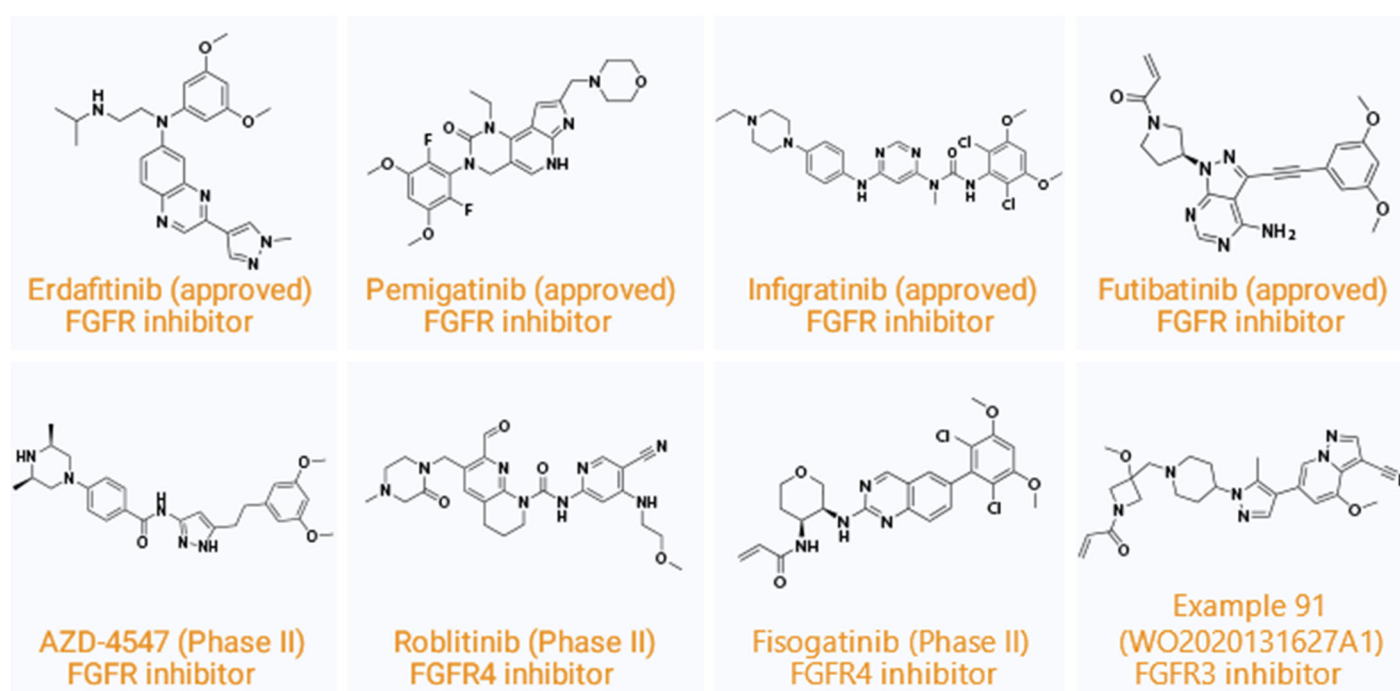


Building Blocks / Pharmaceutical Intermediates / Catalysts & Ligands

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The fibroblast growth factor receptors (FGFRs) are a family of highly conserved transmembrane tyrosine kinases (RTKs), which constitute four members (FGFR1-4)^[1]. The FGF-FGFR axis is involved in signal transduction pathways that regulate cell proliferation, differentiation, embryonic development, migration, survival, angiogenesis and organogenesis. FGFR genomic aberrations have been identified in many types of tumors. For instance, FGFR1 amplifications occur in about 20% of squamous non-small cell lung carcinomas and 10%-15% of breast cancers. FGFR2 translocations occur in 14% of intrahepatic cholangiocarcinomas. FGFR3 mutations have been identified in 60%-80% of non-muscleinvasive bladder carcinomas. In addition, FGFR4 amplifications occur in 50% of hepatocellular carcinomas. Therefore, the FGFR signaling pathway represents a promising target for cancer therapeutics. Up to now, 4 FGFR inhibitors have been approved by FDA and more than 20 FGFR inhibitors have entered into clinical trials^[2-10].



A series of building blocks will be used as molecular fragments in the design of FGFR inhibitors.

[1] European Journal of Medicinal Chemistry (2018), 154, 9-28.

[2] Journal of Medicinal Chemistry (2021), 64, 15, 10666-10679.

[3] European Journal of Medicinal Chemistry (2020), 186, 111884.

[4] European Journal of Medicinal Chemistry (2021), 220, 113499.

[5] Bioorganic & Medicinal Chemistry (2021), 33, 116019.

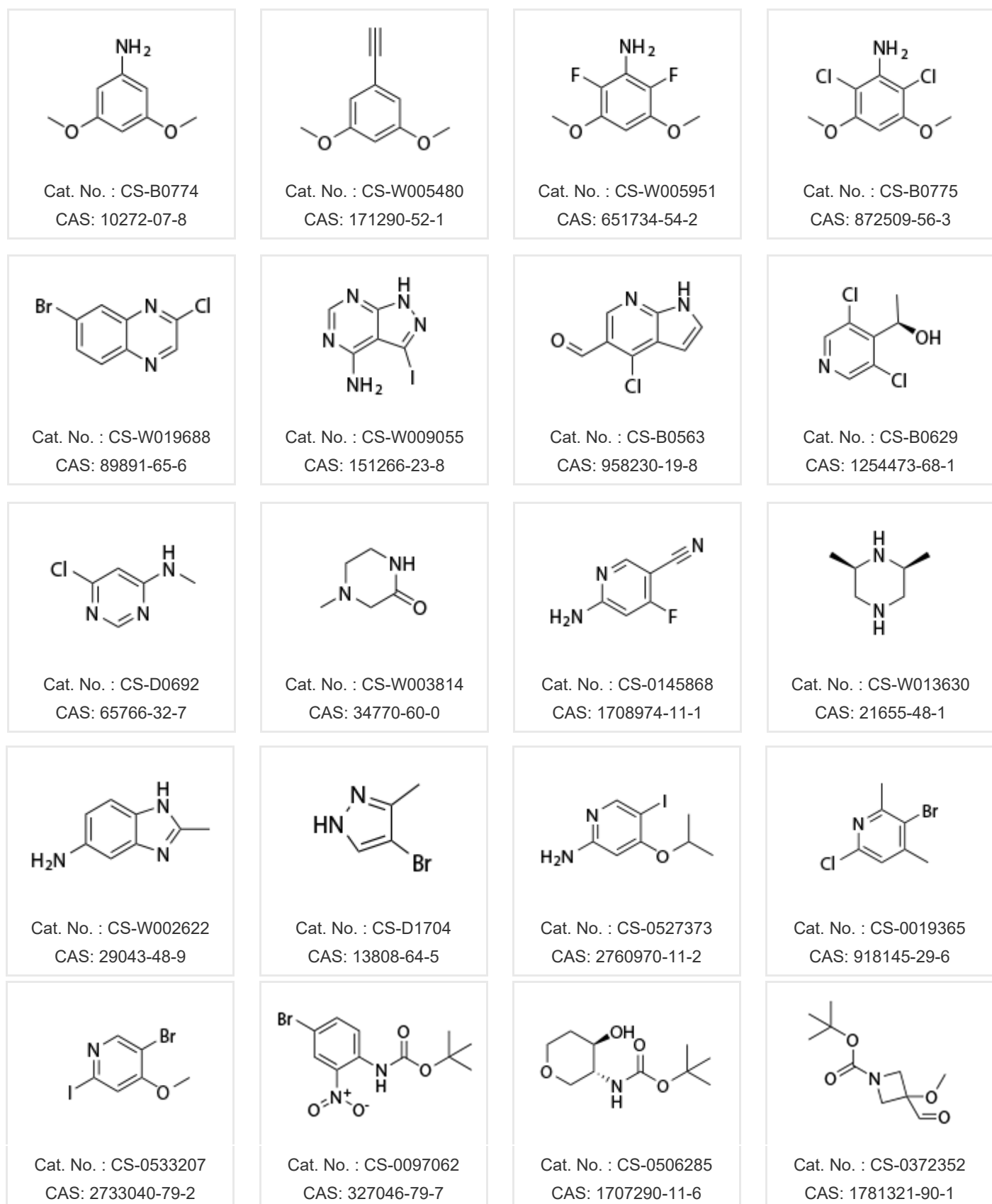
[6] Journal of Medicinal Chemistry (2022), 65, 8, 6017-6038.

[7] Journal of Medicinal Chemistry (2019), 62, 16, 7473-7488.

[8] WO2020131627A1.

[9] WO2020131674A1.

[10] WO2022109577A1.



ChemScene LLC

Tel: 732-484-9848

Fax: 888-484-5008

Email: sales@ChemScene.com

Address: 1 Deer Park Dr, Suite Q, Monmouth Junction, NJ 08852, USA

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