2020 Small Molecules of the Year

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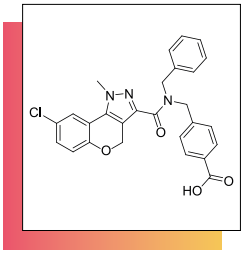
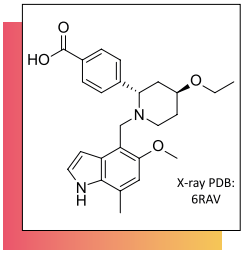


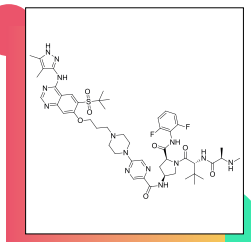
Novartis FXR Agonist

selective FXR partial agonist
orally eff. in NASH model, Ph. I in HV complete
from two 3M compound HTS and LBD
January - LMB763 (nidufexor)
Novartis (GNF), San Diego, CA



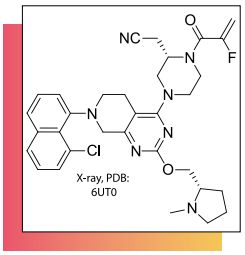
Novartis Factor B Inhibitor

selective factor B serine protease inhibitor
oral, retina penetrant, Ph. I in HV complete
from 250k compound HTS and SBDD lead op.
February – LNP023
Novartis (NIBR), Cambridge, MA



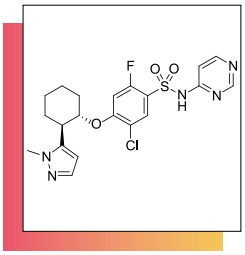
GSK RIPK2 Degrader

IAP-based selective RIPK2 degrader
prolonged PD w/ 0.15 mpk SC Q3D dosing
E3 binder switch and property-based opt.
March - "PROTAC 6"
GlaxoSmithKline, Stevenage, UK / PMCC



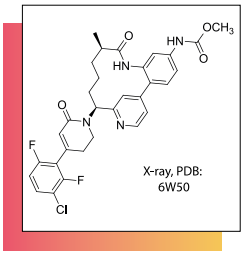
Mirati KRAS Inhibitor

covalent KRAS^{G12C} inhibitor
in clinical development for KRAS^{G12C}+ cancers
from optimization of known starting point
April – MRTX849
Array / Mirati Therapeutics



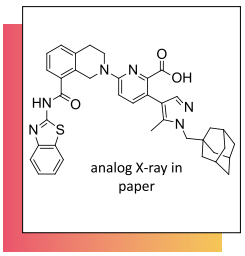
Daiichi Sankyo $Na_V1.7i$

potent, selective $Na_V1.7$ ion channel inhibitor
completed Ph. I in HV, discontinued in Ph. II
from optimization of known starting point
May - DS-1971a
Daiichi Sankyo, Tokyo, JP



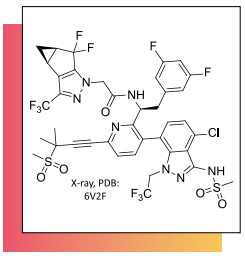
BMS Factor XIa Inhibitor

selective factor XIa serine protease inhibitor
oral in higher spec. / eff. in thrombosis model
from PK optimization of prior series
June – "Compound 6f"
Bristol Myers Squibb, Princeton, NJ



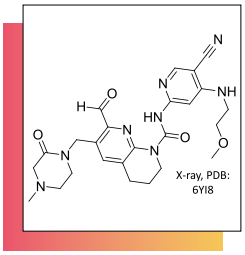
AbbVie BCL-X_L Inhibitor

first-in-class, bioavailable BCL-X_L inhibitor
oral efficacy in xenograft, led to ADC dev.
from SBDD of prior BH3 mimetics
July – A-1331852
AbbVie, North Chicago, IL / Genentech



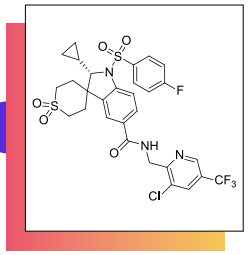
Gilead HIV Capsid Inhibitor

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.
August – GS-6207 (lenacapavir)
Gilead Sciences, Foster City, CA



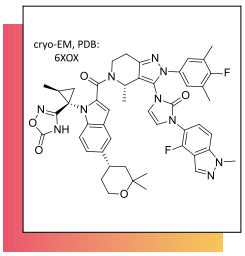
Novartis FGFR4 Inhibitor

oral reversible-covalent FGFR4 kinase inhibitor
first sel. FGFR4i in clinical studies; for HCC
from biochemical HTS and SBDD
September - FGF401 (roblitinib)
Novartis, Basel, CH



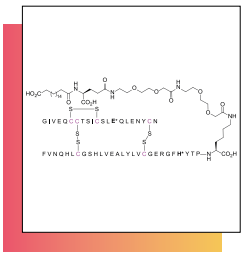
Bayer hGnRH-R Antagonist

oral hGnRH-R hormone receptor antagonist
to treat of uterine fibroids, Ph. I completed
from cell-based 2.5M cmpd HTS + opt.
October - BAY 1214784
Bayer AG, Berlin, DE



Chugai/Lilly GLP-1R Agonist

oral non-peptide GLP-1R GPCR partial agonist
in Ph. I for Type 2 diabetes, HV study complete
from cell-based screen and opt.
November - LY3502970 (OWL833)
Chugai, Shizuoka, JP / Eli Lilly, Indianapolis, IN



Novo Nordisk Oral Insulin

oral, ultralong-acting insulin analog
effective in Ph. IIa, hum. $t_{1/2}$~3 d, 4% F dog
albumin-binding motif + reduced endocytosis
December - OI338
Novo Nordisk, Maaloev, DK

HIGHLIGHTS FROM DRUG DISCOVERY ARTICLES PUBLISHED ONLINE IN 2020

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