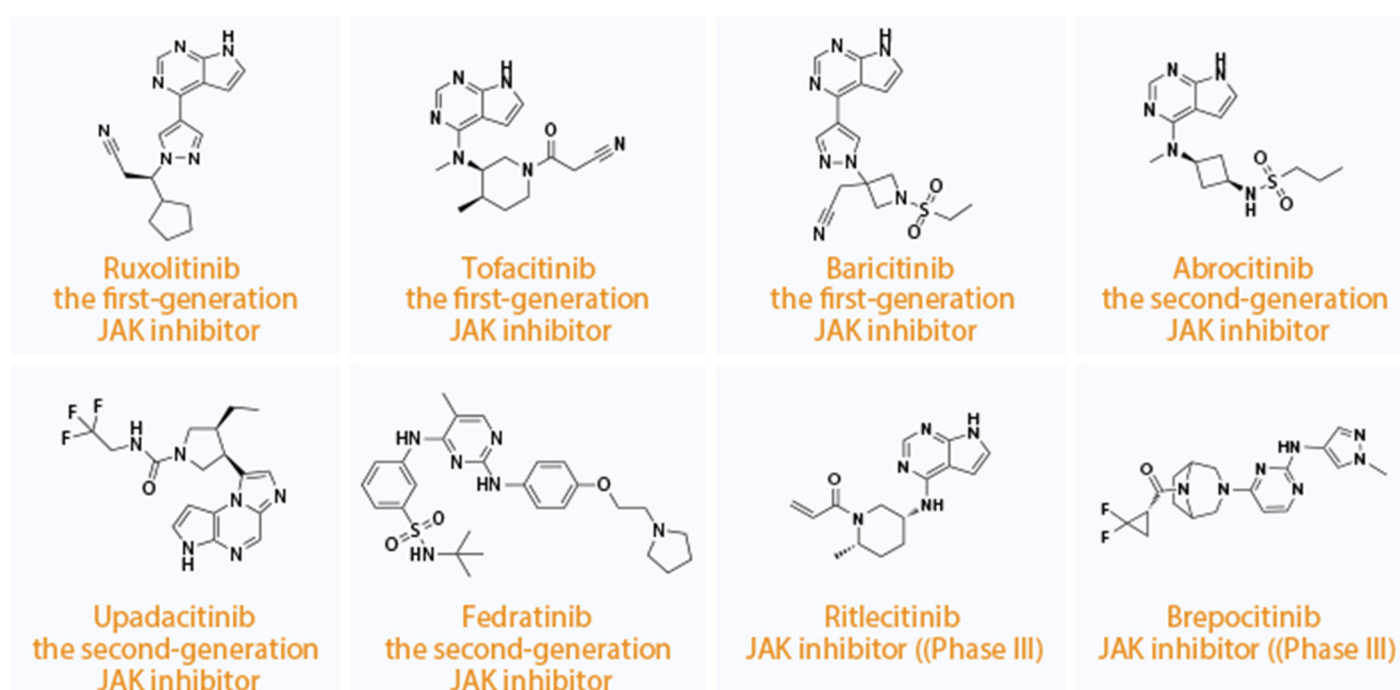


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JAK1 together with JAK2, JAK3, and TYK2 belong to the JAK (Janus-associated kinase) family of cytoplasmic tyrosine kinases that play important roles in cytokine and growth factor mediated signal transduction^[1]. Dysregulated JAK activity leading to a constitutively activated signal transducers and activators of transcription (STAT) is strongly associated with immune-related diseases and cancers. Targeting JAK to interfere the signaling of JAK/STAT pathway has achieved quite success in the treatment of these diseases. In 2011, the first JAK inhibitor Ruxolitinib was approved by FDA for the treatment of patients with intermediate or high-risk myelofibrosis. Upadacitinib is a highly selective JAK1 agent and was launched in U.S. in 2019 for patients with rheumatoid arthritis, it was also approved by FDA for the treatment of psoriatic arthritis in 2021 and atopic dermatitis in 2022. Up to now, 10 JAK inhibitors have been approved for marketing worldwide and more than 80 JAK inhibitors have entered into clinical trials^[2-8].



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

[1] Journal of Medicinal Chemistry (2020), 63, 9, 4517-4527.

[2] European Journal of Medicinal Chemistry (2022), 239, 114551.

[3] European Journal of Medicinal Chemistry (2020), 192, 112155.

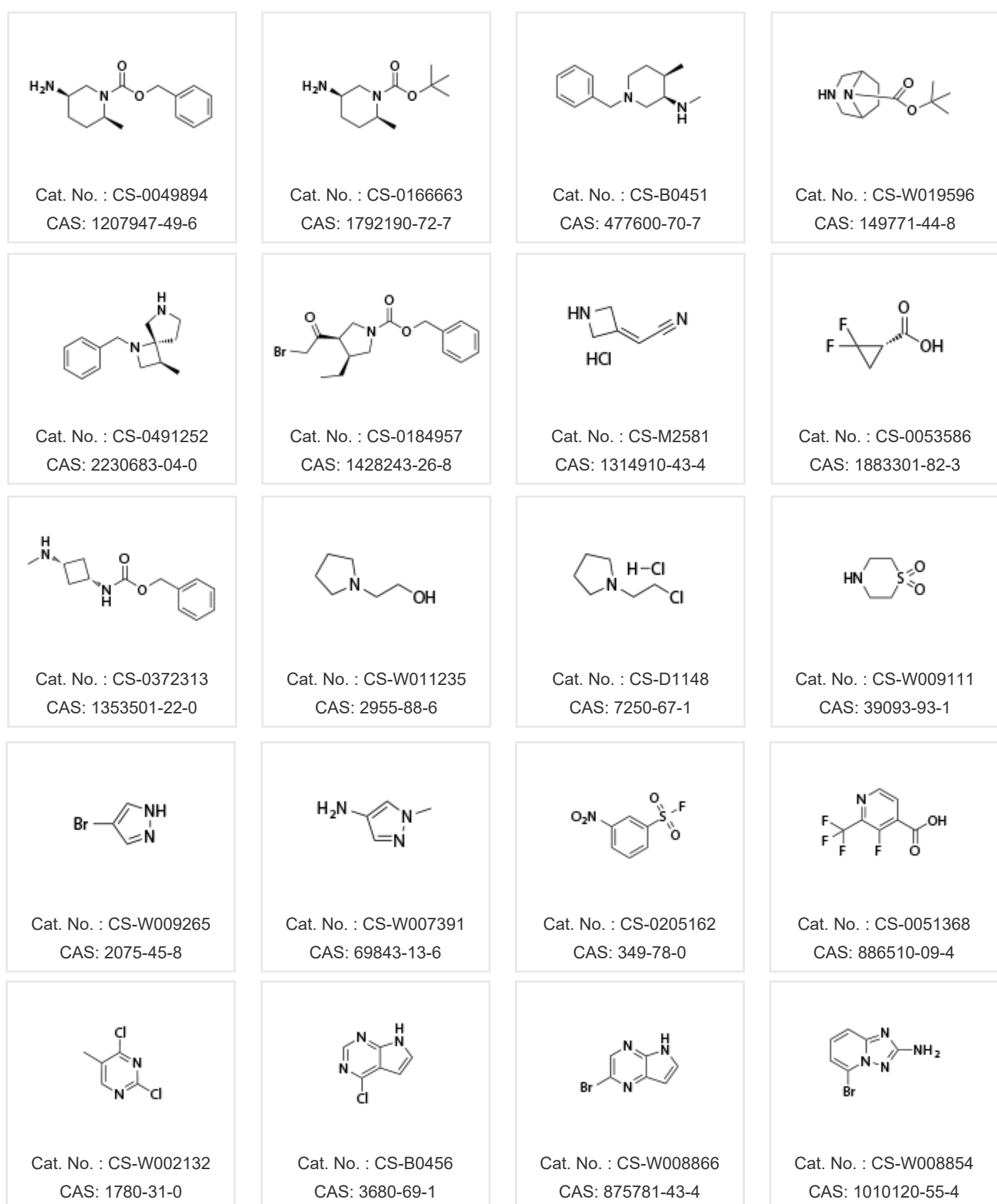
[4] Journal of Medicinal Chemistry (2022), 65, 15, 10674-10690.

[5] Pharmacological Research (2022), 183, 106362.

[6] Journal of Medicinal Chemistry (2020), 63, 10, 5324-5340.

[7] Journal of Medicinal Chemistry (2015), 58, 18, 7596-7602.

[8] Bioorganic & Medicinal Chemistry (2019), 27, 8, 1562-1576.


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