



Faculty of Pharmacy

## **Design and Synthesis of Novel Imatinib Analogs as Antitumor Multi-target Kinase Inhibitors**

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بِسْمِ اللَّهِ الرَّحْمَنِ الرَّحِيمِ

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## List of Abbreviations

<b>7-AAD:</b>	7-aminoactinomycin-D
<b>aa:</b>	Amino acids
<b>A<math>\beta</math>40/42:</b>	Amyloid beta isoforms 40 and 42
<b>ACS</b>	American Cancer Society
<b>ADMET:</b>	Absorption, Distribution, Metabolism, Excretion, Toxicity
<b>AIF:</b>	Apoptosis Inducing Factor
<b>Akt:</b>	AKT8 virus oncogene cellular homolog
<b>ALK</b>	Activin-Like Kinase
<b>ALL:</b>	Acute Lymphoblastic Leukemia
<b>APAF-1:</b>	Apoptotic Protease Activating Factor 1
<b>APO-1:</b>	Apo-enzyme/ Apolipoprotein
<b>APP-695:</b>	Amyloid protein precursor-695
<b>ARD:</b>	Caspase activation and recruitment domain
<b>ATP:</b>	Adenosine Tri-Phosphate
<b>AXL:</b>	Receptor tyrosine kinase
<b>Bax:</b>	BCL (B Cell Lymphoma)-Associated X protein
<b>BBB:</b>	Blood Brain Barrier
<b>BCG:</b>	Bacillus Calmette-Guérin
<b>Bcl-2:</b>	B cell leukemia 2 protein
<b>Bcl-xL:</b>	B cell leukemia extra large
<b>Bcr-Abl:</b>	Ablon leukemia oncogene cellular homolog
<b>BH3:</b>	Bcl-2 Homology-3
<b>BID:</b>	A BH3 domain-only death agonist protein
<b>BM</b>	Bone marrow
<b>BRAF:</b>	B cell receptor activating factor of TNF family
<b>BSA:</b>	Bovine serum albumin
<b>BTK:</b>	Bruton's tyrosine kinase
<b>CASP3:</b>	Caspase 3 gene
<b>CD95:</b>	Cyclin Dependent 95
<b>CDK-4:</b>	Cyclin dependent kinase-4
<b>CH<sub>2</sub>Cl<sub>2</sub>:</b>	Methylene Chloride
<b>c-IAP1:</b>	Cellular inhibitor of apoptosis protein 1
<b>c-IAP2:</b>	Cellular inhibitor of apoptosis protein 2
<b>c-Met:</b>	Tyrosine protein kinase Met
<b>CK:</b>	Casein Kinase

<b>CK1:</b>	Casein Kinase 1
<b>CK1 I:</b>	Casein Kinase 1 inhibitors
<b>CMGC:</b>	Kinase Group CMGC
<b>CML:</b>	Chronic Myeloid Leukemia
<b>CNS:</b>	Central Nervous System
<b>CrKI:</b>	CT10 sarcoma oncogene cellular homolog
<b>CSF-1R:</b>	Colony Stimulating Factor Receptor-1
<b>CYP 171A1 inhibitor:</b>	Cytochrome P 171A1 inhibitor
<b>CYP 450:</b>	Cytochrome P450
<b>D<sub>2</sub>O:</b>	Deuterium Oxide
<b>DAPI:</b>	4'6'-diamidino-2-phenylindole
<b>DCC:</b>	N,N'Dicyclohexylcarbodiimide
<b>DD:</b>	Death Domain
<b>DDR:</b>	Death Domain Receptor
<b>DDX3:</b>	Death Domain X3
<b>DED:</b>	Death Effector Domain
<b>DFG:</b>	A general molecular framework that defines a type II inhibitor consists of a heterocyclic “head” group that recognizes the kinase hinge region, an amide or a urea based linker that traverses across the kinase “gatekeeper” residue, and a “tail” scaffold that occupies the hydrophobic allosteric pocket created by the flip
<b>DIABLO:</b>	(Direct IAP binding protein with low pI) gene on chromosome 12
<b>DISC:</b>	Death-Initiating Signaling Complex
<b>DMAP:</b>	4-dimethylaminopyridine
<b>DNA:</b>	Deoxyribonucleic acid
<b>DRD:</b>	Death receptor dependent
<b>DTP:</b>	Developmental Therapeutic Program
<b>DTT:</b>	Dithiothreitol also known as Cleland's reagent
<b>DVL:</b>	Dishevelled 1 (Homologous to Drosophila Dsh)
<b>EGFR:</b>	Epidermal Growth Factor Receptor
<b>Endo G:</b>	Endonuclease G
<b>ERBB2:</b>	Erythroblast oncogene B, a gene isolated from avian genome
<b>ERK 1/2:</b>	Extracellular signal regulated kinase
<b>FADD:</b>	Fas-associated protein with death domain
<b>FAK:</b>	Focal adhesion kinase
<b>Fas:</b>	TNF superfamily receptor 6

<b>FDA:</b>	Food and Drug Administration
<b>FGF:</b>	Fibroblast Growth Factor
<b>FLASH</b>	Proapoptotic Protein Involved in Activation of Caspase-8
<b>FZD:</b>	Wnt-protein ligand to a Frizzled family
<b>GCT:</b>	Giant Cell Tumor cells
<b>GPCR:</b>	G-protein coupled receptor
<b>Grb2:</b>	Growth factor receptor- <i>bound</i> protein 2
<b>HBA:</b>	Hydrogen Bond Acceptors
<b>HBTU:</b>	Hexafluorophosphate Benzotriazole Tetramethyl Uronium
<b>HEI-193</b>	Human Vestibular Schwannoma cells
<b>HL60:</b>	Acute Myeloid Leukemia
<b>HMC-1</b>	Human Mast Cell line-1
<b>HMG-CoA synthetase:</b>	High mobility group-CoA synthetase
<b>HOBT:</b>	1-hydroxybenzotriazole
<b>Hsp10:</b>	Heat shock protein 10
<b>Hsp60:</b>	Heat shock protein 60
<b>HtrA2:</b>	High temperature requirement serine protease A2
<b>IAPs:</b>	Inhibitors of Apoptosis Proteins
<b>IGFR:</b>	Insulin-like Growth Factor Receptor
<b>IKK<math>\beta</math>:</b>	I $\kappa$ B kinase
<b>JAK:</b>	Janus family tyrosine kinase
<b>JNK:</b>	Jun N-terminal kinase
<b>K562:</b>	First human immortalised myelogenous leukemia line (erythroleukemia)
<b>KD:</b>	Kinase domain
<b>kDa:</b>	Kilo Dalton
<b>KG1a:</b>	Human Leukemia Stem-like cell line
<b>KIT:</b>	Human gene of receptor tyrosine kinase
<b>LBD:</b>	Ligand Binding Domains
<b>LEDs</b>	Light-emitting diodes
<b>LMP:</b>	lysosomal membrane permeabilization
<b>LRP:</b>	Leucine-responsive Regulatory Protein
<b>Lu:</b>	Luminescence Intensity in the presence of the compound
<b>Luc:</b>	Luminescence Intensities in the presence of Kinase
<b>Lu:</b>	Luminescence Intensities in the absence of Kinase
<b>MCF-7:</b>	Breast cancer cell line