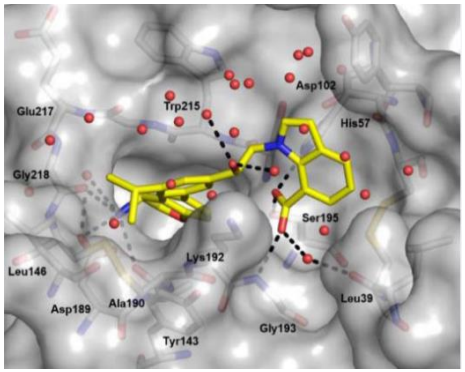
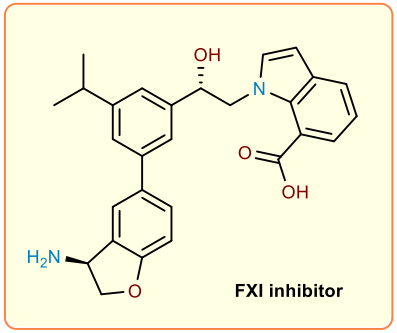
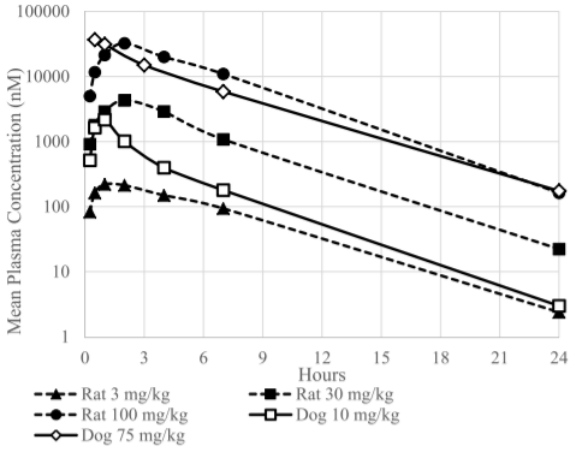
FXI Inhibitor

NOVARTIS

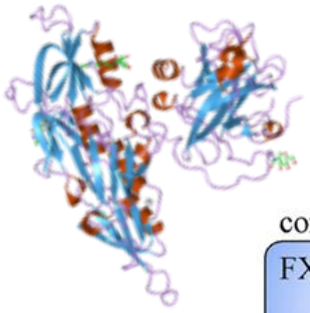


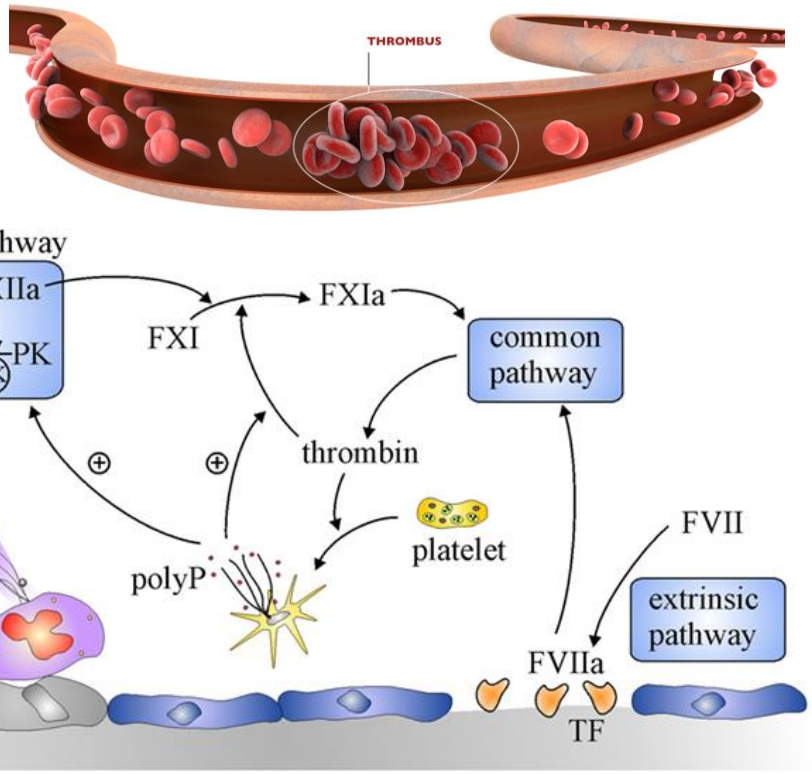
- Scalable asymmetric synthesis of FXI inhibitor for preclinical studies
- Reduction of ketone to chiral alcohol through biocatalysis
- Suzuki−Miyaura cross-coupling facilitated by surfactant chemistry
- Harsh hydrolysis of the nitrile via flow chemistry





Species	PO Dose (mg/kg)	D.N. Cmax (nM)	D.N. AUC_{0-t} (nM*h)	%F
Rat	3	77 ± 4	382 ± 71	10 ± 2
	30	143 ± 39	621 ± 169	19 ± 5
	100	323 ± 64	1770 ± 439	45 ± 11
Dog	10	217 ± 57	560 ± 254	5 ± 2
	75	504 ± 171	2200 ± 620	21 ± 6
IV parameters (1mg/kg)	Cl (ml/min/kg)	AUC0-t (nM*h)	Vdss (L/kg)	T½ (h)
Rat	9.4 ± 1.0	3330 ± 370	1.3 ± 0.2	6.4 ± 0.1
Dog	4.4 ± 0.4	10660 ± 960	0.3 ± 0.0	2.8 ± 0.1

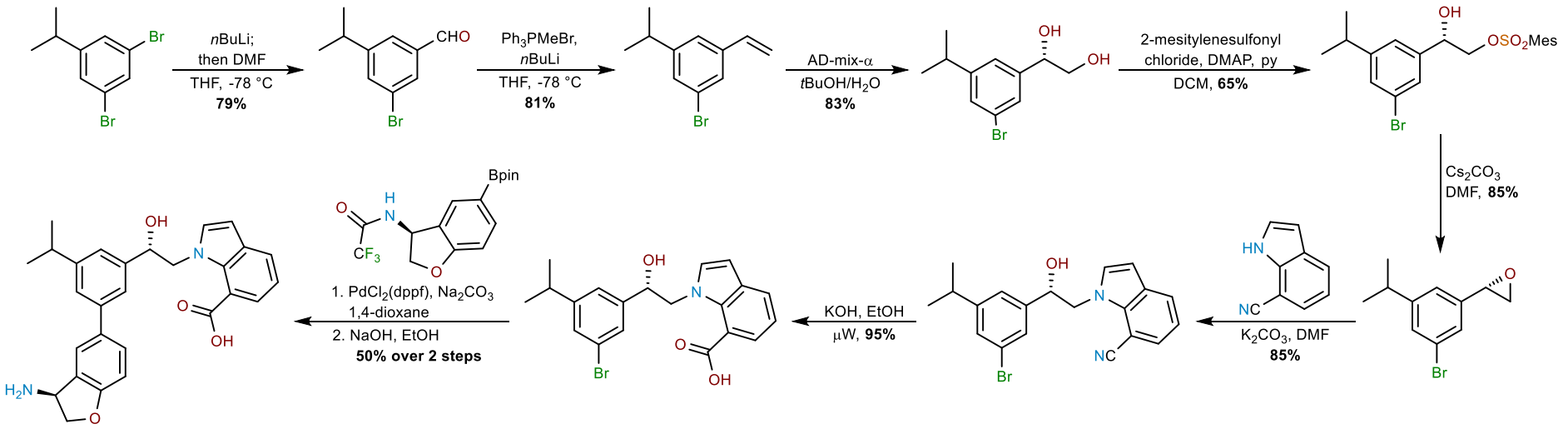




Lorthiois, E. and Roache, J. *J. Med. Chem.* **2020**, *63*, 8088-8113. https://doi.org/10.1021/acs.jmedchem.0c00279
Gao, F. and Wang, J. *Org. Process Res. Dev.* **2020,** DOI: 10.1021/acs.oprd.0c00412. https://doi.org/10.1021/acs.oprd.0c004102

FXI Inhibitor

Medicinal Chemistry Route:



Process Route: