Tyrosine kinases such as anaplastic lymphoma kinase (ALK) are becoming major targets in the development of new chemotherapeutics and anti-inflammatories. ALK plays an important role in the development of the brain; it also drives the progression of several cancers, including anaplastic large-cell lymphoma, neuroblastoma, and non-small cell lung cancer.

When the ALK gene is mutated or fused with other genes, it often produces extra or aberrant proteins. Overactive ALK stimulates JAK/STAT, PI3K/Akt, and ERK, promoting unregulated cell cycle progression, survival, and proliferation. Targeting ALK prevents these downstream effects, limiting cancer cell signaling and tumor growth.

Several ALK inhibitors also inhibit IGF-1R, an additional target in preventing growth of cancer cells. Products that target both of these kinases include LDK378 (L1340), AZD3463 (A9600), and GSK-1838705A (G7540).

References:
2. www.clinicaltrials.gov/show/NCT01685060
8. www.clinicaltrials.gov/show/NCT01284192

Crizotinib (C6935) is a well-characterized ALK inhibitor that also suppresses activity of ROS1 and c-MET. In cancer cells, this compound upregulates expression of pro-apoptotic BIM and downregulates expression of anti-apoptotic survivin to induce apoptosis.

CH5424802 (C2900) targets both wild-type and mutant L1196M ALK, inducing regression of non-small cell lung cancer metastasis in the brain.

Doramapimod (D5868) is an inhibitor of ALK, JNK, and p38 MAPK that suppresses pulmonary inflammation in vivo and in vitro.

ASP-3026 (A7400) is an inhibitor of ALK that lowers tumor burden in lung and intrapleural tumor models.