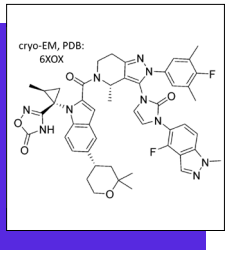
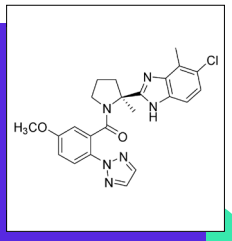
Small Molecules of the Month

November 2020
drughunter.com



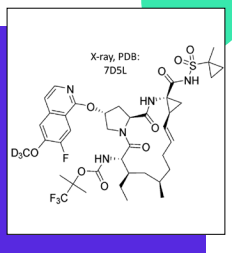
LY3502970 (OWL833)

Oral non-peptide GLP-1R GPCR partial agonist
In Ph. I for Type 2 diabetes, HV study complete
From cell-based screen and opt.
PNAS, Nov. 11, 2020
Chugai, Shizuoka, JP / Eli Lilly, Indianapolis, IN



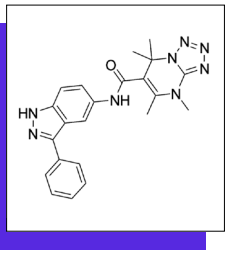
daridorexant

Dual orexin receptor GPCR antagonist
Ph. III efficacy for insomnia, oral 25-50 mg
From optimization of prior clinical candidate
ChemMedChem., Oct. 28, 2020
Idorsia Pharmaceuticals, Allschwil, CH



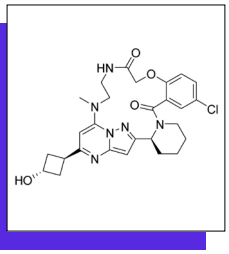
BMS-986144

Pan-genotype HCV NS3/4A protease inhibitor
Proj. oral QD dosing, well-tolerated in rodent
Deuteration reduced CYP TDI
J. Med. Chem., Nov. 23, 2020
Bristol-Myers Squibb, NJ + MA + CT + IN



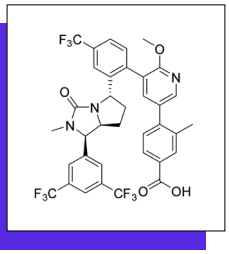
EB-42486

Oral G2019S-LRRK2 mut.-selective kinase inh.
>70x sel. for Parkinson's mut. over WT, non-BP
From 50k cmpd HTS + homology-based opt.
J. Med. Chem., Nov. 16, 2020
ESCAPE Bio, South San Francisco, CA



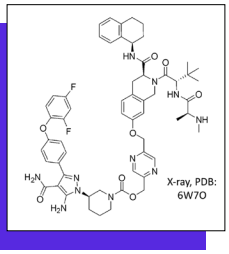
"compound 60b"

RSV D486N-mut. fusion protein inh.
Oral antiviral clinical candidate
From lower barrier to atropisomerism of lead
Bioorg. Med. Chem., Oct. 31, 2020
Taisho Pharmaceutical, Saitama, JP



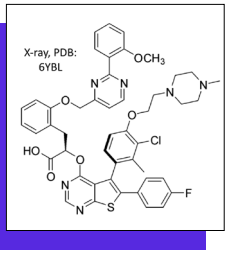
"compound 31"

Cholesteryl ester transfer protein (CETP) inh.
Oral HDL-increasing activity in rodent model
Core replacement from anacetrapib
Bioorg. Med. Chem. Lett., Nov. 6, 2020
Merck, Kenilworth, NJ



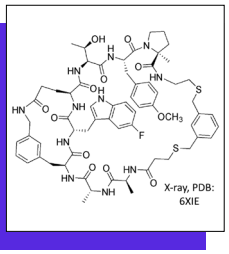
BCPyr

CIAP1-based BTK degrader
CIAP1-degrader-BTK complex crystallized
From BTK and IAP ligands + SBDD
Nature Chem. Biol., Nov. 16, 2020
Pfizer, Groton, CT



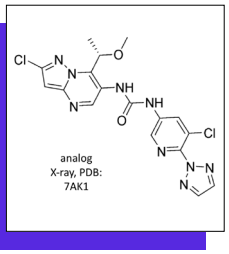
S64315

Potent and selective Mcl-1 PPI inhibitor
Completed Ph. I in AML/MDS (IV weekly)
From NMR fragment screening and SBDD
J. Med. Chem., Nov. 4, 2020
Servier, HU + FR / Vernalis, UK



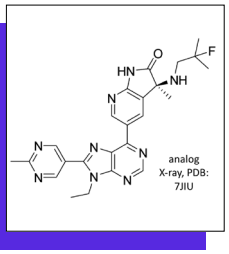
"peptide 78"

Potent macrocyclic PCSK9 PPI inhibitor
1000x optimization of biochem. activity
From mRNA display screen and SBDD
J. Med. Chem., 2020, Nov. 10, 2020
Merck, PA + NJ / UCB Ra Pharma, MA



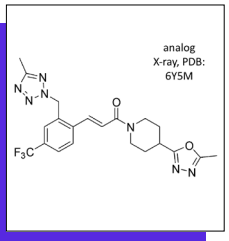
MLT-985

Allosteric MALT1 protease (paracaspase) inh.
Oral QD act. in xenograft; on-target pathology
From 1M cmpd biochem. HTS and opt.
J. Med. Chem., Nov. 20, 2020
Novartis, Basel, CH



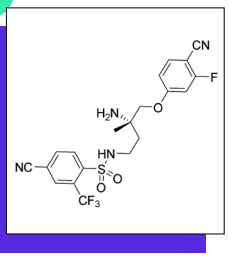
"compound 4d"

Oral selective PI3Kδ kinase inhibitor
<10 mg proj. human dose
From virtual screening and opt.
ACS Med. Chem. Lett., Nov. 19, 2020
Merck, Boston, CA



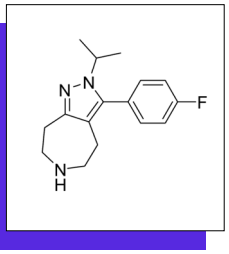
"compound 15a"

Reversible ATX inhibitor w/ alt. binding mode
In vivo PD observed on oral dosing
From HTS screen and opt.
Bioorg. Med. Chem. Lett., Nov. 4, 2020
Novartis, Horsham, UK / Basel, CH



"compound 36"

Oral TRPV4 ion channel antagonist backup
Proj. human dose <100 mg QD for pul. edema
Backup to GSK2798745 / GSK3527497
J. Med. Chem., Nov. 17, 2020
GlaxoSmithKline, Collegeville, PA



"compound 4j"

5-HT2 antagonist and 5-HT7 inverse agonist
Brain penetrant, oral efficacy in rodent models
Backup candidate to JNJ-18038683
Bioorg. Med. Chem. Lett., Nov. 7, 2020
Janssen, San Diego, CA

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