TABLE 102e-2 SOME FDA-APPROVED MOLECULARLY TARGETED AGENTS FOR THE TREATMENT OF CANCER

Drug	Molecular Target	Disease	Mechanism of Action
All-*trans* retinoic acid	PML-RARα oncogene	Acute promyelocytic leukemia M3 AML; t(15;17)	Inhibits transcriptional repression by PML-RARα
Imatinib	Bcr-Abl, c-Abl, c-Kit, PDGFR-α/β	Chronic myeloid leukemia; GIST	Blocks ATP binding to tyrosine kinase active site
Dasatinib, nilotinib, ponatinib, bosutinib	Bcr-Abl (primarily)	Chronic myeloid leukemia	Blocks ATP binding to tyrosine kinase active site
Sunitinib	c-Kit, VEGFR-2, PDGFR-β, Flt-3	GIST; renal cell cancer	Inhibits activated c-Kit and PDGFR in GIST; inhibits VEGFR in RCC
Sorafenib	RAF, VEGFR-2, PDGFR-α/β, Flt-3, c-Kit	RCC; hepatocellular carcinoma; TC	Targets VEGFR pathways in RCC. Possible activity against BRAF in thyroid cancer
Regorafenib	VEGFR-1 to -3, TIE-2, FGFR1, KIT, RET, PDGFR	Colorectal cancer; GIST	Competitive inhibitor of ATP binding site of tyrosine kinase domain multiple kinases
Axitinib	VEGFR-1 to -3	RCC	Competitive inhibitor of ATP binding site of tyrosine kinase domain VEGF receptors
Erlotinib	EGFR	Non-small-cell lung cancer; pancreatic cancer	Competitive inhibitor of the ATP-binding site of the EGFR
Afatinib	EGFR (and other HER family)	Non-small-cell lung cancer	Irreversible inhibitor of ATP-binding site of HER family members
Lapatinib	HER2/neu	Breast cancer	Competitive inhibitor of the ATP binding site of HER2
Crizotinib (Xalkori)	ALK	Non-small-cell lung cancer	Inhibitor of ALK tyrosine kinase
Bortezomib, carfilzomib	Proteasome	Multiple myeloma	Inhibits proteolytic degradation of multiple cellular proteins
Vemurafenib, dabrafenib	BRAF	Melanoma	Inhibitor of serine-threonine kinase domain of V600E mutant of BRAF
Trametinib	MEK	Melanoma	Inhibitor of serine-threonine kinase domain of V600E mutant of MEK
Cabozantinib	RET, MET, VEGFR	MTC	Competitive inhibitor of ATP binding site of tyrosine kinase domain multiple kinases
Vandetanib	RET, VEGFR, EGFR	MTC	Competitive inhibitor of ATP binding site of tyrosine kinase domain multiple kinases
Temsirolimus	mTOR	RCC	Competitive inhibitor of mTOR serine-threonine kinase
Everolimus	mTOR	RCC; breast cancer	Binds to immuophilin FK binding protein-12, which forms complex that inhibits mTOR kinase
Vorinostat, romidepsin	HDAC	CTCL	HDAC inhibitor
Ruxolitinib	JAK-1, -2	Myelofibrosis	Competitive inhibitor of tyrosine kinase
Vismodegib	Hedgehog pathway	Basel cell cancer (skin)	Inhibits smoothened in hedgehog pathway
Monoclonal Antibodies Alone			
Trastuzumab	HER2/neu (ERBB2)	Breast cancer	Binds HER2 on tumor cell surface and induces receptor internalization
Pertuzumab	HER2/neu (ERBB2)	Breast cancer	Binds HER2 on tumor cell surface at distinct site from trastuzumab and prevents binding to other receptors
Cetuximab	EGFR	Colon cancer, squamous cell carcinoma of the head and neck	Binds extracellular domain of EGFR and blocks binding of EGF and TGF-α; induces receptor internalization; potentiates the efficacy of chemotherapy and radiotherapy
Panitumumab	EGFR	Colon cancer	Similar to cetuximab but fully humanized rather than chimeric
Rituximab	CD20	B cell lymphomas and leukemias that express CD20	Multiple potential mechanisms, including direct induction of tumor cell apoptosis and immune mechanisms
Alemtuzumab	CD52	Chronic lymphocytic leukemia and CD52-expressing lymphoid tumors	Immune mechanisms
Bevacizumab	VEGF	Colorectal, lung cancers, RCC, glioblastoma, cervical cancer	Inhibits angiogenesis by high-affinity binding to VEGF
Ziv-aflibercept	VEGF-A, VEGF-B, PLGF	Colorectal cancers	Inhibits angiogenesis by high-affinity binding to VEGF-A, VEGF-B, and PLGF
Ipilimumab	CTLA-4	Melanoma	Blocks CTLA-4, preventing interaction with CD80/86 and T cell inhibition
Denosumab	RANK ligand	Breast, prostate cancer	Inhibits RANK ligand, the primary signal for bone removal
Pembrolizumab	PD-1	Melanoma	Blocks PD-1 preventing interaction with PD-L1 T cell inhibition
Antibody-Chemotherapy Conjugates			
Brentuximab vedotin	CD30	Hodgkin's disease, anaplastic lymphoma	Delivery of chemotherapeutic agent (MMAE) to CD30-expressing tumor cells
Ado-trastuzumab emtansine	HER2	Breast cancer	Delivery of chemotherapeutic agent emtansine to HER2-expressing breast cancer cells

Abbreviations: AML, acute myeloid leukemia; CTCL, cutaneous T cell lymphoma; EGFR, epidermal growth factor receptor; FDA, Food and Drug Administration; Flt-3, fms-like tyrosine kinase-3; GIST, gastrointestinal stromal tumor; MTC, medullary thyroid cancer; mTOR, mammalian target of rapamycin; PDGFR, platelet-derived growth factor receptor; PLGF, placental growth factor; PML-RARα, promyelocytic leukemia-retinoic acid receptor-alpha; RCC, renal cell cancer; t(15;17), translocation between chromosomes 15 and 17; TC, thyroid cancer; TGF-α, transforming growth factor-alpha; VEGFR, vascular endothelial growth factor receptor.