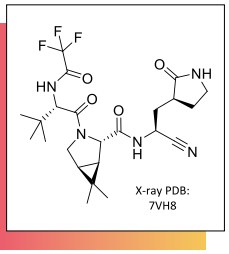
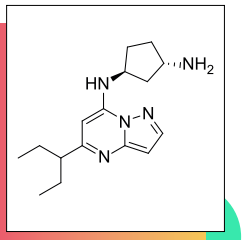
2021 Small Molecules of the Year

drughunter.com



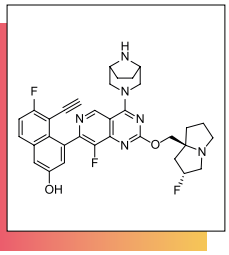
Pfizer CoV-2 M^{Pro} Inhibitor

oral pan-coronavirus antiviral, rev. covalent
Ph. III candidate for COVID-19 (300 mg BID)
from SARS-CoV-1 inhibitor (WO2005113580)
paxlovid (PF-07321332)
Pfizer Worldwide Research



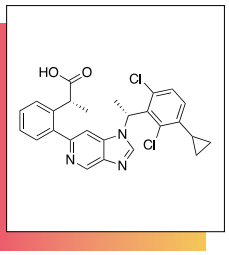
Kronos CDK9 Inhibitor

selective CDK9 inhibitor
oral Ph. I candidate for MYC-amp tumors
from microarray binding assay with lysate
KB-0742
Kronos Bio, Cambridge, MA



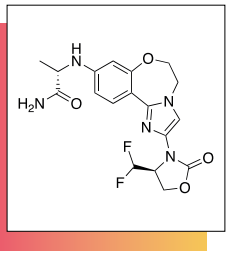
Mirati KRAS^{G12D} Inhibitor

reversible KRAS^{G12D} inhibitor
preclinical efficacy in cancer model
from SBDD around KRASG12C inhibitor
MRTX1133
Mirati Therapeutics, San Diego, CA



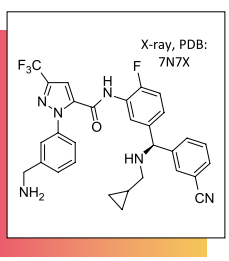
Lilly GLP Molecular Glue

GLP-1R/GLP molecular glue agonist (PAM)
oral blood glucose↓, additive w/ sitaglipin
from 220k cmpd cell-based screen + PK opt.
LSN3318839
Lilly Research Laboratories, Indianapolis, IN



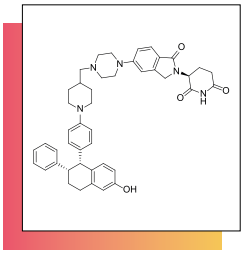
Genentech mPI3Kα Degrader

isoform-selective mutant PI3K$_\alpha$ degrader
oral <9 mg QD, Ph. III in HR+/HER2- BC
from cellular characterization of PI3Ki and opt.
inovalisib (GDC-0077)
Genentech, South San Francisco, CA



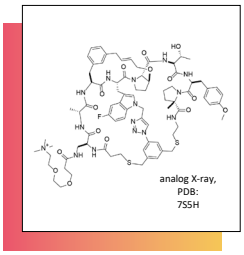
BioCryst Kallikrein Inhibitor

oral plasma kallikrein serine protease inhibitor
approved for prevention of HAE attacks
from structure-based drug design
berotralstat
BioCryst, Birmingham, AL



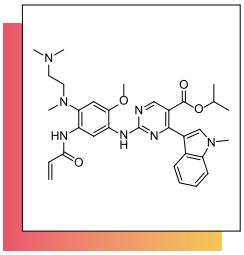
Arvinas ER Chimeric Degrader

CRBN-based heterobifunctional ER degrader
oral Ph. II candidate for ER+/HER2- BC
from ER ligand and CRBN ligand
ARV-471
Arvinas, New Haven, CT



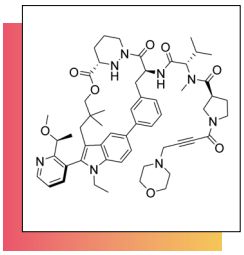
Merck PCSK9 Inhibitors

macrocyclic PCSK9/LDLR PPI inhibitor
oral PD in Ph. I with MK-0616
from mRNA display screen and SBDD
published example: compound 44
Merck & Co.



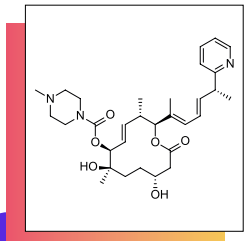
Takeda EGFR ex20 Inhibitor

EGFR exon 20 mutant inhibitor, oral once-daily
Breakthrough Therapy for ex20+ NSCLC (Ph. I)
from cellular screening + SBDD
mobocertinib
ARIAD/Takeda, Cambridge, MA



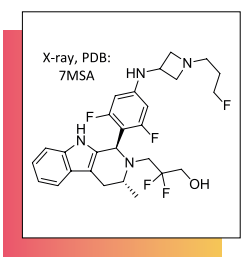
RevMed KRAS^{G12C} Tricomplex Inhibitor

KRAS(G12C)ON-cyclophilin A tri-complex inh.
overcomes KRAS resist. mut. in PDX model
natural product related (sanglifehrin); undiscl.
RM-018
Revolution Medicines, Redwood City, CA



H3Bio SF3b Splicing Modulator

oral splicing modulator (SF3b complex)
7-20 mg 21d+/7d-, Ph. I for myeloid neoplasias
from opt. of pladienolide B natural product
H3B-8800
H3 Biomedicine, Cambridge, MA



Genentech ER Degrader

selective ER degrader (SERD) + full antag.
oral (30 mg QD), Ph. III for ER+, HER2- BC
from profiling >4k cmpds for desired MoA
giredestrant (GDC-9545)
Genentech, San Francisco, US