Representative Issued U.S. Patents

1. *Spiroheptane salicylamides and related compounds as inhibitors of ROCK Spiroheptane salicylamides and related compounds as inhibitors of ROCK.* **Leon M. Smith II**, Vladimir Ladziata, Indawati DeLucca, *et al.* US 10,829,501 Issued Nov 10, 2020.

2. *Macrocyclic factor XIa inhibitors bearing heterocyclic groups*. Donald J. P. Pinto, Michael J. Orwat, **Leon M. Smith II**, *et al.* US 10,273,236 Issued Apr 30, 2019.

3. *Substituted tetrahydroisoquinoline compounds as factor XIa inhibitors.* Michael J. Orwat, Donald J. P. Pinto, **Leon M. Smith II,** Shefali Srivastava. US 10,208,021 Issued Feb 19, 2019.

4. *Diamide macrocycles as factor XIa inhibitors.* **Leon M. Smith II**, Donald J. P. Pinto, James R. Corte, William R. Ewing US 10,160,750 Issued Dec 25, 2018.

5. *Substituted 4,5,6,7-tetrahydropyrazolo[3,4-c]pyridines as factor XIa inhibitors.* Michael J. Orwat, Donald J. P. Pinto, **Leon M. Smith** II, et al. US 10,000,466 Issued Jun 19, 2018.

6. *Dihydropyridone P1 as factor XIa inhibitors.* Wu Yang, James R. Corte, Leon **M. Smith II**, *et al.* US 9,951,071 · Issued Apr 24, 2018

7. *Substituted tetrahydroisoquinoline compounds as factor XIa inhibitors*. Michael J. Orwat, Donald J. P. Pinto, **Leon M. Smith II**, et al. US 9,944,625 · Issued Apr 17, 2018.

8. *Macrocycles as factor XIa inhibitors*. Donald J. P. Pinto, James R. Corte, **Leon M. Smith II**, et al. US 9,902,742 · Issued Feb 27, 2018

9. 9. *Macrocycles with aromatic P2' groups as factor XIa inhibitors.* James R. Corte, Indawati De Lucca, **Leon M. Smith II**, et al. US 9,777,001 Issued Oct 3, 2017

10. *Tetrahydroisoquinolines containing substituted azoles as factor XIa inhibitors*. Donald J. P. Pinto, Charles G. Clarke, **Leon M. Smith II,** et al. US 9,738,655 · Issued Aug 8, 2017.

11. *Macrocycles as factor XIa inhibitors*. Donald J. P. Pinto, James R. Corte, **Leon M. Smith II**, et al. US 9,611,274 · Issued Apr 4, 2017US 9,611,274 · Issued Apr 4, 2017.

12. *Substituted 4,5,6,7-tetrahydropyrazolo[4,3-c]pyridines as factor XIa inhibitors*. Michael J. Orwat, Donald J. P. Pinto, **Leon M. Smith II**, et al. US 9,725,435 · Issued Sep 27, 2016.

13. *Pyrimidinones as factor XIa inhibitors*. Andrew K. Dilger, James R. Corte, **Leon M. Smith II**, et al. US 9,453,018 · Issued Sep 27, 2016.

14. *Substituted tetrahydroisoquinoline compounds as factor XIa inhibitors.* Michael J. Orwat, Donald J. P. Pinto, **Leon M. Smith II,** et al. US 9,447,110 · Issued Sep 20, 2016.

15. *Dihydropyridone P1 as factor XIa inhibitors.* Wu Yang James R. Corte, **Leon M. Smith II,** et al. US 9,409,908 · Issued Aug 9, 2016.

16. *Guanidine substituted tetrahydroisoquinoline compounds as factor XIa inhibitors*. Donald J. P. Pinto, Charles G. Clark, **Leon M. Smith II,** et al. US 9,403,774 · Issued Aug 2, 2016.

17. Substituted 1,2,3,4-tetrahydro-2,6-naphthyridines as factor XIa inhibitors. Michael J. Orwat, Donald J. P. Pinto, **Leon M. Smith II**, et al. US 9,394,276 · Issued Jul 19, 2016.

18. *Dihydropyridone P1 as factor XIa inhibitors*. Wu Yang James R. Corte, **Leon M. Smith II**, et al. US 9,376,444 · Issued Jun 28, 2016.

19. *Guanidine substituted tetrahydroisoquinoline compounds as factor XIa inhibitors*. Donald J. P. Pinto, Charles G. Clark, **Leon M. Smith II**, et al. US 9,315,519 · Issued Apr 19, 2016.

20. *Macrocycles as factor XIa inhibitors*. Donald J. P. Pinto, James R. Corte, **Leon M. Smith II**, et al. US 9,221,818 · Issued Dec 29, 2015.

21. *Substituted tetrahydroisoquinoline compounds as factor XIa inhibitors.* Michael J. Orwat, Donald J. P. Pinto, **Leon M. Smith II**, et al. US 9,192,607 · Issued Nov 24, 2015.

22. *Cyclic P1 linkers as factor XIa inhibitors*. Patrick Y. S. Lam, Charles G. Clark, **Leon M. Smith II**, et al. US 9,108,981 · Issued Aug 18, 2015.

23. *Substituted 1,2,3,4-tetrahydro-2,6-naphthyridines as factor XIa inhibitors*. Michael J. Orwat, Donald J. P. Pinto, **Leon M. Smith II**, et al. US 9,108,951 · Issued Aug 18, 2015.

24. *Substituted tetrahydroisoquinoline compounds as factor XIa inhibitors*. Michael J. Orwat, Donald J. P. Pinto, **Leon M. Smith II**, et al. US 9,000,172 · Issued Apr 7, 2015.

25. *Cyclic P1 linkers as factor XIa inhibitors*. Patrick Y. S. Lam, Charles G. Clark, **Leon M. Smith II**, *et al.* US 8,901,115 · Issued Dec 2, 2014.

26. *Substituted alkylamine derivatives and methods of use.* Guoqing Chen, Jeffrey A. Adams, **Leon M. Smith II,** *et al.* US 8,642,624 · Issued Feb 4, 2014.

27. *Arylpropionamide, arylacrylamide, arylpropynamide, or arylmethylurea analogs as factor XIa inhibitors*. Donald J. P. Pinto, Joanne M. Smallheer, **Leon M. Smith II,** *et al.* US 8,604,056 · Issued Dec 10, 2013.

28. *Dipeptide analogs as coagulation factor inhibitors*. Donald J. P. Pinto, Mimi L. Quan, **Leon M. Smith II**, *et al.* US 8,367,709 Issued Feb 5, 2013.

29. *Arylpropionamide, arylacrylamide, arylpropynamide, or arylmethylurea analogs as factor XIa inhibitors.* Donald J. P. Pinto, Joanne M. Smallheer, **Leon M. Smith II**, *et al.* US 8,252,830 · Issued Aug 28, 2012.

30. *Arylpropionamide, arylacrylamide, arylpropynamide, or arylmethylurea analogs as factor XIa inhibitors*. Donald J. P. Pinto, Joanne M. Smallheer, **Leon M. Smith II,** *et al.* US 7,842,708 · Issued Nov 30, 2010.

31. *Arylpropionamide, arylacrylamide, arylpropynamide, or arylmethylurea analogs as factor XIa inhibitors*. Donald J. P. Pinto, Joanne M. Smallheer **Leon M. Smith II**, *et al.* US 7,626,039 · Issued Dec 1, 2009.

32. *Substituted amine derivatives and methods of use.* Guoqing Chen, Jeffrey A. Adams, **Leon M. Smith II**, *et al.* US 7,514,564 · Issued Apr 7, 2009.

33. *Substituted amine derivatives and methods of use*. Guoqing Chen, Jeffrey A. Adams, **Leon M. Smith II**, *et al.* US 7,105,682 · Issued Sep 12, 2006.

34. *Substituted arylamine derivatives and methods of use*. Daniel Elbaum, Benny C. Askew, Jr., **Leon M. Smith II**, *et al.* US 7,101,868 · Issued Sep 5, 2006.

35. *Substituted alkylamine derivatives and methods of use*. Guoqing Chen, Jeffrey A. Adams, **Leon M. Smith II**, *et al.* US 6,995,162 · Issued Feb 7, 2006

Representative Issued Patent Applications

1. Preparation of bicyclo[3.2.0]heptane bis(amides) as RXFP1 agonists. Dilger, Andrew K.; Smith, Leon M., II; Orwat, Michael J.; Pinto, Donald J. P. WO2023114824 A1 2023-06-22.

2. Preparation of benzothiophene derivatives as RXFP1 agonists. Kumar, Sreekantha Ratna; Pasunoori, Laxman; Srinivas, Pitani Veera Venkata; Duraisamy, Srinivasan Kunchithaptham; Bhogadi, Vikram; Hegde, Subramanya; Orwat, Michael J.; Barre, Durga Buchi Raju; Pinto, Donald J. P.; Smith, Leon M., II et al. WO2023114823 A1 2023-06-22

3. Preparation of tetraline, phenylcyclobutane, and phenylcyclopentane analogs as RXFP1 agonists. Smith, Leon M., II; Pinto, Donald J. P.; Orwat, Michael J. WO2023114818 A1 2023-06-22

4. Norbornyl benzamide derivatives as RXFP1 agonists and their preparation. Su, Shun; Bilder, Donna M.; Clarke, Adam James; Finlay, Heather; Friends, Todd J.; Mathur, Arvind; Myers, Michael C.; Lawrence, R. Michael; Li, Jianqing; Pinto, Donald J.P.; Smith, Leon M., II; et al. WO2023076626 A1 2023-05-04.

5. Norbornyl heteroarylamide derivatives as RXFP1 agonists and their preparation. Clarke, Adam James; Friends, Todd J.; Mathur, Arvind; Myers, Michael C.; Li, Jianqing; Pinto, Donald J.P.; Pabbisetty, Kumar Balashanmuga; Su, Shun; Vokits, Benjamin P.; Barre, Durga Buchi Raju; Smith, Leon M., II; et al. WO2023077070 A1 2023-05-04.

Representative Peer-Reviewed Journal Publications

1. *Discovery of BMS-986177/JNJ-70033093 an inhibitor of FXIa in phase 2 studies for antithrombotic therapy.* Ewing, W. R., Dilger, A. K., **Leon M. Smith II**, *et al.* 260th ACS National Meeting & Exposition, San Francisco, CA, USA, August 23-27, 2020. MEDI-0057 · Aug 23, 2020.

2. *A mild and readily scalable procedure for the N-1-difluoromethylation of ethyl 6-((tert-butyldiphenylsilyl)oxy)-1H-indazole-3-carboxylate and its applications to the N-difluoromethylation of indazole, benzotriazole, imidazole, indole, and pyrazole derivatives.* Hong, Z., Hou, X., Zhao, Rulin; Li, J., Pawluczyk, J., Wang, B., Kempson, J., Khandelwal, P., **Smith II, L. M**., Glunz, P., Mathur. J. Fluorine Chem. 2020, 234, 109514.

3. *Discovery of a parenteral small molecule coagulation Factor XIa inhibitor clinical candidate (BMS-962212).* Pinto, D. J. P., Orwat, M. J., **Smith II, L. M**., *et al.* J. Med. Chem.,2017, 60(23), 9703-9723.

4. *Novel phenylalanine derived diamides as Factor XIa inhibitors*. **Smith II, L. M**.; Orwat, M, J.; Hu, Z.; Pinto. D. J. P. *et al.* Bioorg. & Med. Chem. Lett., 2016, 26 (2), 472-478.

5. *Structure-based design of inhibitors of coagulation factor XIa with novel P1 moieties.* Pinto, D. J. P.; Smallheer, J. M.; Corte, J. R.; Austin, E. J. D.; Wang, C.; Fang, T.; **Smith, L. M.**; *et al.* Bioorg. & Med. Chem. Lett.,2015, 25 (7), 1635-1642.

6. *Arylphthalazines as potent, and orally-bioavailable inhibitors of VEGFR-2*. Duncton, M. A. J.; Piatnitski, E.; Katoch-Rouse, R.; Sherman, D.; Wong, W. C.; Smith II, L. M.; *et al*. Bioorg. & Med. Chem., 2009, 17, 731-740.

7. *Discovery of N-phenyl nicotinamides as potent inhibitors of Kdr.* Dominguez, C.; **Smith, L.**; *et al*. Bioorg. & Med. Chem. Lett., 2007, 17, 6003-6008.

8. N*ovel Tricyclic Azepine Derivatives: Biological Evaluation of Pyrimido[4,5-b]-1,4-benzoxazepines, thiazepines, and diazepines as inhibitors of the Epidermal Growth Factor Receptor Tyrosine Kinase*. **Smith II, L. M.;** Wong, W. *et al.* Bioorg. & Med. Chem. Lett. 2006, 16, 5102-06.

9. Tricyclic Azepines Derivatives: Pyrimido[4,5-b]-1,4-benzoxazepines, A Novel Class of Tyrosine Kinase Inhibitors of Epidermal Growth Factor Receptor. **Smith II, L. M** *et al.* Bioorg. & Med. Chem. Lett., 2006, 16, 1643-46.

10. Arylphthalazines. Part 2: 1-(Isoquinolin-5-yl)-4-arylamino Phthalazines a Potent Inhibitors of VEGF Receptors I and II. Duncton, M.; Piatnitski, E.; Katoch-Rouse, R.; **Smith, L.;** *et al.* Bioorg. & Med. Chem. Lett., 2006, 16, 1579-81.

11. *Oxadiazole Derivatives as a Novel Class of Antimototic Agents: Synthesis, Inhibition of Tubulin Polymerization, and Activity in Tumor Cell Lines.* Ouyang, X.; **Smith, L.;** *et al.* Bioorg. & Med. Chem. Lett., 2006, 16, 1191-96

12. *Preparation of Substituted Pyrimido[4,5-b]-1,4-benzoxazepines, Thiazepines and Diazepines via a Pictet-Spengler-type Cyclization.* Duncton, M.; **Smith II, L.;** Burdzovic-Wizeman, S.; Burns, A.; Liu, H.; Mao, Y. J. Org. Chem., 2005, 70, 9629- 31.