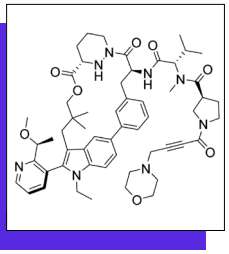
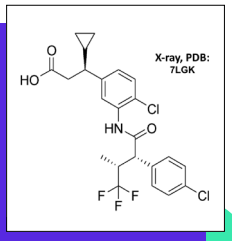
Small Molecules of the Month

April 2021
drughunter.com



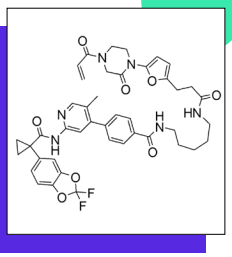
RM-018 | KRAS^{G12C}

KRAS(G12C)ON-cyclophilin A tri-complex inh.
Overcomes KRAS resist. mut. in PDX model
Natural product related (sanglifehrin); undiscl.
Cancer Discov., Apr. 6, 2021
Revolution Medicines, Redwood City, CA



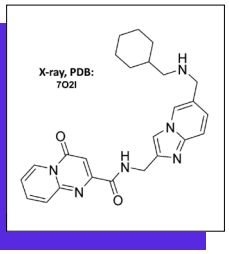
BAY 1101042 | sGC

Oral once-daily sGC activator
Ph. II for CKD + diabetic neuropathy
From cell-based HTS + opt.
J. Med. Chem., Apr. 19, 2021
Bayer AG, Wuppertal, DE



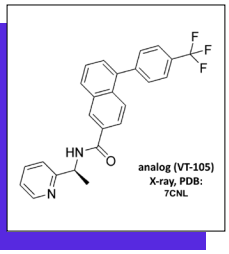
NJH-2-057 | DUBTAC

Covalent allosteric OTUB1-recruiting DUBTAC
Induced deubiq./stabilization of ΔF508-CFTR
From gel-based screen of 702 covalent ligands
bioRxiv, Apr. 30, 2021
UC Berkeley / Novartis (NIBR)



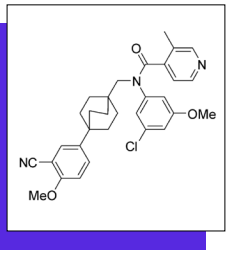
STM-2457 | METTL3

METTL3 RNA modifying enzyme inhibitor
Efficacy in AML PDX model (50 mg/kg IP)
From 250k compound HTS
Nature, Apr. 26, 2021
Storm Therapeutics / University of Cambridge



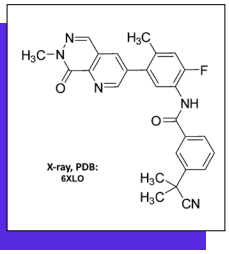
VT-104 | TEAD

Oral pan-TEAD auto-palmitoylation inhibitor
Tumor regression at 3 mg/kg QD
From 160k compound cell-based HTS
Mol. Cancer. Ther., Apr. 13, 2021
Vivace Therapeutics, San Mateo, CA



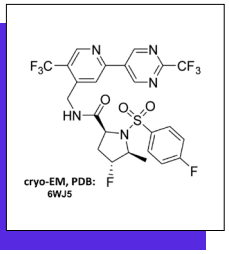
"cmpd 20p" | FXR/TGR5

FXR nucl. receptor + TGR5 GPCR dual agonist
Dual in vivo effects at 100 mpk PO
From merger of literature agonist fragments
Sci. Rep., Apr. 28, 2021
Fuji Yakuhin Co., Ltd., Saitama, JP



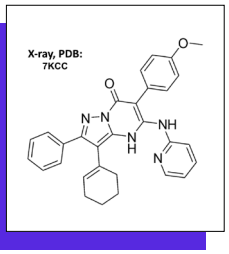
GNE-9815 | RAF

Oral pan-RAF Type II kinase inhibitor tool
Combo. efficacy in KRAS+ models w/ MEKi
SBDD from literature ligands
ACS Med. Chem. Lett., Apr. 21, 2021
Genentech, South San Francisco, CA



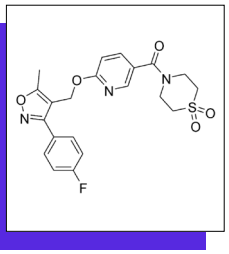
GDC-0334 | TRPA1

Oral TRPA1 ion-channel inhibitor
For asthma, target engagement in HV Ph. I
From ligand-based design, cryo-EM structure
J. Exp. Med., Apr. 5, 2021
Genentech Inc., South San Francisco, CA



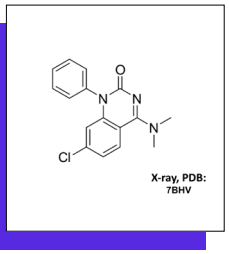
AG-270 | MAT2A

First-in-class oral MAT2A allosteric inhibitor
Synthetic lethal candidate in Ph. I for MTAP-
From >2000 fragment library and SBDD
J. Med. Chem., Apr. 8, 2021
Agios Pharmaceuticals, Cambridge, MA



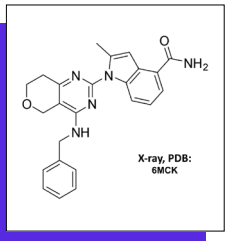
basmisanil | GABAA-α5

CNS-pen. GABAA-α5 neg. allo. mod. (NAM)
Ph. II for Down syndrome (240 mg BID)
From 56k cmpd competition binding HTS
Sci. Rep., Apr. 8, 2021
Roche Innovation Center, Basel, CH



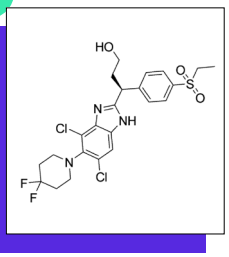
"compound 28" | MAT2A

Potent MAT2A inhibitor in vivo tool
Efficacy in MTAP-mut. xenograft (50 mpk SC)
From fragment-based DD (frag. merging)
J. Med. Chem., Apr. 26, 2021
AstraZeneca, Cambridge, UK



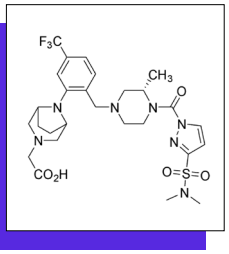
CB-5083 | p97/VCP

P97/VCP ATPase inhibitor (PDE6 off-target)
Ph. I in cancer (discont., dyschromatopsia)
From HTS of NIH compound library
J. Pharmacol. Exp. Ther., Apr. 30, 2021
Cleave Therapeutics, San Francisco, CA



SHR168442 | RORγ

Topical (skin-restricted) RORγ antagonist
Efficacy in psoriasis model / minipig PK
From GSK-805 and met. stability reduction
Sci. Rep., Apr. 28, 2021
Eternity Bioscience, NJ / Shanghai Hengrui, CN



ABD957 | ABHD17

ABHD17 serine hydrolase covalent inhibitor
Reduction of N-Ras signaling, AML cell growth
5k cmpd ser. hydrolase directed screen + opt.
Nature Chem. Biol., Apr. 29, 2021
Scripps (TSRI) / UCSF / Lundbeck

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