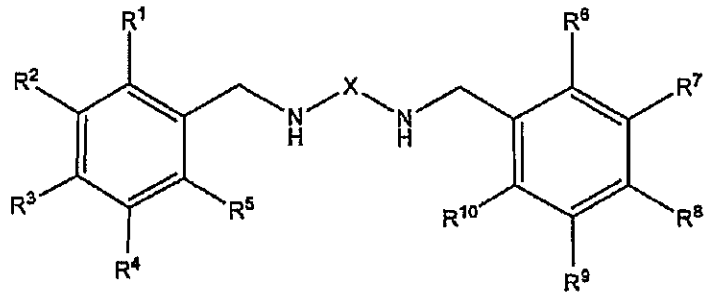
What is claimed is:

1. A compound, or a pharmaceutically acceptable salt or ester thereof, having a structure of formula II:



wherein X is an alkanediyl having a structure of $-C_nH_{2n}-$ wherein n is 2 to 5; and

R^1-R^{10} are each individually H, optionally-substituted alkyl, optionally-substituted alkoxy, optionally-substituted aryl, optionally-substituted cycloalkyl, optionally-substituted heterocyclic, halogen, amino, or hydroxy, provided that at least one of R^3 or R^8 is a 5-membered or 6-membered N-heterocyclic; wherein the N-heterocyclic is selected from pyrrolyl, H-pyrrolyl, pyrrolinyl, pyrrolidinyl, oxazolyl, oxadiazolyl, isoxazolyl, furazanyl, isothiazolyl, pyrazolyl, pyrazolinyl, pyrazolidinyl, imidazolyl, tetrazolyl, dithiazolyl, pyridyl, pyrimidinyl, pyridazinyl, pyrazinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl, or triazinyl,

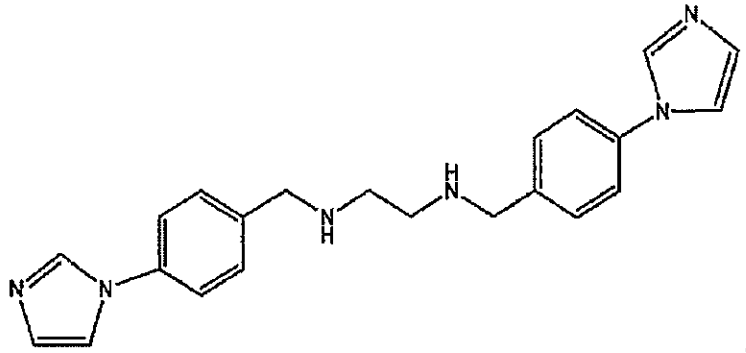
X is $-CH_2-CH_2-$, or R^3 and R^8 are each pyrimidinyl, or X is $-CH_2-CH_2-$ and R^3 and R^8 are each pyrimidinyl.

2. The compound of claim 1, wherein R^3 is a 5-membered or 6-membered N-heterocyclic and R^8 is a 5-membered or 6-membered N-heterocyclic.

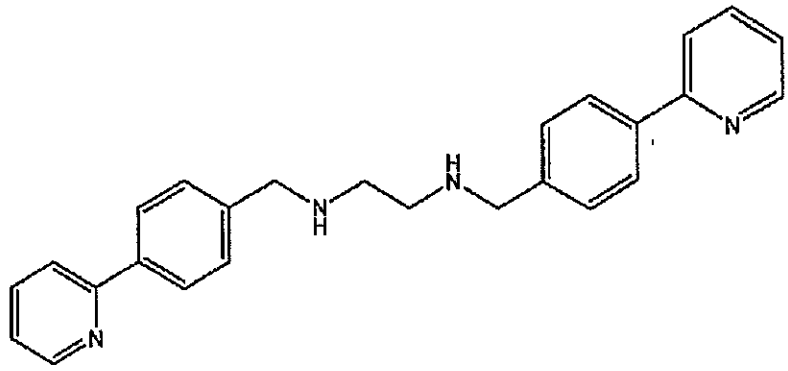
3. The compound of claim 1 or claim 2, wherein the N-heterocyclic is selected from imidazolyl, pyridyl, pyrazolyl, oxadiazolyl, or pyrimidinyl.

4. The compound of claim 1, wherein X is an alkanediyl having a structure of $-C_nH_{2n}-$ wherein n is 2 to 5; and R^1, R^2, R^4, R^5, R^6, R^7, R^9 and R^{10} are each H.

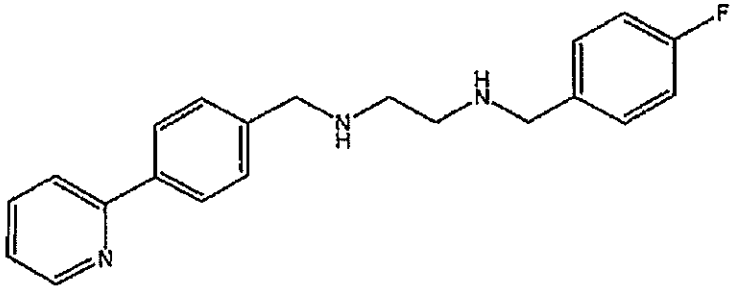
5. The compound of claim 1, wherein the compound is selected from:



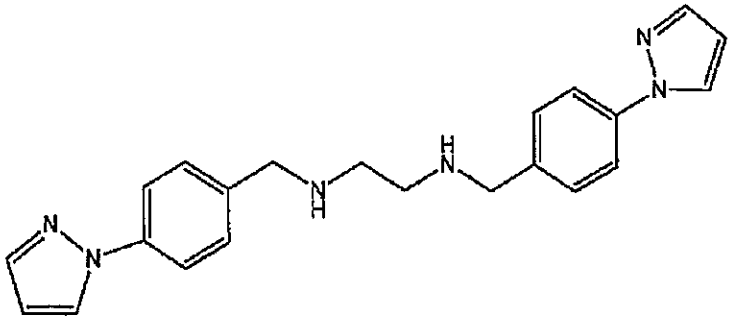
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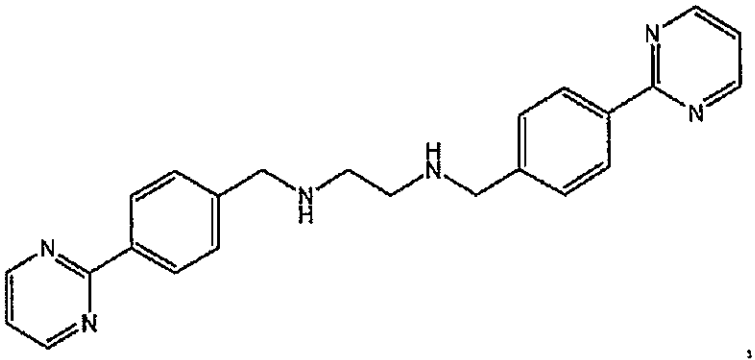
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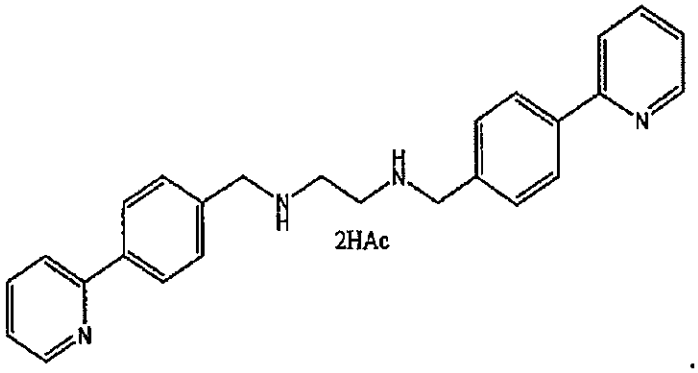
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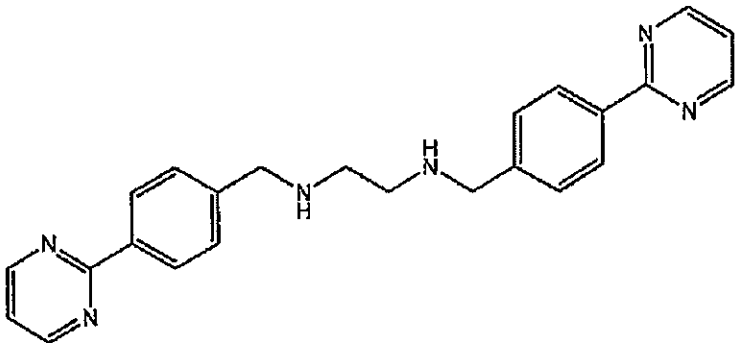
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, or



6. The compound of claim 1, wherein the compound is:



7. The compound of any one of claims 1 to 3, wherein X is $-CH_2-CH_2-$.

8. The compound of claim 1 or 4, wherein R^3 is pyrimidinyl and R^8 is pyrimidinyl.

9. The compound of claim 1, wherein X is $-CH_2-CH_2-$, R^3 is pyrimidinyl, and R^8 is pyrimidinyl.

10. A pharmaceutical composition comprising at least one compound of any one of claims 1 to 9, and at least one pharmaceutically acceptable additive.

11. Use of a compound of any one of claims 1 to 9 in the manufacture of a medicament for treating a pro-inflammatory cytokine release-mediated disorder.

12. Use of a compound of any one of claims 1 to 9 in the manufacture of a medicament for inhibiting pro-inflammatory cytokine release.

13. Use of a compound of any one of claims 1 to 9 in the manufacture of a medicament for treating an FBXO3-mediated disorder or injury, wherein the FBXO3-mediated disorder or injury is selected from malaria, toxic lung exposure, cancer, Alzheimer's, or a burn-related injury.