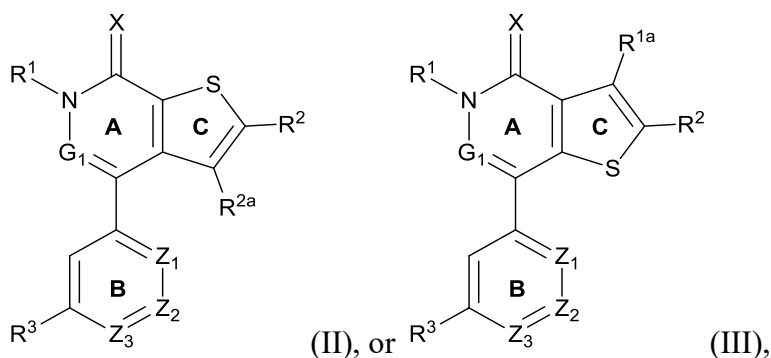


Cell, 19: 523-534 (2005)). BET bromodomain inhibitors have also been shown to reactivate HIV transcription in models of latent T cell infection and latent monocyte infection (Banerjee, et al., J. Leukocyte Biol. doi:10.1189/jlb.0312165). BRDT has an important role in spermatogenesis (Matzuk, et al., Cell 150: 673-684 (2012)).

[0005] Due to this potential as an epigenetic target, a number of small molecule compounds that inhibit the function of BET family proteins have been developed, and many of them have demonstrated promising anti-cancer activities with both solid and hematologic malignancies in preclinical studies. This has led to several early-phase clinical trials. Included among these are RO6870810 (formerly TEN-010), ZEN003694, BMS-986158, CPI-0610, I-BET762, OTX015, FT-1101, INCB054329, PLX51107, GS-5829, and ABBV-075. While these efforts are promising, there is need for better selectivity and improved durability of BET inhibitors that provide enhanced efficacy while reducing toxicity related to off-target effects. The present invention relates to novel BET inhibitors.

SUMMARY

[0005a] In an aspect of the present disclosure, there is provided a compound of Formula (II) or (III):



or a tautomer or stereoisomer thereof, or a pharmaceutically acceptable salt of any of the foregoing, wherein:

X is O;

R¹ is hydrogen, C₁-C₃ alkyl, -(C₁-C₃ alkylene)OH, C₁-C₃ haloalkyl, or C₃-C₄ cycloalkyl;

G₁ is CR^a, wherein:

R^a is hydrogen, halogen, or C₁-C₄ alkyl;

Z₁ is C-W₁-R^c, wherein:

each W₁ is -O- and

R^c is phenyl optionally substituted by R^{c1}, wherein each R^{c1} is independently halogen, C₁-C₄ alkyl, C₃-C₆ cycloalkyl, 3- to 6-membered heterocyclyl, cyano, oxo, C₁-C₄ alkoxy, C₁-C₄ haloalkoxy, C₁-C₄ haloalkyl, -OR¹⁰, -NR¹⁰R¹¹, -C(O)NR¹⁰R¹¹, -NR¹⁰C(O)R¹¹, -S(O)₂R¹⁰, -NR¹⁰S(O)₂R¹¹, or -S(O)₂NR¹⁰R¹¹;

Z₂ is CH;

Z₃ is CH;

R^{1a} and R^{2a} are each independently hydrogen, halogen, C₁-C₄ alkyl, C₃-C₆ cycloalkyl, 3- to 6-membered heterocyclyl, 5- to 10-membered heteroaryl, cyano, oxo, C₁-C₄ haloalkyl, C₁-C₄ alkoxy,