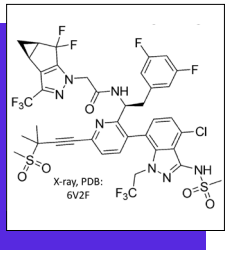
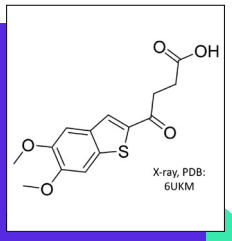
Small Molecules of the Month

August 2020
drughunter.com



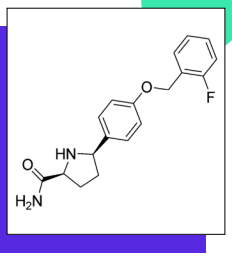
GS-6207 (lenacapavir)

Long-acting HIV capsid PPI-based inhibitor
In Ph. II/III for resistant HIV (SC once/6 mo.)
From HTS for binders, SBDD + opt. for funct.
Nature, Aug. 27, 2020 issue
Gilead Sciences, Foster City, CA



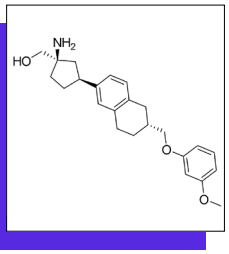
MSA-2

Oral non-nucleoside STING agonist
Single agent systemic activity in I/O model
From 2.4M cmpd cell-based phenotypic screen
Science, Aug. 21, 2020
Merck & Co., Kenilworth, NJ



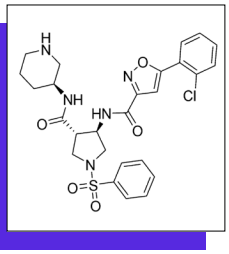
Vixotrigine (BIIB074)

BP, use-dependent sodium channel blocker
Ph. II oral efficacy in trigeminal neuralgia
From cell-based HTS and ligand-based opt.
ACS Med. Chem. Lett., Jul. 16, 2020
Biogen / Convergence / GSK, MA / UK



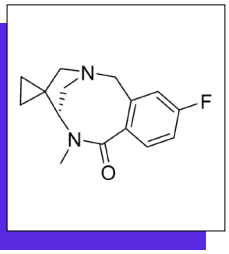
"compound 3d"

Sphingosine-1-phosphate recep. mod. prodrug
For multiple sclerosis, proj. human $t_{1/2}$ of 5d
From opt. of prior $S1P_1$ modulators
ACS Med. Chem. Lett., Aug. 11, 2020
Bristol-Myers Squibb, Princeton, NJ



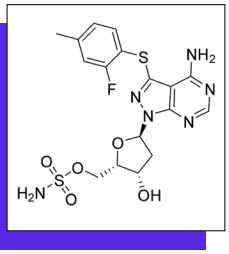
"compound 12j"

Potent ghrelin receptor full agonist
For atrophy/cachexia, not advanced due to PK
From HTS and ligand-based design
J. Med. Chem., Aug. 12, 2020
Astrazeneca, Molndal, SE



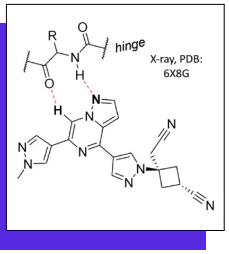
DS34942424

Potent oral non-μ-opioid receptor analgesic
Oral activity in pain model, unknown mech.
Inspired by natural product, conolidine
Bioorg. Med. Chem., Aug. 8, 2020
Daiichi Sankyo, Tokyo, JP



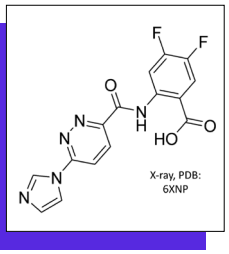
"compound 37"

ATG7 E1 substrate-assisted covalent inhibitor
Autophagy inhibition in vivo (150 mg/kg SC)
From focused HTS of adenosine sulfamates
Bioorg. Med. Chem., Aug. 4, 2020
Takeda, Cambridge, MA



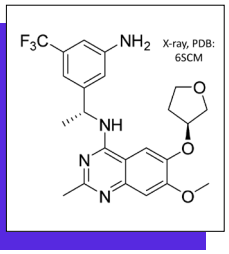
PF-0826647

TYK2-selective kinase inhibitor (JH1 domain)
In Ph. II for inflamm. conditions (oral, QD)
From structure-based design
J. Med. Chem., Aug. 5, 2020
Pfizer, Cambridge, MA / Groton, CT



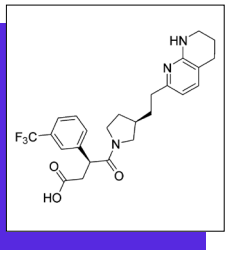
SR-717

Non-nucleoside STING agonist
Single agent systemic activity in I/O model
From 100k cmpd cellular pheno. screen + opt.
Science, Aug. 21, 2020
TSRI / Calibr, La Jolla, CA



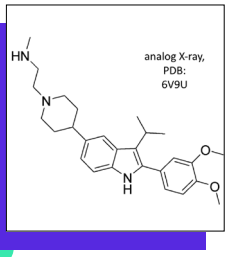
BI-3406

Potent and selective SOS1/KRAS inhibitor
Related cmpd in Ph. I for KRAS+ cancers
From biochemical HTS and SBDD
Cancer Discovery, Aug. 19, 2020
Boehringer Ingelheim, Vienna, AT



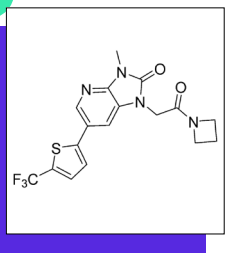
"compound 12"

Potent and selective αvβ5 integrin inhibitor
Selective in vitro tool compound
From internal integrin library and optimization
Eur. J. Med. Chem., Aug. 2, 2020
GlaxoSmithKline, Stevenage, UK



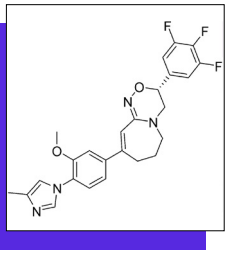
"compound 7f"

Oral toll-like receptors 7/8/9 antagonist
Oral efficacy in autoimmune disease models
From cell-based screen and opt.
ACS Med. Chem. Lett., Jul. 29, 2020
Bristol-Myers Squibb, Princeton, NJ



"compound 12"

Selective GluN2B negative allosteric mod.
Active in brain, proj. oral dose of 120 mg
From cell-based HTS and opt.
J. Med. Chem., Jul. 31, 2020
Janssen R&D, San Diego, CA



"compound 20"

Oral brain penetrant γ-secretase modulator
Oral reduction of CSF $Aβ_{42}$ in model
Rational design from literature starting point
J. Med. Chem., Aug. 13, 2020
Merck & Co., Kenilworth, NJ

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