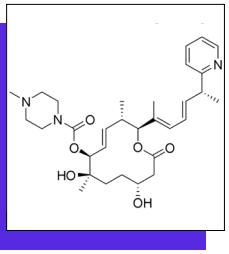
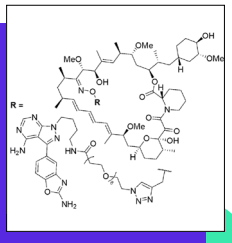
Small Molecules of the Month

June 2021
drughunter.com



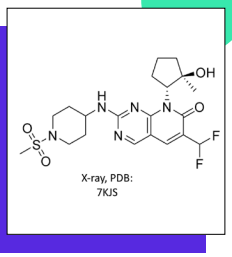
H3B-8800 | SF3b

Oral splicing modulator (SF3b complex)
7–20 mg 21d+/7d–, Ph.I for myeloid neoplasias
From opt. of pladienolide B natural product
Leukemia
H3 Biomedicine, Cambridge, US



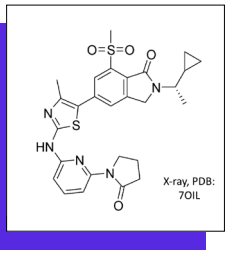
RMC-4529 | mTORC1

mTORC1-selective bi-steric mTOR inhibitor
QW IP activity in xeno., 5552 in Ph.I for cancer
From linking of "rapalog" + mTOR inh. + opt
Nature Chemical Biology
Revolution Medicines, Redwood City, US



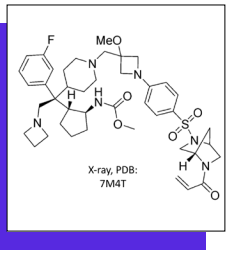
PF-06873600 | CDK2/4/6

Selective CDK2/4/6 inhibitor
Oral agent in Ph. I/IIa for HR+ HER2– cancers
Screen for CDK1/2 sel., SBDD + Free-Wilson
Journal of Medicinal Chemistry
Pfizer, San Diego, US



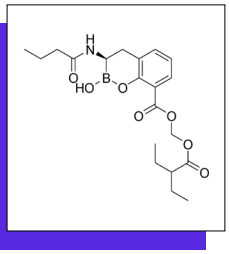
AZD8154 | PI3Kγ,δ

Inhaled dual PI3Kγ,δ kinase inhibitor
Ph.II (3 mg QD) for asthma; withdrawn
From re-opt. of oral PI3Kγ inhibitor
Journal of Medicinal Chemistry
AstraZeneca, Gothenburg, SE



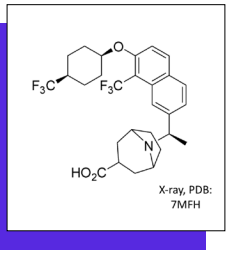
M-1121 | menin-MLL

Orally active covalent menin–MLL PPI inhibitor
Efficacy in xenograft (300 mpk PO QD)
Warhead addition to rev. inh. and opt.
Journal of Medicinal Chemistry
University of Michigan, Ann Arbor, US



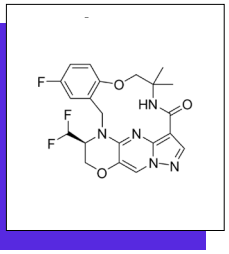
VNRX-7145 | β-Lact.

Oral serine β-lactamase inh. prodrug
Restores ceftibuten activity in model, Ph. I
Hydrolysis transition state mimetic
Journal of Medicinal Chemistry
Venatorx Pharmaceuticals, Malvern, US



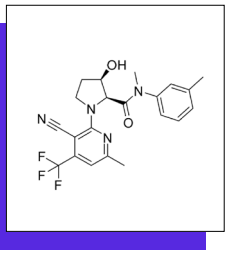
BIO-32546 | ATX

CNS-penetrant non-zinc binding ATX inhibitor
Oral PK/PD and efficacy in inflamm. pain model
From phosphonic acid hit from S1P library
ACS Medicinal Chemistry Letters
Biogen Inc., Cambridge, US



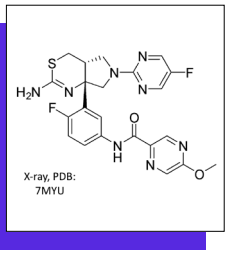
TPX-0131 | ALK

Brain-penetrant mutant ALK kinase inhibitor
Oral, Ph. I/II in ALK+ pre-treated cancers
Undisclosed starting point, SBDD
Molecular Cancer Therapeutics
Turning Point Therapeutics, San Diego, US



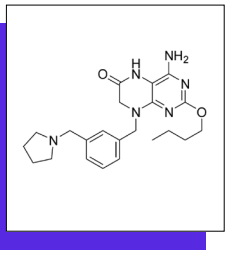
ART558 | Polθ

Allosteric Polθ DNA polymerase inhibitor
Oral activity in BRCA– xenograft (100 mpk QD)
From 165k cmpd biochem. HTS and opt.
Nature Communications
Artios Pharma, Cambridge / ICR, London, UK



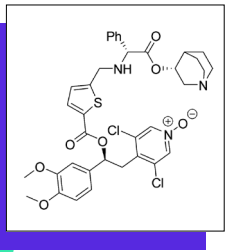
LY3202626 | BACE

Low-dose CNS-penetrant BACE inhibitor
90% red. of CSF Aβ in Ph. II at 9.2 mg/discont.
From opt. vs. CatD and dose red. of prior leads
Journal of Medicinal Chemistry
Eli Lilly, Indianapolis, US



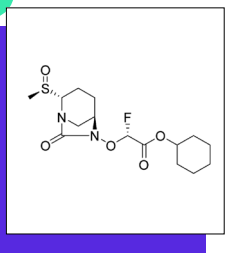
vesatolimod | TLR7

Oral Toll-like receptor TLR7 agonist
3 mg Q2W, Ph. II for HIV/AIDS
From opt. of 8-oxopurine agonist
Science Translational Medicine
Gilead Sciences, Foster City, CA



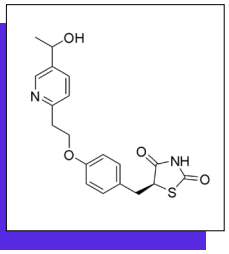
compound 92a | M3/PDE4

Inhaled dual M3 antagonist/PDE4 inhibitor
Intratracheal efficacy in model, not developed
From linking M3 antag. + PDE inh. and opt.
Journal of Medicinal Chemistry
Chiesi Farmaceutici S.p.A., Parma, IT



"compound 21" | β-Lact.

Oral serine β-lactamase inh. prodrug
Efficacy in murine urinary tract infect. model
From SAR of prior scaffold
Journal of Medicinal Chemistry
Shionogi, Toyonaka, JP



Ieriglitazone | PPARγ

Oral PPARγ agonist for CNS diseases
Ph. II and III ongoing for AMN and cALD
One of the metabolites of pioglitazone
Science Translational Medicine
Minoryx Therapeutics S.L., Barcelona, ES