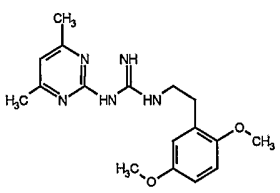
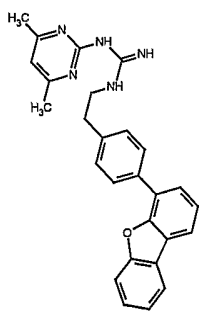
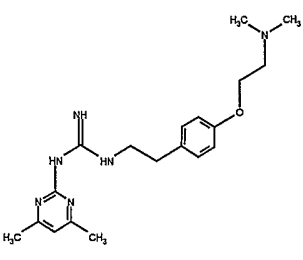
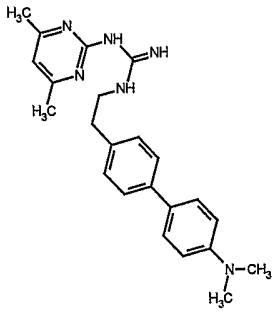
[0097] Further example compounds of the invention are provided in Table 2 below.

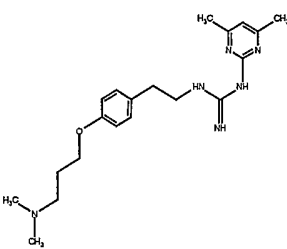
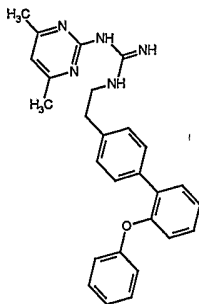
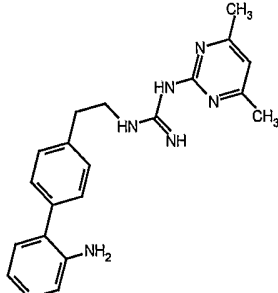
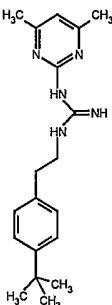
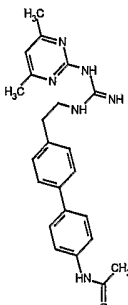
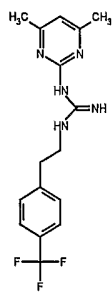
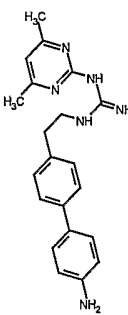
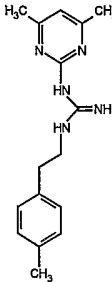
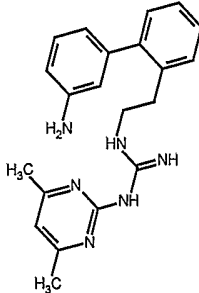
Table 2

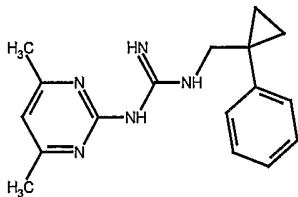
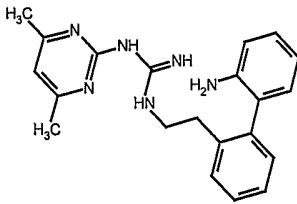
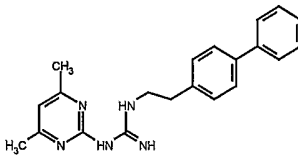
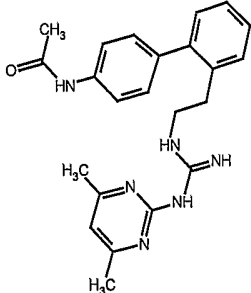
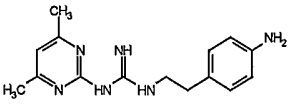
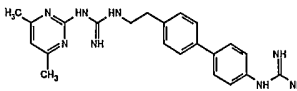
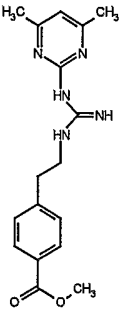
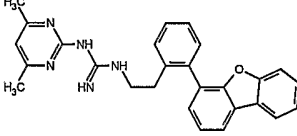
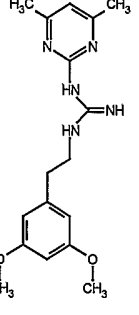
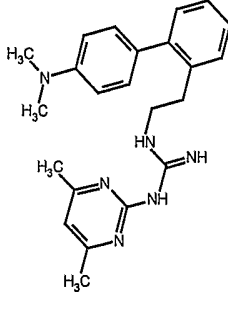
No.	Compound	Synth. Method Ex. No.	No.	Compound	Synth. Method Ex. No.
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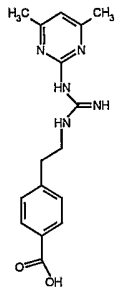
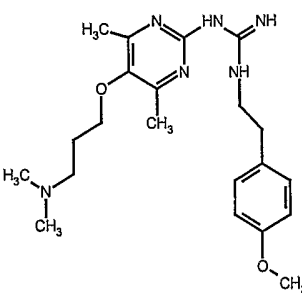
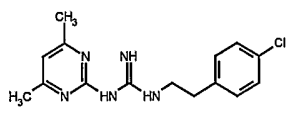
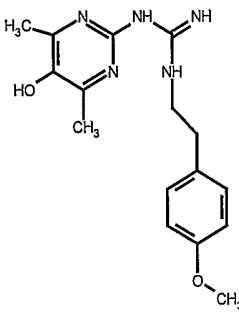
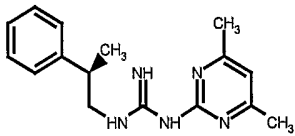
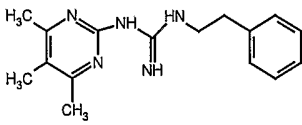
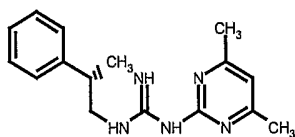
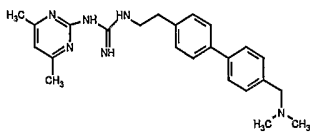
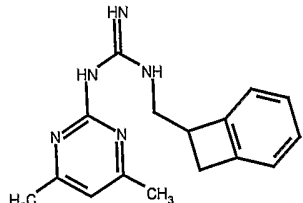
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2.2		8	2.51		8
2.3		8	2.52		8
2.4		1	2.53		8
2.5		8	2.54		8

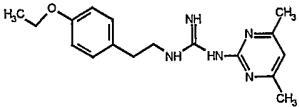
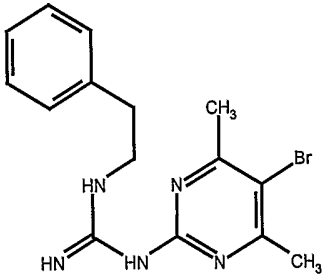
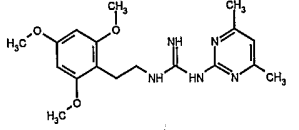
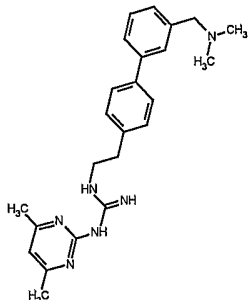
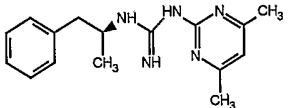
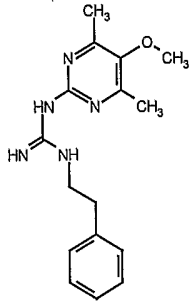
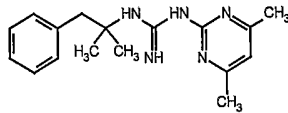
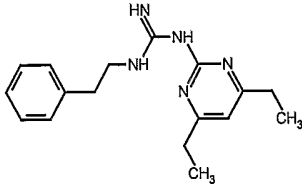
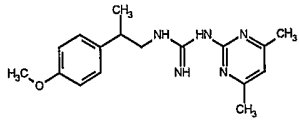
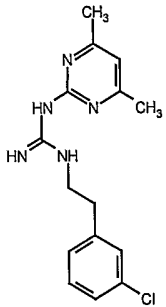
2.6		1	2.55		1
2.7		8	2.56		1
2.8		8	2.57		1
2.9		8	2.58		1
2.10		8	2.59		3

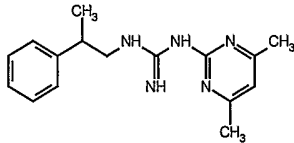
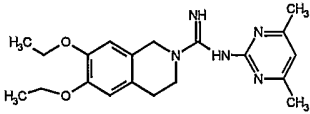
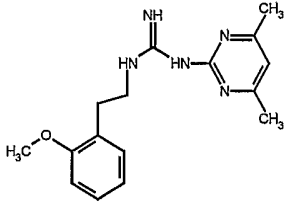
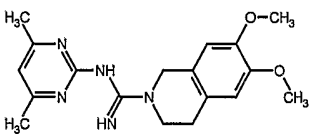
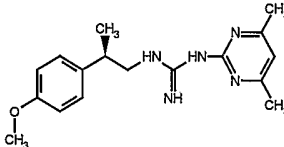
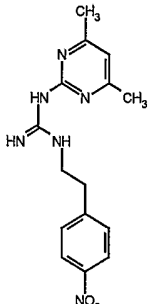
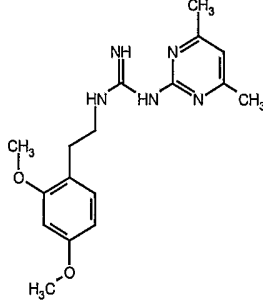
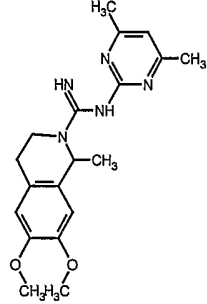
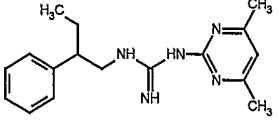
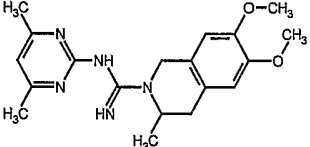
2.11		8	2.60		4
			2.61		4
2.12		8	2.62		4
2.13		8	2.63		4
2.14		8	2.64		6

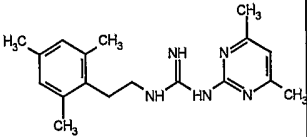
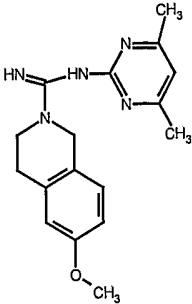
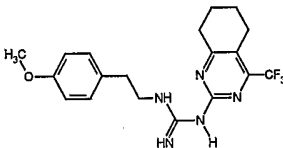
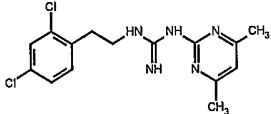
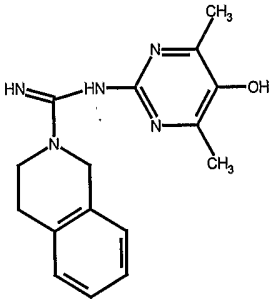
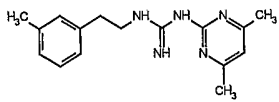
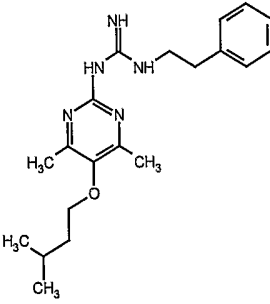
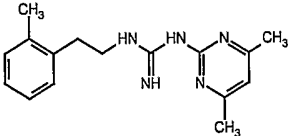
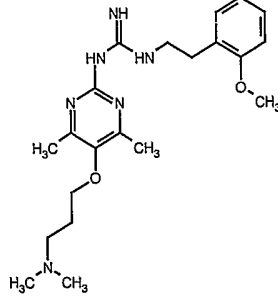
2.15		8	2.65		4
			2.66		4
2.16		8	2.67		4
2.17		1	2.68		4
2.18		1	2.69		5

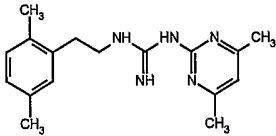
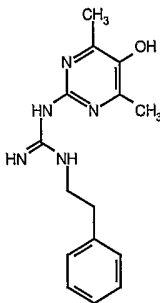
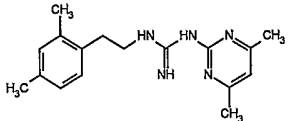
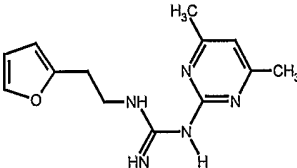
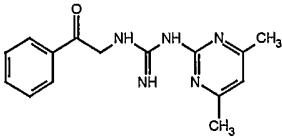
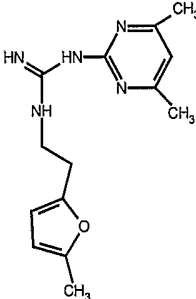
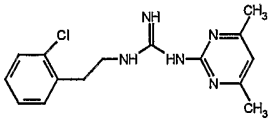
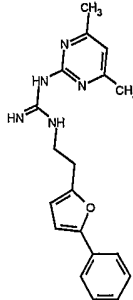
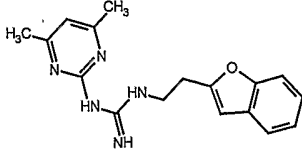
2.19		8	2.70		5
2.20		4	2.71		5
2.21		1	2.72		4
2.22		8	2.73		5
2.23		8	2.74		5

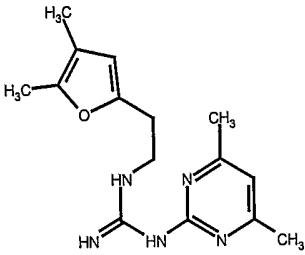
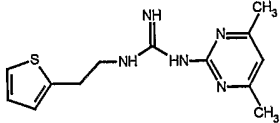
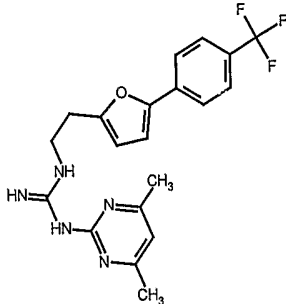
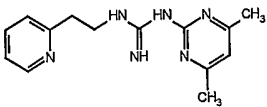
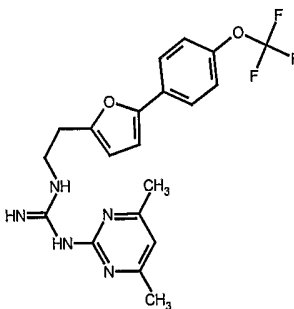
2.24		8	2.75		3
2.25		1	2.76		3
2.26		8	2.77		2
2.27		8	2.78		6
2.28		8			

2.29		8	2.79		3
2.30		8	2.80		6
2.31		8	2.81		3
2.32		8	2.82		3
2.33		8	2.83		1

2.34		8	2.84		2
2.35		8	2.85		2
2.36		8	2.86		1
2.37		8	2.87		2
2.38		8	2.88		2

2.39		8	2.89		2
2.40		2			
2.41		1	2.90		2
2.42		1	2.91		3
2.43		1	2.92		3

2.44		1	2.93		2
2.45		1	2.94		1
2.46		1	2.95		1
2.47		1	2.96		1
			2.97		1

			2.98		1
2.48		1	2.99		1
2.49		1	2.100		1

[0098] It is appreciated that certain features of the invention, which are, for clarity, described in the context of separate embodiments, may also be provided in combination in a single embodiment. Conversely, various features of the invention which are, for brevity, described in the context of a single embodiment, may also be provided separately or in any suitable subcombination.

[0099] As used herein, the term “alkyl” is meant to refer to a saturated hydrocarbon group which is straight-chained or branched. Example alkyl groups include methyl (Me), ethyl (Et), propyl (*e.g.*, *n*-propyl and isopropyl), butyl (*e.g.*, *n*-butyl, isobutyl, *t*-butyl), pentyl (*e.g.*, *n*-pentyl, isopentyl, neopentyl), and the like. An alkyl group can contain from 1 to about 20, from 2 to about 20, from 1 to about 10, from 1 to about 8, from 1 to about 6, from 1 to about 4, or from 1 to about 3 carbon atoms.

[0100] As used herein, “alkenyl” refers to an alkyl group having one or more double carbon-carbon bonds. Example alkenyl groups include ethenyl, propenyl, and the like.

[0101] As used herein, “alkynyl” refers to an alkyl group having one or more triple carbon-carbon bonds. Example alkynyl groups include ethynyl, propynyl, and the like.

[0102] As used herein, “haloalkyl” refers to an alkyl group having one or more halogen substituents. Example haloalkyl groups include CF₃, C₂F₅, CHF₂, CCl₃, CHCl₂, C₂Cl₅, and the like. An alkyl group in which all of the hydrogen atoms are replaced with halogen atoms can be referred to as “perhaloalkyl.”

[0103] As used herein, “aryl” refers to monocyclic or polycyclic aromatic hydrocarbons such as, for example, phenyl, naphthyl, anthracenyl, phenanthrenyl, indanyl, indenyl, and the like. In some embodiments, aryl groups have from 6 to about 20 carbon atoms.

[0104] As used herein, “cycloalkyl” refers to non-aromatic hydrocarbons including cyclized alkyl, alkenyl, and alkynyl groups. Cycloalkyl group can include mono-, bi- or poly-cyclic ring systems. Example cycloalkyl groups include cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl, cycloheptyl, cyclopentenyl, cyclohexenyl, cyclohexadienyl, cycloheptatrienyl, norbornyl, norpinyl, norcarnyl, adamantyl, and the like. Also included in the definition of cycloalkyl are moieties that have one or more aromatic rings fused (i.e., having a bond in common with) to the cycloalkyl ring, for example, benzo derivatives of pentane, hexane, and the like. Cycloalkyl groups can have from 3 to 7, 3 to 6, 3 to 5, or 3 to 4 ring-forming carbon atoms.

[0105] As used herein, “heteroaryl” groups are monocyclic and polycyclic aromatic hydrocarbons that have at least one heteroatom ring member such as sulfur, oxygen, or nitrogen. Heteroaryl groups include, without limitation, pyridyl, pyrimidinyl, pyrazinyl, pyridazinyl, triazinyl, furyl (furanyl), quinolyl, isoquinolyl, thienyl, imidazolyl, thiazolyl, indolyl, pyrrol (pyrrolyl), oxazolyl, benzofuryl, benzothienyl, benzthiazolyl, isoxazolyl, pyrazolyl, triazolyl, tetrazolyl, indazolyl, 1,2,4-thiadiazolyl, isothiazolyl, benzothienyl, purinyl, carbazolyl, benzimidazolyl, 2,3-dihydrobenzofuranyl, 2,3-dihydrobenzothienyl, 2,3-dihydrobenzothienyl-S-oxide, 2,3-dihydrobenzothienyl-S-dioxide, benzoxazolin-2-on-yl, indolinyl, benzodioxolanyl (benzo[1,3]dioxolyl), and the like. In some embodiments, heteroaryl groups can have from 1 to about 20 carbon atoms, and in further embodiments from about 3 to about 20

carbon atoms. In some embodiments, heteroaryl groups have 1 to about 4, 1 to about 3, or 1 to 2 heteroatoms.

[0106] As used herein, “heterocycloalkyl” refers to cycloalkyl groups wherein one or more of the ring-forming carbon atoms is replaced by a heteroatom such as an O, N, or S atom. Also included in the definition of heterocycloalkyl are moieties that have one or more aromatic rings fused (i.e., having a bond in common with) to the nonaromatic heterocyclic ring, for example phthalimidyl, naphthalimidyl pyromellitic diimidyl, phthalanyl, and benzo derivatives of saturated heterocycles such as indolene and isoindolene groups.

[0107] As used herein, “biaryl” refers to aryl substituted by aryl. An example biaryl compound is biphenyl.

[0108] As used herein “biheteroaryl” refers to heteroaryl substituted by heteroaryl. An example biheteroaryl is bipyridyl.

[0109] As used herein, “arylheteroaryl” refers to heteroaryl substituted by aryl. An example arylheteroaryl is phenylfuranyl.

[0110] As used herein, “heteroarylaryl” refers to aryl substituted by heteroaryl. An example heteroarylaryl is tetrazolylphenyl.

[0111] As used herein, “halo” or “halogen” includes fluoro, chloro, bromo, and iodo.

[0112] As used herein, “alkoxy” refers to an -O-alkyl group. Example alkoxy groups include methoxy, ethoxy, propoxy (*e.g.*, n-propoxy and isopropoxy), t-butoxy, and the like. Alkoxy groups can have, for example, from 1 to about 10, 1 to about 8, 1 to about 6, 1 to about 4, or 1 to about 3 carbon atoms.

[0113] As used herein, “thioalkoxy” refers to an alkoxy group in which the O atom is replaced by an S atom.

[0114] As used herein, “aryloxy” refers to an -O-aryl group. An example aryloxy group is phenoxy.

[0115] As used herein, “thioaryloxy” refers to an aryloxy group in which the O atom is replaced by an S atom.

[0116] As used herein, “aralkyl” refers to an alkyl moiety substituted by an aryl group. Example aralkyl groups include benzyl and naphthylmethyl groups. In some embodiments, arylalkyl groups have from 7 to 11 carbon atoms.

[0117] As used herein, “aralkoxy” refers to an alkoxy group substituted by an aryl group.

[0118] As used herein, “mercapto” refers to SH.

[0119] As used herein, “substituted” indicates that at least one hydrogen atom of a chemical group is replaced by a non-hydrogen moiety. Example substituents include F, Cl, Br, I, C₁-C₆ alkyl, C₁-C₆ alkenyl, C₁-C₆ alkynyl, haloalkyl, NR'R'', N₃, NO₂, CN, CNO, CNS, C(=O)OR', R'CO, R'C(=O)O, R'CONR', R'R''NCO, ureido, OR', SR', SO₂-alkyl, SO₂-aryl, and SO₂-NR'R', wherein R' and R'' are each, independently, H or C₁-C₆ alkyl. Alternatively, R' and R'' may be combined, with the nitrogen to which they are attached, to form a 5- to 7- membered heterocyclic ring, for example pyrrolidinyl, piperidinyl, morpholinyl, piperazinyl, and N-methylpiperazinyl. When a chemical group herein is “substituted” it may have up to the full valance of substitution, provided the resulting compound is a stable compound or stable structure; for example, a methyl group may be substituted by 1, 2, or 3 substituents, a methylene group may be substituted by 1 or 2 substituents, a phenyl group may be substituted by 1, 2, 3, 4, or 5 substituents, and the like.

[0120] The compounds described herein can be asymmetric (e.g., having one or more stereocenters). All stereoisomers, such as enantiomers and diastereomers, are intended unless otherwise indicated. Compounds of the present invention that contain asymmetrically substituted carbon atoms can be isolated in optically active or racemic forms. Methods on how to prepare optically active forms from optically active starting materials are known in the art, such as by resolution of racemic mixtures or by stereoselective synthesis.

[0121] Compounds of the invention can also include tautomeric forms, such as keto-enol tautomers. Tautomeric forms can be in equilibrium or sterically locked into one form by appropriate substitution.

[0122] Compounds of the invention can also include all isotopes of atoms occurring in the intermediates or final compounds. Isotopes include those atoms having the same atomic number but different mass numbers. For example, isotopes of hydrogen include tritium and deuterium.

[0123] The present invention also includes pharmaceutically acceptable salts of the compounds described herein. As used herein, “pharmaceutically acceptable salts” refer to derivatives of the disclosed compounds wherein the parent compound is modified by converting an existing acid or base moiety to its salt form. Examples of pharmaceutically acceptable salts include, but are not limited to, mineral or organic acid salts of basic residues such as amines; alkali or organic salts of acidic residues such as carboxylic acids;

and the like. The pharmaceutically acceptable salts of the present invention can be synthesized by conventional chemical methods from the compounds of Formula I which contain a basic or acidic moiety. Generally, the salts can be prepared by reacting the free base or acid with stoichiometric amounts or with an excess of the desired salt-forming inorganic or organic acid or base in a suitable solvent or various combinations of solvents. Lists of suitable salts are found in *Remington's Pharmaceutical Sciences*, 17th ed., Mack Publishing Company, Easton, Pa., 1985, p. 1418, the disclosure of which is hereby incorporated by reference in its entirety.

Synthesis

[0124] Compounds of the invention, including salts and solvates thereof, can be prepared using known organic synthesis techniques and can be synthesized according to any of numerous possible synthetic routes.

[0125] The reactions for preparing compounds of the invention can be carried out in suitable solvents which can be readily selected by one of skill in the art of organic synthesis. Suitable solvents can be substantially nonreactive with the starting materials (reactants), the intermediates, or products at the temperatures at which the reactions are carried out, i.e., temperatures which can range from the solvent's freezing temperature to the solvent's boiling temperature. A given reaction can be carried out in one solvent or a mixture of more than one solvent. Depending on the particular reaction step, suitable solvents for a particular reaction step can be selected.

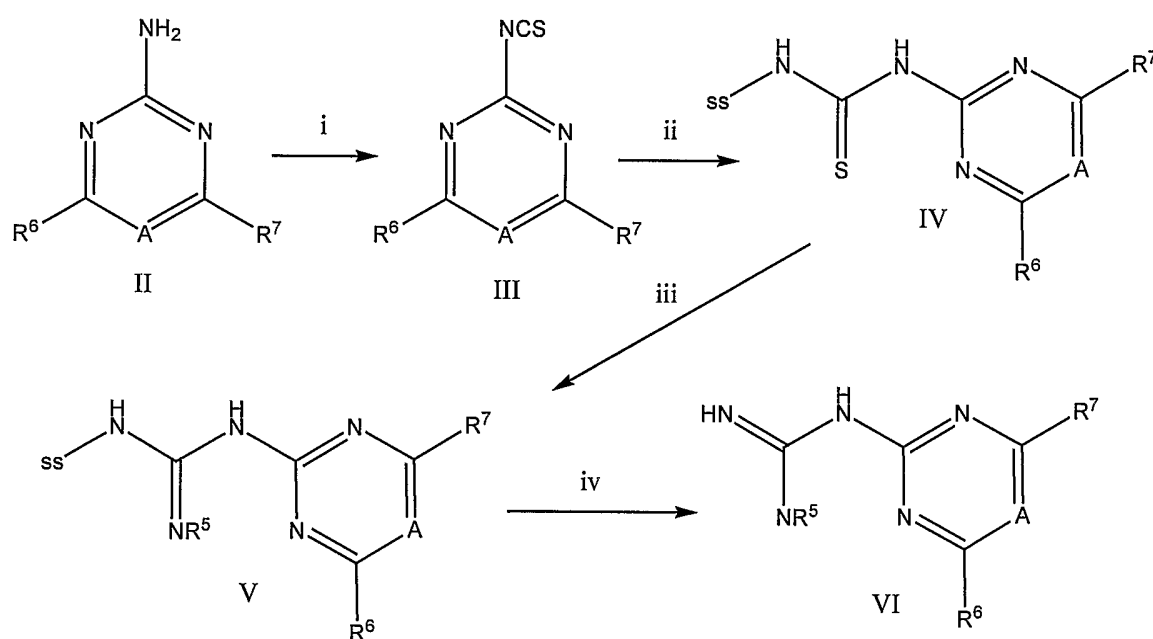
[0126] Preparation of compounds of the invention can involve the protection and deprotection of various chemical groups. The need for protection and deprotection, and the selection of appropriate protecting groups can be readily determined by one skilled in the art. The chemistry of protecting groups can be found, for example, in T.W. Green and P.G.M. Wuts, *Protective Groups in Organic Synthesis*, 3rd. Ed., Wiley & Sons, Inc., New York (1999), which is incorporated herein by reference in its entirety.

[0127] Reactions can be monitored according to any suitable method known in the art. For example, product formation can be monitored by spectroscopic means, such as nuclear magnetic resonance spectroscopy (e.g., ^1H or ^{13}C) infrared spectroscopy, spectrophotometry (e.g., UV-visible), or mass spectrometry, or by chromatography such as high performance liquid chromatography (HPLC) or thin layer chromatography.

[0128] Compounds of the invention can be prepared by solid phase or solution methods such as shown in the Schemes below. According to Scheme 1, a pyrimidinyl or

triazinyl amine (II), available commercially or readily made by methods known in the art, can be converted to its corresponding isothiocyanate derivative (III) by reaction with, for example, a C=S donor (i) such as di-2-pyridylthionocarbonate. The isothiocyanate compound can be attached to solid support (ss) (ii) by means known in the art to form a thiourea linked pyrimidinyl or triazinyl compound (IV). A guanidinyll linkage can be formed from the thiourea linkage by reacting IV with a primary amine such as, for example, R^5NH_2 (iii). The resulting guanidinyll compound (V) can be cleaved from the resin by methods and reagents well known in the art. Typical cleaving reagents (iv) include acidic solutions such as, for example, 35% TFA/ CH_2Cl_2 . The resulting guanidine VI can be further derivatized by methods known in the art and reactions described herein.

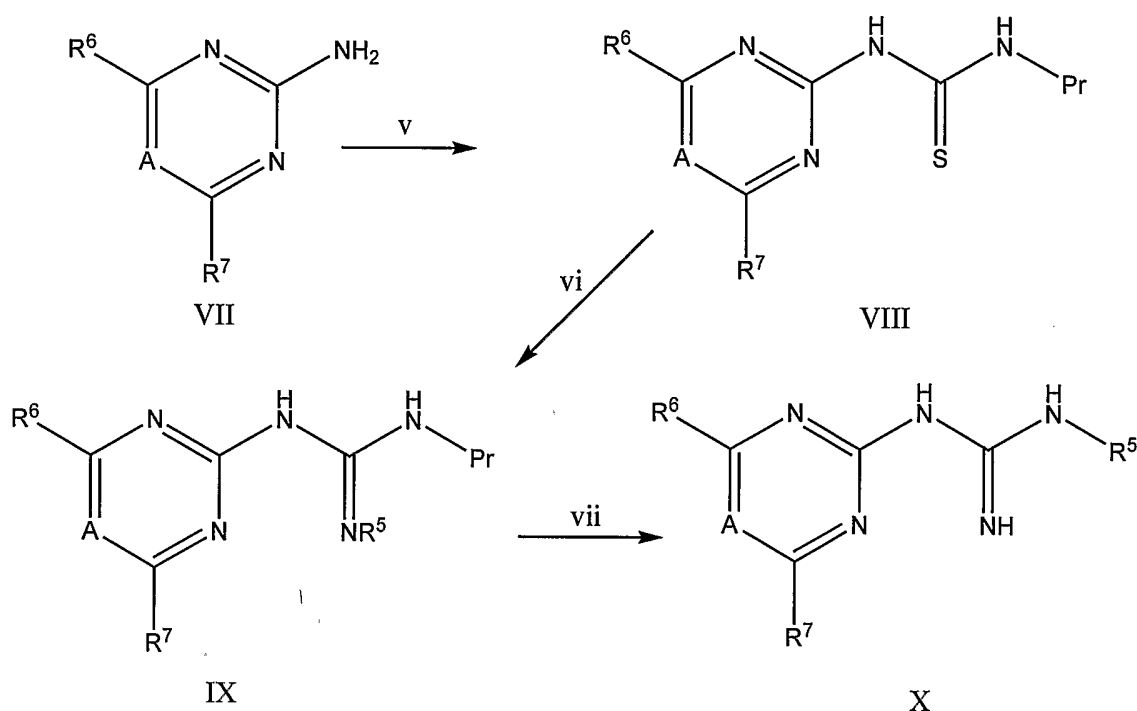
Scheme 1



[0129] Another suitable synthesis of guanidines is provided in Scheme 2 below. A pyrimidinyl or triazinyl amine (VII), available commercially or readily made by methods known in the art, can be converted to its corresponding thiourea (VIII) by reaction with an isothiocyanate (v) (or protected version thereof, e.g. Pr-isothiocyanate where Pr is a protecting group such as Fmoc, benzoyl, benzyloxycarbonyl (Cbz), and the like). The thiourea VIII can be further reacted with a primary amine (vi) to produce the protected

guanidinyll compound IX which can be optionally deprotected by standard methods to yield guanidinyll compounds of Formula X. Suitable deprotecting agents (vii) include, for example, acids or bases such as PS-Trisamine or HCl. Other suitable deprotecting agents include reducing agents such as palladium (Pd/C and H₂).

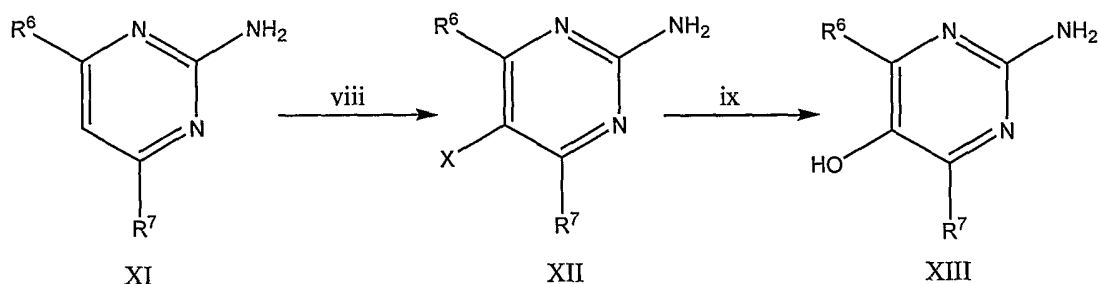
Scheme 2



[0130] Scheme 3 below illustrates the preparation of 5-substituted 2-aminopyrimidines useful as intermediates in the preparation of compounds of the invention. A 2-aminopyrimidine of Formula XI can be reacted with a halogenating reagent (viii) to prepare the 5-halo-2-aminopyrimidine of Formula XII. Suitable halogenating reagents are well known in the art and include, for example, Br₂. The halogen (X) can be replaced by a hydroxy group by reaction of a compound of Formula XII with a suitable hydroxylating reagent (ix) such as Ba(OH)₂ to prepared the 5-hydroxy compound depicted in Formula XIII. The 5-hydroxy compounds can be used according to the syntheses of Schemes 1 and 2 for the preparation of guanidinyll compounds of the invention.

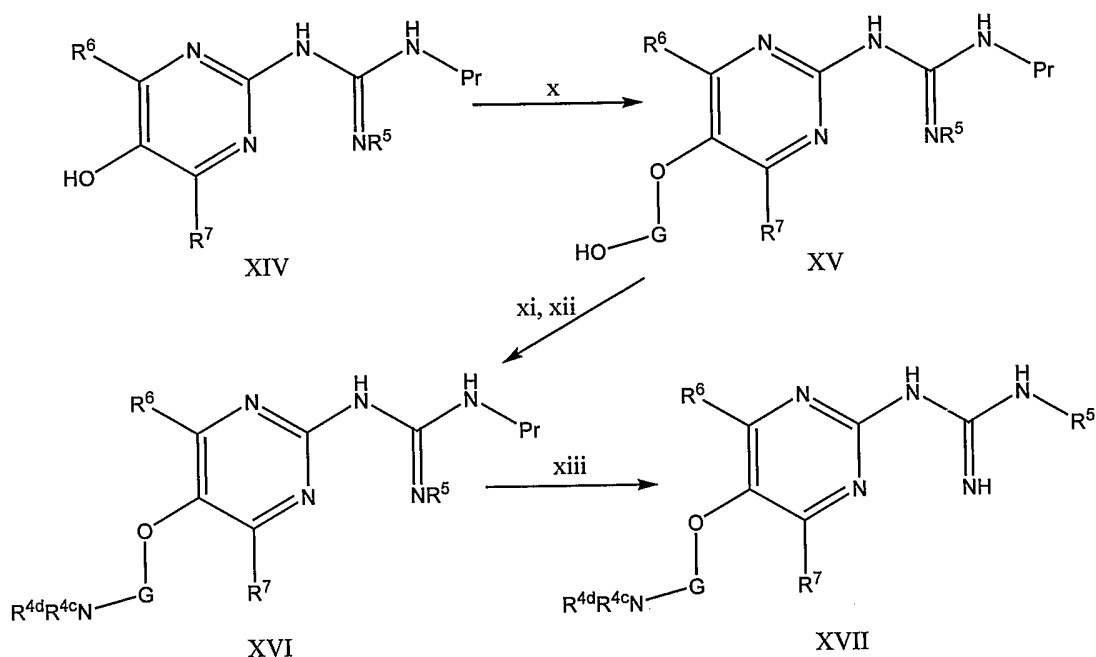
[0131]

Scheme 3



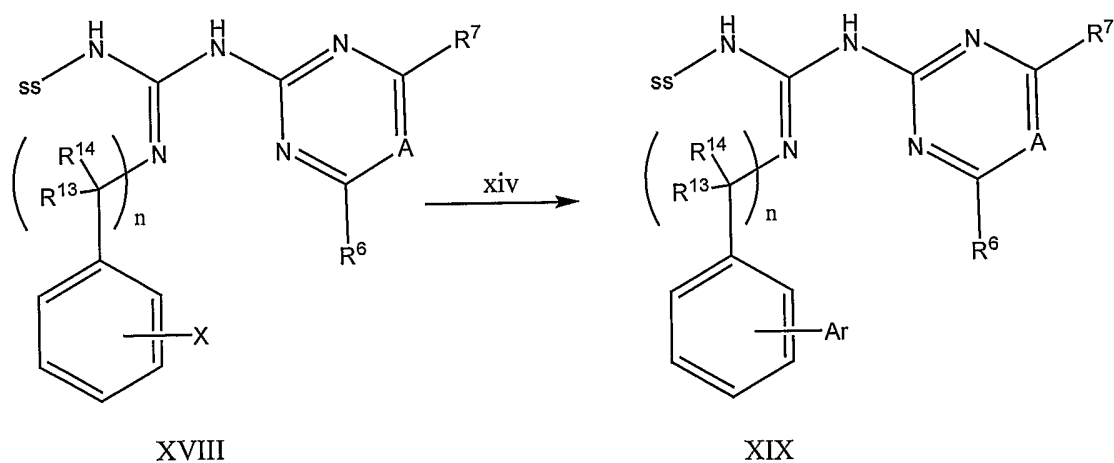
[0132] Pyrimidinyl compounds of the invention can be further modified at the 5-position by methods provided in Scheme 4 below. 5-Hydroxy compounds of Formula XIV can be reacted, for example, with reagents of Formula X-G-OH (x), where X is halo and G is an alkylene group (e.g., $-(\text{CR}^{4a}\text{R}^{4b})_n-$) to prepare hydroxy compounds of Formula XV. reagents of Formula X-G-OH can be obtained commercially or readily prepared according to methods known in the art. The resulting hydroxy compound of Formula XV can be converted to an amine of Formula XVI by reaction with a hydroxy activating group (xi) such as a mesyl or tosyl chloride followed by reaction with a primary or secondary amine of Formula $\text{NHR}^{4c}\text{R}^{4d}$ (xii). The resulting amine compound of Formula XVI can then be deprotected by reaction with a deprotecting agent (xiii) according to standard methods and/or further derivatized to produce compounds of the present invention.

Scheme 4

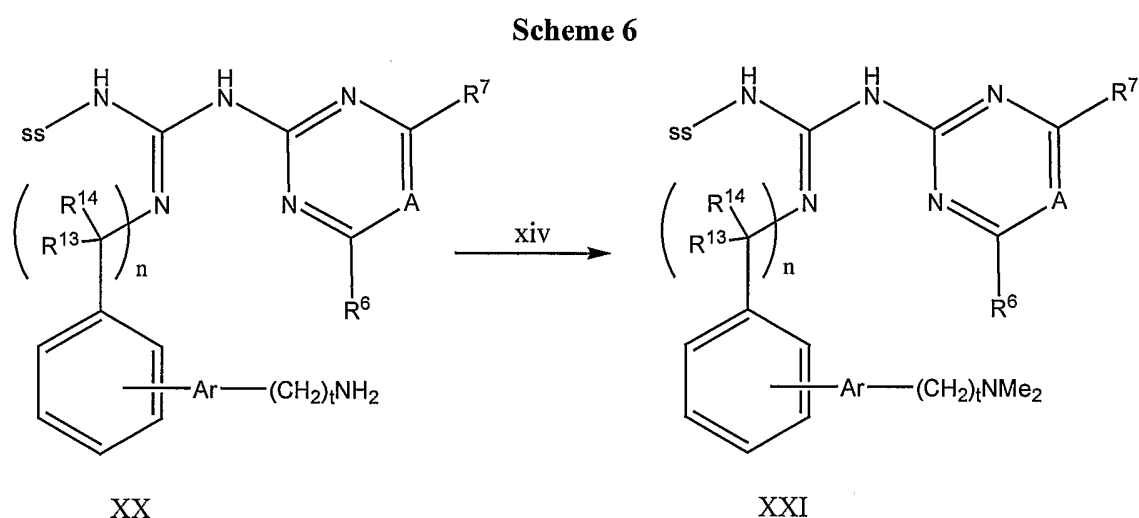


[0133] Scheme 5 below provides a general method for preparing further substituted guanidines of the present invention. A guanidinyln resin of Formula XVIII, where X is halo, can be converted to an aromatic substituted guanidinyln resin of Formula XIX using a Suzuki coupling reagent of Formula $\text{ArB}(\text{OH})_2$ (xiv) where Ar is an optionally substituted aromatic moiety. Conditions for Suzuki couplings are well known in the art. The resulting aromatic substituted guanidinyln can be cleaved from the resin using any of numerous cleaving reagents and conditions known in the art to produce compounds of the present invention.

Scheme 5



[0134] Scheme 6 below provides a general method for preparing further substituted guanidines of the present invention. A guanidinyln resin of Formula XX, where Ar is substituted or unsubstituted aromatic, can be converted to the guanidinyln resin of Formula XXI by reductive amination. The reductive amination reagent (xiv) can be any of numerous reagents known in the art such as formaldehyde in the presence of NaBH_3CN . The resulting guanidinyln moiety can be cleaved from the resin using any of numerous cleaving reagents and conditions known in the art to produce compounds of the present invention.



[0135] Aromaticalkyleneamines as intermediates for preparing compounds of the present invention can be prepared, for example, by combining aromatic aldehyde (commercially available, e.g., benzaldehyde) with ammonium acetate in nitromethane to form a corresponding nitroalkene (e.g., Ph-CH=CH-NO_2). The nitroalkene can then be reduced with a reducing agent such as lithium aluminum hydride (LAH) to produce the corresponding aromaticalkyleneamine, which can be used in preparation of guanidinyln compounds of the invention according to, for example, Schemes 1 and 2.

[0136] N-Alkylation of the guanidinyln moiety in compounds of the present invention can be carried out by any suitable alkylation method known in the art. Example alkylating reagents include methyl iodide, ethyl iodide, ethyl bromide, isopropyl iodide, hexyl iodide, benzyl bromide, allyl iodide, and the like.

Methods of Use

[0137] The compounds described herein can be useful in modulating the activity of an infectious agent, such as a virus or other disease-causing agent. Modulation refers to an ability to increase or decrease (inhibit) the activity of an infectious agent. In some embodiments, infectious activity is decreased or inhibited. Methods of measuring activity of infectious agents are well known in the art and include, for example, determination of virus titer levels in a medium, cell, or infected host and determination of relative levels of nucleic acids or proteins in a medium, cell, or host that are characteristic of infection by the infectious agent.

[0138] The present compounds can inhibit translation of nucleic acids, such as translation mediated by an internal ribosome entry site (IRES). Without being bound to theory, it is believed that binding of the present compounds to an IRES blocks IRES-mediated translation. Because numerous viral agents and other agent contain IRES, the present compounds are useful in inhibiting viral replication.

[0139] The compounds described herein can be useful in treating viral infections, such as infections caused by viruses that can replicate in a medium, cell, or host via a mechanism involving directly or indirectly an internal ribosome entry site (IRES). Accordingly, administration of one or more compounds of the present invention to patients having a viral infection or prone to contracting a viral infection can result in prevention of infection by the viral agent, elimination of infection, or lessening of the severity of infection.

[0140] Example viruses that can undergo IRES-mediated replication include, for example, a variety of picornaviruses such as poliovirus, rhinovirus, hepatitis A virus, coxsackievirus, and other members of the picornaviridae group. There are numerous other viruses not belonging to the picornaviral group that also use internal ribosome entry for translation. An example is hepatitis C virus (a flavivirus) and infectious bronchitis virus (a coronavirus). In addition, mRNAs encoding reverse transcriptase of duck and human hepatitis B virus, vesicular stomatitis virus NS protein, adenovirus DNA polymerase, and Sendai virus P/C protein have been shown to use internal initiation of ribosome entry. Further still, internal ribosome entry has been shown for translation in the retrovirus family (e.g., murine leukemia virus, the pestivirus family, and plant poty viruses).

[0141] Suitable assays to screen for agents that block IRES element activity can be carried out by constructing a dicistronic mRNA characterized by the presence of two different reporter genes, wherein the translation of one gene is under IRES element control and translation of the other gene is under the control of the host-cell cap structure and

cellular 5'-UTR sequence. Such a construct makes it possible to identify agents, using either cell-free or cell-based assays, that block IRES element activity without adversely affecting the process that cells use to initiate translation of their own mRNA. This and other assays for detecting binding of compounds to IRES and blocking of IRES-mediated translation are described, for example, in U.S. Pat. No. 6,579,674, which is incorporated herein by reference in its entirety. An example assay is provided in Example 10 below.

[0142] Compounds of the invention can also be used as a diagnostic tools to determine whether a particular nucleic acid, such as an RNA, shows IRES-mediated translation.

Pharmaceutical Compositions, Dosage, and Administration

[0143] When employed as pharmaceuticals, the compounds of Formula I can be administered in the form of pharmaceutical compositions. These compositions can be administered by a variety of routes including oral, rectal, transdermal, subcutaneous, intravenous, intramuscular, and intranasal, and can be prepared in a manner well known in the pharmaceutical art.

[0144] Pharmaceutical compositions of the invention contain, as the active ingredient, one or more of the compounds of Formula I above in combination with one or more pharmaceutically acceptable carriers. In making the compositions of the invention, the active ingredient is typically mixed with a pharmaceutically acceptable carrier, diluted by a pharmaceutically acceptable carrier or enclosed within such a carrier in the form of, for example, a capsule, sachet, paper, or other container. When the pharmaceutically acceptable carrier serves as a diluent, it can be a solid, semi-solid, or liquid material, which acts as a vehicle, carrier or medium for the active ingredient. Thus, the compositions can be in the form of tablets, pills, powders, lozenges, sachets, cachets, elixirs, suspensions, emulsions, solutions, syrups, aerosols (as a solid or in a liquid medium), ointments containing, for example, up to 10% by weight of the active compound, soft and hard gelatin capsules, suppositories, sterile injectable solutions, and sterile packaged powders.

[0145] In preparing a formulation, the active compound can be milled to provide the appropriate particle size prior to combining with the other ingredients. If the active compound is substantially insoluble, it can be milled to a particle size of less than 200 mesh. If the active compound is substantially water soluble, the particle size can be

adjusted by milling to provide a substantially uniform distribution in the formulation, e.g. about 40 mesh.

[0146] Some examples of suitable pharmaceutically acceptable carriers include lactose, dextrose, sucrose, sorbitol, mannitol, starches, gum acacia, calcium phosphate, alginates, tragacanth, gelatin, calcium silicate, microcrystalline cellulose, polyvinylpyrrolidone, cellulose, water, syrup, and methyl cellulose. The formulations can additionally include: lubricating agents such as talc, magnesium stearate, and mineral oil; wetting agents; emulsifying and suspending agents; preserving agents such as methyl- and propylhydroxy-benzoates; sweetening agents; and flavoring agents. The compositions of the invention can be formulated so as to provide quick, sustained or delayed release of the active ingredient after administration to the patient by employing procedures known in the art.

[0147] The compositions can be formulated in a unit dosage form, each dosage containing from about 5 to about 100 mg, more usually about 10 to about 30 mg, of the active ingredient. The term "unit dosage forms" refers to physically discrete units suitable as unitary dosages for human subjects and other mammals, each unit containing a predetermined quantity of active material calculated to produce the desired therapeutic effect, in association with a suitable pharmaceutical pharmaceutically acceptable carrier.

[0148] The active compound can be effective over a wide dosage range and is generally administered in a pharmaceutically effective amount. It will be understood, however, that the amount of the compound actually administered will usually be determined by a physician, according to the relevant circumstances, including the condition to be treated, the chosen route of administration, the actual compound administered, the age, weight, and response of the individual patient, the severity of the patient's symptoms, and the like.

[0149] For preparing solid compositions such as tablets, the principal active ingredient is mixed with a pharmaceutically acceptable carrier to form a solid preformulation composition containing a homogeneous mixture of a compound of the present invention. When referring to these preformulation compositions as homogeneous, the active ingredient is typically dispersed evenly throughout the composition so that the composition can be readily subdivided into equally effective unit dosage forms such as tablets, pills and capsules. This solid preformulation is then subdivided into unit dosage forms of the type described above containing from, for example, 0.1 to about 500 mg of the active ingredient of the present invention.

[0150] The tablets or pills of the present invention can be coated or otherwise compounded to provide a dosage form affording the advantage of prolonged action. For example, the tablet or pill can comprise an inner dosage and an outer dosage component, the latter being in the form of an envelope over the former. The two components can be separated by an enteric layer which serves to resist disintegration in the stomach and permit the inner component to pass intact into the duodenum or to be delayed in release. A variety of materials can be used for such enteric layers or coatings, such materials including a number of polymeric acids and mixtures of polymeric acids with such materials as shellac, cetyl alcohol, and cellulose acetate.

[0151] The liquid forms in which the compounds and compositions of the present invention can be incorporated for administration orally or by injection include aqueous solutions, suitably flavored syrups, aqueous or oil suspensions, and flavored emulsions with edible oils such as cottonseed oil, sesame oil, coconut oil, or peanut oil, as well as elixirs and similar pharmaceutical vehicles.

[0152] Compositions for inhalation or insufflation include solutions and suspensions in pharmaceutically acceptable, aqueous or organic solvents, or mixtures thereof, and powders. The liquid or solid compositions may contain suitable pharmaceutically acceptable pharmaceutically acceptable carriers as described supra. In some embodiments, the compositions are administered by the oral or nasal respiratory route for local or systemic effect. Compositions in can be nebulized by use of inert gases. Nebulized solutions may be breathed directly from the nebulizing device or the nebulizing device can be attached to a face masks tent, or intermittent positive pressure breathing machine. Solution, suspension, or powder compositions can be administered orally or nasally from devices which deliver the formulation in an appropriate manner.

[0153] The amount of compound or composition administered to a patient will vary depending upon what is being administered, the purpose of the administration, such as prophylaxis or therapy, the state of the patient, the manner of administration, and the like. In therapeutic applications, compositions can be administered to a patient already suffering from a disease in an amount sufficient to cure or at least partially arrest the symptoms of the disease and/or its complications. An amount adequate to accomplish this is referred to as a "therapeutically effective amount." Effective doses will depend on the disease condition being treated as well as by the judgement of the attending clinician depending upon factors such as the severity of the disease, the age, weight and general condition of the patient, and the like.

[0154] The compositions administered to a patient can be in the form of pharmaceutical compositions described above. These compositions can be sterilized by conventional sterilization techniques, or may be sterile filtered. Aqueous solutions can be packaged for use as is, or lyophilized, the lyophilized preparation being combined with a sterile aqueous carrier prior to administration. The pH of the compound preparations typically will be between 3 and 11, more preferably from 5 to 9 and most preferably from 7 to 8. It will be understood that use of certain of the foregoing pharmaceutically acceptable carriers, carriers, or stabilizers will result in the formation of pharmaceutical salts.

[0155] The therapeutic dosage of the compounds of the present invention can vary according to, for example, the particular use for which the treatment is made, the manner of administration of the compound, the health and condition of the patient, and the judgement of the prescribing physician. The proportion or concentration of a compound of the invention in a pharmaceutical composition can vary depending upon a number of factors including dosage, chemical characteristics (e.g., hydrophobicity), and the route of administration. For example, the compounds of the invention can be provided in an aqueous physiological buffer solution containing about 0.1 to about 10% w/v of the compound for parenteral administration. Some typical dose ranges are from about 1 $\mu\text{g/kg}$ to about 1 g/kg of body weight per day. In some embodiments, the dose range is from about 0.01 mg/kg to about 100 mg/kg of body weight per day. The dosage is likely to depend on such variables as the type and extent of progression of the disease or disorder, the overall health status of the particular patient, the relative biological efficacy of the compound selected, formulation of the pharmaceutically acceptable carrier, and its route of administration. Effective doses can be extrapolated from dose-response curves derived from in vitro or animal model test systems.

[0156] The present invention also includes pharmaceutical kits useful, for example, in the treatment or prevention of inflammatory diseases, which comprise one or more containers containing a pharmaceutical composition comprising a therapeutically effective amount of a compound of Formula I. Such kits can further include, if desired, one or more of various conventional pharmaceutical kit components, such as, for example, containers with one or more pharmaceutically acceptable carriers, additional containers, etc., as will be readily apparent to those skilled in the art. Instructions, either as inserts or as labels, indicating quantities of the components to be administered, guidelines for

administration, and/or guidelines for mixing the components, can also be included in the kit.

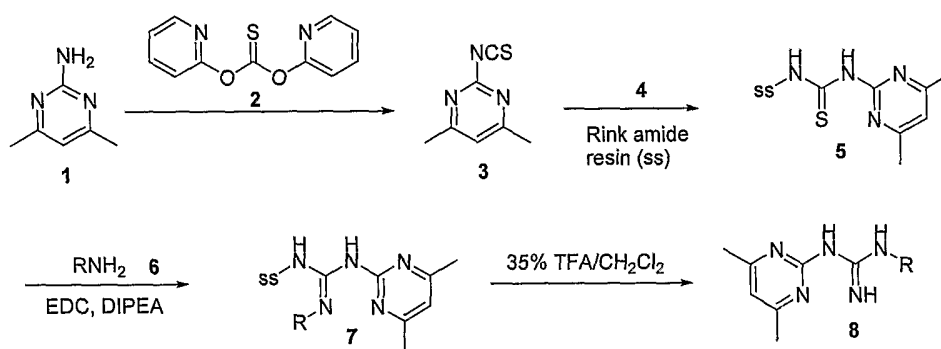
[0157] The invention will be described in greater detail by way of specific examples. The following examples are offered for illustrative purposes, and are not intended to limit the invention in any manner. Those of skill in the art will readily recognize a variety of noncritical parameters which can be changed or modified to yield essentially the same results.

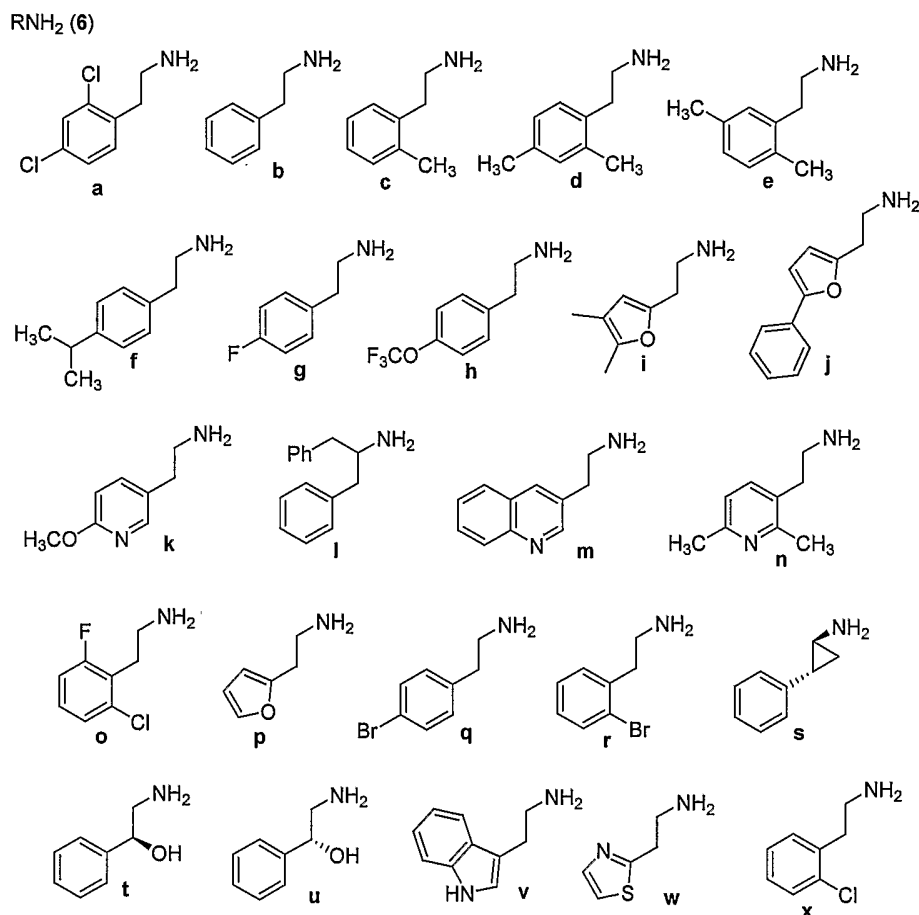
EXAMPLES

Example 1

Solid-Phase Synthesis of Guanidines

Scheme A





Step 1: Deprotection of Argogel Rink amide resin (4).

[0158] A solution of 20% piperidine in DMF was added to commercially available Argogel®-Rink-NH-Fmoc resin (10 g, 0.37 mmol/g); and the mixture was swirled for 3 to 5 h at room temperature (rt). The resin was filtered and washed sequentially with DMF (3X), CH₂Cl₂ (3X), MeOH (3X) and CH₂Cl₂ (3X) to provide resin 4.

Step 2: Preparation of Thiourea-resin (5).

[0159] A mixture of 2-amino-4,6-dimethylpyrimidine (2.77 g, 22.5 mmol, 1 eq) and di-2-pyridyl thionocarbonate (4.98 g, 21.38 mmol, 0.95 eq) in dry dichloroethane (200 mL) was refluxed for 5 hr. The reaction was cooled to rt and treated with Fmoc-deprotected Rink amide resin 4 (10g, 0.37 mmol/g). After swirling under an atmosphere of nitrogen gas for 12h at rt, the resin was filtered and washed sequentially with CH₂Cl₂ (2X), MeOH (2X) and CH₂Cl₂ (2X) and dried in a vacuum oven over P₂O₅ for 14 h at rt to provide Thiourea-resin 5 (ss in Scheme A indicates solid support or resin).

Step 3: Preparation of Guanidine-resin (7).

[0160] A solution of 1-[3-(dimethylamino)propyl]-3-ethylcarbodiimide hydrochloride (EDC, 0.33 g, 1.75 mmol) and diisopropylethylamine (DIPEA, 0.92 mL, 5.25 mmol) in dry CH₂Cl₂ (5 to 7 mL) was added to thiourea-resin **4** (500 mg, 0.175 mmol) in a Argonaut Quest 210 parallel synthesizer. After agitating the reaction mixture for 30 min at rt, the desired amine **6** (1.75 mmol, purchased from commercial vendors or prepared by the method outlined in Example 7) was added to the reaction mixture. The agitation was continued for an additional 20 h at 40 °C after which, the resin was filtered and sequentially washed with DMF (3X), CH₂Cl₂ (3X), MeOH (3X) and CH₂Cl₂ (2X) to provide guanidine-resin **7**.

Step 4: Preparation of Guanidine (8).

[0161] Guanidine-resin **7** was treated with a mixture of 35% TFA/CH₂Cl₂ for 2h at rt and the acid solution was collected by filtration. The resin was washed with additional CH₂Cl₂ (5 mL) and the combined washings were concentrated using a SpeedVac (Savant Instruments Inc.). The crude residue obtained was further purified by reverse phase preparative HPLC (Agilent Prep HPLC-MSD 1100 with a Gilson 215 fraction collector, using a Phenomenex Luna 250 x 21.2 mm column, flow rate of 30ml/min, Buffer A = 1%AcOH in water, Buffer B = Acetonitrile) to provide guanidine **8** as the acetate salt.

Example 1a

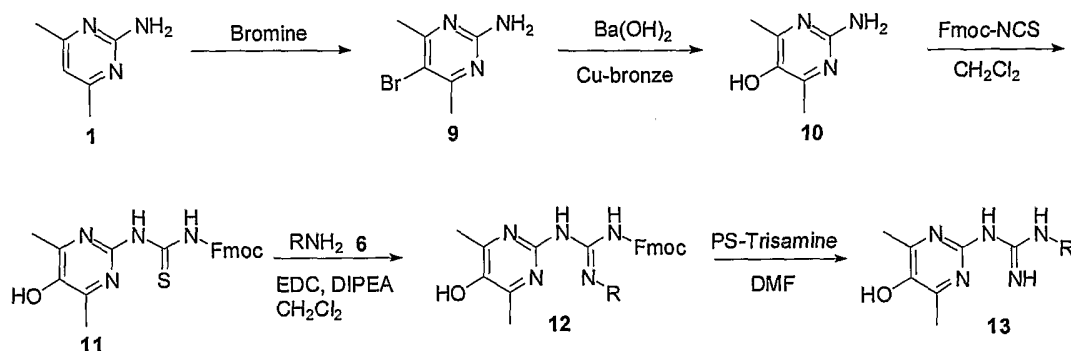
N-[2-(2-Chloro-phenyl)-ethyl]-N'-(4,6-dimethyl-pyrimidin-2-yl)-guanidine (**8x**).

[0162] This compound was prepared using the general procedure described in Example 1 using 2-(2-chloro-phenyl)-ethylamine **6x** to provide guanidine **8x** as the acetate salt. ¹H NMR (CD₃OD, 300 MHz) δ : 7.39 (m, 2H), 7.28 (m, 2H), 3.74 (t, 2H, $J = 6.7$), 3.16 (t, 2H, $J = 6.7$) 2.37 (s, 6H). LCMS: LC retention time 2.5 min.; MS (ES⁺) 304.0 (MH⁺).

Example 2

Solution Synthesis of Guanidines Using Fmoc-Isothiocyanate

Scheme B



Step 1: Preparation of 2-amino-4,6-dimethyl-5-hydroxy-pyrimidine (10).

[0163] Bromine (1.76 mL, 34.4 mmol) was added dropwise to a cold solution (0 °C) of pyrimidine **1** (4 g, 32.4 mmol) in glacial acetic acid (40 mL). After stirring in the ice bath for 30 min, the precipitated solid was collected by filtration and further washed with a small volume of glacial acetic acid (20 – 30 mL). The solid was then dissolved in hot H₂O (400 mL) and the resulting solution was cooled and basified by the dropwise addition of 4N NaOH. The resulting white precipitate was collected by filtration to provide **9** (2.17g). ¹H NMR (DMSO-*d*₆, 300 MHz) δ: 6.62 (bs, 2H), 2.33 (s, 6H). LCMS: LC retention time 2.44 min.; MS (ES⁺) 204.0 (MH⁺).

[0164] A mixture of Ba(OH)₂ (3.12 g, 9.9 mmol), Cu-bronze powder (20 mg, 0.3 mmol, Aldrich) and **9** (2.17 g) in H₂O (9 mL) was heated in a sealed tube at 180 °C for 20h. The reaction mixture was cooled to rt, diluted with H₂O (10 mL) and boiled for 5 min to remove ammonia. After neutralization with 30% v/v H₂SO₄ (~2 mL) the reaction mixture was filtered through celite and the aqueous filtrate was concentrated under vacuum. The resulting residue was suspended in hot EtOH and the suspension filtered. The ethanolic filtrate was further concentrated under vacuum and the resulting solid was suspended in hot acetone and the suspension filtered. The acetone filtrate was then concentrated under vacuum to provide **10** (470 mg) as a white solid. ¹H NMR (DMSO-*d*₆, 300 MHz) δ: 7.96 (s, 1H), 5.85 (bs, 2H), 2.29 (s, 6H). LCMS: LC retention time 0.46 min.; MS (ES⁺) 140.0 (MH⁺).

Step 2: Preparation of guanidine (13).

[0165] Fmoc-isothiocyanate (0.21 g, 0.75 mmol, Novabiochem) was added to a solution of **10** (0.64 g, 0.75 mmol) in acetone (4 mL). After stirring for 12 h at rt the acetone was evaporated under vacuum to provide crude **11**, which was used without any further purification.

[0166] EDC (0.28 g, 1.5 mmol) and DIPEA (3 mmol, 0.39 mmol) were added to a cold (0 °C) solution of **11** (0.75 mmol) in dry CH₂Cl₂ (7.5 mL). After stirring for 15 min the desired amine **6** (0.75 mmol, purchased from commercial vendors or prepared by using the method described in example 7) was added and the reaction mixture was stirred for 12h at rt. The solvent was evaporated under vacuum to provide a crude mixture containing **12**, which was used without any further purification.

[0167] The crude mixture containing **12** was dissolved in DMF (2 mL) and treated with PS-Trisamine resin (1 teaspoon, Argonaut). After swirling for 12h at rt, the reaction mixture was filtered and the resin was washed with additional CH₂Cl₂. The combined filtrates were evaporated under vacuum and the crude residue was further purified by reverse phase HPLC (as described in example 1) to provide **13**.

[0168] In an slightly modified procedure, **1** was reacted directly with Fmoc-isothiocyanate to provide the corresponding Fmoc-thiourea. Further reaaction with primary or secondary amines using EDC to activate the thiourea provided the corresponding Fmoc protected guanidine. The Fmoc protecting group was removed using PS-trisamine in DMF to provide the final guanidine product (e.g., unsubstituted at the 4-position of the pyrimidine ring).

Example 2a

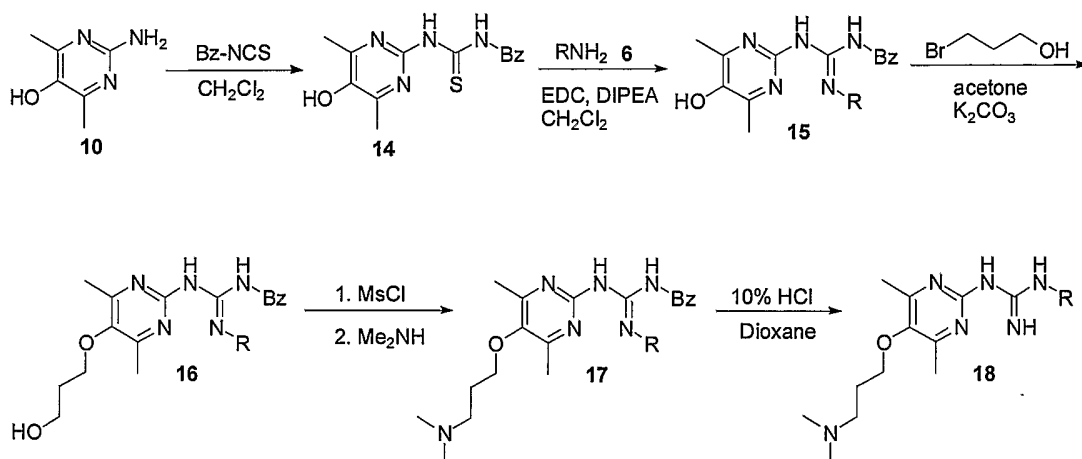
N-(5-Hydroxy-4,6-dimethyl-pyrimidin-2-yl)-*N'*-[2-(4-methoxy-phenyl)-ethyl]-guanidine (**13h**).

[0169] This compound was prepared according to the general procedure described in Example 2 using phenethylamine **6h** to provide guanidine **13h** as the acetate salt. ¹H NMR (CD₃OD, 300 MHz) δ: 6.99 (d, 2H, *J* = 8.2), 6.66 (d, 2H, *J* = 8.2), 3.55 (s, 3H), 3.43 (t, 2H, *J* = 6.7), 2.73 (t, 2H, *J* = 6.7) 2.11 (s, 6H). LCMS: LC retention time 2.29 min.; MS (ES⁺) 316.0 (MH⁺).

Example 3

Solution Synthesis of Guanidines Using Benzoyl Isothiocyanate

Scheme C



[0170] Benzoyl isothiocyanate (0.26 mL, 1.94 mmol) was added to a solution of pyrimidine **10** (0.27 g, 1.94 mmol) in acetone:CH₂Cl₂ (1:1, 12mL). After stirring for 12h at rt, the solvent was removed under vacuum to provide crude **14** that was used without any further purification. ¹H NMR (DMSO-*d*₆, 300 MHz) δ : 9.37 (s, 1H), 7.97 (d, 2H, *J* = 7.14), 7.69 (m, 1H), 7.59 (m, 2H), 2.35 (s, 6H). LCMS: LC retention time 2.97 min.; MS (ES⁺) 303.1 (MH⁺).

[0171] EDC (0.32 g, 3.3 mmol), DIPEA (0.56 mL, 3.3 mmol) were added to a cold (0 °C) solution of **14** (0.25 g, 0.83 mmol) in dry CH₂Cl₂ (16 mL). After stirring for 15 min, the desired amine **6** (3.31 mmol, purchased from commercial vendors or prepared by using the method described in example 7) was added. After stirring for an additional 12h at rt, the reaction mixture was diluted with CH₂Cl₂ and the organic layer was sequentially washed with 5% HCl, brine, dried (MgSO₄) and concentrated to provide crude **15** which was used without any further purification.

[0172] A mixture of crude **15** (0.15 g, 0.36 mmol), bromopropanol (0.03 mL, 0.36 mmol) and K₂CO₃ (0.069g, 0.5 mmol) in acetone (1 mL) was refluxed for 12 h. The reaction mixture was cooled to rt and diluted with EtOAc. The organic layer was sequentially extracted with H₂O, brine, dried (MgSO₄) and concentrated to provide crude **16**, which was used without any further purification.

[0173] Methansulfonyl chloride (0.032 mL, 0.4 mL) was added to a cold solution (0 °C) of crude **16** (obtained above), triethylamine (0.07 mL, 0.5 mmol) and DMAP (catalytic) in dry CH₂Cl₂ (0.6 mL). After stirring for 12 h at rt, the reaction mixture was diluted with CH₂Cl₂ and the organic layer was washed with H₂O, brine, dried (MgSO₄) and concentrated. The crude residue obtained was dissolved in a solution of dimethylamine in THF (5 mL of a 2 M solution, Aldrich). After stirring for 12 h at 40 °C,

the reaction was concentrated under vacuum to provide crude **17**, which was used without any further purification.

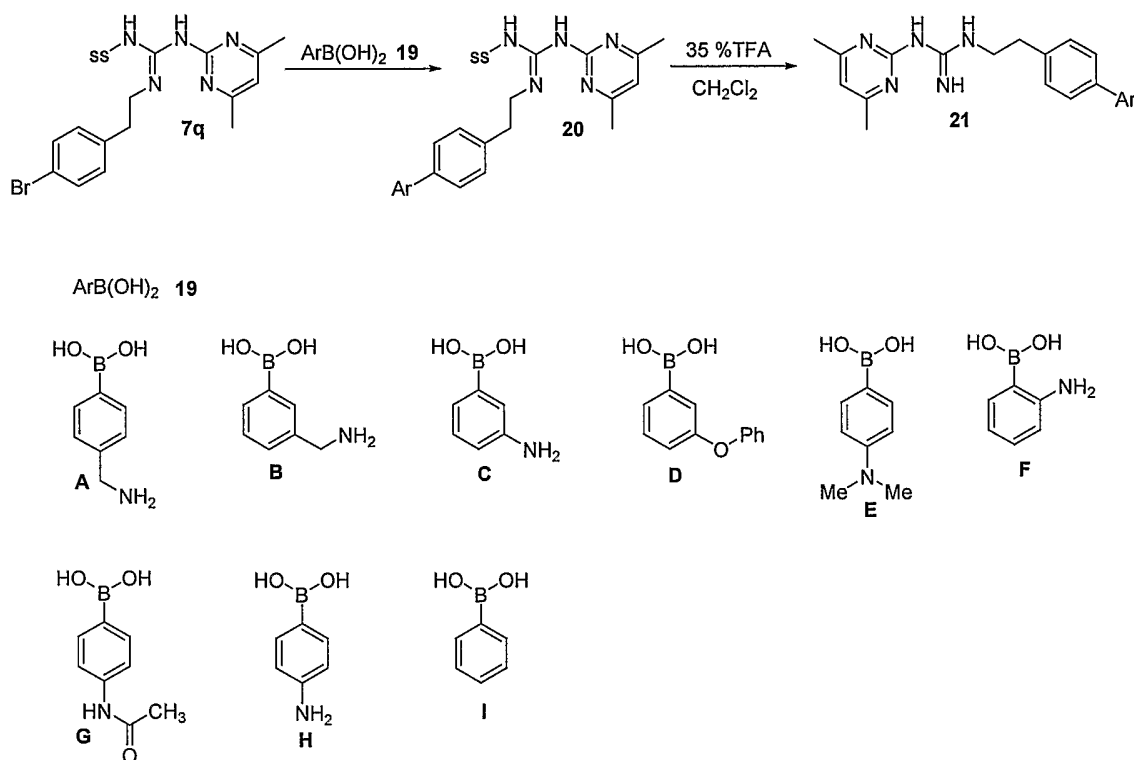
[0174] A mixture of crude **17** (obtained above) and 10% aq. HCl (4 mL) in dioxane (2 mL) was refluxed for 12h after which the solvent was removed by concentration under vacuum to provide crude **18**. Purification of the crude residue by reverse phase preparative HPLC provided guanidine **18** (as described in Example 1) as the acetate salt.

Example 3a

N-[5-(3-Dimethylamino-propoxy)-4,6-dimethyl-pyrimidin-2-yl]-*N'*-phenethyl-guanidine (**18b**)

[0175] This compound was prepared according to the general procedure described in Example 3 using phenethylamine **6b** to provide guanidine **18b** as the acetate salt. ¹H NMR (CD₃OD, 300 MHz) δ : 7.21 (m, 5H), 3.77 (t, 2H, $J = 6.2$), 3.58 (t, 2H, $J = 6.8$), 2.90 (t, 2H, $J = 6.2$), 2.56 (m, 2H), 1.91 (m, 2H), 1.80 (s, 6H). LCMS: LC retention time 1.85 min.; MS (ES⁺) 371.1 (MH⁺).

[0176]

Example 4**Modification of Guanidines via Suzuki Coupling: Method 1****Scheme D***Step 1: Preparation of Guanidine-resin (20).*

[0177] Guanidine resin **7q** (loading approximately 0.34 mmol/g) was prepared according to the general procedure described in Example 1 using 2-(4-bromo-phenyl)-ethylamine **6q**.

[0178] A solution of the boronic acid **19** (0.15g, 1 mmol, 6 eq) in EtOH (1.8 mL) was added to a suspension of guanidine-resin **7q** (0.5 g, 0.34 mmol/g, 1 eq) in ethyleneglycol dimethylether (DME, 4 mL). A solution of Na_2CO_3 (0.21 g, 2 mmol, 13.3 eq) in H_2O (1 mL) was added followed by a solution of tetrakis(triphenylphosphine) palladium (29 mg, 0.025 mmol, 0.17 eq) in dioxane (0.45 mL). After swirling under a nitrogen atmosphere for 12h at 70 °C, the resin was filtered and sequentially washed with H_2O (3X), DME: H_2O (1:1, 3X), DME (3X), H_2O (3X), gl. Acetic acid: H_2O (1:1, 3X), gl. Acetic acid (3X), CH_2Cl_2 (3X) and MeOH (3X).

Step 2: Preparation of Guanidine (21).

[0179] Guanidine-resin **20** was treated with a mixture of 35% TFA/CH₂Cl₂ for 2h at rt and the acid solution was collected by filtration. The resin was washed with additional CH₂Cl₂ (5 mL) and the combined washings were concentrated using a SpeedVac (Savant Instruments Inc.). The crude residue obtained was further purified by reverse phase preparative HPLC to provide Guanidine **21** (as described in Example 1) as the acetate salt.

Example 4a

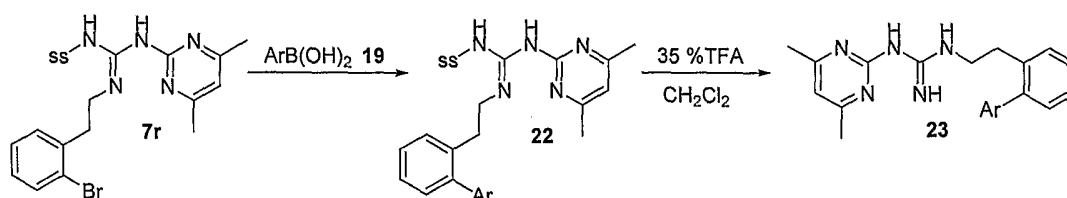
N-[2-(2'-Amino-biphenyl-4-yl)-ethyl]-*N'*-(4,6-dimethyl-pyrimidin-2-yl)-guanidine (**21F**)

[0180] This compound was prepared using the general procedure described in Example 4 using 3-amino-phenylboronic acid **19F** to provide guanidine **21F** as the acetate salt. ¹H NMR (CD₃OD, 300 MHz) δ : 7.23 (m, 4H), 6.91 (m, 1H), 6.82 (m, 1H), 6.80 (s, 1H), 6.65 – 6.55 (m, 2H), 3.58 (t, 2H, $J = 6.74$), 2.90 (t, 2H, $J = 6.74$), 2.21 (s, 6H). LCMS: LC retention time 2.51 min.; MS (ES⁺) 361.1 (MH⁺).

Example 5

Modification of Guanidines via Suzuki Coupling: Method 2

Scheme E



[0181] This method was identical to Example 4 except that Guanidine-resin **7r** was used as the starting material.

Example 5a

N-[2-(4'-Dimethylamino-biphenyl-2-yl)-ethyl]-*N'*-(4,6-dimethyl-pyrimidin-2-yl)-guanidine (**23E**)

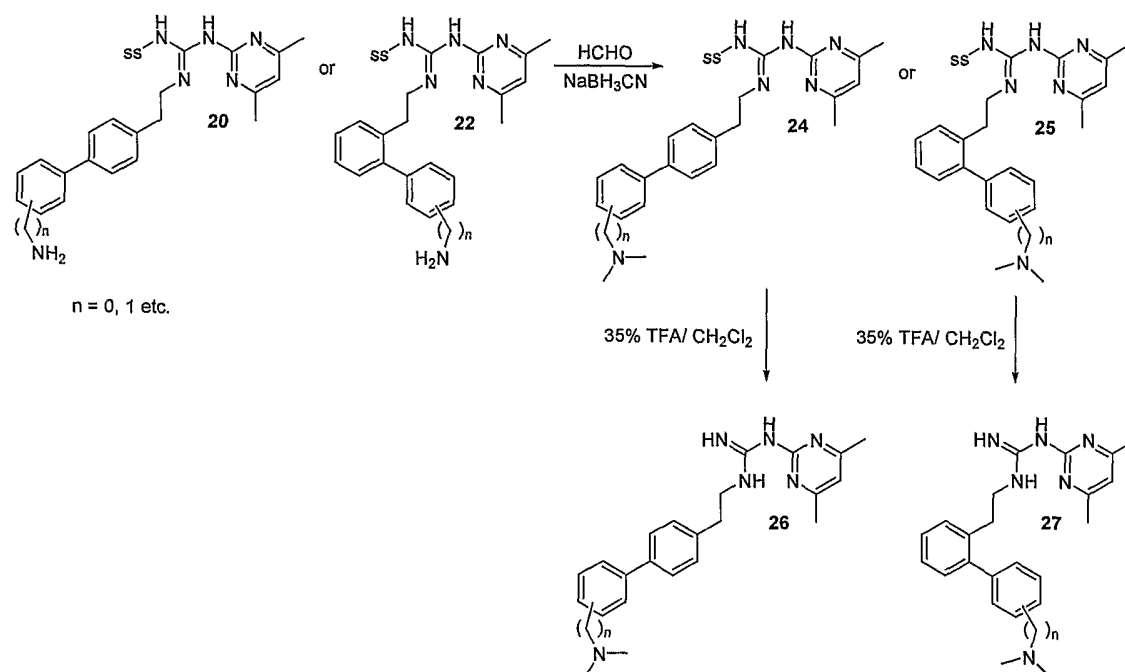
[0182] This compound was prepared using the general procedure described in Example 5 using 3-amino-phenylboronic acid **19E** to provide guanidine **23E** as the acetate salt. ¹H NMR (CD₃OD, 300 MHz) δ : 7.27 (m, 1H), 7.17 (m, 2H), 7.07 (m, 1H), 6.99 (d, 2H, $J = 8.71$), 6.84 (s, 1H), 6.62 (d, 2H, $J = 8.70$), 3.36 (t, 2H, $J = 6.62$), 2.99 (t, 2H, $J =$

6.69), 2.79 (s, 6H), 2.25 (s, 6H). LCMS: LC retention time 2.57 min.; MS (ES^+) 403.1 (MH^+).

Example 6

Solid-Phase Reductive Amination

Scheme F



Preparation of guanidine-resin **24** or **25**.

[0183] Guanidine-resin **20** (0.56 g, 0.21 mmol) prepared using boronic acids such as **19A**, **B**, **C**, **F** and **H** (bearing free amine groups) was suspended in MeOH (4 mL) and treated with formaldehyde (1.5 mL of a 35% solution in water) and glacial acetic acid (4 drops). After agitating for 5 min, NaBH_3CN (1 teaspoon) was added and the mixture was agitated for an additional 2h at rt. The resin was then filtered and washed with MeOH (3X) and CH_2Cl_2 (3X) to provide guanidine resin **26** or **27**.

Preparation of guanidine **26** or **27**.

[0184] Guanidine-resin **24** or **25** was treated with a mixture of 35% TFA/ CH_2Cl_2 for 2h at rt and the acid solution was collected by filtration. The resin was washed with additional CH_2Cl_2 (5 mL) and the combined washings were concentrated using a SpeedVac (Savant Instruments Inc.). The crude residue obtained was further purified by

reverse phase preparative HPLC to provide Guanidine **26** or **27** (as described in Example 1) as the acetate salt.

Example 6a

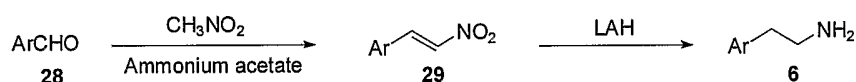
***N*-[2-(3'-Dimethylaminomethyl-biphenyl-4-yl)-ethyl]-*N'*-(4,6-dimethyl-pyrimidin-2-yl)-guanidine (26A)**

[0185] This compound was prepared using the general procedure described in Example 6 using guanidine-resin **20A** to provide guanidine **26A** as the acetate salt. ¹H NMR (CD₃OD, 300 MHz) δ: 7.55 (m, 4H), 7.39 (m, 1H), 2.29 (m, 3H), 6.85 (s, 1H), 3.65 (t, 2H, *J* = 6.8), 2.97 (t, 2H, *J* = 6.8), 2.48 (s, 6H), 2.25 (s, 6H). LCMS: LC retention time 2.02 min.; MS (ES⁺) 390.1 (MH⁺).

Example 7

Preparation of 2-Arylethylamines 6.

Scheme G



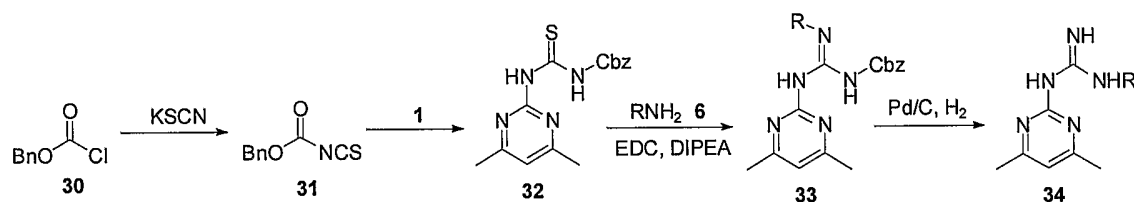
[0186] A mixture of a commercially available aromatic aldehyde **28** (6.56 mmol) and ammonium acetate (6.7 mmol, 0.52 g) was refluxed in nitromethane (20 mL) for 30 min. The reddish solution thus formed was cooled to rt and allowed to stand for 12 – 16 h during which time nitroalkene **29** crystallized out. The crystalline **29** thus obtained was collected by filtration, air-dried and used without any further purification.

[0187] A solution of **29** (3.6 mmol) in dry THF (10 mL) was added to a cold (0 °C) suspension of LAH (0.33 g, 7.2 mmol) in dry THF (15 mL) via a canula under a nitrogen atmosphere. After stirring under nitrogen for 12 h at rt, the reaction was cooled in an ice bath and very carefully quenched by the dropwise addition of H₂O (0.33 mL). After stirring for another 30 min, a solution of 4 M NaOH (0.33 mL) was added followed by additional H₂O (1 mL). The resulting suspension was stirred for 1 h after which, it was filtered through a bed of celite. The filter bed was washed with additional THF and the combined filtrates were concentrated to provide amine **6**, which was used without any further purification.

Example 7a

2-(5-Phenyl-furan-2-yl)-ethylamine (6j)

[0188] This compound was prepared using the general procedure described in example 7 to provide **6j**. ^1H NMR (CDCl_3 , 300 MHz) δ : 7.63 (d, 2H, $J = 7.2$), 7.36 (m, 2H), 7.22 (m, 2H), 6.55 (d, 1H, $J = 3.2$), 6.14 (d, 1H, $J = 3.2$), 3.03 (t, 2H, $J = 6.6$), 2.83 (t, 2H, $J = 6.6$).

Example 8**Preparation of Guanidines Using CbzNCS****Scheme H**

[0189] Synthesis of (benzyloxycarbonyl) isothiocyanate **30** was carried out using a modification of *J. Org. Chem.* **1986**, 51, 1277-82. A suspension of finely powdered potassium isothiocyanate (50 g) in 400 mL of anhydrous ethyl acetate under nitrogen was cooled to 0 °C and treated dropwise with benzyl chloroformate (23 mL). The reaction mixture was allowed to warm to room temperature slowly and then stirred under nitrogen overnight. The reaction mixture was filtered through Celite and evaporated to dryness to give a crude yellow oil (26.8 g) as a mixture of benzylthiocyanate and product (1:4) that was used without further purification in the next step.

[0190] Crude (benzyloxycarbonyl)isothiocyanate **31** (7.0 g) was added to a stirred mixture of 4,6-dimethylpyrimidine **1** (4.3 g) in CH_2Cl_2 (300 mL). The reaction was allowed to proceed at room temperature for 48 hours and then evaporated to dryness. Recrystallization from hot EtOAc and hexanes gave pure thiourea **32** (6.5 g). ^1H NMR (CDCl_3 , 300 MHz) δ : 7.42–7.34 (m, 5H), 6.76 (s, 1H), 5.29 (s, 2H), 2.43 (s, 6H).

[0191] A solution of thiourea **32** (0.1 mmol) in CH_2Cl_2 (2 mL) was added to alkylamines (0.2 mmol), and diisopropylethylamine (0.2 mmol) and cooled to 0 °C. EDCI (0.2 mmol) was added, and the solution was stirred under nitrogen. After 1 h the ice bath was removed and the solution was stirred overnight at room temperature. The reaction

mixture was then coevaporated with silica gel and purified by silica chromatography using a gradient of 100% hexanes to 100% EtOAc to provide Cbz-guanidine **33**.

[0192] A solution of Cbz-guanidine **33** (50mg) in EtOH (2 mL and as much EtOAc as necessary to affect a solution) was added to a flask containing 10% Pd/C (10 mg). This was then hydrogenated for 8 hours at 40psi, filtered thru Celite and evaporated to dryness to provide guanidine **34**.

Example 8a

N-(4,6-dimethyl-pyrimidin-2-yl)-*N'*-phenethyl-guanidine (**34b**)

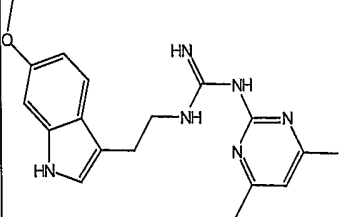
[0193] This compound was prepared according to the general procedure described in example 2 using phenethylamine **6h** to provide guanidine **34h**. ¹H NMR (CDCl₃, 300 MHz) δ : 7.26 (m, 5H), 6.41 (s, 1H), 6.55 (s, 1H), 3.56 (t, 2H, $J = 6.8$), 2.92 (t, 2H, $J = 6.8$), 2.29 (s, 6H). LCMS: LC retention time 2.65 min.; MS (ES⁺) 270.1.0 (MH⁺).

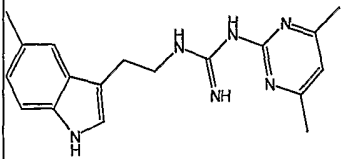
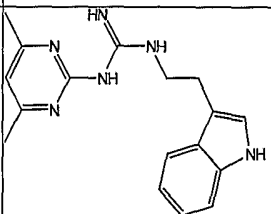
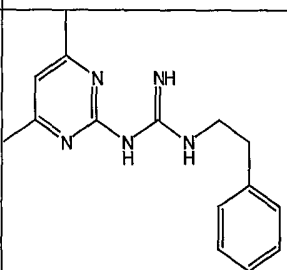
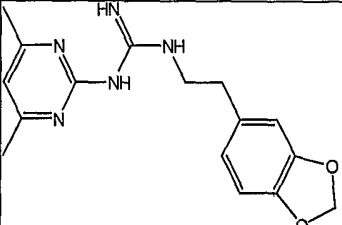
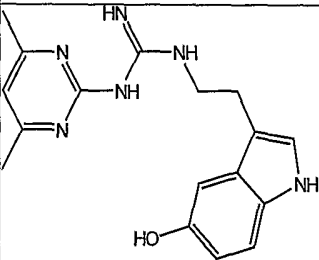
Example 9

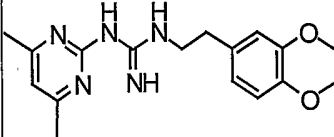
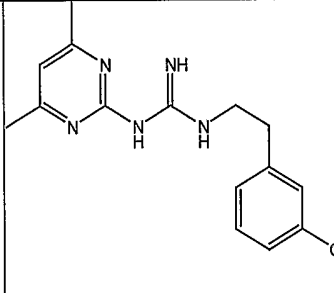
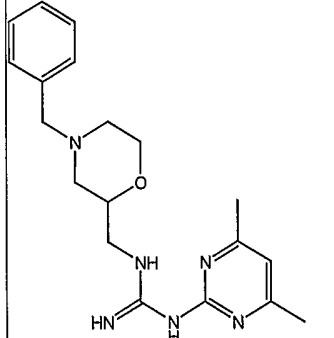
Compound Activity

[0194] Compounds of the invention were tested for inhibition of HCV-IRES dependent translation according to the assay described in Example 10. IC₅₀ data is provided below in Table 3. Compounds having an IC₅₀ less than about 100 μ m are considered to be active.

Table 3

Identifier	Compound	HCV-IRES, IC ₅₀ (μ M)
1.4		10.4

1.9		10.1
1.72		2.9
1.43		12.1
1.69		13.1
1.71		2.8

1.79		15.8
1.83		13.7
1.96		12.9

Example 10**HCV Dual Reporter *In vitro* Expression Assay**

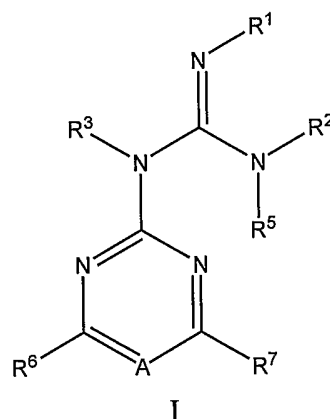
[0195] This assay uses in vitro expression of two reporter genes for *Renilla* luciferase and firefly luciferase. The assay template is a DNA plasmid containing a gene for *Renilla* luciferase that has been cloned downstream of a T7 RNA polymerase promoter. The *Renilla* luciferase gene is followed by a viral IRES containing 5'-UTR sequence (Zhang, H. *et al* (1999) *Antimicrobial Agents and Chemotherapy*, **43**, 347.) fused to a gene for firefly luciferase. The assay is carried out in a eukaryotic coupled transcription/translation system (Promega Gold TnT[®] T7 Express 96, Catalog # L5600). Messenger RNA from 125 ng dual reporter plasmid template is transcribed and translated in rabbit reticulocyte lysate in the presence or absence of test compound. Compounds are

tested in black 96 well microtiter plates with an assay volume of 25 μ L. Each test well contains 20 μ L Gold TnT^R rabbit reticulocyte lysate, 2.5 μ L test compound, and 2.5 μ L of 50 ng/ μ L plasmid DNA. Wells containing a DNA template with an inverted viral IRES containing 5'-UTR sequence fused to a firefly luciferase gene are tested simultaneously on each plate as a control for read-through of the second reporter gene. Signal generated from this inverted control plasmid are used to normalize the signal generated in the presence of test compound. The transcription/translation reaction is incubated for 90 minutes at 30°C. The substrate for firefly luciferase (Promega Dual-GloTM Luciferase Assay System, Catalog #E2940) is added and the light output quantitated on a Perkin-Elmer TopCount. The firefly light is quenched by addition of the substrate for *Renilla* luciferase (Promega Stop & Glo) and the *Renilla* light output is quantitated on a TopCount. Compounds are tested for their ability to specifically bind and inhibit the IRES-mediated translation (firefly reporter protein) while having negligible effect on normal cellular translation (*Renilla* reporter protein).

[0196] Various modifications of the invention, in addition to those described herein, will be apparent to those skilled in the art from the foregoing description. Such modifications are also intended to fall within the scope of the appended claims. Each reference cited in the present application is incorporated herein by reference in its entirety.

WHAT IS CLAIMED:

1. A compound of Formula I:



or pharmaceutically acceptable salt form thereof, wherein:

R^1 is H or COOR^{1a} ;

R^{1a} is H or $\text{C}_1\text{-C}_{10}$ alkyl, aryl, cycloalkyl, or aralkyl;

R^2 and R^3 are each, independently, H, $\text{C}_1\text{-C}_{10}$ alkyl, or $\text{C}_3\text{-C}_7$ cycloalkyl;

A is N or CR^4 ;

R^4 is H, halo, $\text{C}_1\text{-C}_6$ alkyl, $\text{C}_1\text{-C}_6$ haloalkyl, $\text{C}_3\text{-C}_7$ cycloalkyl, $\text{C}_2\text{-C}_6$ alkenyl, $\text{C}_2\text{-C}_6$ alkynyl, OH, alkoxy, aryloxy, aralkoxy, cycloalkyloxy, cycloalkylalkyloxy, heterocycloalkyloxy, heterocycloalkylalkyloxy, heteroaryloxy, heteroarylalkyloxy, cyano, nitro, hydroxy, mercapto, or $\text{O}(\text{CR}^{4a}\text{R}^{4b})_a\text{NR}^{4c}\text{R}^{4d}$;

R^{4a} and R^{4b} are each, independently, H or $\text{C}_1\text{-C}_4$ alkyl;

R^{4c} and R^{4d} are each, independently, H, $\text{C}_1\text{-C}_4$ alkyl, $\text{C}_3\text{-C}_7$ cycloalkyl, $\text{C}_1\text{-C}_4$ haloalkyl, aryl, $\text{C}(\text{O})\text{-(C}_1\text{-C}_6\text{ alkyl)}$, $\text{C}(\text{O})\text{-aryl}$, $\text{C}(\text{O})\text{-(C}_3\text{-C}_7\text{ cycloalkyl)}$, $\text{C}(\text{O})\text{O-(C}_1\text{-C}_6\text{ alkyl)}$, $\text{C}(\text{O})\text{O-aryl}$, or $\text{C}(\text{O})\text{O-(C}_3\text{-C}_7\text{ cycloalkyl)}$, or R^{4c} and R^{4d} together with the N atom to which they are attached form a 5- or 6-membered heterocycle;

a is 1, 2, 3, 4, 5, or 6;

R^5 is $\text{N(R}^{5a})\text{-Q}$;

R^{5a} is H or $\text{C}_1\text{-C}_6$ alkyl;

Q is aryl, heteroaryl, cycloalkyl, or heterocycloalkyl, wherein Q is optionally substituted by one or more $\text{C}_1\text{-C}_{10}$ alkyl, $\text{C}_2\text{-C}_{10}$ alkenyl, $\text{C}_2\text{-C}_{10}$ alkynyl, alkoxy, aryloxy, aralkoxy, aralkyl, OH, SH, thioalkoxy, halo, $\text{C}_1\text{-C}_{10}$ haloalkyl, haloalkoxy, COOH , $\text{C}(\text{O})\text{-(C}_1\text{-C}_6\text{ alkyl)}$, $\text{C}(\text{O})\text{-(C}_3\text{-C}_7\text{ cycloalkyl)}$, $\text{C}(\text{O})\text{-aryl}$, $\text{C}(\text{O})\text{O-(C}_1\text{-C}_6\text{ alkyl)}$, $\text{C}(\text{O})\text{O-(C}_3\text{-C}_7\text{ cycloalkyl)}$, $\text{C}(\text{O})\text{O-aryl}$, $\text{C}(\text{O})\text{NR}^{Q1}\text{R}^{Q2}$, NO_2 , CN, or $\text{NR}^{Q3}\text{R}^{Q4}$;

R^{Q1} and R^{Q2} are each, independently, H, C₁-C₆ alkyl, C₃-C₆ cycloalkyl, aryl, or R^{Q1} and R^{Q2} together with the N atom to which they are attached form a 5- or 6-membered heterocycle;

R^{Q3} and R^{Q4} are each, independently, H, C₁-C₆ alkyl, aryl, C(O)-C₁-C₆ alkyl, C(O)-(C₃-C₇ cycloalkyl), C(O)-aryl, C(O)O-(C₁-C₆ alkyl), C(O)O-(C₃-C₇ cycloalkyl), C(O)O-aryl, or R^{Q1} and R^{Q2} together with the N atom to which they are attached form a 5- or 6-membered heterocycle;

or R^5 is phenyl, naphthyl, or heteroaryl, wherein said naphthyl or heteroaryl is substituted by one or more OH or O(CR⁸R⁹)_pY and wherein said phenyl is substituted by one or more O(CR⁸R⁹)_pY;

R^8 and R^9 are each, independently, H or C₁-C₄ alkyl;

p is 1, 2, 3, 4, 5, or 6;

Y is Y¹ or Y²;

Y¹ is NR¹⁰R¹¹, C₃-C₇ cycloalkyl, heterocycloalkyl, or heteroaryl, wherein Y¹ is optionally substituted by one or more halo, C₁-C₆ alkyl, C₁-C₆ haloalkyl, C₂-C₆ alkenyl, C₂-C₆ alkynyl, C₃-C₇ cycloalkyl, aryl, heteroaryl, heterocycloalkyl, OH, SH, CN, NO₂, COOH, C(O)-(C₁-C₆ alkyl), C(O)-(C₃-C₇ cycloalkyl), C(O)-aryl, C(O)O-(C₁-C₆ alkyl), C(O)O-(C₃-C₇ cycloalkyl), C(O)O-aryl, NH₂, NH(C₁-C₄ alkyl), N(C₁-C₄ alkyl)₂, NHC(O)O-(C₁-C₆ alkyl), NHC(O)O-aryl or (CH₂)_qOH;

R^{10} and R^{11} are each, independently, H, (C₁-C₆)alkyl, C(O)-(C₁-C₆ alkyl), C(O)-(C₃-C₇ cycloalkyl), C(O)-aryl, C(O)O-(C₁-C₆ alkyl), C(O)O-(C₃-C₇ cycloalkyl), C(O)O-aryl, aryl, heteroaryl, cycloalkyl, or heterocycloalkyl, or R^{10} and R^{11} together with the N atom to which they are attached form a 5- or 6- membered heterocycle;

q is 0, 1, 2, or 3;

Y² is OR^{12a} or OSO₂R^{12b};

R^{12a} is H, C₁-C₁₀ alkyl, C₁-C₁₀ alkenyl, C₁-C₁₀ alkynyl, aryl, heteroaryl, C₃-C₇ cycloalkyl, or heterocycloalkyl;

R^{12b} is H, C₁-C₆ alkyl, aryl, or NH₂;

or R^5 is cycloalkyl or heterocycloalkyl, wherein said cycloalkyl or heterocycloalkyl is optionally substituted by one or more halo, C₁-C₁₀ alkyl, C₁-C₁₀ haloalkyl, C₂-C₁₀ alkenyl, C₂-C₁₀ alkynyl, aryl, heteroaryl, cycloalkyl, heterocycloalkyl, alkoxy, aryloxy, aralkoxy, aralkyl, OH, SH, thioalkoxy, haloalkoxy, COOH, C(O)-(C₁-C₆ alkyl), C(O)-(C₃-

C₇ cycloalkyl), C(O)-aryl, C(O)O-(C₁-C₆ alkyl), C(O)O-(C₃-C₇ cycloalkyl), C(O)O-aryl, CONR^{5b}R^{5c}, NO₂, CN, NR^{5d}R^{5e}, or O(CR⁸R⁹)_pY;

R^{5b} and R^{5c} are each, independently, H, C₁-C₆ alkyl, C₃-C₆ cycloalkyl, aryl, or R^{5b} and R^{5c} together with the N atom to which they are attached form a 5- or 6-membered heterocycle;

R^{5d} and R^{5e} are each, independently, H, C₁-C₆ alkyl, aryl, C(O)-C₁-C₆ alkyl, C(O)-(C₃-C₇ cycloalkyl), C(O)-aryl, C(O)O-(C₁-C₆ alkyl), C(O)O-(C₃-C₇ cycloalkyl), C(O)O-aryl, or R^{5d} and R^{5e} together with the N atom to which they are attached form a 5- or 6-membered heterocycle;

or R⁵ is -(CR¹³R¹⁴)_n-Z;

n is 1, 2, 3, 4, 5, 6, 7, or 8;

R¹³ and R¹⁴ are each, independently, H or C₁-C₆ alkyl, C₂-C₆ alkenyl, C₂-C₆ alkynyl, OH, SH, aryl, or aralkyl, or R¹³ and R¹⁴ together form C₃-C₇ cycloalkyl, oxo, or sulfido;

Z is naphthyl, anthracenyl, heteroaryl, cycloalkyl, heterocycloalkyl, biaryl, biheteroaryl, arylheteroaryl, or heteroarylaryl, each of which is optionally substituted by one or more R¹⁵, wherein when Z is morpholino, Z is substituted by at least one R¹⁵;

or Z is phenyl optionally substituted by at least one R¹⁶;

R¹⁵ is halo, C₁-C₁₀ alkyl, C₁-C₁₀ haloalkyl, C₂-C₁₀ alkenyl, C₂-C₁₀ alkynyl, alkoxy, aryloxy, aralkoxy, aralkyl, OH, SH, guanidiny, thioalkoxy, haloalkoxy, COOH, C(O)-(C₁-C₆ alkyl), C(O)-(C₃-C₇ cycloalkyl), C(O)-aryl, C(O)O-(C₁-C₆ alkyl), C(O)O-(C₃-C₇ cycloalkyl), C(O)O-aryl, CONR^{18a}R^{19a}, NO₂, CN, (CH₂)_tNR^{18b}R^{19b}, heteroaryl, heterocycloalkyl, aryl, C₃-C₇ cycloalkyl, or O(CR²⁰R²¹)_rX;

R¹⁶ is halo, C₁-C₁₀ alkyl, C₁-C₁₀ haloalkyl, C₂-C₁₀ alkenyl, C₂-C₁₀ alkynyl, alkoxy, aryloxy, aralkoxy, aralkyl, OH, SH, guanidiny, thioalkoxy, haloalkoxy, COOH, C(O)-(C₁-C₆ alkyl), C(O)-(C₃-C₇ cycloalkyl), C(O)-aryl, C(O)O-(C₁-C₆ alkyl), C(O)O-(C₃-C₇ cycloalkyl), C(O)O-aryl, CONR^{18c}R^{19c}, NO₂, CN, (CH₂)_tNR^{18d}R^{19d}, heteroaryl, heterocycloalkyl, aryl, C₃-C₇ cycloalkyl, or O(CR²⁰R²¹)_rX;

R^{18a} and R^{19a} are each, independently, H or C₁-C₆ alkyl, or R^{18a} and R^{19a} together with the N atom to which they are attached form a 5- or 6-membered heterocycle;

R^{18b} and R^{19b} are each, independently, H, C₁-C₆ alkyl, aryl, C(O)-C₁-C₆ alkyl, C(O)-(C₃-C₇ cycloalkyl), C(O)-aryl, C(O)O-(C₁-C₆ alkyl), C(O)O-(C₃-C₇

cycloalkyl), C(O)O-aryl, or R^{18b} and R^{19b} together with the N atom to which they are attached form a 5- or 6-membered heterocycle;

R^{18c} and R^{19c} are each, independently, H or C₁-C₆ alkyl, or R^{18c} and R^{19c} together with the N atom to which they are attached form a heterocycle;

R^{18d} and R^{19d} are each, independently, H, C₁-C₆ alkyl, aryl, C(O)-C₁-C₆ alkyl, C(O)-(C₃-C₇ cycloalkyl), C(O)-aryl, C(O)O-(C₁-C₆ alkyl), C(O)O-(C₃-C₇ cycloalkyl), C(O)O-aryl, or R^{18d} and R^{19d} together with the N atom to which they are attached form a 5- or 6-membered heterocycle;

R²⁰ and R²¹ are each, independently, H or C₁-C₆ alkyl;

r is 0, 1, 2, 3, 4, 5, or 6;

t is 0, 1, or 2;

X is X¹ or X²;

X¹ is NR²²R²³, C₃-C₇ cycloalkyl, aryl, heteroaryl, or heterocycloalkyl, wherein X¹ is optionally substituted by one or more halo, C₁-C₆ alkyl, C₃-C₇ cycloalkyl, C₁-C₆ haloalkyl, aryl, heteroaryl, heterocycloalkyl, CN, NO₂, OH, COOH, C(O)-C₁-C₆ alkyl, C(O)-(C₃-C₇ cycloalkyl), C(O)-aryl, C(O)O-(C₁-C₆ alkyl), C(O)O-(C₃-C₇ cycloalkyl), C(O)O-aryl, NH₂, NH(C₁-C₄ alkyl), N(C₁-C₄ alkyl)₂, NHC(O)O-(C₁-C₆ alkyl), NHC(O)O-aryl or (CH₂)_sOH;

R²² and R²³ are each, independently, H, C₁-C₆ alkyl, aryl, heteroaryl, heterocycloalkyl, cycloalkyl, C(O)-C₁-C₆ alkyl, C(O)-(C₃-C₇ cycloalkyl), C(O)-aryl, C(O)O-(C₁-C₆ alkyl), C(O)O-(C₃-C₇ cycloalkyl), C(O)O-aryl, or R²² and R²³ together with the N atom to which they are attached form a 5- or 6-membered heterocycle;

s is 0, 1, 2, or 3;

X² is OH or OSO₂R²⁴;

R²⁴ is H, C₁-C₆ alkyl, aryl, or NH₂;

or R⁵ and R² together with the N atom to which they are attached form heterocycloalkyl optionally substituted by halo, C₁-C₄ alkyl, OH, SH, alkoxy or aryloxy; and

R⁶ and R⁷ are each, independently, H, halo, C₁-C₆ alkyl, C₁-C₆ haloalkyl, C₂-C₆ alkenyl, C₂-C₆ alkynyl, alkoxy, aryloxy, or aralkoxy, or R⁶ and R⁷ together with the atoms to which they are attached form a fused cycloalkyl, heterocycloalkyl, aryl, or heteroaryl group;

with the proviso that when R¹ is COOR^{1A}; R⁵ is not phenyl substituted by methyl;

with the proviso that when R^5 is cycloalkyl or heterocycloalkyl, R^5 is not piperidinyl, tetrahydrothiophenyl, pyrazol-3-one, or oxo or dioxo derivatives thereof,
with the proviso that when R^4 is OH, R^6 and R^7 are not both C_4 alkyl;
with the proviso that when R^5 is $-(CR^{13}R^{14})_n-Z$ and Z is phenyl substituted by at least one halo, n is greater than 1;
with the proviso that when R^5 is $-(CR^{13}R^{14})_n-Z$ and Z is phenyl substituted by one C_1 - C_4 alkoxy, said C_1 - C_4 alkoxy is located at the 2- or 3- position of said phenyl;
with the proviso that when R^5 is $-(CR^{13}R^{14})_n-Z$ and Z is phenyl substituted by two C_1 - C_4 alkoxy, said two C_1 - C_4 alkoxy are located at the 2- and 4-, 2- and 5-, or 2- and 6- positions of said phenyl; and
with the proviso that when R^5 is $-(CR^{13}R^{14})_n-Z$ and Z is unsubstituted phenyl, R^4 is other than H and C_1 - C_6 alkyl or R^{13} is other than H.

2. The compound of claim 1 wherein R^1 is H.
3. The compound of claim 1 wherein R^2 and R^3 are each H.
4. The compound of claim 1 wherein A is CR^4 .
5. The compound of claim 1 wherein R^4 is H.
6. The compound of claim 1 wherein R^4 is C_1 - C_4 alkyl.
7. The compound of claim 1 wherein R^4 is methyl.
8. The compound of claim 1 wherein R^4 is OH.
9. The compound of claim 1 wherein R^4 is or $O(CR^{4a}R^{4b})_aNR^{4c}R^{4d}$.
10. The compound of claim 1 wherein R^6 and R^7 are each C_1 - C_6 alkyl.
11. The compound of claim 1 wherein at least one of R^6 and R^7 is C_1 - C_6 alkyl.
12. The compound of claim 1 wherein at least one of R^6 and R^7 is methyl.

13. The compound of claim 1 wherein both R^6 and R^7 are methyl.
14. The compound of claim 1 wherein R^5 is $-(CR^{13}R^{14})_n-Z$.
15. The compound of claim 1 wherein Z is phenyl substituted by at least one $O(CR^{20}R^{21})_rX$.
16. The compound of claim 1 wherein n is 1 or 2.
17. The compound of claim 1 wherein n is 2.
18. The compound of claim 1 wherein R^5 is $-(CR^{13}R^{14})_n-Z$ and n is 1 or 2.
19. The compound of claim 1 wherein R^5 is phenyl substituted by at least one $O(CR^8R^9)_pY$.
20. The compound of claim 1 wherein R^5 is heteroaryl substituted by at least one $O(CR^8R^9)_pY$.
21. The compound of claim 1 wherein R^5 is substituted or unsubstituted cycloalkyl or heterocycloalkyl.
22. The compound of claim 1 wherein R^{16} is C_2-C_{10} alkyl, C_2-C_{10} alkenyl, C_2-C_{10} alkynyl, C_2-C_{10} alkoxy, aryloxy, aralkoxy, aralkyl, OH, SH, thioalkoxy, haloalkyl, haloalkoxy, COOH, $C(O)-(C_1-C_6 \text{ alkyl})$, $C(O)-(C_3-C_7 \text{ cycloalkyl})$, $C(O)\text{-aryl}$, $C(O)O-(C_1-C_6 \text{ alkyl})$, $C(O)O-(C_3-C_7 \text{ cycloalkyl})$, $C(O)O\text{-aryl}$, $CONR^{18a}R^{19a}$, NO_2 , CN, $(CH_2)_tNR^{18b}R^{19b}$, heteroaryl, heterocycloalkyl, aryl, $C_3-C_7 \text{ cycloalkyl}$, or $O(CR^{20}R^{21})_rX$.
23. The compound of claim 1 wherein R^{16} is C_2-C_{10} alkenyl, C_2-C_{10} alkynyl, C_2-C_{10} alkoxy, aryloxy, aralkoxy, aralkyl, OH, SH, thioalkoxy, haloalkyl, haloalkoxy, COOH, $C(O)-(C_1-C_6 \text{ alkyl})$, $C(O)-(C_3-C_7 \text{ cycloalkyl})$, $C(O)\text{-aryl}$, $C(O)O-(C_1-C_6 \text{ alkyl})$, $C(O)O-(C_3-C_7 \text{ cycloalkyl})$, $C(O)O\text{-aryl}$, $CONR^{18a}R^{19a}$, NO_2 , CN, $(CH_2)_tNR^{18b}R^{19b}$, heteroaryl, heterocycloalkyl, aryl, $C_3-C_7 \text{ cycloalkyl}$, or $O(CR^{20}R^{21})_rX$.

24. The compound of claim 1 wherein R^5 is $-(CR^{13}R^{14})_n-Z$ and Z is substituted or unsubstituted pyridinyl, pyrimidinyl, furanyl, thienyl, quinolinyl, isoquinolinyl, indolyl, benzo[1,3]dioxolyl, or benzoimidazolyl.
25. The compound of claim 1 wherein R^5 is $-(CR^{13}R^{14})_n-Z$ and Z is furanyl, 2-methylfuranyl, 2,3-dimethylfuranyl, 2-phenylfuranyl, or benzofuranyl.
26. The compound of claim 1 wherein R^5 is $-(CR^{13}R^{14})_n-Z$ and at least one of R^{13} and R^{14} is methyl or OH.
27. The compound of claim 1 wherein R^5 is $-(CR^{13}R^{14})_n-Z$ and Z is phenyl substituted by at least one $O(CR^{20}R^{21})_rX$.
28. The method of claim 1 wherein R^5 is $-(CR^{13}R^{14})_n-Z$ and Z is substituted or unsubstituted biaryl, biheteroaryl, arylheteroaryl, or heteroarylaryl.
29. The compound of claim 1 wherein:
 R^5 is $N(R^{5a})-Q$;
 or R^5 is phenyl, naphthyl, or heteroaryl, wherein said naphthyl or heteroaryl is substituted by one or more OH or $O(CR^8R^9)_pY$ and wherein said phenyl is substituted by one or more $O(CR^8R^9)_pY$;
 or R^5 is cycloalkyl or heterocycloalkyl, wherein said cycloalkyl or heterocycloalkyl is optionally substituted by one or more halo, C_1-C_{10} alkyl, C_1-C_{10} haloalkyl, C_2-C_{10} alkenyl, C_2-C_{10} alkynyl, alkoxy, aryloxy, aralkoxy, aralkyl, OH, SH, thioalkoxy, haloalkoxy, COOH, $C(O)-(C_1-C_6 \text{ alkyl})$, $C(O)-(C_3-C_7 \text{ cycloalkyl})$, $C(O)\text{-aryl}$, $C(O)O-(C_1-C_6 \text{ alkyl})$, $C(O)O-(C_3-C_7 \text{ cycloalkyl})$, $C(O)O\text{-aryl}$, $CONR^{5b}R^{5c}$, NO_2 , CN, $NR^{5d}R^{5e}$, or $O(CR^8R^9)_pY$;
 or R^5 is $-(CR^{13}R^{14})_n-Z$.
30. The compound of claim 1 wherein:
 R^5 is $N(R^{5a})-Q$;

or R^5 is phenyl, naphthyl, or heteroaryl, wherein said naphthyl or heteroaryl is substituted by one or more OH or $O(CR^8R^9)_pY$ and wherein said phenyl is substituted by one or more $O(CR^8R^9)_pY$;

or R^5 is $-(CR^{13}R^{14})_n-Z$.

31. The compound of claim 1 wherein:

R^1 is H;

R^2 and R^3 are each, independently, H or C_1-C_6 alkyl;

A is CR^4 ;

R^4 is H, C_1-C_4 alkyl, C_1-C_4 haloalkyl, C_3-C_7 cycloalkyl, C_1-C_4 alkoxy, aryloxy, aralkoxy, hydroxy, or $O(CH_2)_aNR^{4c}R^{4d}$;

R^{4c} and R^{4d} are each, independently, H, C_1-C_4 alkyl, or R^{4c} and R^{4d} together with the N atom to which they are attached form a 5- or 6-membered heterocycle;

a is 1 or 2;

R^5 is NH-Q;

Q is aryl, heteroaryl, cycloalkyl, or heterocycloalkyl, wherein Q is optionally substituted by one or more C_1-C_{10} alkyl, C_2-C_{10} alkenyl, C_2-C_{10} alkynyl, alkoxy, aryloxy, aralkoxy, aralkyl, OH, SH, thioalkoxy, halo, C_1-C_{10} haloalkyl, haloalkoxy, COOH, $C(O)-(C_1-C_6 \text{ alkyl})$, $C(O)-(C_3-C_7 \text{ cycloalkyl})$, $C(O)\text{-aryl}$, $C(O)O-(C_1-C_6 \text{ alkyl})$, $C(O)O-(C_3-C_7 \text{ cycloalkyl})$, $C(O)O\text{-aryl}$, $C(O)NR^{Q1}R^{Q2}$, NO_2 , CN, or $NR^{Q3}R^{Q4}$;

R^{Q1} and R^{Q2} are each, independently, H, C_1-C_6 alkyl, C_3-C_6 cycloalkyl, aryl, or R^{Q1} and R^{Q2} together with the N atom to which they are attached form a 5- or 6-membered heterocycle;

R^{Q3} and R^{Q4} are each, independently, H, C_1-C_6 alkyl, aryl, $C(O)-C_1-C_6$ alkyl, $C(O)-(C_3-C_7 \text{ cycloalkyl})$, $C(O)\text{-aryl}$, $C(O)O-(C_1-C_6 \text{ alkyl})$, $C(O)O-(C_3-C_7 \text{ cycloalkyl})$, $C(O)O\text{-aryl}$, or R^{Q1} and R^{Q2} together with the N atom to which they are attached form a 5- or 6-membered heterocycle;

or R^5 is phenyl, naphthyl, or heteroaryl, wherein said naphthyl or heteroaryl is substituted by one or more OH or $O(CR^8R^9)_pY$ and wherein said phenyl is substituted by one or more $O(CR^8R^9)_pY$;

R^8 and R^9 are each, independently, H or C_1-C_4 alkyl;

p is 1, 2, or 3;

Y is Y^1 or Y^2 ;

Y^1 is $NR^{10}R^{11}$;

R^{10} and R^{11} are each, independently, H, C_1 - C_6 alkyl, $C(O)$ -(C_1 - C_6 alkyl), $C(O)$ -(C_3 - C_7 cycloalkyl), $C(O)$ -aryl, $C(O)O$ -(C_1 - C_6 alkyl), $C(O)O$ -(C_3 - C_7 cycloalkyl), $C(O)O$ -aryl, aryl, heteroaryl, cycloalkyl, or heterocycloalkyl, or R^{10} and R^{11} together with the N atom to which they are attached form a 5- or 6- membered heterocycle;

Y^2 is OR^{12a} or OSO_2R^{12b} ;

R^{12a} is H, C_1 - C_{10} alkyl, C_1 - C_{10} alkenyl, C_1 - C_{10} alkynyl, aryl, heteroaryl, C_3 - C_7 cycloalkyl, or heterocycloalkyl;

R^{12b} is H, C_1 - C_6 alkyl, aryl, or NH_2 ;

or R^5 is cycloalkyl optionally substituted by one or more halo, C_1 - C_{10} alkyl, C_1 - C_{10} haloalkyl, C_2 - C_{10} alkenyl, C_2 - C_{10} alkynyl, alkoxy, aryloxy, aralkoxy, aralkyl, OH, SH, thioalkoxy, haloalkoxy, COOH, $C(O)$ -(C_1 - C_6 alkyl), $C(O)$ -(C_3 - C_7 cycloalkyl), $C(O)$ -aryl, $C(O)O$ -(C_1 - C_6 alkyl), $C(O)O$ -(C_3 - C_7 cycloalkyl), $C(O)O$ -aryl, $CONR^{5b}R^{5c}$, NO_2 , CN, $NR^{5d}R^{5e}$, or $O(CR^8R^9)_pY$;

R^{5b} and R^{5c} are each, independently, H, C_1 - C_6 alkyl, C_3 - C_6 cycloalkyl, aryl, or R^{5b} and R^{5c} together with the N atom to which they are attached form a 5- or 6- membered heterocycle;

R^{5d} and R^{5e} are each, independently, H, C_1 - C_6 alkyl, aryl, $C(O)$ - C_1 - C_6 alkyl, $C(O)$ -(C_3 - C_7 cycloalkyl), $C(O)$ -aryl, $C(O)O$ -(C_1 - C_6 alkyl), $C(O)O$ -(C_3 - C_7 cycloalkyl), $C(O)O$ -aryl, or R^{5d} and R^{5e} together with the N atom to which they are attached form a 5- or 6-membered heterocycle;

or R^5 is $-(CR^{13}R^{14})_n-Z$;

n is 1, 2, or 3;

R^{13} and R^{14} are each, independently, H or C_1 - C_4 alkyl;

Z is naphthyl, anthracenyl, or heteroaryl, wherein said naphthyl, anthracenyl, or heteroaryl, is optionally substituted by one or more R^{15} ;

or Z is phenyl optionally substituted by at least one R^{16} ;

R^{15} is halo, C_1 - C_{10} alkyl, C_1 - C_{10} haloalkyl, C_2 - C_{10} alkenyl, C_2 - C_{10} alkynyl, alkoxy, aryloxy, aralkoxy, aralkyl, OH, SH, thioalkoxy, haloalkoxy, COOH, $C(O)$ -(C_1 - C_6 alkyl), $C(O)$ -(C_3 - C_7 cycloalkyl), $C(O)$ -aryl, $C(O)O$ -(C_1 - C_6 alkyl), $C(O)O$ -(C_3 - C_7 cycloalkyl), $C(O)O$ -aryl, $CONR^{18a}R^{19a}$, NO_2 , CN, $(CH_2)_tNR^{18b}R^{19b}$, heteroaryl, heterocycloalkyl, aryl, C_3 - C_7 cycloalkyl, or $O(CR^{20}R^{21})_rX$;

R^{16} is C_2 - C_{10} alkenyl, C_2 - C_{10} alkynyl, C_2 - C_{10} alkoxy, aryloxy, aralkoxy, aralkyl, OH, SH, thioalkoxy, haloalkyl, haloalkoxy, COOH, $C(O)$ -(C_1 - C_6 alkyl),

C(O)-(C₃-C₇ cycloalkyl), C(O)-aryl, C(O)O-(C₁-C₆ alkyl), C(O)O-(C₃-C₇ cycloalkyl), C(O)O-aryl, CONR^{18a}R^{19a}, NO₂, CN, (CH₂)_tNR^{18b}R^{19b}, heteroaryl, heterocycloalkyl, aryl, C₃-C₇ cycloalkyl, or O(CR²⁰R²¹)_rX;

R^{18a} and R^{19a} are each, independently, H or C₁-C₆ alkyl, or R^{18a} and R^{19a} together with the N atom to which they are attached form a 5- or 6-membered heterocycle;

R^{18b} and R^{19b} are each, independently, H, C₁-C₆ alkyl, aryl, C(O)-C₁-C₆ alkyl, C(O)-(C₃-C₇ cycloalkyl), C(O)-aryl, C(O)O-(C₁-C₆ alkyl), C(O)O-(C₃-C₇ cycloalkyl), C(O)O-aryl, or R^{18b} and R^{19b} together with the N atom to which they are attached form a 5- or 6-membered heterocycle;

R²⁰ and R²¹ are each, independently, H or C₁-C₄ alkyl;

r is 0, 1, or 2;

t is 0, 1, or 2;

X is X¹ or X²;

X¹ is NR²²R²³, C₃-C₇ cycloalkyl, aryl, heteroaryl, or heterocycloalkyl, wherein X¹ is optionally substituted by one or more halo, C₁-C₆ alkyl, C₃-C₇ cycloalkyl, C₁-C₆ haloalkyl, aryl, heteroaryl, heterocycloalkyl, CN, NO₂, OH, COOH, C(O)-C₁-C₆ alkyl, C(O)-(C₃-C₇ cycloalkyl), C(O)-aryl, C(O)O-(C₁-C₆ alkyl), C(O)O-(C₃-C₇ cycloalkyl), C(O)O-aryl, NH₂, NH(C₁-C₄ alkyl), N(C₁-C₄ alkyl)₂, NHC(O)O-(C₁-C₆ alkyl), NHC(O)O-aryl or (CH₂)_sOH;

R²² and R²³ are each, independently, H, C₁-C₆ alkyl, aryl, heteroaryl, heterocycloalkyl, cycloalkyl, C(O)-C₁-C₆ alkyl, C(O)-(C₃-C₇ cycloalkyl), C(O)-aryl, C(O)O-(C₁-C₆ alkyl), C(O)O-(C₃-C₇ cycloalkyl), C(O)O-aryl, or R²² and R²³ together with the N atom to which they are attached form a 5- or 6-membered heterocycle;

s is 0, 1, 2, or 3;

X² is OH, NH₂, or OSO₂R²⁴;

R²⁴ is H, C₁-C₆ alkyl, aryl, or NH₂; and

R⁶ and R⁷ are each, independently, H or C₁-C₆ alkyl;

with the proviso that when R⁵ is -(CR¹³R¹⁴)_n-Z and Z is unsubstituted phenyl, R⁴ is other than H and C₁-C₆ alkyl.

32. The compound of claim 1 wherein:

R¹ is H;

R² and R³ are each H;

A is CH; and

R⁶ and R⁷ are each methyl.

33. The compound of claim 1 wherein:

R¹ is H;

R² and R³ are each H;

A is CH;

R⁵ is $-(\text{CR}^{13}\text{R}^{14})_n\text{-Z}$;

n is 1 or 2; and

R⁶ and R⁷ are each methyl.

34. The compound of claim 1 wherein:

A is CR⁴;

R⁴ is hydroxy, alkoxy, cyloalkyloxy, aryloxy, heteroaryloxy, heterocycloalkyloxy, aralkoxy, cycloalkylalkyloxy, heteroarylalkyloxy, heterocycloalkylalkyloxy, or $\text{O}(\text{CR}^{4a}\text{R}^{4b})_a\text{NR}^{4c}\text{R}^{4d}$;

R^{4a} and R^{4b} are each, independently, H or C₁-C₄ alkyl;

R^{4c} and R^{4d} are each, independently, H, C₁-C₄ alkyl, C₃-C₇ cycloalkyl, C₁-C₄ haloalkyl, aryl, C(O)-(C₁-C₆ alkyl), C(O)-aryl, C(O)-(C₃-C₇ cycloalkyl), C(O)O-(C₁-C₆ alkyl), C(O)O-aryl, or C(O)O-(C₃-C₇ cycloalkyl), or R^{4c} and R^{4d} together with the N atom to which they are attached form a 5- or 6-membered heterocycle; and

a is 1, 2, 3, 4, 5, or 6.

35. The compound of claim 1 wherein:

A is CR⁴;

R⁴ is hydroxy, alkoxy, cyloalkyloxy, aryloxy, aralkoxy, heterocycloalkyloxy, heterocycloalkylalkyloxy, or $\text{O}(\text{CR}^{4a}\text{R}^{4b})_a\text{NR}^{4c}\text{R}^{4d}$;

R^{4a} and R^{4b} are each, independently, H or C₁-C₄ alkyl;

R^{4c} and R^{4d} are each, independently, H, C₁-C₄ alkyl, C₃-C₇ cycloalkyl, C₁-C₄ haloalkyl, aryl, C(O)-(C₁-C₆ alkyl), C(O)-aryl, C(O)-(C₃-C₇ cycloalkyl), C(O)O-(C₁-C₆ alkyl), C(O)O-aryl, or C(O)O-(C₃-C₇ cycloalkyl), or R^{4c} and R^{4d} together with the N atom to which they are attached form a 5- or 6-membered heterocycle;

a is 1, 2, 3, 4, 5, or 6; and

R⁶ and R⁷ are each, independently, H, halo, C₁-C₃ alkyl, or C₁-C₆ haloalkyl.

36. The compound of claim 1 wherein:

R^1 , R^2 , and R^3 are each H;

A is CR^4 ;

R^4 is hydroxy, alkoxy, cyloalkoxy, aryloxy, aralkoxy, heterocycloalkoxy, heterocycloalkylalkoxy, or $O(CR^{4a}R^{4b})_aNR^{4c}R^{4d}$;

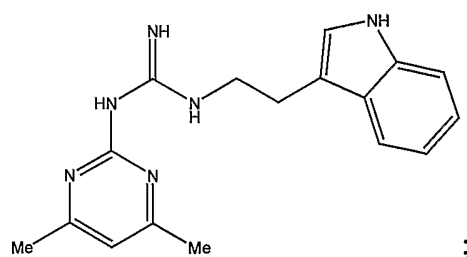
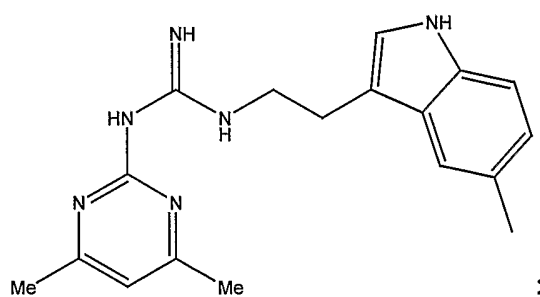
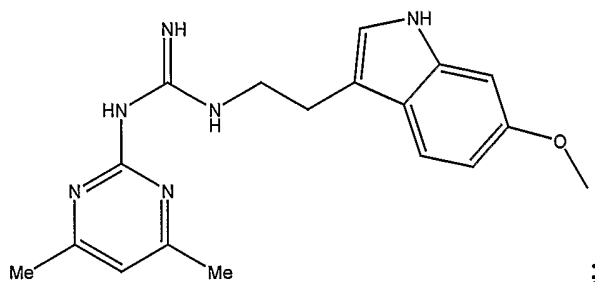
R^{4a} and R^{4b} are each, independently, H or C_1 - C_4 alkyl;

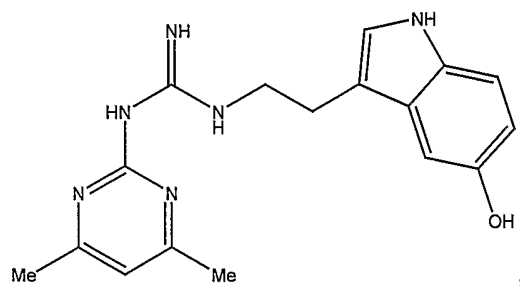
R^{4c} and R^{4d} are each, independently, H, C_1 - C_4 alkyl, C_3 - C_7 cycloalkyl, C_1 - C_4 haloalkyl, aryl, $C(O)$ -(C_1 - C_6 alkyl), $C(O)$ -aryl, $C(O)$ -(C_3 - C_7 cycloalkyl), $C(O)O$ -(C_1 - C_6 alkyl), $C(O)O$ -aryl, or $C(O)O$ -(C_3 - C_7 cycloalkyl), or R^{4c} and R^{4d} together with the N atom to which they are attached form a 5- or 6-membered heterocycle;

a is 1, 2, 3, 4, 5, or 6; and

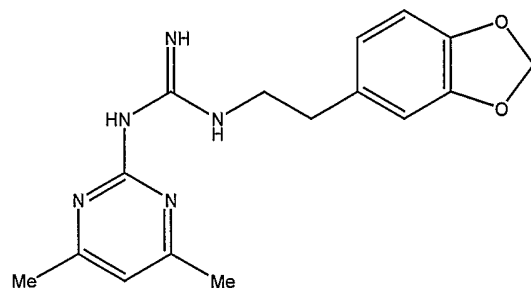
R^6 and R^7 are each, independently, H, halo, C_1 - C_3 alkyl, or C_1 - C_6 haloalkyl.

37. A compound of claim 1 having the Formula:

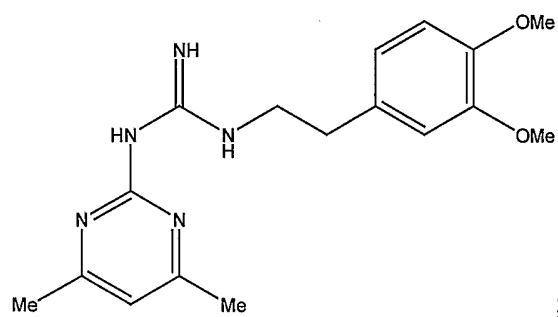




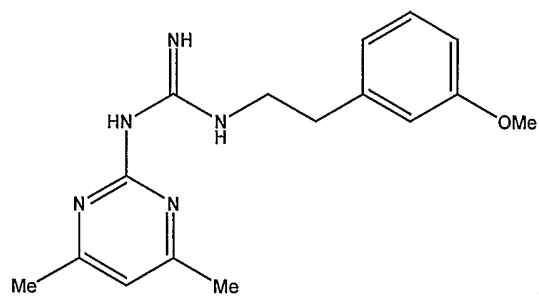
;



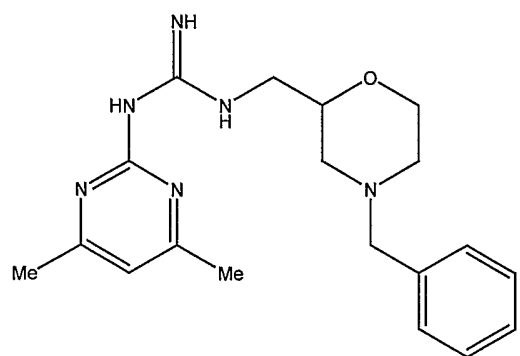
;



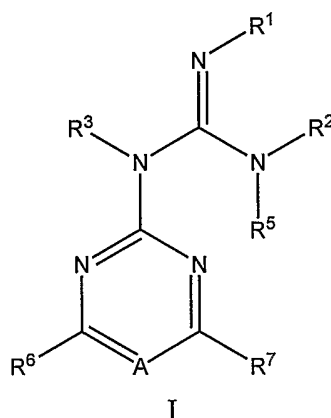
;



; or



38. A compound of Formula I:



or pharmaceutically acceptable salt form thereof, wherein:

R^1 is H or COOR^{1a} ;

R^{1a} is H or $\text{C}_1\text{-C}_{10}$ alkyl, aryl, cycloalkyl, or aralkyl;

R^2 and R^3 are each, independently, H, $\text{C}_1\text{-C}_{10}$ alkyl, or $\text{C}_3\text{-C}_7$ cycloalkyl;

A is CR^4 ;

R^4 is OH, alkoxy, aryloxy, aralkoxy, cycloalkyloxy, cycloalkylalkyloxy, heterocycloalkyloxy, heterocycloalkylalkyloxy, heteroaryloxy, heteroarylalkyloxy, or $\text{O}(\text{CR}^{4a}\text{R}^{4b})_a\text{NR}^{4c}\text{R}^{4d}$;

R^{4a} and R^{4b} are each, independently, H or $\text{C}_1\text{-C}_4$ alkyl;

R^{4c} and R^{4d} are each, independently, H, $\text{C}_1\text{-C}_4$ alkyl, $\text{C}_3\text{-C}_7$ cycloalkyl, $\text{C}_1\text{-C}_4$ haloalkyl, aryl, $\text{C}(\text{O})\text{-(C}_1\text{-C}_6\text{ alkyl)}$, $\text{C}(\text{O})\text{-aryl}$, $\text{C}(\text{O})\text{-(C}_3\text{-C}_7\text{ cycloalkyl)}$, $\text{C}(\text{O})\text{O-(C}_1\text{-C}_6\text{ alkyl)}$, $\text{C}(\text{O})\text{O-aryl}$, or $\text{C}(\text{O})\text{O-(C}_3\text{-C}_7\text{ cycloalkyl)}$, or R^{4c} and R^{4d} together with the N atom to which they are attached form a 5- or 6-membered heterocycle;

a is 1, 2, 3, 4, 5, or 6;

R^5 is $\text{N(R}^{5a}\text{)-Q}$;

R^{5a} is H or $\text{C}_1\text{-C}_6$ alkyl;

Q is aryl, heteroaryl, cycloalkyl, or heterocycloalkyl, wherein Q is optionally substituted by one or more $\text{C}_1\text{-C}_{10}$ alkyl, $\text{C}_2\text{-C}_{10}$ alkenyl, $\text{C}_2\text{-C}_{10}$ alkynyl, alkoxy, aryloxy, aralkoxy, aralkyl, OH, SH, thioalkoxy, halo, $\text{C}_1\text{-C}_{10}$ haloalkyl, haloalkoxy, COOH , $\text{C}(\text{O})\text{-(C}_1\text{-C}_6\text{ alkyl)}$, $\text{C}(\text{O})\text{-(C}_3\text{-C}_7\text{ cycloalkyl)}$, $\text{C}(\text{O})\text{-aryl}$, $\text{C}(\text{O})\text{O-(C}_1\text{-C}_6\text{ alkyl)}$, $\text{C}(\text{O})\text{O-(C}_3\text{-C}_7\text{ cycloalkyl)}$, $\text{C}(\text{O})\text{O-aryl}$, $\text{C}(\text{O})\text{NR}^{\text{Q1}}\text{R}^{\text{Q2}}$, NO_2 , CN, or $\text{NR}^{\text{Q3}}\text{R}^{\text{Q4}}$;

R^{Q1} and R^{Q2} are each, independently, H, $\text{C}_1\text{-C}_6$ alkyl, $\text{C}_3\text{-C}_6$ cycloalkyl, aryl, or R^{Q1} and R^{Q2} together with the N atom to which they are attached form a 5- or 6-membered heterocycle;

R^{Q3} and R^{Q4} are each, independently, H, C₁-C₆ alkyl, aryl, C(O)-C₁-C₆ alkyl, C(O)-(C₃-C₇ cycloalkyl), C(O)-aryl, C(O)O-(C₁-C₆ alkyl), C(O)O-(C₃-C₇ cycloalkyl), C(O)O-aryl, or R^{Q1} and R^{Q2} together with the N atom to which they are attached form a 5- or 6-membered heterocycle;

or R^5 is aryl or heteroaryl, wherein said aryl or heteroaryl is optionally substituted by one or more OH or O(CR⁸R⁹)_pY;

R^8 and R^9 are each, independently, H or C₁-C₄ alkyl;

p is 1, 2, 3, 4, 5, or 6;

Y is Y¹ or Y²;

Y¹ is NR¹⁰R¹¹, C₃-C₇ cycloalkyl, heterocycloalkyl, or heteroaryl, wherein Y¹ is optionally substituted by one or more halo, C₁-C₆ alkyl, C₁-C₆ haloalkyl, C₂-C₆ alkenyl, C₂-C₆ alkynyl, C₃-C₇ cycloalkyl, aryl, heteroaryl, heterocycloalkyl, OH, SH, CN, NO₂, COOH, C(O)-(C₁-C₆ alkyl), C(O)-(C₃-C₇ cycloalkyl), C(O)-aryl, C(O)O-(C₁-C₆ alkyl), C(O)O-(C₃-C₇ cycloalkyl), C(O)O-aryl, NH₂, NH(C₁-C₄ alkyl), N(C₁-C₄ alkyl)₂, NHC(O)O-(C₁-C₆ alkyl), NHC(O)O-aryl or (CH₂)_qOH;

R^{10} and R^{11} are each, independently, H, (C₁-C₆)alkyl, C(O)-(C₁-C₆ alkyl), C(O)-(C₃-C₇ cycloalkyl), C(O)-aryl, C(O)O-(C₁-C₆ alkyl), C(O)O-(C₃-C₇ cycloalkyl), C(O)O-aryl, aryl, heteroaryl, cycloalkyl, or heterocycloalkyl, or R^{10} and R^{11} together with the N atom to which they are attached form a 5- or 6- membered heterocycle;

q is 0, 1, 2, or 3;

Y² is OR^{12a} or OSO₂R^{12b};

R^{12a} is H, C₁-C₁₀ alkyl, C₁-C₁₀ alkenyl, C₁-C₁₀ alkynyl, aryl, heteroaryl, C₃-C₇ cycloalkyl, or heterocycloalkyl;

R^{12b} is H, C₁-C₆ alkyl, aryl, or NH₂;

or R^5 is cycloalkyl or heterocycloalkyl, wherein said cycloalkyl or heterocycloalkyl is optionally substituted by one or more halo, C₁-C₁₀ alkyl, C₁-C₁₀ haloalkyl, C₂-C₁₀ alkenyl, C₂-C₁₀ alkynyl, aryl, heteroaryl, cycloalkyl, heterocycloalkyl, alkoxy, aryloxy, aralkoxy, aralkyl, OH, SH, thioalkoxy, haloalkoxy, COOH, C(O)-(C₁-C₆ alkyl), C(O)-(C₃-C₇ cycloalkyl), C(O)-aryl, C(O)O-(C₁-C₆ alkyl), C(O)O-(C₃-C₇ cycloalkyl), C(O)O-aryl, CONR^{5b}R^{5c}, NO₂, CN, NR^{5d}R^{5e}, or O(CR⁸R⁹)_pY;

R^{5b} and R^{5c} are each, independently, H, C₁-C₆ alkyl, C₃-C₆ cycloalkyl, aryl, or R^{5b} and R^{5c} together with the N atom to which they are attached form a 5- or 6-membered heterocycle;

R^{5d} and R^{5e} are each, independently, H, C_1 - C_6 alkyl, aryl, $C(O)$ - C_1 - C_6 alkyl, $C(O)$ -(C_3 - C_7 cycloalkyl), $C(O)$ -aryl, $C(O)O$ -(C_1 - C_6 alkyl), $C(O)O$ -(C_3 - C_7 cycloalkyl), $C(O)O$ -aryl, or R^{5d} and R^{5e} together with the N atom to which they are attached form a 5- or 6-membered heterocycle;

or R^5 is $-(CR^{13}R^{14})_n-Z$;

n is 1, 2, 3, 4, 5, 6, 7, or 8;

R^{13} and R^{14} are each, independently, H or C_1 - C_6 alkyl, C_2 - C_6 alkenyl, C_2 - C_6 alkynyl, OH, SH, aryl, or aralkyl, or R^{13} and R^{14} together form C_3 - C_7 cycloalkyl, oxo, or sulfido;

Z is aryl, heteroaryl, cycloalkyl, heterocycloalkyl, biaryl, biheteroaryl, arylheteroaryl, or heteroarylaryl, each of which is optionally substituted by one or more R^{15} ;

R^{15} is halo, C_1 - C_{10} alkyl, C_1 - C_{10} haloalkyl, C_2 - C_{10} alkenyl, C_2 - C_{10} alkynyl, alkoxy, aryloxy, aralkoxy, aralkyl, OH, SH, guanidiny, thioalkoxy, haloalkoxy, COOH, $C(O)$ -(C_1 - C_6 alkyl), $C(O)$ -(C_3 - C_7 cycloalkyl), $C(O)$ -aryl, $C(O)O$ -(C_1 - C_6 alkyl), $C(O)O$ -(C_3 - C_7 cycloalkyl), $C(O)O$ -aryl, $CONR^{18a}R^{19a}$, NO_2 , CN , $(CH_2)_tNR^{18b}R^{19b}$, heteroaryl, heterocycloalkyl, aryl, C_3 - C_7 cycloalkyl, or $O(CR^{20}R^{21})_rX$;

R^{18a} and R^{19a} are each, independently, H or C_1 - C_6 alkyl, or R^{18a} and R^{19a} together with the N atom to which they are attached form a 5- or 6-membered heterocycle;

R^{18b} and R^{19b} are each, independently, H, C_1 - C_6 alkyl, aryl, $C(O)$ - C_1 - C_6 alkyl, $C(O)$ -(C_3 - C_7 cycloalkyl), $C(O)$ -aryl, $C(O)O$ -(C_1 - C_6 alkyl), $C(O)O$ -(C_3 - C_7 cycloalkyl), $C(O)O$ -aryl, or R^{18b} and R^{19b} together with the N atom to which they are attached form a 5- or 6-membered heterocycle;

R^{18c} and R^{19c} are each, independently, H or C_1 - C_6 alkyl, or R^{18c} and R^{19c} together with the N atom to which they are attached form a heterocycle;

R^{18d} and R^{19d} are each, independently, H, C_1 - C_6 alkyl, aryl, $C(O)$ - C_1 - C_6 alkyl, $C(O)$ -(C_3 - C_7 cycloalkyl), $C(O)$ -aryl, $C(O)O$ -(C_1 - C_6 alkyl), $C(O)O$ -(C_3 - C_7 cycloalkyl), $C(O)O$ -aryl, or R^{18d} and R^{19d} together with the N atom to which they are attached form a 5- or 6-membered heterocycle;

R^{20} and R^{21} are each, independently, H or C_1 - C_6 alkyl;

r is 0, 1, 2, 3, 4, 5, or 6;

t is 0, 1, or 2;

X is X^1 or X^2 ;

X^1 is $NR^{22}R^{23}$, C_3 - C_7 cycloalkyl, aryl, heteroaryl, or heterocycloalkyl, wherein X^1 is optionally substituted by one or more halo, C_1 - C_6 alkyl, C_3 - C_7 cycloalkyl, C_1 - C_6 haloalkyl, aryl, heteroaryl, heterocycloalkyl, CN, NO_2 , OH, COOH, $C(O)$ - C_1 - C_6 alkyl, $C(O)$ -(C_3 - C_7 cycloalkyl), $C(O)$ -aryl, $C(O)O$ -(C_1 - C_6 alkyl), $C(O)O$ -(C_3 - C_7 cycloalkyl), $C(O)O$ -aryl, NH_2 , NH (C_1 - C_4 alkyl), N (C_1 - C_4 alkyl) $_2$, $NHC(O)O$ -(C_1 - C_6 alkyl), $NHC(O)O$ -aryl or $(CH_2)_sOH$;

R^{22} and R^{23} are each, independently, H, C_1 - C_6 alkyl, aryl, heteroaryl, heterocycloalkyl, cycloalkyl, $C(O)$ - C_1 - C_6 alkyl, $C(O)$ -(C_3 - C_7 cycloalkyl), $C(O)$ -aryl, $C(O)O$ -(C_1 - C_6 alkyl), $C(O)O$ -(C_3 - C_7 cycloalkyl), $C(O)O$ -aryl, or R^{22} and R^{23} together with the N atom to which they are attached form a 5- or 6-membered heterocycle;

s is 0, 1, 2, or 3;

X^2 is OH or OSO_2R^{24} ;

R^{24} is H, C_1 - C_6 alkyl, aryl, or NH_2 ;

or R^5 and R^2 together with the N atom to which they are attached form heterocycloalkyl optionally substituted by halo, C_1 - C_4 alkyl, OH, SH, alkoxy or aryloxy; and

R^6 and R^7 are each, independently, H, halo, C_1 - C_6 alkyl, C_1 - C_6 haloalkyl, C_2 - C_6 alkenyl, C_2 - C_6 alkynyl, alkoxy, aryloxy, or aralkoxy, or R^6 and R^7 together with the atoms to which they are attached form a fused cycloalkyl, heterocycloalkyl, aryl, or heteroaryl group.

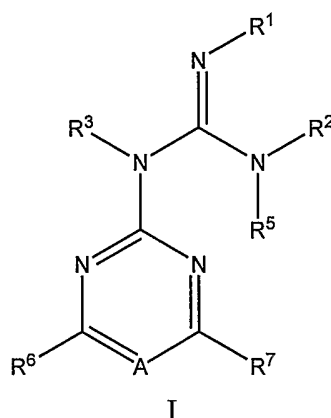
39. The compound of claim 38 wherein R^4 is OH, C_1 - C_6 alkoxy, or $O(CR^{4a}R^{4b})_aNR^{4c}R^{4d}$.

40. The compound of claim 38 wherein R^4 is OH or C_1 - C_6 alkoxy,

41. A composition comprising a compound of claim 1 and a pharmaceutically acceptable carrier.

42. A composition comprising a compound of claim 38 and a pharmaceutically acceptable carrier.

43. A method of modulating activity of an infectious agent comprising contacting said infectious agent with a compound of Formula I:



or pharmaceutically acceptable salt form thereof, wherein:

R^1 is H or COOR^{1a} ;

R^{1a} is H or $\text{C}_1\text{-C}_{10}$ alkyl, aryl, cycloalkyl, or aralkyl;

R^2 and R^3 are each, independently, H, $\text{C}_1\text{-C}_{10}$ alkyl, or $\text{C}_3\text{-C}_7$ cycloalkyl;

A is N or CR^4 ;

R^4 is H, halo, $\text{C}_1\text{-C}_6$ alkyl, $\text{C}_1\text{-C}_6$ haloalkyl, $\text{C}_3\text{-C}_7$ cycloalkyl, $\text{C}_2\text{-C}_6$ alkenyl, $\text{C}_2\text{-C}_6$ alkynyl, OH, alkoxy, aryloxy, aralkoxy, cycloalkyloxy, cycloalkylalkyloxy, heterocycloalkyloxy, heterocycloalkylalkyloxy, heteroaryloxy, heteroarylalkyloxy, cyano, nitro, hydroxy, mercapto, or $\text{O}(\text{CR}^{4a}\text{R}^{4b})_a\text{NR}^{4c}\text{R}^{4d}$;

R^{4a} and R^{4b} are each, independently, H or $\text{C}_1\text{-C}_4$ alkyl;

R^{4c} and R^{4d} are each, independently, H, $\text{C}_1\text{-C}_4$ alkyl, $\text{C}_3\text{-C}_7$ cycloalkyl, $\text{C}_1\text{-C}_4$ haloalkyl, aryl, $\text{C}(\text{O})\text{-(C}_1\text{-C}_6\text{ alkyl)}$, $\text{C}(\text{O})\text{-aryl}$, $\text{C}(\text{O})\text{-(C}_3\text{-C}_7\text{ cycloalkyl)}$, $\text{C}(\text{O})\text{O-(C}_1\text{-C}_6\text{ alkyl)}$, $\text{C}(\text{O})\text{O-aryl}$, or $\text{C}(\text{O})\text{O-(C}_3\text{-C}_7\text{ cycloalkyl)}$, or R^{4c} and R^{4d} together with the N atom to which they are attached form a 5- or 6-membered heterocycle;

a is 1, 2, 3, 4, 5, or 6;

R^5 is $\text{N(R}^{5a}\text{)-Q}$;

R^{5a} is H or $\text{C}_1\text{-C}_6$ alkyl;

Q is aryl, heteroaryl, cycloalkyl, or heterocycloalkyl, wherein Q is optionally substituted by one or more $\text{C}_1\text{-C}_{10}$ alkyl, $\text{C}_2\text{-C}_{10}$ alkenyl, $\text{C}_2\text{-C}_{10}$ alkynyl, alkoxy, aryloxy, aralkoxy, aralkyl, OH, SH, thioalkoxy, halo, $\text{C}_1\text{-C}_{10}$ haloalkyl, haloalkoxy, COOH , $\text{C}(\text{O})\text{-(C}_1\text{-C}_6\text{ alkyl)}$, $\text{C}(\text{O})\text{-(C}_3\text{-C}_7\text{ cycloalkyl)}$, $\text{C}(\text{O})\text{-aryl}$, $\text{C}(\text{O})\text{O-(C}_1\text{-C}_6\text{ alkyl)}$, $\text{C}(\text{O})\text{O-(C}_3\text{-C}_7\text{ cycloalkyl)}$, $\text{C}(\text{O})\text{O-aryl}$, $\text{C}(\text{O})\text{NR}^{Q1}\text{R}^{Q2}$, NO_2 , CN, or $\text{NR}^{Q3}\text{R}^{Q4}$;

R^{Q1} and R^{Q2} are each, independently, H, $\text{C}_1\text{-C}_6$ alkyl, $\text{C}_3\text{-C}_6$ cycloalkyl, aryl, or R^{Q1} and R^{Q2} together with the N atom to which they are attached form a 5- or 6-membered heterocycle;

R^{Q3} and R^{Q4} are each, independently, H, C_1 - C_6 alkyl, aryl, $C(O)$ - C_1 - C_6 alkyl, $C(O)$ -(C_3 - C_7 cycloalkyl), $C(O)$ -aryl, $C(O)O$ -(C_1 - C_6 alkyl), $C(O)O$ -(C_3 - C_7 cycloalkyl), $C(O)O$ -aryl, or R^{Q1} and R^{Q2} together with the N atom to which they are attached form a 5- or 6-membered heterocycle;

or R^5 is aryl, heteroaryl, cycloalkyl, or heterocycloalkyl, wherein said aryl, heteroaryl, cycloalkyl, or heterocycloalkyl is optionally substituted by one or more halo, C_1 - C_{10} alkyl, C_1 - C_{10} haloalkyl, C_2 - C_{10} alkenyl, C_2 - C_{10} alkynyl, aryl, heteroaryl, cycloalkyl, heterocycloalkyl, alkoxy, aryloxy, aralkoxy, aralkyl, CN, NO_2 , OH, SH, thioalkoxy, haloalkoxy, COOH, $C(O)$ -(C_1 - C_6 alkyl), $C(O)$ -aryl, $C(O)$ -(C_3 - C_7 cycloalkyl), $C(O)O$ -(C_1 - C_6 alkyl), $C(O)O$ -aryl, or $C(O)O$ -(C_3 - C_7 cycloalkyl), $CONR^{5b}R^{5c}$, $NR^{5d}R^{5e}$, or $O(CR^8R^9)_pY$;

R^{5b} and R^{5c} are each, independently, H, C_1 - C_6 alkyl, C_3 - C_6 cycloalkyl, aryl, or R^{5b} and R^{5c} together with the N atom to which they are attached form a 5- or 6-membered heterocycle;

R^{5d} and R^{5e} are each, independently, H, C_1 - C_6 alkyl, aryl, $C(O)$ - C_1 - C_6 alkyl, $C(O)$ -(C_3 - C_7 cycloalkyl), $C(O)$ -aryl, $C(O)O$ -(C_1 - C_6 alkyl), $C(O)O$ -(C_3 - C_7 cycloalkyl), $C(O)O$ -aryl, or R^{5d} and R^{5e} together with the N atom to which they are attached form a 5- or 6-membered heterocycle;

R^8 and R^9 are each, independently, H or C_1 - C_6 alkyl;

p is 1, 2, 3, 4, 5, or 6;

Y is $NR^{10}R^{11}$, OR^{12a} , OSO_2R^{12b} , C_3 - C_7 cycloalkyl, heterocycloalkyl, or heteroaryl, wherein Y is optionally substituted by one or more halo, C_1 - C_6 alkyl, C_1 - C_6 haloalkyl, C_2 - C_6 alkenyl, C_2 - C_6 alkynyl, C_3 - C_7 cycloalkyl, aryl, heteroaryl, heterocycloalkyl, OH, SH, CN, NO_2 , COOH, $C(O)$ -(C_1 - C_6 alkyl), $C(O)$ -(C_3 - C_7 cycloalkyl), $C(O)$ -aryl, $C(O)O$ -(C_1 - C_6 alkyl), $C(O)O$ -(C_3 - C_7 cycloalkyl), $C(O)O$ -aryl, NH_2 , $NH(C_1$ - C_4 alkyl), $N(C_1$ - C_4 alkyl) $_2$, $NHC(O)O$ -(C_1 - C_6 alkyl), $NHC(O)O$ -aryl or $(CH_2)_qOH$;

R^{10} and R^{11} are each, independently, H, $(C_1$ - $C_6)$ alkyl, $C(O)$ -(C_1 - C_6 alkyl), $C(O)$ -(C_3 - C_7 cycloalkyl), $C(O)$ -aryl, $C(O)O$ -(C_1 - C_6 alkyl), $C(O)O$ -(C_3 - C_7 cycloalkyl), $C(O)O$ -aryl, aryl, heteroaryl, cycloalkyl, or heterocycloalkyl, or R^{10} and R^{11} together with the N atom to which they are attached form a 5- or 6- membered heterocycle;

q is 0, 1, 2, or 3;

R^{12a} is H, C₁-C₁₀ alkyl, C₁-C₁₀ alkenyl, C₁-C₁₀ alkynyl, aryl, heteroaryl, C₃-C₇ cycloalkyl, or heterocycloalkyl;

R^{12b} is H, C₁-C₆ alkyl, aryl, or NH₂;

or R^5 is $-(CR^{13}R^{14})_n-Z$;

n is 1, 2, 3, 4, 5, 6, 7, or 8;

R^{13} and R^{14} are each, independently, H, C₁-C₆ alkyl, C₂-C₆ alkenyl, C₂-C₆ alkynyl, OH, aryl, or aralkyl, or R^{13} and R^{14} together form cycloalkyl, oxo, or sulfido;

Z is aryl, heteroaryl, cycloalkyl, heterocycloalkyl, biaryl, biheteroaryl, arylheteroaryl, heteroarylaryl, each of which is optionally substituted by one or more R^{15} ,

R^{15} is halo, C₁-C₁₀ alkyl, C₁-C₁₀ haloalkyl, C₂-C₁₀ alkenyl, C₂-C₁₀ alkynyl, alkoxy, aryloxy, aralkoxy, aralkyl, OH, SH, guanidiny, thioalkoxy, haloalkoxy, COOH, C(O)-(C₁-C₆ alkyl), C(O)-(C₃-C₇ cycloalkyl), C(O)-aryl, C(O)O-(C₁-C₆ alkyl), C(O)O-(C₃-C₇ cycloalkyl), C(O)O-aryl, CONR^{18a}R^{19a}, NO₂, CN, (CH₂)_tNR^{18b}R^{19b}, heteroaryl, heterocycloalkyl, aryl, C₃-C₇ cycloalkyl, or O(CR²⁰R²¹)_rX;

R^{18a} and R^{19a} are each, independently, H or C₁-C₆ alkyl, or R^{18a} and R^{19a} together with the N atom to which they are attached form a 5- or 6-membered heterocycle;

R^{18b} and R^{19b} are each, independently, H, C₁-C₆ alkyl, aryl, C(O)-C₁-C₆ alkyl, C(O)-(C₃-C₇ cycloalkyl), C(O)-aryl, C(O)O-(C₁-C₆ alkyl), C(O)O-(C₃-C₇ cycloalkyl), C(O)O-aryl, or R^{18b} and R^{19b} together with the N atom to which they are attached form a 5- or 6-membered heterocycle;

R^{20} and R^{21} are each, independently, H or C₁-C₆ alkyl;

r is 0, 1, 2, 3, 4, 5, or 6;

t is 0, 1, or 2;

X is NR²²R²³, OH, NH₂, OSO₂R²⁴, C₃-C₇ cycloalkyl, aryl, heteroaryl, or heterocycloalkyl, wherein X is optionally substituted by one or more halo, C₁-C₆ alkyl, C₃-C₇ cycloalkyl, C₁-C₆ haloalkyl, aryl, heteroaryl, heterocycloalkyl, CN, NO₂, OH, COOH, C(O)-C₁-C₆ alkyl, C(O)-(C₃-C₇ cycloalkyl), C(O)-aryl, C(O)O-(C₁-C₆ alkyl), C(O)O-(C₃-C₇ cycloalkyl), C(O)O-aryl, NH₂, NH(C₁-C₄ alkyl), N(C₁-C₄ alkyl)₂, NHC(O)O-(C₁-C₆ alkyl), NHC(O)O-aryl or (CH₂)_sOH;

R^{22} and R^{23} are each, independently, H, C₁-C₆ alkyl, aryl, heteroaryl, heterocycloalkyl, cycloalkyl, C(O)-C₁-C₆ alkyl, C(O)-(C₃-C₇ cycloalkyl), C(O)-aryl, C(O)O-(C₁-C₆ alkyl), C(O)O-(C₃-C₇ cycloalkyl), C(O)O-aryl, or R^{22} and R^{23} together with the N atom to which they are attached form a 5- or 6-membered heterocycle;

s is 0, 1, 2, or 3;

R^{24} is H, C_1 - C_6 alkyl, aryl, or NH_2 ;

or R^5 and R^2 together with the N atom to which they are attached form heterocycloalkyl optionally substituted by one or more halo, C_1 - C_4 alkyl, OH, SH, alkoxy or aryloxy; and

R^6 and R^7 are each, independently, H, halo, C_1 - C_6 alkyl, C_1 - C_6 haloalkyl, C_2 - C_6 alkenyl, C_2 - C_6 alkynyl, alkoxy, aryloxy, or aralkoxy, or R^6 and R^7 together with the atoms to which they are attached form a fused cycloalkyl, heterocycloalkyl, aryl, or heteroaryl group.

44. The method of claim 43 wherein said infectious agent is a virus.
45. The method of claim 43 wherein said infectious agent is a virus that can replicate by an IRES-mediated pathway.
46. The method of claim 43 wherein said infectious agent is hepatitis C virus.
47. The method of claim 43 wherein said modulating is inhibiting.
48. The method of claim 43 wherein R^1 is H.
49. The method of claim 43 wherein R^2 and R^3 are each H.
50. The method of claim 43 wherein A is CR^4 .
51. The method of claim 43 wherein R^4 is H.
52. The method of claim 43 wherein R^4 is C_1 - C_4 alkyl.
53. The method of claim 43 wherein R^4 is methyl.
54. The method of claim 43 wherein R^4 is OH, alkoxy, aryloxy, aralkoxy, cycloalkyloxy, cycloalkylalkyloxy, heterocycloalkyloxy, heterocycloalkylalkyloxy, heteroaryloxy, heteroarylalkyloxy, or $O(CR^{4a}R^{4b})_aNR^{4c}R^{4d}$.

55. The method of claim 43 wherein R^4 is OH, alkoxy, or $O(CR^{4a}R^{4b})_aNR^{4c}R^{4d}$.
56. The method of claim 43 wherein R^4 is or $O(CR^{4a}R^{4b})_aNR^{4c}R^{4d}$.
57. The method of claim 43 wherein R^6 and R^7 are each C_1 - C_6 alkyl.
58. The method of claim 43 wherein at least one of R^6 and R^7 is C_1 - C_6 alkyl.
59. The method of claim 43 wherein at least one of R^6 and R^7 is methyl.
60. The method of claim 43 wherein both R^6 and R^7 are methyl.
61. The method of claim 43 wherein R^5 is $-(CR^{13}R^{14})_n-Z$.
62. The method of claim 43 wherein Z is phenyl substituted by at least one $O(CR^{20}R^{21})_rX$.
63. The method of claim 43 wherein n is 1 or 2.
64. The method of claim 43 wherein n is 2.
65. The method of claim 43 wherein R^5 is $-(CR^{13}R^{14})_n-Z$ and n is 1 or 2.
66. The method of claim 43 wherein R^5 is phenyl substituted by at least one $O(CR^8R^9)_pY$.
67. The method of claim 43 wherein R^5 is heteroaryl substituted by at least one $O(CR^8R^9)_pY$.
68. The method of claim 43 wherein R^5 is substituted or unsubstituted cycloalkyl or heterocycloalkyl.

69. The method of claim 43 wherein R^5 is $-(CR^{13}R^{14})_n-Z$ and Z is substituted or unsubstituted pyridinyl, pyrimidinyl, furanyl, thienyl, quinolinyl, isoquinolinyl, indolyl, benzo[1,3]dioxolyl, or benzoimidazolyl.
70. The method of claim 43 wherein R^5 is $-(CR^{13}R^{14})_n-Z$ and Z is furanyl, 2-methylfuranyl, 2,3-dimethylfuranyl, 2-phenylfuranyl, or benzofuranyl.
71. The method of claim 43 wherein R^5 is $-(CR^{13}R^{14})_n-Z$ and at least one of R^{13} and R^{14} is methyl or OH.
72. The method of claim 43 wherein R^5 is $-(CR^{13}R^{14})_n-Z$ and Z is phenyl substituted by at least one $O(CR^{20}R^{21})_rX$.
73. The method of claim 43 wherein R^5 is $-(CR^{13}R^{14})_n-Z$ and Z is substituted or unsubstituted biaryl, biheteroaryl, arylheteroaryl, or heteroarylaryl.
74. The method of claim 43 wherein R^5 is $N(R^{5a})-Q$.
75. The method of claim 43 wherein R^5 is substituted or unsubstituted aryl, heteroaryl, cycloalkyl, or heterocycloalkyl.
76. The method of claim 43 wherein:
 R^5 is $N(R^{5a})-Q$;
 or R^5 is aryl, heteroaryl, cycloalkyl, or heterocycloalkyl, wherein said aryl, heteroaryl, cycloalkyl, or heterocycloalkyl is optionally substituted by one or more halo, C_1 - C_{10} alkyl, C_1 - C_{10} haloalkyl, C_2 - C_{10} alkenyl, C_2 - C_{10} alkynyl, alkoxy, aryloxy, aralkoxy, aralkyl, CN, NO_2 , OH, SH, thioalkoxy, haloalkoxy, COOH, $C(O)-(C_1-C_6 \text{ alkyl})$, $C(O)-\text{aryl}$, $C(O)-(C_3-C_7 \text{ cycloalkyl})$, $C(O)O-(C_1-C_6 \text{ alkyl})$, $C(O)O-\text{aryl}$, or $C(O)O-(C_3-C_7 \text{ cycloalkyl})$, $CONR^{5b}R^{5c}$, $NR^{5d}R^{5e}$, or $O(CR^8R^9)_pY$;
 or R^5 is $-(CR^{13}R^{14})_n-Z$.
77. The method of claim 43 wherein:
 R^1 is H;
 R^2 and R^3 are each, independently, H, C_1 - C_6 alkyl;

A is CR⁴;

R⁴ is H, C₁-C₆ alkyl, C₁-C₆ haloalkyl, alkoxy, or O(CR^{4a}R^{4b})_aNR^{4c}R^{4d};

R^{4a} and R^{4b} are each H;

R^{4c} and R^{4d} are each, independently, H, C₁-C₄ alkyl, C₃-C₇ cycloalkyl, C₁-C₄ haloalkyl, aryl, C(O)-(C₁-C₆ alkyl), C(O)-aryl, C(O)-(C₃-C₇ cycloalkyl), C(O)O-(C₁-C₆ alkyl), C(O)O-aryl, or C(O)O-(C₃-C₇ cycloalkyl), or R^{4c} and R^{4d} together with the N atom to which they are attached form a 5- or 6-membered heterocycle;

a is 1, 2, or 3;

R⁵ is NH-Q;

Q is aryl, heteroaryl, cycloalkyl, or heterocycloalkyl, wherein Q is optionally substituted by one or more C₁-C₁₀ alkyl, C₂-C₁₀ alkenyl, C₂-C₁₀ alkynyl, alkoxy, aryloxy, aralkoxy, aralkyl, OH, SH, thioalkoxy, halo, C₁-C₁₀ haloalkyl, haloalkoxy, COOH, C(O)-(C₁-C₆ alkyl), C(O)-(C₃-C₇ cycloalkyl), C(O)-aryl, C(O)O-(C₁-C₆ alkyl), C(O)O-(C₃-C₇ cycloalkyl), C(O)O-aryl, C(O)NR^{Q1}R^{Q2}, NO₂, CN, or NR^{Q3}R^{Q4};

R^{Q1} and R^{Q2} are each, independently, H, C₁-C₆ alkyl, C₃-C₆ cycloalkyl, aryl, or R^{Q1} and R^{Q2} together with the N atom to which they are attached form a 5- or 6-membered heterocycle;

R^{Q3} and R^{Q4} are each, independently, H, C₁-C₆ alkyl, aryl, C(O)-C₁-C₆ alkyl, C(O)-(C₃-C₇ cycloalkyl), C(O)-aryl, C(O)O-(C₁-C₆ alkyl), C(O)O-(C₃-C₇ cycloalkyl), C(O)O-aryl, or R^{Q1} and R^{Q2} together with the N atom to which they are attached form a 5- or 6-membered heterocycle;

or R⁵ is aryl, heteroaryl, cycloalkyl, or heterocycloalkyl, wherein said aryl, heteroaryl, cycloalkyl, or heterocycloalkyl is optionally substituted by one or more halo, C₁-C₁₀ alkyl, C₁-C₁₀ haloalkyl, C₂-C₁₀ alkenyl, C₂-C₁₀ alkynyl, alkoxy, aryloxy, aralkoxy, aralkyl, CN, NO₂, OH, SH, thioalkoxy, haloalkoxy, COOH, C(O)-(C₁-C₆ alkyl), C(O)-aryl, C(O)-(C₃-C₇ cycloalkyl), C(O)O-(C₁-C₆ alkyl), C(O)O-aryl, or C(O)O-(C₃-C₇ cycloalkyl), CONR^{5b}R^{5c}, NR^{5d}R^{5e}, or O(CR⁸R⁹)_pY;

R^{5b} and R^{5c} are each, independently, H, C₁-C₆ alkyl, C₃-C₆ cycloalkyl, aryl, or R^{5b} and R^{5c} together with the N atom to which they are attached form a 5- or 6-membered heterocycle;

R^{5d} and R^{5e} are each, independently, H, C₁-C₆ alkyl, aryl, C(O)-C₁-C₆ alkyl, C(O)-(C₃-C₇ cycloalkyl), C(O)-aryl, C(O)O-(C₁-C₆ alkyl), C(O)O-(C₃-C₇ cycloalkyl), C(O)O-aryl, or R^{5d} and R^{5e} together with the N atom to which they are attached form a 5- or 6-membered heterocycle;

R^8 and R^9 are each, independently, H or C_1 - C_6 alkyl;

p is 1 or 2;

Y is $NR^{10}R^{11}$, OR^{12a} , OSO_2R^{12b} , C_3 - C_7 cycloalkyl, heterocycloalkyl, or heteroaryl, wherein Y is optionally substituted by one or more halo, C_1 - C_6 alkyl, C_1 - C_6 haloalkyl, C_2 - C_6 alkenyl, C_2 - C_6 alkynyl, C_3 - C_7 cycloalkyl, aryl, heteroaryl, heterocycloalkyl, OH, SH, CN, NO_2 , COOH, $C(O)$ -(C_1 - C_6 alkyl), $C(O)$ -(C_3 - C_7 cycloalkyl), $C(O)$ -aryl, $C(O)O$ -(C_1 - C_6 alkyl), $C(O)O$ -(C_3 - C_7 cycloalkyl), $C(O)O$ -aryl, NH_2 , NH (C_1 - C_4 alkyl), N (C_1 - C_4 alkyl) $_2$, $NHC(O)O$ -(C_1 - C_6 alkyl), $NHC(O)O$ -aryl or $(CH_2)_qOH$;

R^{10} and R^{11} are each, independently, H, C_1 - C_6 alkyl, $C(O)$ -(C_1 - C_6 alkyl), $C(O)$ -(C_3 - C_7 cycloalkyl), $C(O)$ -aryl, $C(O)O$ -(C_1 - C_6 alkyl), $C(O)O$ -(C_3 - C_7 cycloalkyl), $C(O)O$ -aryl, aryl, heteroaryl, cycloalkyl, or heterocycloalkyl, or R^{10} and R^{11} together with the N atom to which they are attached form a 5- or 6- membered heterocycle;

q is 0, 1, 2, or 3;

R^{12a} is H, C_1 - C_{10} alkyl, C_1 - C_{10} alkenyl, C_1 - C_{10} alkynyl, aryl, heteroaryl, C_3 - C_7 cycloalkyl, or heterocycloalkyl;

R^{12b} is H, C_1 - C_6 alkyl, aryl, or NH_2 ;

or R^5 is $-(CR^{13}R^{14})_n-Z$;

n is 1, 2, or 3;

R^{13} and R^{14} are each, independently, H or C_1 - C_4 alkyl;

Z is aryl, heteroaryl, cycloalkyl, or heterocycloalkyl, wherein said aryl, heteroaryl, cycloalkyl, or heterocycloalkyl is optionally substituted by one or more R^{15} ,

R^{15} is halo, C_1 - C_6 alkyl, C_1 - C_6 haloalkyl, C_2 - C_6 alkenyl, C_2 - C_6 alkynyl, alkoxy, aryloxy, aralkoxy, aralkyl, OH, SH, thioalkoxy, haloalkoxy, COOH, $C(O)$ -(C_1 - C_6 alkyl), $C(O)$ -(C_3 - C_7 cycloalkyl), $C(O)$ -aryl, $C(O)O$ -(C_1 - C_6 alkyl), $C(O)O$ -(C_3 - C_7 cycloalkyl), $C(O)O$ -aryl, $CONR^{18a}R^{19a}$, NO_2 , CN, $(CH_2)_tNR^{18b}R^{19b}$, heteroaryl, heterocycloalkyl, aryl, C_3 - C_7 cycloalkyl, or $O(CR^{20}R^{21})_rX$;

R^{18a} and R^{19a} are each, independently, H or C_1 - C_6 alkyl, or R^{18a} and R^{19a} together with the N atom to which they are attached form a 5- or 6- membered heterocycle;

R^{18b} and R^{19b} are each, independently, H, C_1 - C_6 alkyl, aryl, $C(O)$ - C_1 - C_6 alkyl, $C(O)$ -(C_3 - C_7 cycloalkyl), $C(O)$ -aryl, $C(O)O$ -(C_1 - C_6 alkyl), $C(O)O$ -(C_3 -

C₇ cycloalkyl), C(O)O-aryl, or R^{18b} and R^{19b} together with the N atom to which they are attached form a 5- or 6-membered heterocycle;

R²⁰ and R²¹ are each, independently, H or C₁-C₄ alkyl;

r is 0, 1, 2, or 3;

t is 0, 1, or 2;

X is NR²²R²³, OH, NH₂, OSO₂R²⁴, C₃-C₇ cycloalkyl, aryl, heteroaryl, or heterocycloalkyl, wherein X is optionally substituted by one or more halo, C₁-C₆ alkyl, C₃-C₇ cycloalkyl, C₁-C₆ haloalkyl, aryl, heteroaryl, heterocycloalkyl, CN, NO₂, OH, COOH, C(O)-C₁-C₆ alkyl, C(O)-(C₃-C₇ cycloalkyl), C(O)-aryl, C(O)O-(C₁-C₆ alkyl), C(O)O-(C₃-C₇ cycloalkyl), C(O)O-aryl, NH₂, NH(C₁-C₄ alkyl), N(C₁-C₄ alkyl)₂, NHC(O)O-(C₁-C₆ alkyl), NHC(O)O-aryl or (CH₂)_sOH;

R²² and R²³ are each, independently, H, C₁-C₆ alkyl, aryl, heteroaryl, heterocycloalkyl, cycloalkyl, C(O)-C₁-C₆ alkyl, C(O)-(C₃-C₇ cycloalkyl), C(O)-aryl, C(O)O-(C₁-C₆ alkyl), C(O)O-(C₃-C₇ cycloalkyl), C(O)O-aryl, or R²² and R²³ together with the N atom to which they are attached form a 5- or 6-membered heterocycle;

s is 0 or 1;

R²⁴ is H, C₁-C₆ alkyl, aryl, or NH₂; and

R⁶ and R⁷ are each, independently, H, C₁-C₄ alkyl, C₁-C₄ alkoxy.

78. The method of claim 43 wherein:

R¹ is H;

R² and R³ are each H;

A is CH; and

R⁶ and R⁷ are each methyl.

79. The method of claim 43 wherein:

R¹ is H;

R² and R³ are each H;

A is CH;

R⁵ is -(CR¹³R¹⁴)_n-Z;

n is 1 or 2; and

R⁶ and R⁷ are each methyl.

80. The method of claim 43 wherein:

A is CR⁴; and

R⁴ is alkoxy, aryloxy, aralkoxy, cycloalkyloxy, cycloalkylalkyloxy, heterocycloalkyloxy, heterocycloalkylalkyloxy, heteroaryloxy, heteroarylalkyloxy, hydroxy, or O(CR^{4a}R^{4b})_aNR^{4c}R^{4d}.

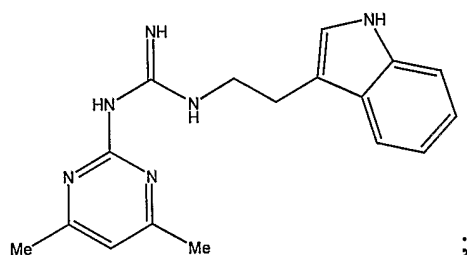
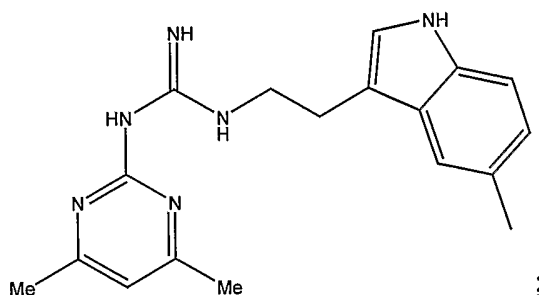
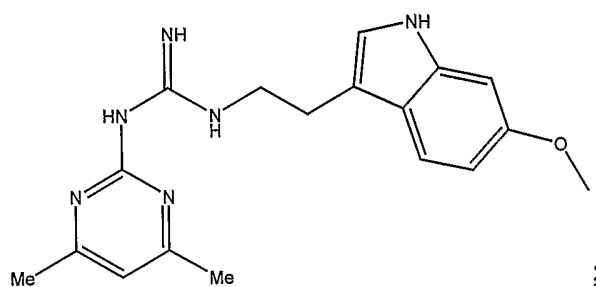
81. The method of claim 43 wherein:

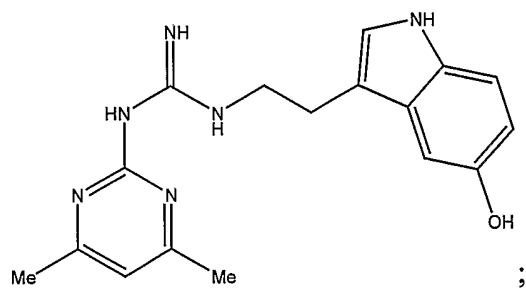
A is CR⁴;

R⁴ is alkoxy, aryloxy, aralkoxy, cycloalkyloxy, cycloalkylalkyloxy, heterocycloalkyloxy, heterocycloalkylalkyloxy, heteroaryloxy, heteroarylalkyloxy, hydroxy, or O(CR^{4a}R^{4b})_aNR^{4c}R^{4d}; and

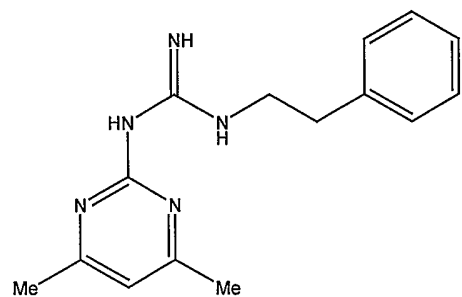
R⁶ and R⁷ are each, independently, H, halo, C₁-C₃ alkyl, or C₁-C₆ haloalkyl.

82. The method of claim 43 wherein said compound has the Formula:

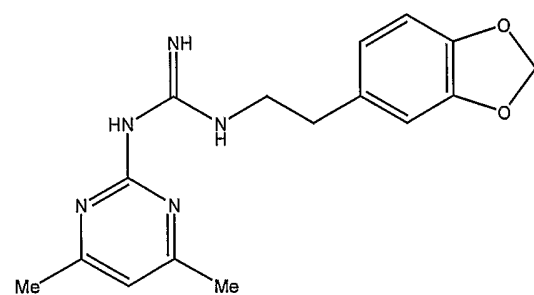




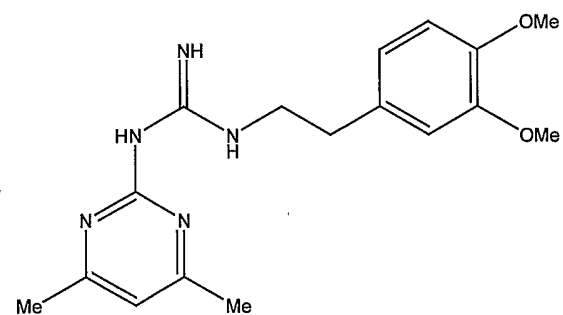
;



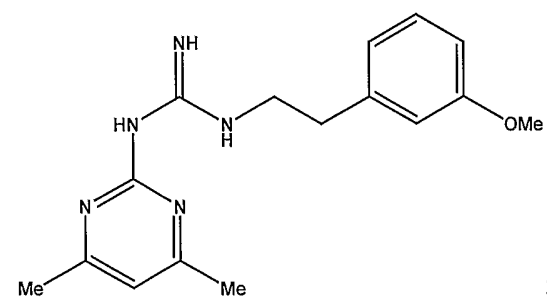
;



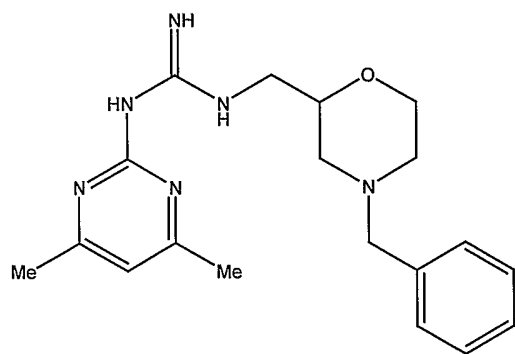
;



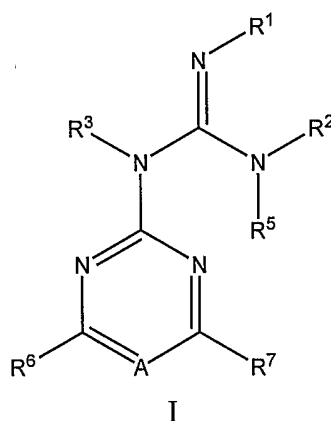
;



; or



83. A method of treating a viral infection in a patient comprising administering to said patient a therapeutically effective amount of a compound of Formula I:



or pharmaceutically acceptable salt form thereof, wherein:

R^1 is H or COOR^{1a} ;

R^{1a} is H or $\text{C}_1\text{-C}_{10}$ alkyl, aryl, cycloalkyl, or aralkyl;

R^2 and R^3 are each, independently, H, $\text{C}_1\text{-C}_{10}$ alkyl, or $\text{C}_3\text{-C}_7$ cycloalkyl;

A is N or CR^4 ;

R^4 is H, halo, $\text{C}_1\text{-C}_6$ alkyl, $\text{C}_1\text{-C}_6$ haloalkyl, $\text{C}_3\text{-C}_7$ cycloalkyl, $\text{C}_2\text{-C}_6$ alkenyl, $\text{C}_2\text{-C}_6$ alkynyl, OH, alkoxy, aryloxy, aralkoxy, cycloalkyloxy, cycloalkylalkyloxy, heterocycloalkyloxy, heterocycloalkylalkyloxy, heteroaryloxy, heteroarylalkyloxy, cyano, nitro, hydroxy, mercapto, or $\text{O}(\text{CR}^{4a}\text{R}^{4b})_a\text{NR}^{4c}\text{R}^{4d}$;

R^{4a} and R^{4b} are each, independently, H or $\text{C}_1\text{-C}_4$ alkyl;

R^{4c} and R^{4d} are each, independently, H, $\text{C}_1\text{-C}_4$ alkyl, $\text{C}_3\text{-C}_7$ cycloalkyl, $\text{C}_1\text{-C}_4$ haloalkyl, aryl, $\text{C}(\text{O})\text{-(C}_1\text{-C}_6\text{ alkyl)}$, $\text{C}(\text{O})\text{-aryl}$, $\text{C}(\text{O})\text{-(C}_3\text{-C}_7\text{ cycloalkyl)}$, $\text{C}(\text{O})\text{O-(C}_1\text{-C}_6\text{ alkyl)}$, $\text{C}(\text{O})\text{O-aryl}$, or $\text{C}(\text{O})\text{O-(C}_3\text{-C}_7\text{ cycloalkyl)}$, or R^{4c} and R^{4d} together with the N atom to which they are attached form a 5- or 6-membered heterocycle;

a is 1, 2, 3, 4, 5, or 6;

R^5 is $N(R^{5a})-Q$;

R^{5a} is H or C_1-C_6 alkyl;

Q is aryl, heteroaryl, cycloalkyl, or heterocycloalkyl, wherein Q is optionally substituted by one or more C_1-C_{10} alkyl, C_2-C_{10} alkenyl, C_2-C_{10} alkynyl, alkoxy, aryloxy, aralkoxy, aralkyl, OH, SH, thioalkoxy, halo, C_1-C_{10} haloalkyl, haloalkoxy, COOH, $C(O)-(C_1-C_6 \text{ alkyl})$, $C(O)-(C_3-C_7 \text{ cycloalkyl})$, $C(O)\text{-aryl}$, $C(O)O-(C_1-C_6 \text{ alkyl})$, $C(O)O-(C_3-C_7 \text{ cycloalkyl})$, $C(O)O\text{-aryl}$, $C(O)NR^{Q1}R^{Q2}$, NO_2 , CN, or $NR^{Q3}R^{Q4}$;

R^{Q1} and R^{Q2} are each, independently, H, C_1-C_6 alkyl, C_3-C_6 cycloalkyl, aryl, or R^{Q1} and R^{Q2} together with the N atom to which they are attached form a 5- or 6-membered heterocycle;

R^{Q3} and R^{Q4} are each, independently, H, C_1-C_6 alkyl, aryl, $C(O)-C_1-C_6$ alkyl, $C(O)-(C_3-C_7 \text{ cycloalkyl})$, $C(O)\text{-aryl}$, $C(O)O-(C_1-C_6 \text{ alkyl})$, $C(O)O-(C_3-C_7 \text{ cycloalkyl})$, $C(O)O\text{-aryl}$, or R^{Q1} and R^{Q2} together with the N atom to which they are attached form a 5- or 6-membered heterocycle;

or R^5 is aryl, heteroaryl, cycloalkyl, or heterocycloalkyl, wherein said aryl, heteroaryl, cycloalkyl, or heterocycloalkyl is optionally substituted by one or more halo, C_1-C_{10} alkyl, C_1-C_{10} haloalkyl, C_2-C_{10} alkenyl, C_2-C_{10} alkynyl, aryl, heteroaryl, cycloalkyl, heterocycloalkyl, alkoxy, aryloxy, aralkoxy, aralkyl, CN, NO_2 , OH, SH, thioalkoxy, haloalkoxy, COOH, $C(O)-(C_1-C_6 \text{ alkyl})$, $C(O)\text{-aryl}$, $C(O)-(C_3-C_7 \text{ cycloalkyl})$, $C(O)O-(C_1-C_6 \text{ alkyl})$, $C(O)O\text{-aryl}$, or $C(O)O-(C_3-C_7 \text{ cycloalkyl})$, $CONR^{5b}R^{5c}$, $NR^{5d}R^{5e}$, or $O(CR^8R^9)_pY$;

R^{5b} and R^{5c} are each, independently, H, C_1-C_6 alkyl, C_3-C_6 cycloalkyl, aryl, or R^{5b} and R^{5c} together with the N atom to which they are attached form a 5- or 6-membered heterocycle;

R^{5d} and R^{5e} are each, independently, H, C_1-C_6 alkyl, aryl, $C(O)-C_1-C_6$ alkyl, $C(O)-(C_3-C_7 \text{ cycloalkyl})$, $C(O)\text{-aryl}$, $C(O)O-(C_1-C_6 \text{ alkyl})$, $C(O)O-(C_3-C_7 \text{ cycloalkyl})$, $C(O)O\text{-aryl}$, or R^{5d} and R^{5e} together with the N atom to which they are attached form a 5- or 6-membered heterocycle;

R^8 and R^9 are each, independently, H or C_1-C_6 alkyl;

p is 1, 2, 3, 4, 5, or 6;

Y is $NR^{10}R^{11}$, OR^{12a} , OSO_2R^{12b} , C_3-C_7 cycloalkyl, heterocycloalkyl, or heteroaryl, wherein Y is optionally substituted by one or more halo, C_1-C_6 alkyl, C_1-C_6 haloalkyl, C_2-C_6 alkenyl, C_2-C_6 alkynyl, C_3-C_7 cycloalkyl, aryl, heteroaryl, heterocycloalkyl, OH, SH, CN, NO_2 , COOH, $C(O)-(C_1-C_6 \text{ alkyl})$, $C(O)-(C_3-C_7$

cycloalkyl), C(O)-aryl, C(O)O-(C₁-C₆ alkyl), C(O)O-(C₃-C₇ cycloalkyl), C(O)O-aryl, NH₂, NH(C₁-C₄ alkyl), N(C₁-C₄ alkyl)₂, NHC(O)O-(C₁-C₆ alkyl), NHC(O)O-aryl or (CH₂)_qOH;

R¹⁰ and R¹¹ are each, independently, H, (C₁-C₆)alkyl, C(O)-(C₁-C₆ alkyl), C(O)-(C₃-C₇ cycloalkyl), C(O)-aryl, C(O)O-(C₁-C₆ alkyl), C(O)O-(C₃-C₇ cycloalkyl), C(O)O-aryl, aryl, heteroaryl, cycloalkyl, or heterocycloalkyl, or R¹⁰ and R¹¹ together with the N atom to which they are attached form a 5- or 6- membered heterocycle;

q is 0, 1, 2, or 3;

R^{12a} is H, C₁-C₁₀ alkyl, C₁-C₁₀ alkenyl, C₁-C₁₀ alkynyl, aryl, heteroaryl, C₃-C₇ cycloalkyl, or heterocycloalkyl;

R^{12b} is H, C₁-C₆ alkyl, aryl, or NH₂;

or R⁵ is -(CR¹³R¹⁴)_n-Z;

n is 1, 2, 3, 4, 5, 6, 7, or 8;

R¹³ and R¹⁴ are each, independently, H, C₁-C₆ alkyl, C₂-C₆ alkenyl, C₂-C₆ alkynyl, OH, aryl, or aralkyl, or R¹³ and R¹⁴ together form cycloalkyl, oxo, or sulfido;

Z is aryl, heteroaryl, cycloalkyl, heterocycloalkyl, biaryl, biheteroaryl, arylheteroaryl, heteroarylaryl, each of which is optionally substituted by one or more R¹⁵,

R¹⁵ is halo, C₁-C₁₀ alkyl, C₁-C₁₀ haloalkyl, C₂-C₁₀ alkenyl, C₂-C₁₀ alkynyl, alkoxy, aryloxy, aralkoxy, aralkyl, OH, SH, guanidiny, thioalkoxy, haloalkoxy, COOH, C(O)-(C₁-C₆ alkyl), C(O)-(C₃-C₇ cycloalkyl), C(O)-aryl, C(O)O-(C₁-C₆ alkyl), C(O)O-(C₃-C₇ cycloalkyl), C(O)O-aryl, CONR^{18a}R^{19a}, NO₂, CN, (CH₂)_tNR^{18b}R^{19b}, heteroaryl, heterocycloalkyl, aryl, C₃-C₇ cycloalkyl, or O(CR²⁰R²¹)_rX;

R^{18a} and R^{19a} are each, independently, H or C₁-C₆ alkyl, or R^{18a} and R^{19a} together with the N atom to which they are attached form a 5- or 6- membered heterocycle;

R^{18b} and R^{19b} are each, independently, H, C₁-C₆ alkyl, aryl, C(O)-C₁-C₆ alkyl, C(O)-(C₃-C₇ cycloalkyl), C(O)-aryl, C(O)O-(C₁-C₆ alkyl), C(O)O-(C₃-C₇ cycloalkyl), C(O)O-aryl, or R^{18b} and R^{19b} together with the N atom to which they are attached form a 5- or 6-membered heterocycle;

R²⁰ and R²¹ are each, independently, H or C₁-C₆ alkyl;

r is 0, 1, 2, 3, 4, 5, or 6;

t is 0, 1, or 2;

X is $\text{NR}^{22}\text{R}^{23}$, OH, NH_2 , $\text{OSO}_2\text{R}^{24}$, $\text{C}_3\text{-C}_7$ cycloalkyl, aryl, heteroaryl, or heterocycloalkyl, wherein X is optionally substituted by one or more halo, $\text{C}_1\text{-C}_6$ alkyl, $\text{C}_3\text{-C}_7$ cycloalkyl, $\text{C}_1\text{-C}_6$ haloalkyl, aryl, heteroaryl, heterocycloalkyl, CN, NO_2 , OH, COOH, $\text{C(O)-C}_1\text{-C}_6$ alkyl, $\text{C(O)-(C}_3\text{-C}_7\text{ cycloalkyl)}$, C(O)-aryl , $\text{C(O)O-(C}_1\text{-C}_6\text{ alkyl)}$, $\text{C(O)O-(C}_3\text{-C}_7\text{ cycloalkyl)}$, C(O)O-aryl , NH_2 , $\text{NH(C}_1\text{-C}_4\text{ alkyl)}$, $\text{N(C}_1\text{-C}_4\text{ alkyl)}_2$, $\text{NHC(O)O-(C}_1\text{-C}_6\text{ alkyl)}$, NHC(O)O-aryl or $(\text{CH}_2)_s\text{OH}$;

R^{22} and R^{23} are each, independently, H, $\text{C}_1\text{-C}_6$ alkyl, aryl, heteroaryl, heterocycloalkyl, cycloalkyl, $\text{C(O)-C}_1\text{-C}_6$ alkyl, $\text{C(O)-(C}_3\text{-C}_7\text{ cycloalkyl)}$, C(O)-aryl , $\text{C(O)O-(C}_1\text{-C}_6\text{ alkyl)}$, $\text{C(O)O-(C}_3\text{-C}_7\text{ cycloalkyl)}$, C(O)O-aryl , or R^{22} and R^{23} together with the N atom to which they are attached form a 5- or 6-membered heterocycle;

s is 0, 1, 2, or 3;

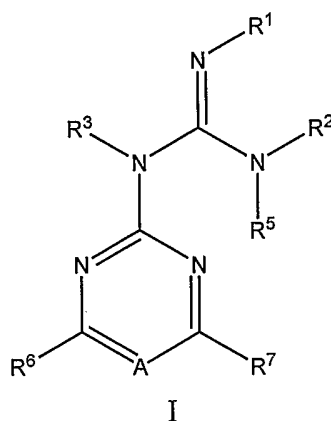
R^{24} is H, $\text{C}_1\text{-C}_6$ alkyl, aryl, or NH_2 ;

or R^5 and R^2 together with the N atom to which they are attached form heterocycloalkyl optionally substituted by one or more halo, $\text{C}_1\text{-C}_4$ alkyl, OH, SH, alkoxy or aryloxy; and

R^6 and R^7 are each, independently, H, halo, $\text{C}_1\text{-C}_6$ alkyl, $\text{C}_1\text{-C}_6$ haloalkyl, $\text{C}_2\text{-C}_6$ alkenyl, $\text{C}_2\text{-C}_6$ alkynyl, alkoxy, aryloxy, or aralkoxy, or R^6 and R^7 together with the atoms to which they are attached form a fused cycloalkyl, heterocycloalkyl, aryl, or heteroaryl group.

84. The method of claim 83 wherein said viral infection is a hepatitis C viral infection.

85. A method of inhibiting translation of a nucleic acid wherein translation of said nucleic acid is mediated by an internal ribosome entry site (IRES), comprising contacting said nucleic acid with a compound of Formula I:



or pharmaceutically acceptable salt form thereof, wherein:

R^1 is H or COOR^{1a} ;

R^{1a} is H or $\text{C}_1\text{-C}_{10}$ alkyl, aryl, cycloalkyl, or aralkyl;

R^2 and R^3 are each, independently, H, $\text{C}_1\text{-C}_{10}$ alkyl, or $\text{C}_3\text{-C}_7$ cycloalkyl;

A is N or CR^4 ;

R^4 is H, halo, $\text{C}_1\text{-C}_6$ alkyl, $\text{C}_1\text{-C}_6$ haloalkyl, $\text{C}_3\text{-C}_7$ cycloalkyl, $\text{C}_2\text{-C}_6$ alkenyl, $\text{C}_2\text{-C}_6$ alkynyl, OH, alkoxy, aryloxy, aralkoxy, cycloalkyloxy, cycloalkylalkyloxy, heterocycloalkyloxy, heterocycloalkylalkyloxy, heteroaryloxy, heteroarylalkyloxy, cyano, nitro, hydroxy, mercapto, or $\text{O}(\text{CR}^{4a}\text{R}^{4b})_a\text{NR}^{4c}\text{R}^{4d}$;

R^{4a} and R^{4b} are each, independently, H or $\text{C}_1\text{-C}_4$ alkyl;

R^{4c} and R^{4d} are each, independently, H, $\text{C}_1\text{-C}_4$ alkyl, $\text{C}_3\text{-C}_7$ cycloalkyl, $\text{C}_1\text{-C}_4$ haloalkyl, aryl, $\text{C}(\text{O})\text{-(C}_1\text{-C}_6\text{ alkyl)}$, $\text{C}(\text{O})\text{-aryl}$, $\text{C}(\text{O})\text{-(C}_3\text{-C}_7\text{ cycloalkyl)}$, $\text{C}(\text{O})\text{O-(C}_1\text{-C}_6\text{ alkyl)}$, $\text{C}(\text{O})\text{O-aryl}$, or $\text{C}(\text{O})\text{O-(C}_3\text{-C}_7\text{ cycloalkyl)}$, or R^{4c} and R^{4d} together with the N atom to which they are attached form a 5- or 6-membered heterocycle;

a is 1, 2, 3, 4, 5, or 6;

R^5 is $\text{N(R}^{5a})\text{-Q}$;

R^{5a} is H or $\text{C}_1\text{-C}_6$ alkyl;

Q is aryl, heteroaryl, cycloalkyl, or heterocycloalkyl, wherein Q is optionally substituted by one or more $\text{C}_1\text{-C}_{10}$ alkyl, $\text{C}_2\text{-C}_{10}$ alkenyl, $\text{C}_2\text{-C}_{10}$ alkynyl, alkoxy, aryloxy, aralkoxy, aralkyl, OH, SH, thioalkoxy, halo, $\text{C}_1\text{-C}_{10}$ haloalkyl, haloalkoxy, COOH , $\text{C}(\text{O})\text{-(C}_1\text{-C}_6\text{ alkyl)}$, $\text{C}(\text{O})\text{-(C}_3\text{-C}_7\text{ cycloalkyl)}$, $\text{C}(\text{O})\text{-aryl}$, $\text{C}(\text{O})\text{O-(C}_1\text{-C}_6\text{ alkyl)}$, $\text{C}(\text{O})\text{O-(C}_3\text{-C}_7\text{ cycloalkyl)}$, $\text{C}(\text{O})\text{O-aryl}$, $\text{C}(\text{O})\text{NR}^{\text{Q1}}\text{R}^{\text{Q2}}$, NO_2 , CN, or $\text{NR}^{\text{Q3}}\text{R}^{\text{Q4}}$;

R^{Q1} and R^{Q2} are each, independently, H, $\text{C}_1\text{-C}_6$ alkyl, $\text{C}_3\text{-C}_6$ cycloalkyl, aryl, or R^{Q1} and R^{Q2} together with the N atom to which they are attached form a 5- or 6-membered heterocycle;

R^{Q3} and R^{Q4} are each, independently, H, $\text{C}_1\text{-C}_6$ alkyl, aryl, $\text{C}(\text{O})\text{-C}_1\text{-C}_6$ alkyl, $\text{C}(\text{O})\text{-(C}_3\text{-C}_7\text{ cycloalkyl)}$, $\text{C}(\text{O})\text{-aryl}$, $\text{C}(\text{O})\text{O-(C}_1\text{-C}_6\text{ alkyl)}$, $\text{C}(\text{O})\text{O-(C}_3\text{-C}_7\text{ cycloalkyl)}$, $\text{C}(\text{O})\text{O-aryl}$, or R^{Q1} and R^{Q2} together with the N atom to which they are attached form a 5- or 6-membered heterocycle;

or R^5 is aryl, heteroaryl, cycloalkyl, or heterocycloalkyl, wherein said aryl, heteroaryl, cycloalkyl, or heterocycloalkyl is optionally substituted by one or more halo, $\text{C}_1\text{-C}_{10}$ alkyl, $\text{C}_1\text{-C}_{10}$ haloalkyl, $\text{C}_2\text{-C}_{10}$ alkenyl, $\text{C}_2\text{-C}_{10}$ alkynyl, aryl, heteroaryl, cycloalkyl, heterocycloalkyl, alkoxy, aryloxy, aralkoxy, aralkyl, CN, NO_2 , OH, SH, thioalkoxy, haloalkoxy, COOH , $\text{C}(\text{O})\text{-(C}_1\text{-C}_6\text{ alkyl)}$, $\text{C}(\text{O})\text{-aryl}$, $\text{C}(\text{O})\text{-(C}_3\text{-C}_7\text{ cycloalkyl)}$, $\text{C}(\text{O})\text{O-(C}_1\text{-C}_6\text{ alkyl)}$, $\text{C}(\text{O})\text{O-(C}_3\text{-C}_7\text{ cycloalkyl)}$, $\text{C}(\text{O})\text{O-aryl}$, or R^{Q1} and R^{Q2} together with the N atom to which they are attached form a 5- or 6-membered heterocycle;

C₆ alkyl), C(O)O-aryl, or C(O)O-(C₃-C₇ cycloalkyl), CONR^{5b}R^{5c}, NR^{5d}R^{5e}, or O(CR⁸R⁹)_pY;

R^{5b} and R^{5c} are each, independently, H, C₁-C₆ alkyl, C₃-C₆ cycloalkyl, aryl, or R^{5b} and R^{5c} together with the N atom to which they are attached form a 5- or 6-membered heterocycle;

R^{5d} and R^{5e} are each, independently, H, C₁-C₆ alkyl, aryl, C(O)-C₁-C₆ alkyl, C(O)-(C₃-C₇ cycloalkyl), C(O)-aryl, C(O)O-(C₁-C₆ alkyl), C(O)O-(C₃-C₇ cycloalkyl), C(O)O-aryl, or R^{5d} and R^{5e} together with the N atom to which they are attached form a 5- or 6-membered heterocycle;

R⁸ and R⁹ are each, independently, H or C₁-C₆ alkyl;

p is 1, 2, 3, 4, 5, or 6;

Y is NR¹⁰R¹¹, OR^{12a}, OSO₂R^{12b}, C₃-C₇ cycloalkyl, heterocycloalkyl, or heteroaryl, wherein Y is optionally substituted by one or more halo, C₁-C₆ alkyl, C₁-C₆ haloalkyl, C₂-C₆ alkenyl, C₂-C₆ alkynyl, C₃-C₇ cycloalkyl, aryl, heteroaryl, heterocycloalkyl, OH, SH, CN, NO₂, COOH, C(O)-(C₁-C₆ alkyl), C(O)-(C₃-C₇ cycloalkyl), C(O)-aryl, C(O)O-(C₁-C₆ alkyl), C(O)O-(C₃-C₇ cycloalkyl), C(O)O-aryl, NH₂, NH(C₁-C₄ alkyl), N(C₁-C₄ alkyl)₂, NHC(O)O-(C₁-C₆ alkyl), NHC(O)O-aryl or (CH₂)_qOH;

R¹⁰ and R¹¹ are each, independently, H, (C₁-C₆)alkyl, C(O)-(C₁-C₆ alkyl), C(O)-(C₃-C₇ cycloalkyl), C(O)-aryl, C(O)O-(C₁-C₆ alkyl), C(O)O-(C₃-C₇ cycloalkyl), C(O)O-aryl, aryl, heteroaryl, cycloalkyl, or heterocycloalkyl, or R¹⁰ and R¹¹ together with the N atom to which they are attached form a 5- or 6- membered heterocycle;

q is 0, 1, 2, or 3;

R^{12a} is H, C₁-C₁₀ alkyl, C₁-C₁₀ alkenyl, C₁-C₁₀ alkynyl, aryl, heteroaryl, C₃-C₇ cycloalkyl, or heterocycloalkyl;

R^{12b} is H, C₁-C₆ alkyl, aryl, or NH₂;

or R⁵ is -(CR¹³R¹⁴)_n-Z;

n is 1, 2, 3, 4, 5, 6, 7, or 8;

R¹³ and R¹⁴ are each, independently, H, C₁-C₆ alkyl, C₂-C₆ alkenyl, C₂-C₆ alkynyl, OH, aryl, or aralkyl, or R¹³ and R¹⁴ together form cycloalkyl, oxo, or sulfido;

Z is aryl, heteroaryl, cycloalkyl, heterocycloalkyl, biaryl, biheteroaryl, arylheteroaryl, heteroarylaryl, each of which is optionally substituted by one or more R¹⁵,

R^{15} is halo, C_1 - C_{10} alkyl, C_1 - C_{10} haloalkyl, C_2 - C_{10} alkenyl, C_2 - C_{10} alkynyl, alkoxy, aryloxy, aralkoxy, aralkyl, OH, SH, guanidiny, thioalkoxy, haloalkoxy, COOH, $C(O)$ -(C_1 - C_6 alkyl), $C(O)$ -(C_3 - C_7 cycloalkyl), $C(O)$ -aryl, $C(O)O$ -(C_1 - C_6 alkyl), $C(O)O$ -(C_3 - C_7 cycloalkyl), $C(O)O$ -aryl, $CONR^{18a}R^{19a}$, NO_2 , CN, $(CH_2)_tNR^{18b}R^{19b}$, heteroaryl, heterocycloalkyl, aryl, C_3 - C_7 cycloalkyl, or $O(CR^{20}R^{21})_rX$;

R^{18a} and R^{19a} are each, independently, H or C_1 - C_6 alkyl, or R^{18a} and R^{19a} together with the N atom to which they are attached form a 5- or 6-membered heterocycle;

R^{18b} and R^{19b} are each, independently, H, C_1 - C_6 alkyl, aryl, $C(O)$ - C_1 - C_6 alkyl, $C(O)$ -(C_3 - C_7 cycloalkyl), $C(O)$ -aryl, $C(O)O$ -(C_1 - C_6 alkyl), $C(O)O$ -(C_3 - C_7 cycloalkyl), $C(O)O$ -aryl, or R^{18b} and R^{19b} together with the N atom to which they are attached form a 5- or 6-membered heterocycle;

R^{20} and R^{21} are each, independently, H or C_1 - C_6 alkyl;

r is 0, 1, 2, 3, 4, 5, or 6;

t is 0, 1, or 2;

X is $NR^{22}R^{23}$, OH, NH_2 , OSO_2R^{24} , C_3 - C_7 cycloalkyl, aryl, heteroaryl, or heterocycloalkyl, wherein X is optionally substituted by one or more halo, C_1 - C_6 alkyl, C_3 - C_7 cycloalkyl, C_1 - C_6 haloalkyl, aryl, heteroaryl, heterocycloalkyl, CN, NO_2 , OH, COOH, $C(O)$ - C_1 - C_6 alkyl, $C(O)$ -(C_3 - C_7 cycloalkyl), $C(O)$ -aryl, $C(O)O$ -(C_1 - C_6 alkyl), $C(O)O$ -(C_3 - C_7 cycloalkyl), $C(O)O$ -aryl, NH_2 , $NH(C_1$ - C_4 alkyl), $N(C_1$ - C_4 alkyl) $_2$, $NHC(O)O$ -(C_1 - C_6 alkyl), $NHC(O)O$ -aryl or $(CH_2)_sOH$;

R^{22} and R^{23} are each, independently, H, C_1 - C_6 alkyl, aryl, heteroaryl, heterocycloalkyl, cycloalkyl, $C(O)$ - C_1 - C_6 alkyl, $C(O)$ -(C_3 - C_7 cycloalkyl), $C(O)$ -aryl, $C(O)O$ -(C_1 - C_6 alkyl), $C(O)O$ -(C_3 - C_7 cycloalkyl), $C(O)O$ -aryl, or R^{22} and R^{23} together with the N atom to which they are attached form a 5- or 6-membered heterocycle;

s is 0, 1, 2, or 3;

R^{24} is H, C_1 - C_6 alkyl, aryl, or NH_2 ;

or R^5 and R^2 together with the N atom to which they are attached form heterocycloalkyl optionally substituted by one or more halo, C_1 - C_4 alkyl, OH, SH, alkoxy or aryloxy; and

R^6 and R^7 are each, independently, H, halo, C_1 - C_6 alkyl, C_1 - C_6 haloalkyl, C_2 - C_6 alkenyl, C_2 - C_6 alkynyl, alkoxy, aryloxy, or aralkoxy, or R^6 and R^7 together with the atoms to which they are attached form a fused cycloalkyl, heterocycloalkyl, aryl, or heteroaryl group.

86. The method of claim 85 wherein said nucleic acid is derived from a virus.
87. The method of claim 85 wherein said nucleic acid is derived from hepatitis C virus.