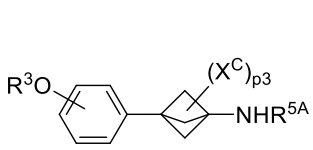
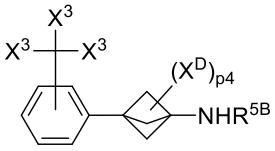
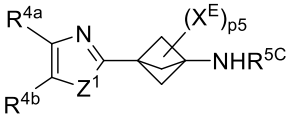
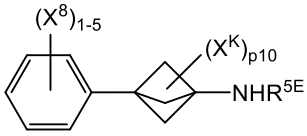
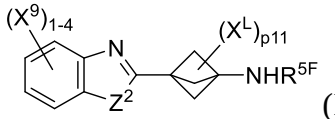
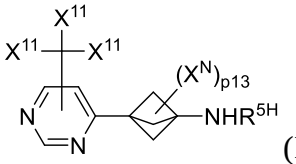
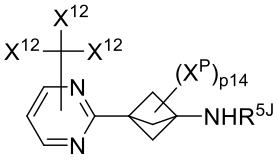
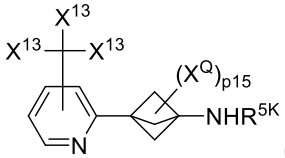
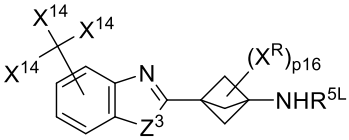
WHAT IS CLAIMED IS:

1. A compound selected from:


(Ic),

(Id),

(Ie),

(Im),

(In),

(Ip),

(Iq),

(Ir) and

(Is),

wherein:

each X^3, each X^{11}, each X^{12}, each X^{13} and each X^{14} are independently hydrogen, deuterium, an unsubstituted C_{1-4} alkyl, fluoro or chloro, provided that at least two of X^3 is fluoro or chloro, provided that at

least two of X^{11} is fluoro or chloro, provided that at least two of X^{12} is fluoro or chloro, provided that at least two of X^{13} is fluoro or chloro, and provided that at least two of X^{14} is fluoro or chloro;

each X^8 and each X^9 are independently deuterium, fluoro or chloro;

R^{5A}, R^{5B}, R^{5E}, R^{5F}, R^{5H}, R^{5J}, R^{5K} and R^{5L} are independently hydrogen, deuterium or an unsubstituted C_{1-4} alkyl;

R^{5C} is selected from the group consisting of hydrogen, deuterium, an unsubstituted C_{1-4} alkyl and $C(=O)R^{12}$;

R^{4a} and R^{4b} are independently hydrogen, deuterium, an unsubstituted C_{1-4} alkyl, a hydroxy substituted C_{1-4} alkyl or $-C(X^{16})_3$, provided that at least one of R^{4a} and R^{4b} is $-C(X^{16})_3$;

R^{12} is selected from the group consisting of hydrogen, deuterium, an unsubstituted C_{1-30} alkyl and an unsubstituted C_{2-30} alkenyl;

each X^{16} is independently hydrogen, deuterium, an unsubstituted C_{1-4} alkyl, fluoro or chloro, provided that at least two of X^{16} is fluoro or chloro;

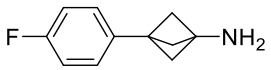
Z^1, Z^2 and Z^3 are independently nitrogen, oxygen or sulfur;

each X^C, each X^D, each X^E, each X^K, each X^L, each X^N, each X^P, each X^Q and each X^R are independently deuterium, chloro or fluoro;

p3, p4, p5, p10, p11, p13, p14, p15 and p16 are independently 0, 1, 2, 3, 4, 5 or 6;

or a pharmaceutically acceptable salt thereof; and

wherein the compound is not:



, or a pharmaceutically acceptable salt thereof.

2. The compound of Claim 1, or a pharmaceutically acceptable salt thereof, of Formula (Ie).

3. The compound of Claim 2, or a pharmaceutically acceptable salt thereof, wherein Z^1 is sulfur.

4. The compound of any one of Claims 1-3, or a pharmaceutically acceptable salt thereof, wherein R^{4a} is $-C(X^{16})_3$; and R^{4b} is hydrogen.

5. The compound of Claim 4, or a pharmaceutically acceptable salt thereof, wherein each X^{16} is independently hydrogen, deuterium, fluoro or chloro, provided that at least two of X^{16} is fluoro or chloro.

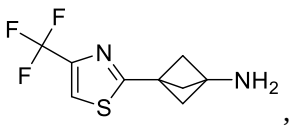
6. The compound of any one of Claims 1-5, or a pharmaceutically acceptable salt thereof, wherein p5 is 0.

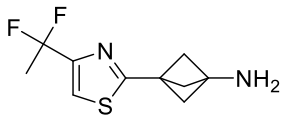
7. The compound of any one of Claims 1-6, or a pharmaceutically acceptable salt thereof, wherein R^{5C} is hydrogen.

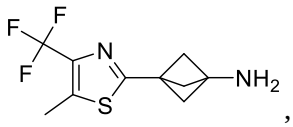
8. The compound of Claim 2, or a pharmaceutically acceptable salt thereof, wherein R^{4a} is $-C(X^{16})_3$; and R^{4b} is an unsubstituted C_{1-4} alkyl.

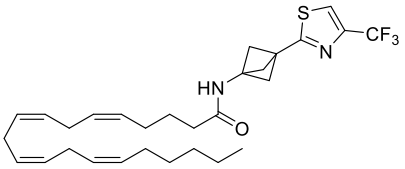
9. The compound of Claim 4 or a pharmaceutically acceptable salt thereof,, wherein each X^{16} is fluoro.

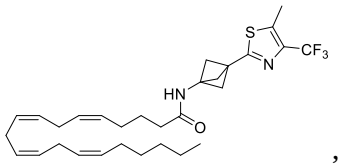
10. The compound of Claim 8, or a pharmaceutically acceptable salt thereof, wherein each X^{16} is fluoro.

11. The compound of any one of Claims 1-7, or a pharmaceutically acceptable salt thereof, wherein the compound is selected from the group consisting of ,

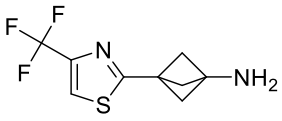


, 

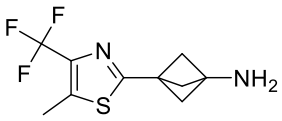
, 

and 

, or a pharmaceutically acceptable salt of any of the foregoing.

12. The compound of Claim 8, or a pharmaceutically acceptable salt thereof, wherein the compound is 

, or a pharmaceutically acceptable salt thereof.

13. The compound of Claim 8, or a pharmaceutically acceptable salt thereof, wherein the compound is 

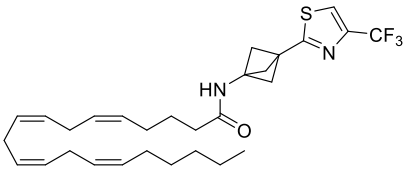
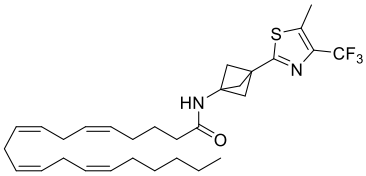
, or a pharmaceutically acceptable salt thereof.

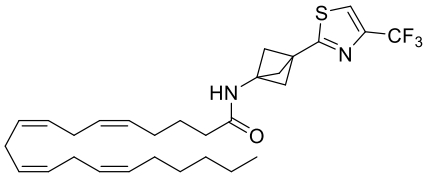
14. The compound of any one of Claims 1-6, or a pharmaceutically acceptable salt thereof, wherein R^{5C} is $C(=O)R^{12}$.

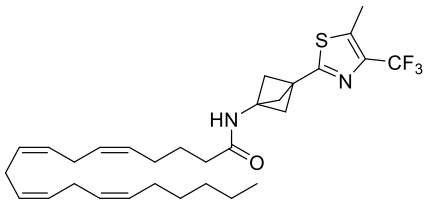
15. The compound of Claim 11, or a pharmaceutically acceptable salt thereof, wherein R^{12} is an unsubstituted C_{1-30} alkyl or an unsubstituted C_{2-30} alkenyl.

16. The compound of Claim 12, or a pharmaceutically acceptable salt thereof, wherein R^{12} is an unsubstituted C_{2-30} alkenyl.

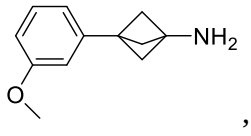
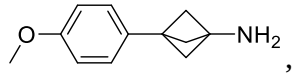
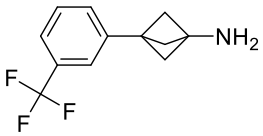
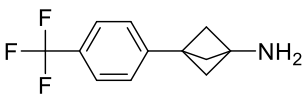
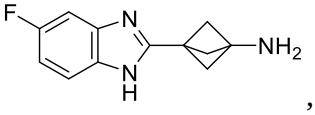
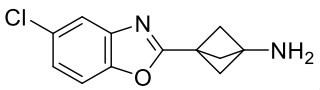
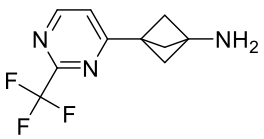
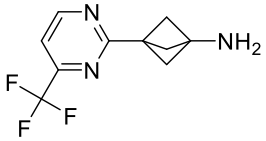
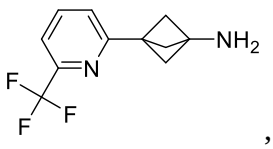
17. The compound of Claim 16, wherein the unsubstituted C_{2-30} alkenyl is selected from the group consisting of, $-(CH_2)_7CH=CH(CH_2)_3CH_3$, $-(CH_2)_7CH=CHCH_2CH=CH(CH_2)_4CH_3$, $-(CH_2)_7CH=CH(CH_2)_7CH_3$, $-(CH_2)_7CH=CHCH_2CH=CH(CH_2)_4CH_3$, $-(CH_2)_7CH=CH(CH_2)_7CH_3$, $-(CH_2)_7CH=CHCH_2CH=CHCH_2CH=CHCH_2CH_3$, $-(CH_2)_9CH=CH(CH_2)_5CH_3$, $-(CH_2)_3CH=CHCH_2CH=CHCH_2CH=CHCH_2CH=CH(CH_2)_4CH_3$, $-(CH_2)_{11}CH=CH(CH_2)_7CH_3$, $-(CH_2)_3CH=CHCH_2CH=CHCH_2CH=CHCH_2CH=CHCH_2CH=CHCH_2CH_3$, $-(CH_2)_4CH=CHCH(CH_3)_2$ and $-(CH_2)_2CH=CHCH_2CH=CHCH_2CH=CHCH_2CH=CHCH_2CH=CHCH_2CH=CHCH_2CH_3$.

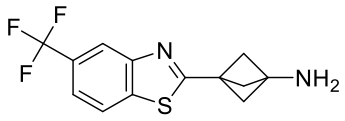
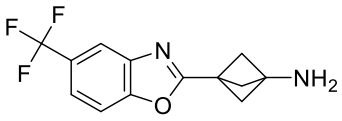
18. The compound of any one of Claims 14-17, or a pharmaceutically acceptable salt thereof, wherein the compound is selected from the group consisting of  and , or a pharmaceutically acceptable salt of any of the foregoing.

19. The compound of Claim 18, or a pharmaceutically acceptable salt thereof, wherein the compound is , or a pharmaceutically acceptable salt thereof.

20. The compound of Claim 18, or a pharmaceutically acceptable salt thereof, wherein the compound is , or a pharmaceutically acceptable salt thereof.

21. The compound of Claim 1, or a pharmaceutically acceptable salt thereof, of Formula (Ic), Formula (Id), Formula (Im), Formula (In), Formula (Ip), Formula (Iq), Formula (Ir) or Formula (Is), or a pharmaceutically acceptable salt of any of the foregoing.

22. The compound of Claim 1, or a pharmaceutically acceptable salt thereof, wherein the compound is selected from the group consisting of , , , , , , , , , .

 and , or a pharmaceutically acceptable salt of any of the foregoing.

23. A compound of any one of Claims 1-22, or a pharmaceutically acceptable salt of any of the foregoing, for use in reducing or at least partially preventing pain or fever.

24. Use of the compound of any one of Claims 1-22, or a pharmaceutically acceptable salt of any of the foregoing, and an opioid analgesic and/or a non-steroidal anti-inflammatory drug (NSAID), in the manufacture of a medicament for reducing or at least partially preventing pain or fever.

25. The use of Claim 24, wherein the opioid analgesic is selected from the group consisting of morphine, codeine, hydrocodone, oxycodone, fentanyl, pethidine, methadone, pentazocine, sufentanil, levorphanol, dihydrocodeine, nalbuphine, butorphanol, tramadol, meptazinol, buprenorphine, dipipanone, alfentanil, remifentanil, oxymorphone, tapentadol, propoxyphene and hydromorphone; and wherein the NSAID is selected from the group consisting of celecoxib, ketorolac, ketoprofen, indomethacin, sulindac, etodolac, mefenamic acid, meclofenamic acid, meclofenamate sodium, flufenamic acid, tolmetin, diclofenac, diclofenac sodium, ibuprofen, naproxen, naproxen sodium, fenoprofen, flurbiprofen, oxaprozin, piroxicam, meloxicam, ampiroxicam, droxicam, lornoxicam, cinnoxicam, sudoxicam, and tenoxicam.

26. The use of Claim 24 or Claim 25, wherein the pain is selected from the group consisting of acute pain, post-operative pain, chronic pain, nociceptive pain, osteoarthritis, rheumatoid arthritis, neuropathic pain, migraine, visceral pain, mixed pain, lower back pain, cancer pain and fibromyalgia pain.