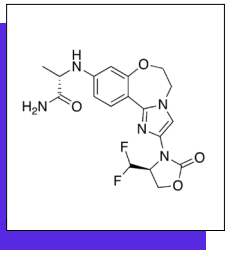
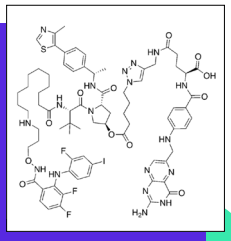
Small Molecules of the Month

May 2021
drughunter.com



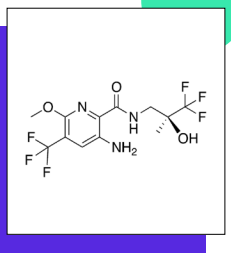
inavolisib | mPI3Kα

Isoform-selective mutant PI3Kα degrader
Oral <9 mg QD, Ph. III in HR+/HER2- BC
From cellular characterization of PI3Ki and opt.
bioRxiv, May 13, 2021
Genentech, South San Francisco, CA



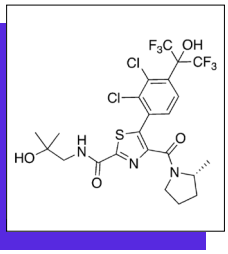
Folate-MS432 | MEK1/2

Folate receptor-dependent PROTAC conjugate
FOLR1-dependent MEK1/2 degrad. in vitro
From conjugation of folate to PROTAC
J. Am. Chem. Soc., May 10, 2021
Harvard Medical / Mt. Sinai



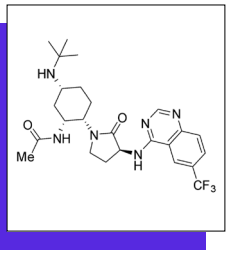
Icenticaftor | CFTR

Mutant + WT CFTR Cl channel potentiator
Oral 300 mg BID, Ph. II in COPD and CF
From 1M cmpd cell-based HTS + opt.
J. Med. Chem., May 24, 2021
Novartis, Horsham, UK / Cambridge, MA



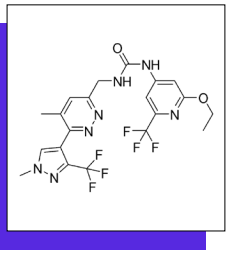
JNJ-61803534 | RORγt

Oral RORγt inverse agonist
Ph. I in HV up to 200 mg w/ PD, discontinued
From HTS + opt.
Scientific Reports, May 26, 2021
Janssen R&D, La Jolla, CA



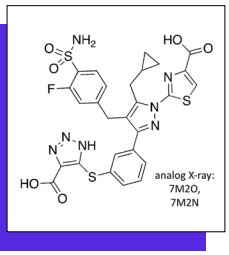
BMS-753426 | CCR2

Sel. CCR2 chemokine receptor antagonist
Oral efficacy (25 mpk BID) in inflamm. models
From PK opt. of prior candidate
ACS Med. Chem. Lett., May 25, 2021
Bristol Myers Squibb, Princeton, NJ



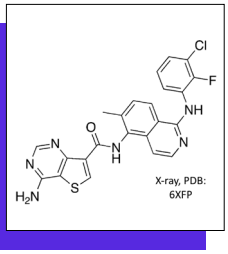
GLPG2938 | S1PR2

Selective S1PR2 antagonist preclin. candidate
Oral efficacy (1 mpk BID) in fibrosis model
Scaffold hop from literature starting points
J. Med. Chem., May 3, 2021
Galapagos NV, Mechelen, Belgium



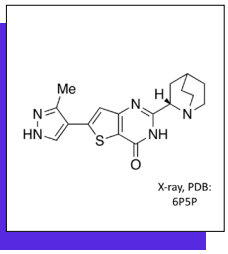
Compound 7 | GO/LDHA

LDHA and GO dual inhibitor
In vitro activity and X-ray vs. both targets
From SBDD of LDHA and GO inhibitors
ACS Med. Chem. Lett., May 20, 2021
Chinook Therapeutics, Seattle, WA



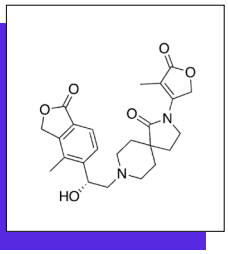
belvarafenib | RAF

Type II RAF dimer kinase inhibitor
Oral 450 mg BID, Ph. II in BRAF/RAS cancers
Demonstrated activity in NRAS-mut. tumors
Nature, May 5, 2021
Genentech, CA / Hanmi Pharma, KR



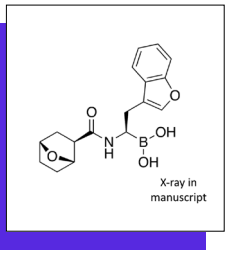
simurosertib | CDC7

CDC7 serine/threonine kinase inhibitor
Oral 50 mg QD, Ph. II in solid tumors compl.
From homology model pharmacophore + opt.
Sci. Adv., May 21, 2021
Takeda Pharmaceutical, Kanagawa, JP



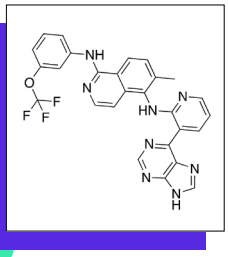
MK-8153 | ROMK

ROMK potassium channel blocker
Oral eff. in hypertension model (1 mpk QD)
Backup candidate to MK-7145 (Ph. Ib)
J. Med. Chem., May 26, 2021
Merck & Co., Kenilworth, NJ



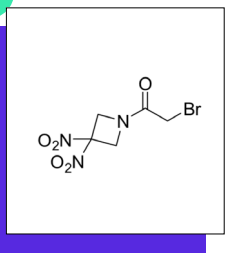
M3258 | LMP7

Sel. reversible cov. immunoproteosome inh.
Oral efficacy (1 mpk) in xeno., Ph. I in MM
From SBDD
Mol. Cancer Ther., May 27, 2021
Merck KGaA, Darmstadt, DE



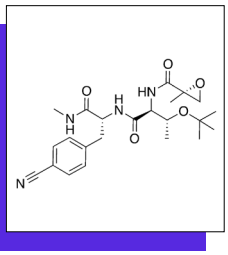
LUT014 | BRAF

Topical BRAF inhibitor (gel) for EGFRi rash
Ph. I in mCRC with EGFRi-related rash
Paradoxical activ. of MAPK to counter EGFRi
Cancer Discovery, May 25, 2021
Lutris-Parma, Tel Aviv, IL / MSKCC, NY



RRx-001 | pleiotropic

Surprisingly well-tolerated clinical molecule
Ph. III candidate in SCLC (4 mg IV QW)
From aerospace compound phenotypic screen
J. Med. Chem., May 27, 2021
EpicentRx Inc., La Jolla, CA



Compound 6 | BTK

Epoxide-based covalent BTK inhibitor
Cysteine reactive, Kinact/Ki ~ 6500
From covalent DEL library screening
Bioorg. & Med. Chem. Lett., May 19, 2021
X-Chem Inc., Waltham, MA

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