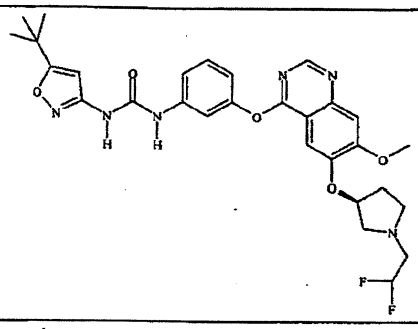
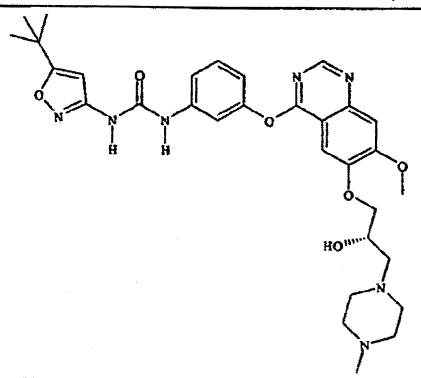
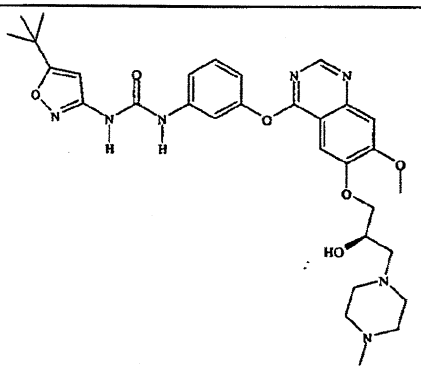
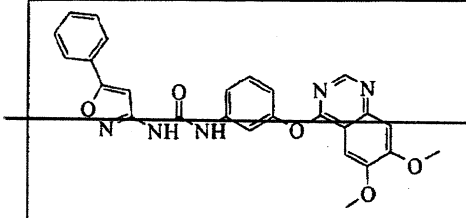
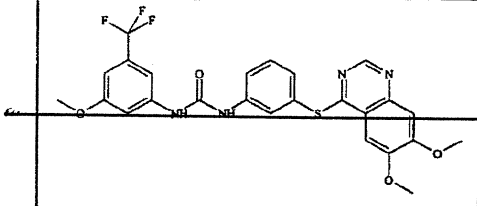
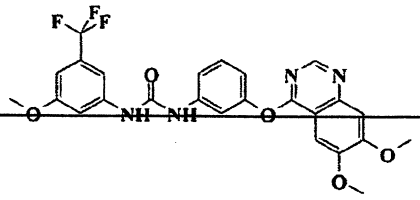
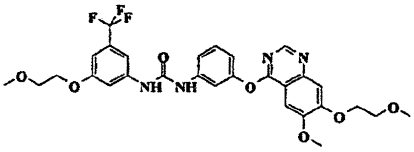
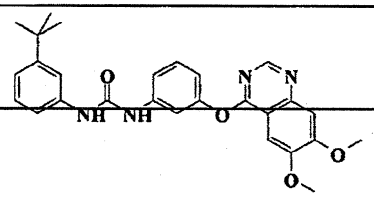
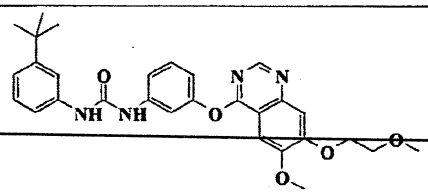
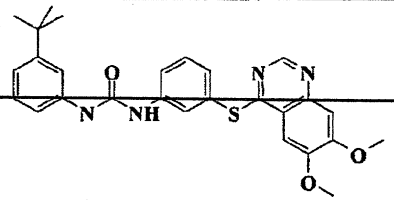
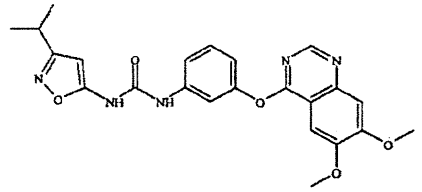
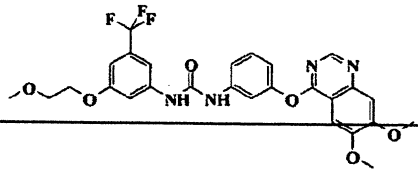
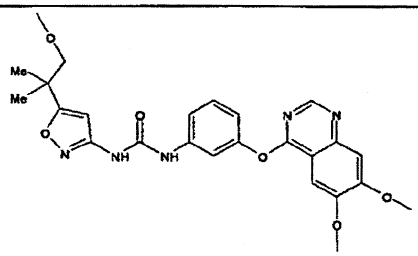
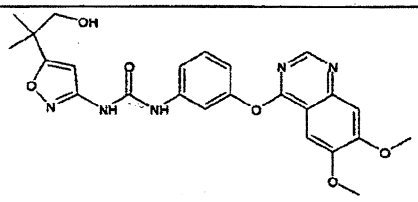
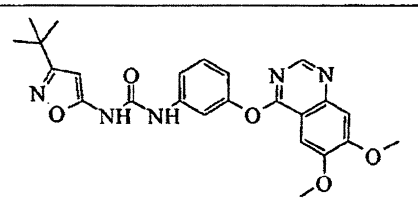
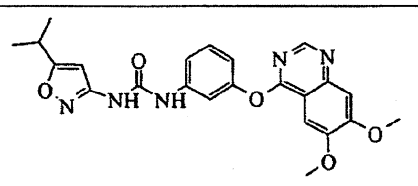
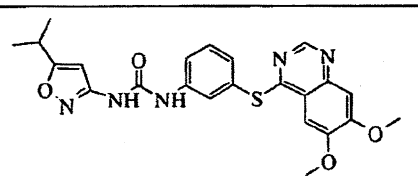
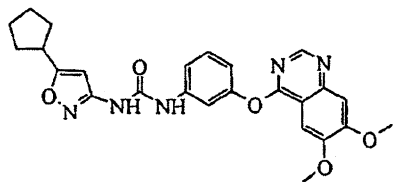
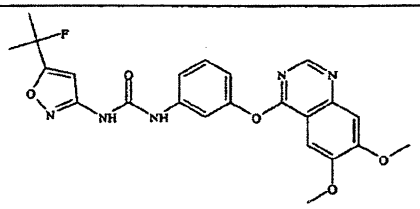
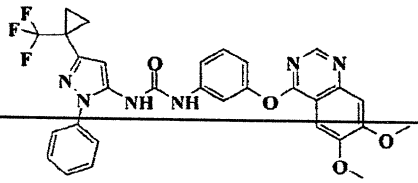
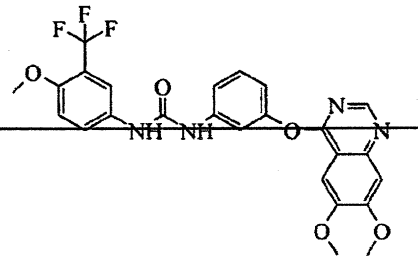
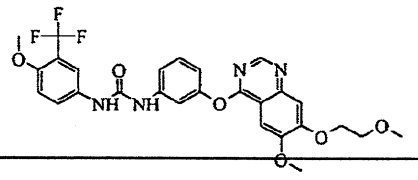
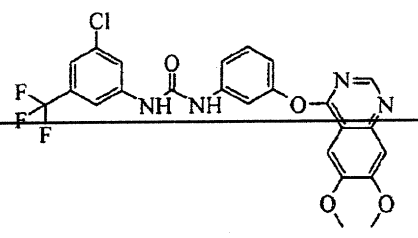
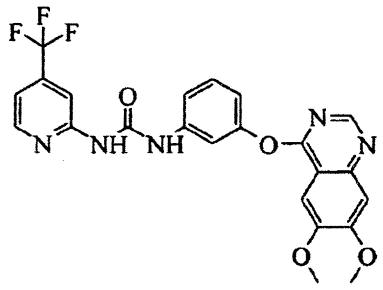
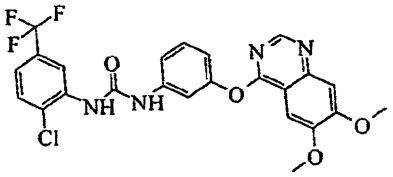
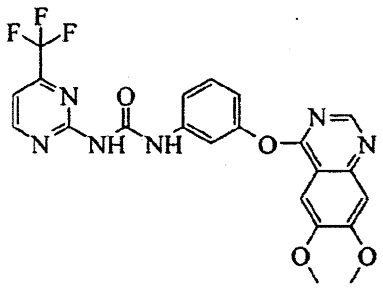
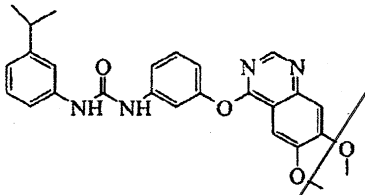
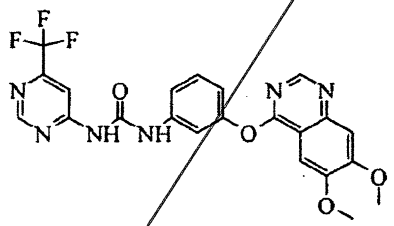
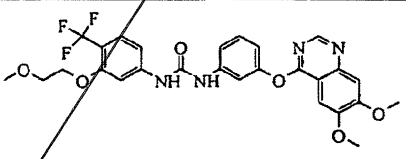
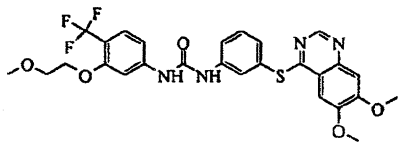
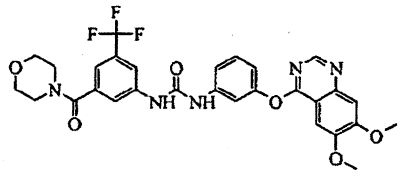
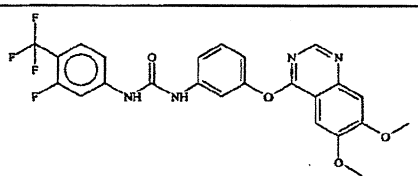
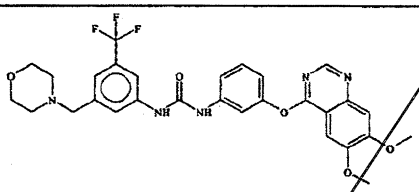
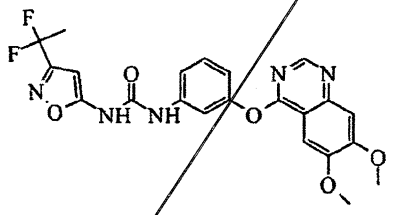
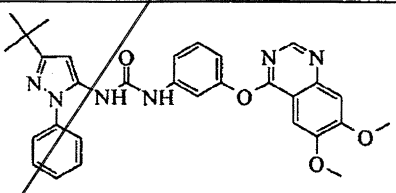
	Name	pMEK IC50 (nM)	A375 Viability EC50 (nM)	BRAF V600E Kd (nM)	BRAF WT Kd nM	RAF1 Kd nM	S35
	Ex 110 (S)-1-(5-tert-butylisoxazol-3-yl)-3-(3-(6-(1-(2,2-difluoroethyl)pyrrolidin-3-yloxy)-7-methoxyquinazolin-4-yloxy)phenyl)urea	A	A	A	B	A	C
	Ex 111 (S)-1-(5-tert-butylisoxazol-3-yl)-3-(3-(6-(2-hydroxy-3-(4methylpiperazin-1-yl)propoxy)-7-methoxyquinazolin-4-yloxy)phenyl)urea	A	B	A	B	A	D
	Ex 112 (R)-1-(5-tert-butylisoxazol-3-yl)-3-(3-(6-(2-hydroxy-3-(4methylpiperazin-1-yl)propoxy)-7-methoxyquinazolin-4-yloxy)phenyl)urea	B	C	A	C	B	D
	Ex 113 1-(3-(6,7-dimethoxyquinazolin-4-yloxy)phenyl)-3-(5-phenylisoxazol-3-yl)urea	C	D	B	C	A	B
	Ex 115 1-(3-(6,7-dimethoxyquinazolin-4-ylthio)phenyl)-3-(3-methoxy-5-(trifluoromethyl)phenyl)urea	D	D	B	C	B	C

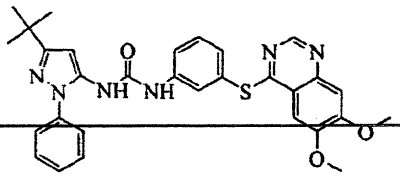
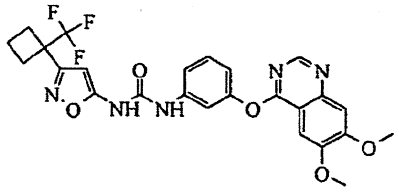
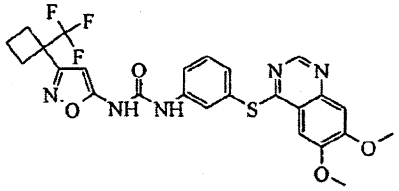
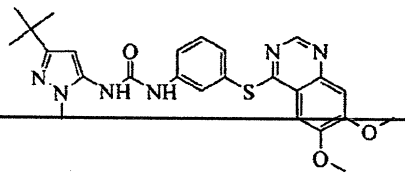
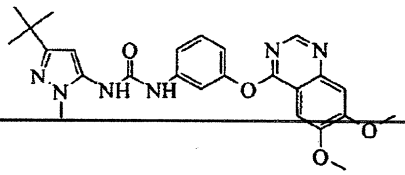
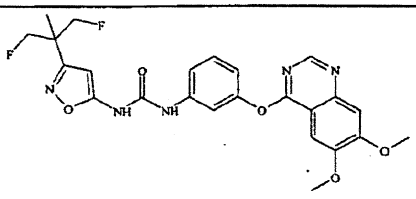
	Name	pMEK IC50 (nM)	A375 Viability EC50 (nM)	BRAF V600E Kd (nM)	BRAF WT Kd nM	RAF 1 Kd nM	S35
	Ex 116 1-(3-(6,7-dimethoxyquinazolin-4-yloxy)phenyl)-3-(3-methoxy-5-(trifluoromethyl)phenyl)urea	D	D	B	C	B	B
	Ex 117 1-(3-(6-methoxy-7-(2-methoxyethoxy)quinazolin-4-yloxy)phenyl)-3-(3-(2-methoxyethoxy)-5-(trifluoromethyl)phenyl)urea	D	D	B	C	B	C
	Ex 118 1-(3-tert-butylphenyl)-3-(3-(6,7-dimethoxyquinazolin-4-yloxy)phenyl)urea	B	D	A	B	A	C*
	Ex 119 1-(3-tert-butylphenyl)-3-(3-(6-methoxy-7-(2-methoxyethoxy)quinazolin-4-yloxy)phenyl)urea	B	D	A	B	B	C*
	Ex 120 1-(3-tert-butylphenyl)-3-(3-(6,7-dimethoxyquinazolin-4-ylthio)phenyl)urea	B	D	A	B	A	C*
	Ex 122 1-(3-(6,7-dimethoxyquinazolin-4-yloxy)phenyl)-3-(3-isopropylisoxazol-5-yl)urea	B	D	A	A	A	C

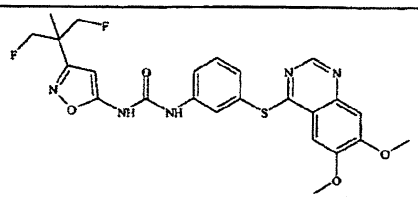
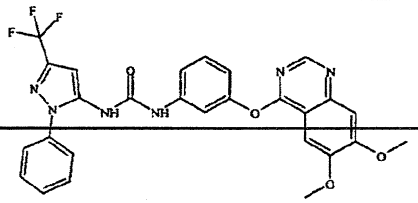
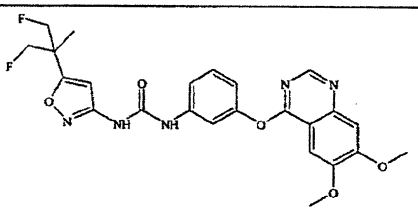
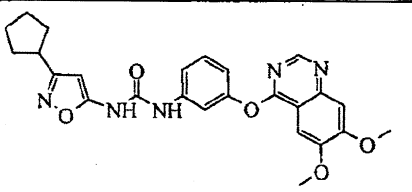
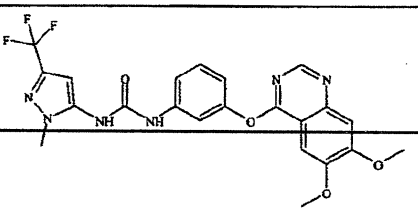
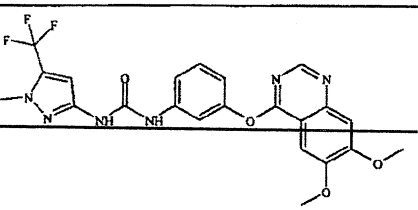
	Name	pMEK IC50 (nM)	A375 Viability EC50 (nM)	BRAF V600E Kd (nM)	BRAF WT Kd nM	RAF 1 Kd nM	S35
	Ex 129 1-(3-(6,7-dimethoxyquinazolin-4-yloxy)phenyl)-3-(3-(2-methoxyethoxy)-5-(trifluoromethyl)phenyl)urea	D	D	B	D	B	B
	Ex 130 1-(3-(6,7-dimethoxyquinazolin-4-yloxy)phenyl)-3-(5-(1-methoxy-2-methylpropan-2-yl)isoxazol-3-yl)urea	B	D	B	D	D	C
	Ex 131 1-(3-(6,7-dimethoxyquinazolin-4-yloxy)phenyl)-3-(5-(1-hydroxy-2-methylpropan-2-yl)isoxazol-3-yl)urea	C	D	A	B	A	C
	Ex 132 1-(3-tert-butylisoxazol-5-yl)-3-(3-(6,7-dimethoxyquinazolin-4-yloxy)phenyl)urea	A	A	A	C	C	C
	Ex 133 1-(3-(6,7-dimethoxyquinazolin-4-yloxy)phenyl)-3-(5-isopropylisoxazol-3-yl)urea	B	C	A	A	A	C*
	Ex 134 1-(3-(6,7-dimethoxyquinazolin-4-ylthio)phenyl)-3-(5-isopropylisoxazol-3-yl)urea	B	D	A	A	A	C*

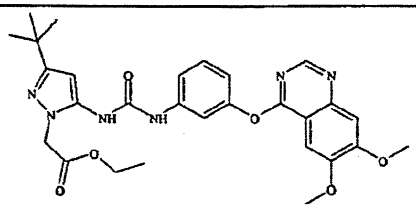
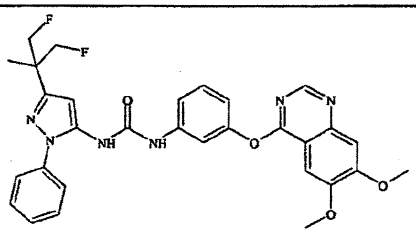
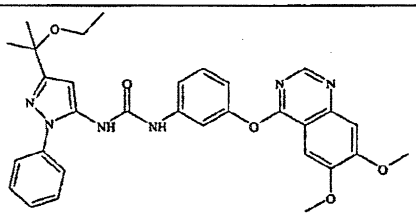
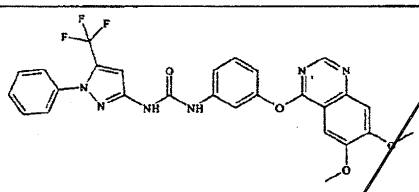
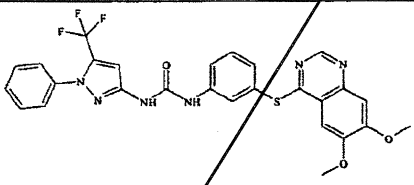
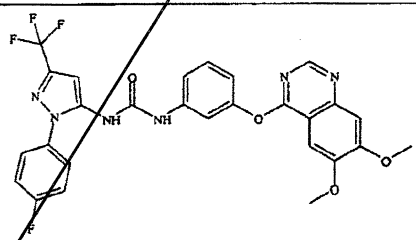
	Name	pMEK IC50 (nM)	A375 Viability EC50 (nM)	BRAF V600E Kd (nM)	BRAF WT Kd nM	RAF 1 Kd nM	S35
	Ex 135 1-(5-cyclopentylisoxazol-3-yl)-3-(3-(6,7-dimethoxyquinazolin-4-yloxy)phenyl) urea	A	B	A	A	A	C*
	Ex 136 1-(3-(6,7-dimethoxyquinazolin-4-yloxy)phenyl)-3-(5-(2-fluoropropan-2-yl)isoxazol-3-yl)urea	A	B	A	A	A	C*
	Ex 137 1-(3-(6,7-dimethoxyquinazolin-4-yloxy)phenyl)-3-(1-phenyl-3-(1-(trifluoromethyl)cyclopropyl)-1H-pyrazol-5-yl)urea	A	C	C	D	D	D*
	Ex 138 1-(3-(6,7-dimethoxyquinazolin-4-yloxy)phenyl)-3-(4-methoxy-3-(trifluoromethyl)phenyl)urea	B	D	A	B	A	B
	Ex 139 1-(4-methoxy-3-(trifluoromethyl)phenyl)-3-(3-(6-methoxy-7-(2-methoxyethoxy)quinazolin-4-yloxy)phenyl) urea	B	D	A	A	A	C*
	Ex 140 1-(3-chloro-5-(trifluoromethyl)phenyl)-3-(3-(6,7-dimethoxyquinazolin-4-yloxy) phehyl)urea	D	D	C	D	C	B

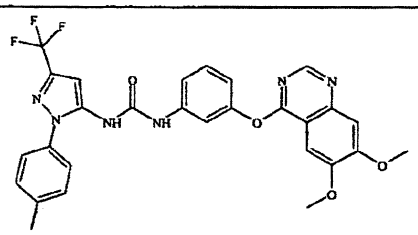
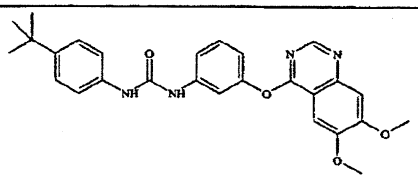
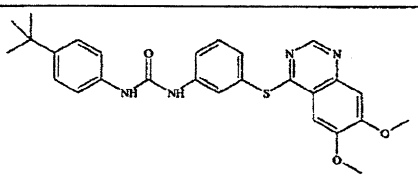
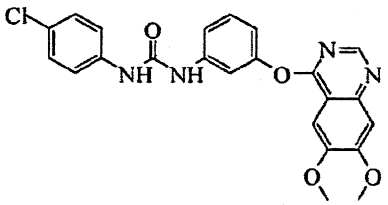
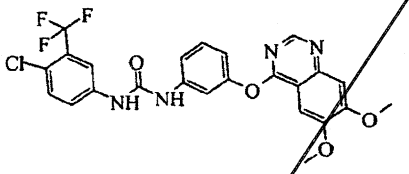
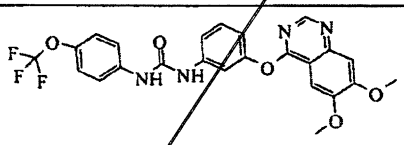
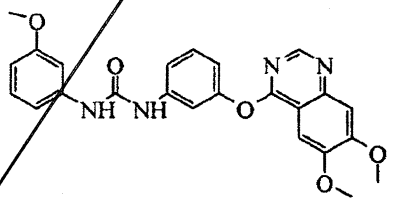
	Name	pMEK IC50 (nM)	A375 Viability EC50 (nM)	BRAF V600E Kd (nM)	BRAF WT Kd nM	RAF 1 Kd nM	S35
	Ex 141 1-(3-(6,7-dimethoxyquinazolin-4-yloxy)phenyl)-3-(4-(trifluoromethyl)pyridin-2-yl)urea	C	D	A	A	A	C
	Ex 142 1-(2-chloro-5-(trifluoromethyl)phenyl)-3-(3-(6,7-dimethoxyquinazolin-4-yloxy)phenyl) urea	D	D	B	D	B	B
	Ex 143 1-(3-(6,7-dimethoxyquinazolin-4-yloxy)phenyl)-3-(4-(trifluoromethyl)pyrimidin-2-yl)urea	D	D	B	D	B	A
	Ex 144 1-(3-(6,7-dimethoxyquinazolin-4-yloxy)phenyl)-3-(3-isopropylphenyl)urea	B	D	A	B	A	C*
	Ex 146 1-(3-(6,7-dimethoxyquinazolin-4-yloxy)phenyl)-3-(6-(trifluoromethyl)pyrimidin-4-yl)urea	D	D	A	B	B	B*
	Ex 147 1-(3-(6,7-dimethoxyquinazolin-4-yloxy)phenyl)-3-(3-(2-methoxyethoxy)-4-(trifluoromethyl)phenyl) urea	D	D	B	D	C	B*

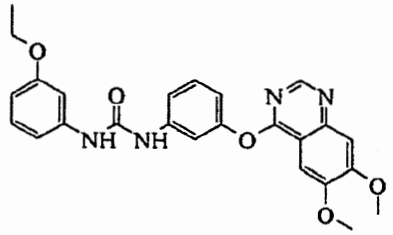
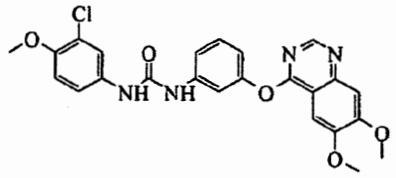
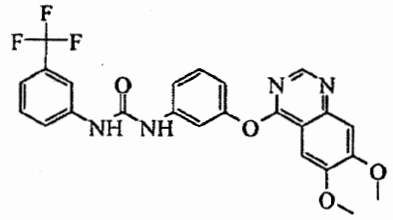
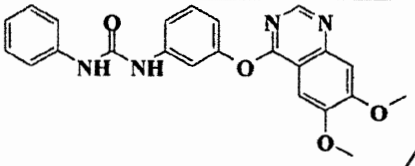
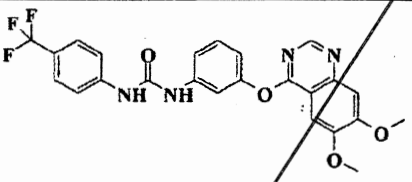
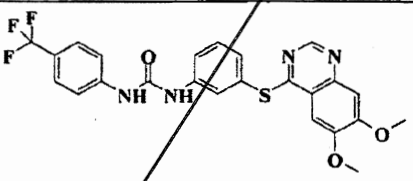
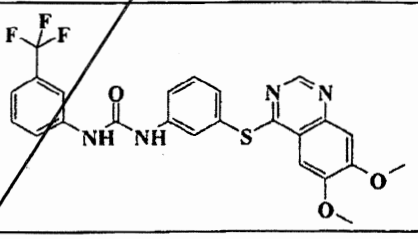
	Name	pMEK IC50 (nM)	A375 Viability EC50 (nM)	BRAF V600E Kd (nM)	BRAF WT Kd nM	RAF 1 Kd nM	S35
	Ex 148 1-(3-(6,7-Dimethoxyquinazolin-4-ylthio)phenyl)-3-(3-(2-methoxyethoxy)-4-(trifluoromethyl)phenyl) urea	D	D	C	D	D	B*
	Ex 149 1-(3-(6,7-dimethoxyquinazolin-4-yloxy)phenyl)-3-(3-(morpholine-4-carbonyl)-5-(trifluoromethyl)phenyl)urea	D	D	C	D	D	B*
	Ex 150 1-(3-(6,7-dimethoxyquinazolin-4-yloxy)phenyl)-3-(3-fluoro-4-(trifluoromethyl)phenyl)urea	D	D	B	C	C	C*
	Ex 151 1-(3-(6,7-dimethoxyquinazolin-4-yloxy)phenyl)-3-(3-(morpholinomethyl)-5-(trifluoromethyl)phenyl)urea	D	D	A	D	B	C*
	Ex 152 1-(3-(1,1-difluoroethyl)isoxazol-5-yl)-3-(3-(6,7-dimethoxyquinazolin-4-yloxy)phenyl) urea	C	C	A	B	B	C*
	Ex 153 1-(3-tert-butyl-1-phenyl-1H-pyrazol-5-yl)-3-(3-(6,7-dimethoxyquinazolin-4-yloxy)phenyl) urea	A	ND	C	D	D	D*

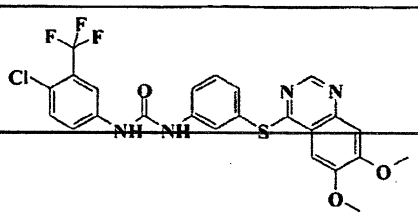
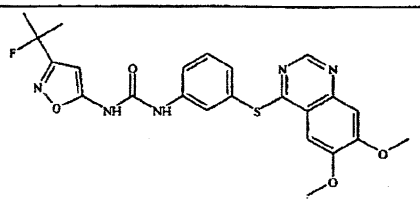
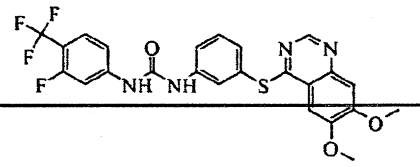
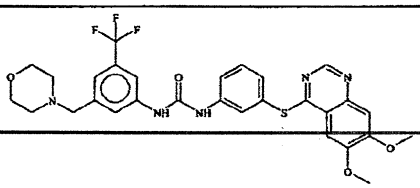
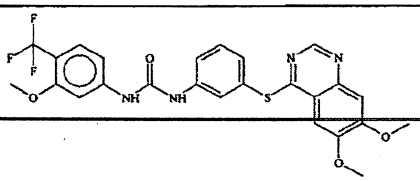
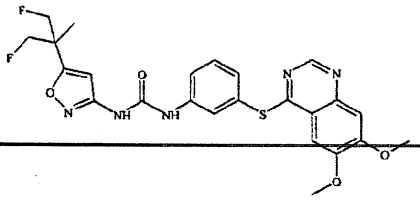
	Name	pMEK IC50 (nM)	A375 Viability EC50 (nM)	BRAF V600E Kd (nM)	BRAF WT Kd nM	RAF 1 Kd nM	S35
	Ex 154 1-(3-tert-butyl-1-phenyl-1H-pyrazol-5-yl)-3-(3-(6,7-dimethoxyquinazolin-4-ylthio)phenyl)urea	A	ND	D	D	D	D*
	Ex 155 1-(3-(6,7-dimethoxyquinazolin-4-yloxy)phenyl)-3-(3-(1-(trifluoromethyl)cyclobutyl)isoxazol-5-yl)urea	B	D	B	D	D	C*
	Ex 156 1-(3-(6,7-dimethoxyquinazolin-4-ylthio)phenyl)-3-(3-(1-(trifluoromethyl)cyclobutyl)isoxazol-5-yl)urea	C	D	C	D	D	C*
	Ex 157 1-(3-tert-butyl-1-methyl-1H-pyrazol-5-yl)-3-(3-(6,7-dimethoxyquinazolin-4-ylthio)phenyl)urea	A	D	A	C	B	C*
	Ex 158 1-(3-tert-butyl-1-methyl-1H-pyrazol-5-yl)-3-(3-(6,7-dimethoxyquinazolin-4-yloxy)phenyl)urea	B	D	A	D	C	C*
	Ex 159 1-[3-(1,3-difluoro-2-methylpropan-2-yl)isoxazol-5-yl]-3-[3-(6,7-dimethoxyquinazolin-4-yloxy]phenyl)urea	B	D	B	C	C	D*

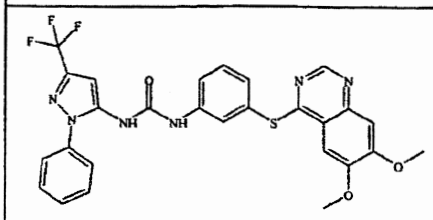
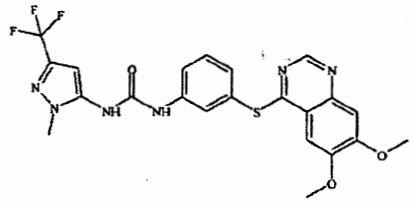
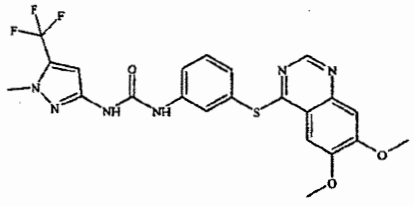
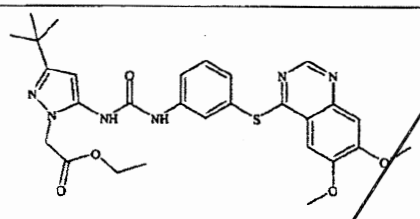
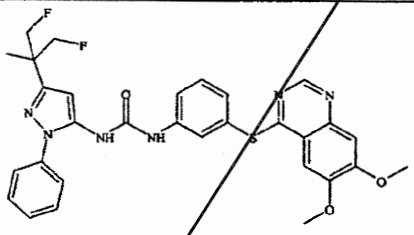
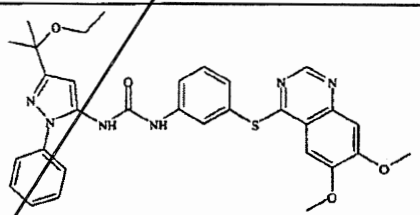
	Name	pMEK IC50 (nM)	A375 Viability EC50 (nM)	BRAF V600E Kd (nM)	BRAF WT Kd nM	RAF 1 Kd nM	S35
	Ex 160 1-[3-(1,3-difluoro-2-methylpropan-2-yl)isoxazol-5-yl]-3-[3-(6,7-dimethoxyquinazolin-4-ylthio]phenyl) urea	A	D	A	C	B	C*
	Ex 161 1-[3-(6,7-dimethoxyquinazolin-4-yloxy)phenyl]-3-[1-phenyl-3-(trifluoromethyl)-1*H*-pyrazol-5-yl]urea	A	B	C	D	D	C*
	Ex 162 1-[5-(1,3-difluoro-2-methylpropan-2-yl)isoxazol-3-yl]-3-[3-(6,7-dimethoxyquinazolin-4-yloxy)phenyl] urea	A	A	A	B	A	C*
	Ex 163 1-(3-cyclopentylisoxazol-5-yl)-3-(3-(6,7-dimethoxyquinazolin-4-yloxy)phenyl) urea	D	D	B	D	C	C*
	Ex 164 1-[3-(6,7-dimethoxyquinazolin-4-yloxy)phenyl]-3-[1-methyl-3-(trifluoromethyl)-1*H*-pyrazol-5-yl]urea	B	D	A	A	A	C*
	Ex 165 1-[3-(6,7-dimethoxyquinazolin-4-yloxy) phenyl]-3-[1-methyl-5-(trifluoromethyl)-1*H*-pyrazol-3-yl]urea	B	C	A	A	A	C*

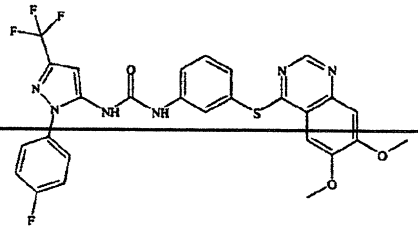
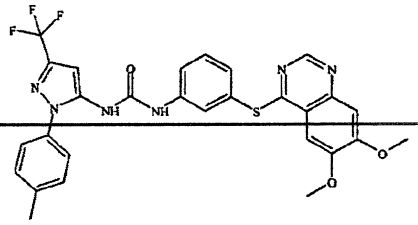
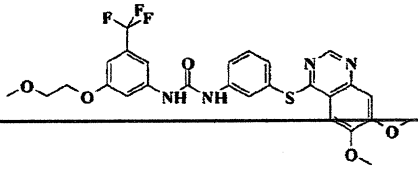
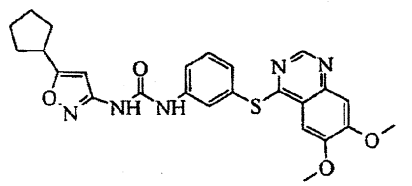
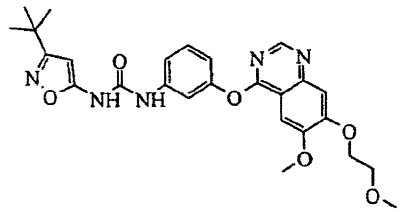
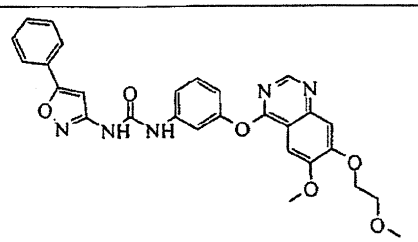
	Name	pMEK IC50 (nM)	A375 Viability EC50 (nM)	BRAF V600E Kd (nM)	BRAF WT Kd nM	RAF 1 Kd nM	S35
	Ex 166 ethyl 2-(3-*tert*-butyl-5-{3-[3-(6,7-dimethoxyquinazolin-4-yloxy)phenyl]ureido}-1*H*-pyrazol-1-yl)acetate	C	D	B	D	D	C*
	Ex 167 1-[3-(1,3-difluoro-2-methylpropan-2-yl)-1-phenyl-1*H*-pyrazol-5-yl]-3-[3-(6,7-dimethoxyquinazolin-4-yloxy)phenyl]urea	A	C	D	D	D	D*
	Ex 168 1-[3-(6,7-dimethoxyquinazolin-4-yloxy)phenyl]-3-[3-(2-ethoxypropan-2-yl)-1-phenyl-1*H*-pyrazol-5-yl]urea	A	D	C	D	D	C*
	Ex 169 1-[3-(6,7-dimethoxyquinazolin-4-yloxy)phenyl]-3-[1-phenyl-5-(trifluoromethyl)-1*H*-pyrazol-3-yl]urea	B	D	B	D	C	C*
	Ex 170 1-[3-(6,7-dimethoxyquinazolin-4-ylthio)phenyl]-3-[1-phenyl-5-(trifluoromethyl)-1*H*-pyrazol-3-yl]urea	B	B	D	D	D	B*
	Ex 171 1-[3-(6,7-dimethoxyquinazolin-4-yloxy)phenyl]-3-[1-(4-fluorophenyl)-3-(trifluoromethyl)-1*H*-pyrazol-5-yl]urea	B	B	C	D	D	C*

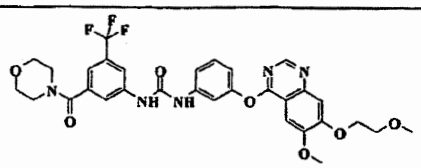
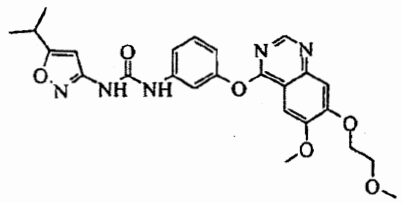
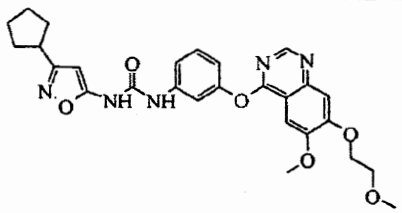
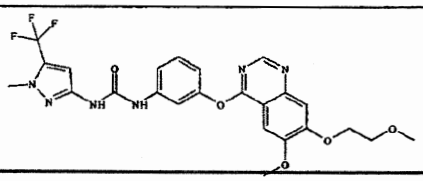
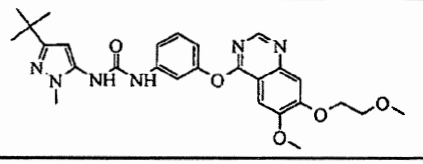
	Name	pMEK IC50 (nM)	A375 Viability EC50 (nM)	BRAF V600E Kd (nM)	BRAF WT Kd nM	RAF 1 Kd nM	S35
	Ex 172 1-[3-(6,7-dimethoxyquinazolin-4-yloxy)phenyl]-3-[1-*p*-tolyl-3-(trifluoromethyl)-1*H*-pyrazol-5-yl]urea	A	A	C	D	D	C*
	Ex 173 1-(4-tert-butylphenyl)-3-(3-(6,7-dimethoxyquinazolin-4-yloxy)phenyl)urea	B	D	A	C	B	C
	Ex 174 1-(4-tert-butylphenyl)-3-(3-(6,7-dimethoxyquinazolin-4-ylthio)phenyl)urea	D	D	B	D	B	C
	Ex 175 1-(4-chlorophenyl)-3-(3-(6,7-dimethoxyquinazolin-4-yloxy)phenyl)urea	D	D	A	A	A	C
	Ex 176 1-(4-chloro-3-(trifluoromethyl)phenyl)-3-(3-(6,7-dimethoxyquinazolin-4-yloxy)phenyl)urea	B	D	A	C	B	C
	Ex 177 1-(3-(6,7-dimethoxyquinazolin-4-yloxy)phenyl)-3-(4-(trifluoromethoxy)phenyl)urea	D	D	A	B	A	C
	Ex 178 1-(3-(6,7-dimethoxyquinazolin-4-yloxy)phenyl)-3-(3-methoxyphenyl)urea	D	D	A	C	B	B*

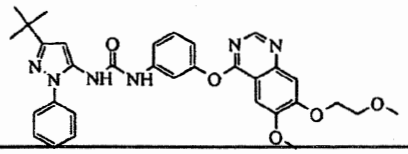
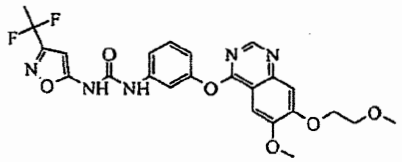
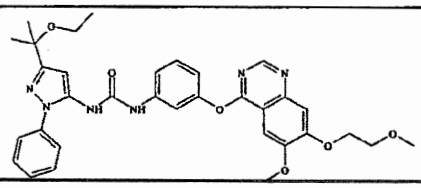
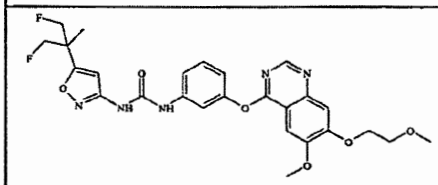
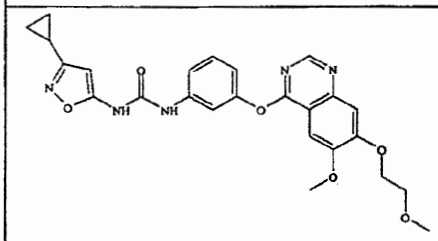
	Name	pMEK IC50 (nM)	A375 Viability EC50 (nM)	BRAF V600E Kd (nM)	BRAF WT Kd nM	RAF 1 Kd nM	S35
	Ex 179 1-(3-(6,7-dimethoxyquinazolin-4-yloxy)phenyl)-3-(3-ethoxyphenyl)urea	D	D	A	C	B	B*
	Ex 180 1-(3-chloro-4-methoxyphenyl)-3-(3-(6,7-dimethoxyquinazolin-4-yloxy)phenyl)urea	D	D	A	A	A	B*
	Ex 181 1-(3-(6,7-dimethoxyquinazolin-4-yloxy)phenyl)-3-(3-(trifluoromethyl)phenyl)urea	D	D	A	A	A	C*
	Ex 182 1-(3-(6,7-dimethoxyquinazolin-4-yloxy)phenyl)-3-phenylurea	D	D	D	D	D	B
	Ex 183 1-(3-(6,7-dimethoxyquinazolin-4-yloxy)phenyl)-3-(4-(trifluoromethyl)phenyl)urea	C	D	A	B	A	C*
	Ex 184 1-(3-(6,7-dimethoxyquinazolin-4-ylthio)phenyl)-3-(4-(trifluoromethyl)phenyl)urea	B	C	B	C	B	C*
	Ex 185 1-(3-(6,7-dimethoxyquinazolin-4-ylthio)phenyl)-3-(3-(trifluoromethyl)phenyl)urea	C	D	A	B	A	C*

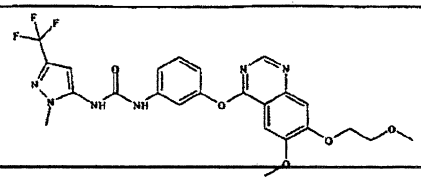
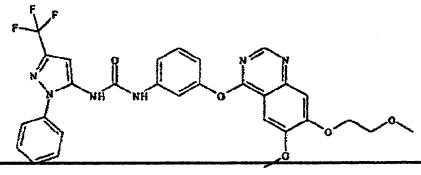
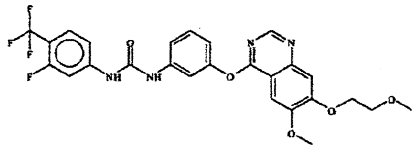
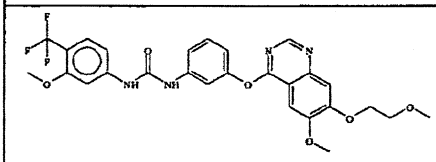
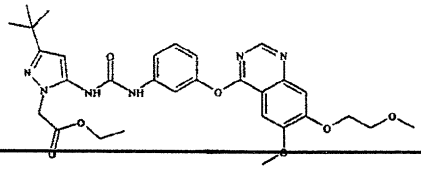
	Name	pMEK IC50 (nM)	A375 Viability EC50 (nM)	BRAF V600E Kd (nM)	BRAF WT Kd nM	RAF 1 Kd nM	S35
	Ex 186 1-(4-chloro-3-(trifluoromethyl)phenyl)-3-(3-(6,7-dimethoxyquinazolin-4-ylthio)phenyl) urea	B	C	B	D	D	B*
	Ex 187 1-(3-(6,7-dimethoxyquinazolin-4-ylthio)phenyl)-3-(3-(2-fluoropropan-2-yl)isoxazol-5-yl)urea	A	D	A	B	A	C*
	Ex 188 1-(3-(6,7-dimethoxyquinazolin-4-ylthio)phenyl)-3-(3-fluoro-4-(trifluoromethyl)phenyl)urea	D	D	B	D	C	B*
	Ex 189 1-(3-(6,7-dimethoxyquinazolin-4-ylthio)phenyl)-3-(3-(morpholinomethyl)-5-(trifluoromethyl)phenyl)urea	C	C	B	D	C	C*
	Ex 190 1-(3-(6,7-dimethoxyquinazolin-4-ylthio)phenyl)-3-(3-methoxy-4-(trifluoromethyl)phenyl)urea	D	D	C	D	D	B*
	Ex 191 1-[5-(1,3-difluoro-2-methylpropan-2-yl)isoxazol-3-yl]-3-[3-(6,7-dimethoxyquinazolin-4-ylthio)phenyl] urea	A	A	A	B	A	C*

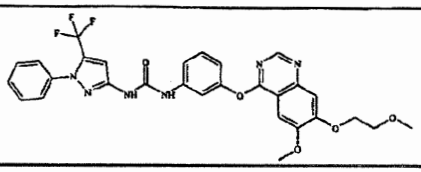
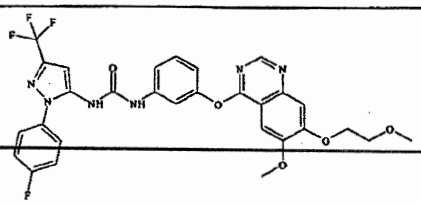
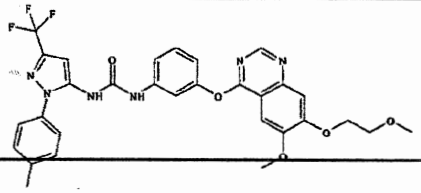
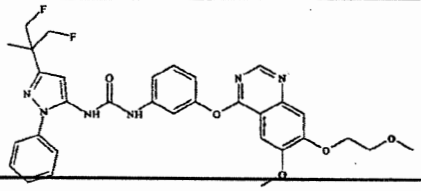
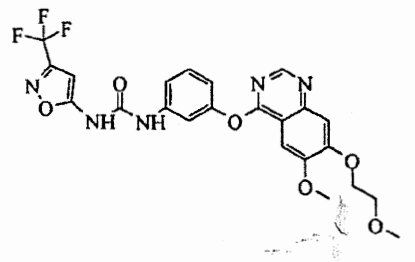
	Name	pMEK IC50 (nM)	A375 Viability EC50 (nM)	BRAF V600E Kd (nM)	BRAF WT Kd nM	RAF 1 Kd nM	S35
	Ex 192 1-[3-(6,7-dimethoxyquinazolin-4-ylthio)phenyl]-3-[1-phenyl-3-(trifluoromethyl)-1*H*-pyrazol-5-yl]urea	A	B	C	D	D	C*
	Ex 193 1-[3-(6,7-dimethoxyquinazolin-4-ylthio)phenyl]-3-[1-methyl-3-(trifluoromethyl)-1*H*-pyrazol-5-yl]urea	A	C	A	A	A	D*
	Ex 194 1-[3-(6,7-dimethoxyquinazolin-4-ylthio)phenyl]-3-[1-methyl-5-(trifluoromethyl)-1*H*-pyrazol-3-yl]urea	B	C	A	A	A	C*
	Ex 195 ethyl 2-(3-*tert*-butyl-5-{3-[3-(6,7-dimethoxyquinazolin-4-ylthio)phenyl]ureido}-1*H*-pyrazol-1-yl)acetate	B	D	B	D	D	C*
	Ex 196 1-[3-(1,3-difluoro-2-methylpropan-2-yl)-1-phenyl-1*H*-pyrazol-5-yl]-3-[3-(6,7-dimethoxyquinazolin-4-ylthio)phenyl]urea	A	D	D	D	D	D*
	Ex 197 1-[3-(6,7-dimethoxyquinazolin-4-ylthio)phenyl]-3-[3-(2-ethoxypropan-2-yl)-1-phenyl-1*H*-pyrazol-5-yl]urea	B	D	B	D	D	C*

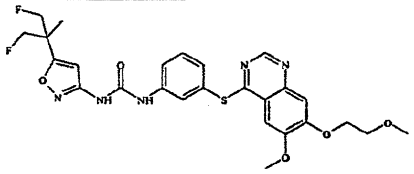
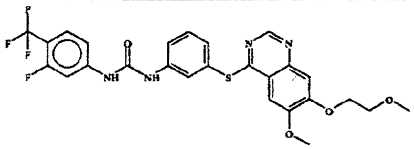
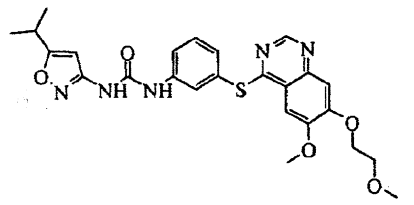
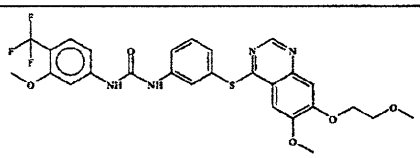
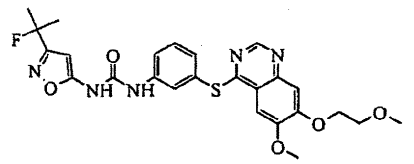
	Name	pMEK IC50 (nM)	A375 Viability EC50 (nM)	BRAF V600E Kd (nM)	BRAF WT Kd nM	RAF 1 Kd nM	S35
	Ex 198 1-[3-(6,7-dimethoxyquinazolin-4-ylthio)phenyl]-3-[1-(4-fluorophenyl)-3-(trifluoromethyl)-1*H*-pyrazol-5-yl]urea	B	C	C	D	D	C*
	Ex 199 1-[3-(6,7-dimethoxyquinazolin-4-ylthio)phenyl]-3-[1-*p*-tolyl-3-(trifluoromethyl)-1*H*-pyrazol-5-yl]urea	A	D	D	D	D	D*
	Ex 200 1-(3-(6,7-dimethoxyquinazolin-4-ylthio)phenyl)-3-(3-(2-methoxyethoxy)-5-(trifluoromethyl)phenyl)urea	D	D	C	C	D	C
	Ex 201 1-(5-cyclopentylisoxazol-3-yl)-3-(3-(6,7-dimethoxyquinazolin-4-ylthio)phenyl) urea	B	D	A	B	A	C*
	Ex 202 1-(3-tert-butylisoxazol-5-yl)-3-(3-(6-methoxy-7-(2-methoxyethoxy)quinazolin-4-yloxy)phenyl)urea	A	D	A	B	B	C
	Ex 203 1-(3-(6-Methoxy-7-(2-methoxyethoxy)quinazolin-4-yloxy)phenyl)-3-(5-phenylisoxazol-3-yl)urea	D	D	D	D	D	B

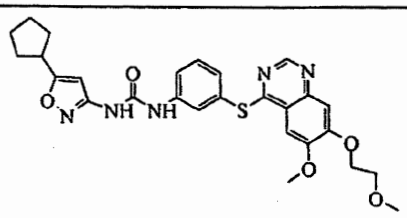
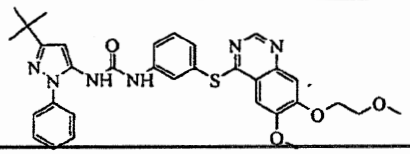
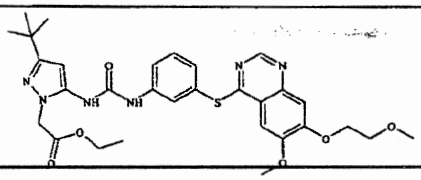
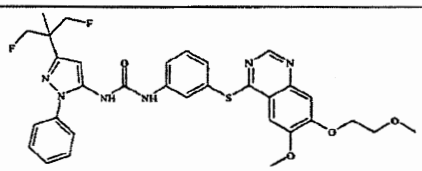
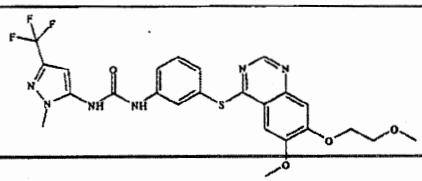
	Name	pMEK IC50 (nM)	A375 Viability EC50 (nM)	BRAF V600E Kd (nM)	BRAF WT Kd nM	RAF 1 Kd nM	S35
	Ex 205 1-(3-(6-methoxy-7-(2-methoxyethoxy)quinazolin-4-yloxy)phenyl)-3-(3-(morpholine-4-carbonyl)-5-(trifluoromethyl)phenyl)urea	D	D	B	D	D	C*
	Ex 206 1-(5-isopropylisoxazol-3-yl)-3-(3-(6-methoxy-7-(2-methoxyethoxy)quinazolin-4-yloxy)phenyl) urea	C	D	A	A	A	C*
	Ex 207 1-(3-cyclopentylisoxazol-5-yl)-3-(3-(6-methoxy-7-(2-methoxyethoxy)quinazolin-4-yloxy)phenyl) urea	D	D	A	C	B	C*
	Ex 208 1-{3-[6-methoxy-7-(2-methoxyethoxy)quinazolin-4-yloxy]phenyl}-3-[1-methyl-5-(trifluoromethyl)-1*H*-pyrazol-3-yl]urea	D	D	A	A	A	C*
	Ex 209 1-(3-tert-butyl-1-methyl-1H-pyrazol-5-yl)-3-(3-(6-methoxy-7-(2-methoxyethoxy)quinazolin-4-yloxy)phenyl) urea	C	D	B	D	D	C*

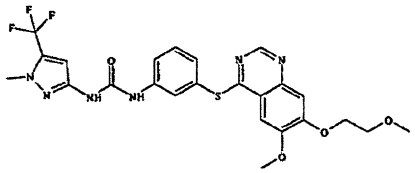
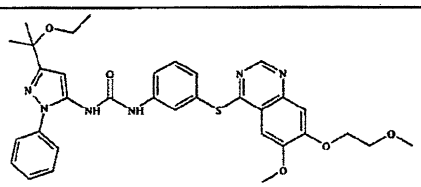
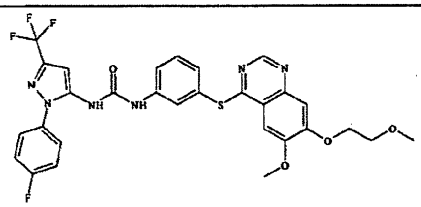
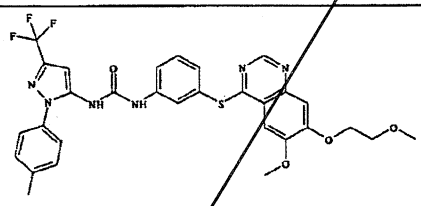
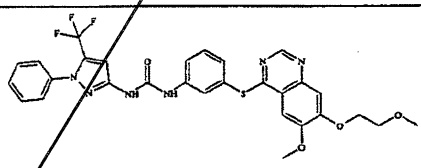
	Name	pMEK IC50 (nM)	A375 Viability EC50 (nM)	BRAF V600E Kd (nM)	BRAF WT Kd nM	RAF 1 Kd nM	S35
	Ex 210 1-(3-tert-butyl-1-phenyl-1H-pyrazol-5-yl)-3-(3-(6-methoxy-7-(2-methoxyethoxy)quinazolin-4-yloxy)phenyl)urea	A	ND	D	D	D	D*
	Ex 211 1-(3-(1,1-difluoroethyl)isoxazol-5-yl)-3-(3-(6-methoxy-7-(2-methoxyethoxy)quinazolin-4-yloxy)phenyl) urea	D	D	B	C	B	C*
	Ex 212 1-[3-(2-ethoxypropan-2-yl)-1-phenyl-1*H*-pyrazol-5-yl]-3-{3-[6-methoxy-7-(2-methoxyethoxy)quinazolin-4-yloxy]phenyl} urea	C	D	B	D	D	C*
	Ex 213 1-[5-(1,3-difluoro-2-methylpropan-2-yl)isoxazol-3-yl]-3-{3-[6-methoxy-7-(2-methoxyethoxy)quinazolin-4-yloxy]phenyl} urea	A	A	A	B	A	D*
	Ex 214 1-(3-cyclopropylisoxazol-5-yl)-3-(3-(6-methoxy-7-(2-methoxyethoxy)quinazolin-4-yloxy)phenyl)urea	D	D	A	A	A	C*

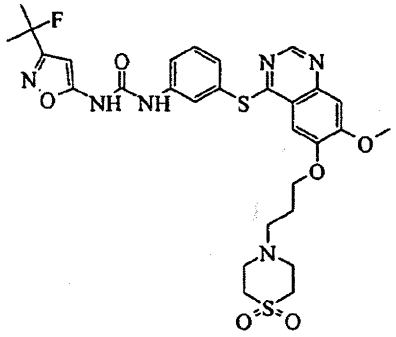
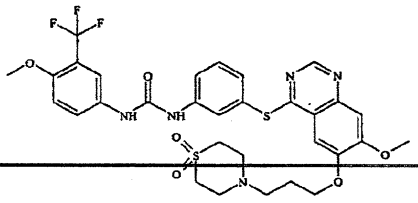
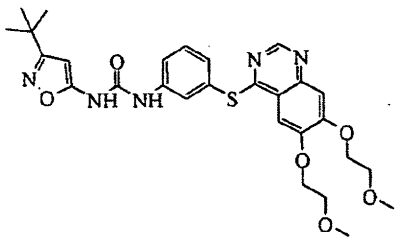
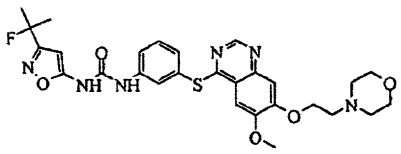
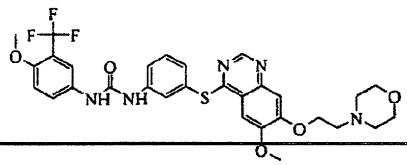
	Name	pMEK IC50 (nM)	A375 Viability EC50 (nM)	BRAF V600E Kd (nM)	BRAF WT Kd nM	RAF 1 Kd nM	S35
	Ex 220 1-{3-[6-methoxy-7-(2-methoxyethoxy)quinazolin-4-yloxy]phenyl}-3-[1-methyl-3-(trifluoromethyl)-1*H*-pyrazol-5-yl]urea	C	D	A	A	A	C*
	Ex 221 1-{3-[6-methoxy-7-(2-methoxyethoxy)quinazolin-4-yloxy]phenyl}-3-[1-phenyl-3-(trifluoromethyl)-1*H*-pyrazol-5-yl]urea	B	C	B	D	D	C*
	Ex 222 1-(3-fluoro-4-(trifluoromethyl)phenyl)-3-(3-(6-methoxy-7-(2-methoxyethoxy)quinazolin-4-yloxy)phenyl)urea	D	D	B	C	B	C*
	Ex 223 1-(3-methoxy-4-(trifluoromethyl)phenyl)-3-(3-(6-methoxy-7-(2-methoxyethoxy)quinazolin-4-yloxy)phenyl)urea	D	D	B	D	C	C*
	Ex 224 ethyl 2-[3-*tert*-butyl-5-(3-{3-[6-methoxy-7-(2-methoxyethoxy)quinazolin-4-yloxy]phenyl}ureido)-1*H*-pyrazol-1-yl]acetate hydrochlorid	D	D	D	D	D	A*

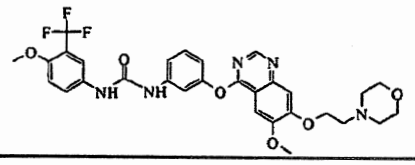
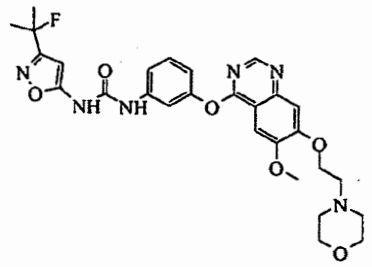
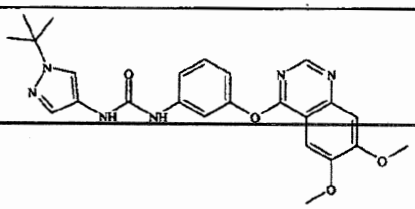
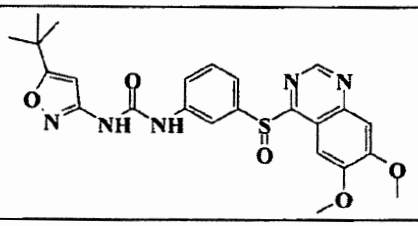
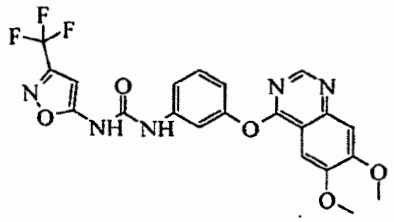
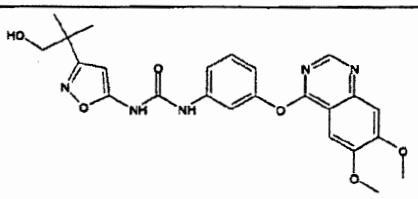
	Name	pMEK IC50 (nM)	A375 Viability EC50 (nM)	BRAF V600E Kd (nM)	BRAF WT Kd nM	RAF 1 Kd nM	S35
	e						
	Ex 225 1-{3-[6-methoxy-7-(2-methoxyethoxy)quinazolin-4-yloxy]phenyl}-3-[1-phenyl-5-(trifluoromethyl)-1*H*-pyrazol-3-yl]urea	C	D	B	D	D	C*
	Ex 226 1-[1-(4-fluorophenyl)-3-(trifluoromethyl)-1*H*-pyrazol-5-yl]-3-{3-[6-methoxy-7-(2-methoxyethoxy)quinazolin-4-yloxy]phenyl}urea	B	D	C	D	D	C*
	Ex 227 1-{3-[6-methoxy-7-(2-methoxyethoxy)quinazolin-4-yloxy]phenyl}-3-[1-*p*-tolyl-3-(trifluoromethyl)-1*H*-pyrazol-5-yl]urea	B	B	C	D	D	C*
	Ex 228 1-[3-(1,3-difluoro-2-methylpropan-2-yl)-1-phenyl-1*H*-pyrazol-5-yl]-3-{3-[6-methoxy-7-(2-methoxyethoxy)quinazolin-4-yloxy]phenyl}urea	A	D	C	D	D	D*
	Ex 229 1-(3-(6-methoxy-7-(2-methoxyethoxy)quinazolin-4-yloxy)phenyl)-3-(3-(trifluoromethyl)isoxazol-5-yl)urea	D	D	A	B	A	C*

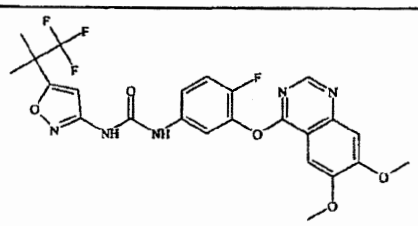
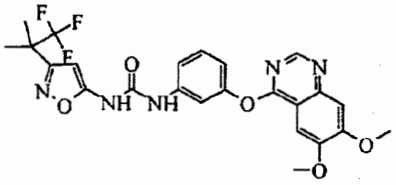
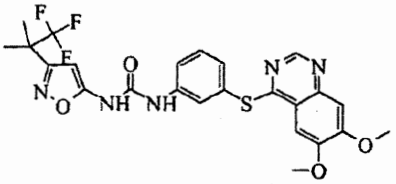
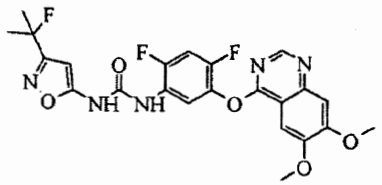
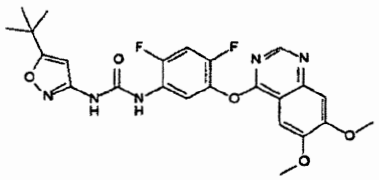
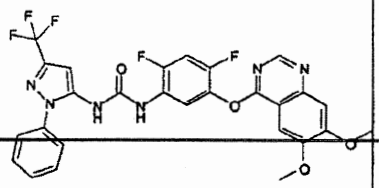
	Name	pMEK IC50 (nM)	A375 Viability EC50 (nM)	BRAF V600E Kd (nM)	BRAF WT Kd nM	RAF 1 Kd nM	S35
	Ex 230 1-[5-(1,3-difluoro-2-methylpropan-2-yl)isoxazol-3-yl]-3-{3-[6-methoxy-7-(2-methoxyethoxy)quinazolin-4-ylthio]phenyl} urea	A	B	A	C	B	C*
	Ex 231 1-(3-fluoro-4-(trifluoromethyl)phenyl)-3-(3-(6-methoxy-7-(2-methoxyethoxy)quinazolin-4-ylthio)phenyl) urea	D	D	C	D	D	B*
	Ex 232 1-(5-isopropylisoxazol-3-yl)-3-(3-(6-methoxy-7-(2-methoxyethoxy)quinazolin-4-ylthio) phenyl)urea	B	D	A	A	A	C*
	Ex 233 1-(3-methoxy-4-(trifluoromethyl)phenyl)-3-(3-(6-methoxy-7-(2-methoxyethoxy)quinazolin-4-ylthio)phenyl) urea	D	D	C	D	D	C*
	Ex 234 1-(3-(2-fluoropropan-2-yl)isoxazol-5-yl)-3-(3-(6-methoxy-7-(2-methoxyethoxy)quinazolin-4-ylthio)phenyl) urea	A	D	A	B	B	C*

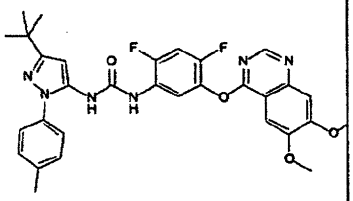
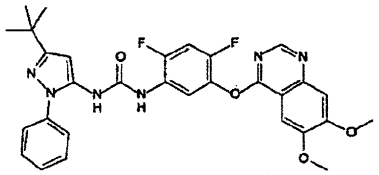
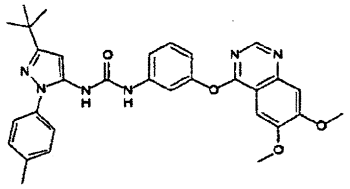
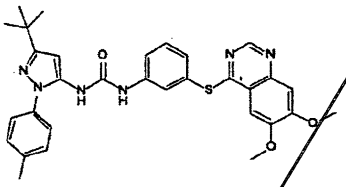
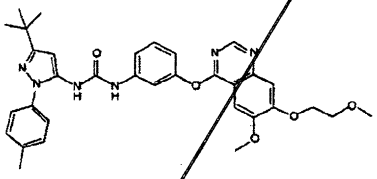
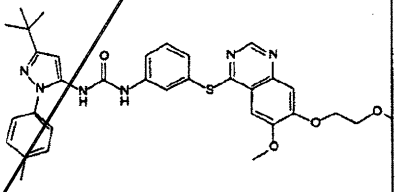
	Name	pMEK IC50 (nM)	A375 Viability EC50 (nM)	BRAF V600E Kd (nM)	BRAF WT Kd nM	RAF 1 Kd nM	S35
	Ex 235 1-(5-cyclopentylisoxazol-3-yl)-3-(3-(6-methoxy-7-(2-methoxyethoxy)quinazolin-4-ylthio)phenyl)urea	B	D	A	B	A	C*
	Ex 236 1-(3-tert-butyl-1-phenyl-1H-pyrazol-5-yl)-3-(3-(6-methoxy-7-(2-methoxyethoxy)quinazolin-4-ylthio)phenyl)urea	A	ND	D	D	D	D*
	Ex 237 ethyl 2-[3-*tert*-butyl-5-(3-{3-[6-methoxy-7-(2-methoxyethoxy)quinazolin-4-ylthio]phenyl}ureido)-1*H*-pyrazol-1-yl]acetate	C	D	C	D	D	C*
	Ex 238 1-[3-(1,3-difluoro-2-methylpropan-2-yl)-1-phenyl-1*H*-pyrazol-5-yl]-3-{3-[6-methoxy-7-(2-methoxyethoxy)quinazolin-4-ylthio]phenyl}urea	A	D	D	D	D	D*
	Ex 239 1-{3-[6-methoxy-7-(2-methoxyethoxy)quinazolin-4-ylthio]phenyl}-3-[1-methyl-3-(trifluoromethyl)-1*H*-pyrazol-5-	B	D	A	A	A	D*

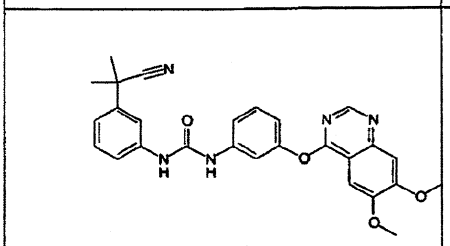
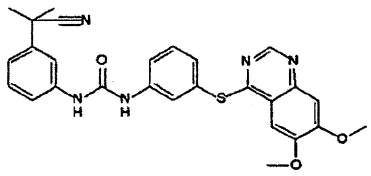
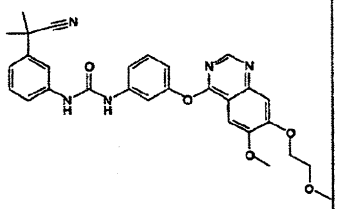
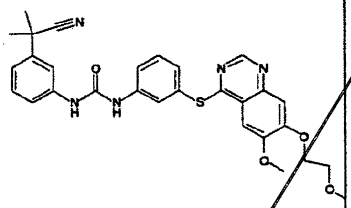
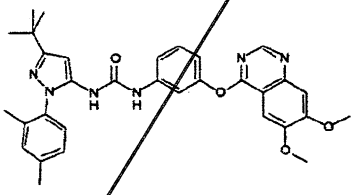
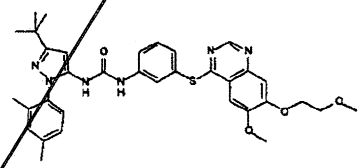
	Name	pMEK IC50 (nM)	A375 Viability EC50 (nM)	BRAF V600E Kd (nM)	BRAF WT Kd nM	RAF 1 Kd nM	S35
	yl]urea						
	Ex 240 1-{3-[6-methoxy-7-(2-methoxyethoxy)quinazolin-4-ylthio]phenyl}-3-[1-methyl-3-(trifluoromethyl)-1*H*-pyrazol-5-yl]urea	B	D	A	A	A	C*
	Ex 241 1-[3-(2-ethoxypropan-2-yl)-1-phenyl-1*H*-pyrazol-5-yl]-3-{3-[6-methoxy-7-(2-methoxyethoxy)quinazolin-4-ylthio]phenyl} urea	C	D	B	D	D	C*
	Ex 242 1-[1-(4-fluorophenyl)-3-(trifluoromethyl)-1*H*-pyrazol-5-yl]-3-{3-[6-methoxy-7-(2-methoxyethoxy)quinazolin-4-ylthio]phenyl} urea	C	D	D	D	D	C*
	Ex 243 1-{3-[6-methoxy-7-(2-methoxyethoxy)quinazolin-4-ylthio]phenyl}-3-[1-*p*-tolyl-3-(trifluoromethyl)-1*H*-pyrazol-5-yl]urea	B	B	D	D	D	C*
	Ex 244 1-{3-[6-methoxy-7-(2-methoxyethoxy)quinazolin-4-ylthio]phenyl}-3-[1-phenyl-5-	D	D	D	D	D	C*

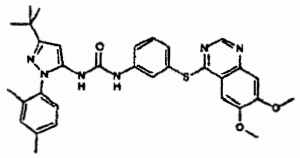
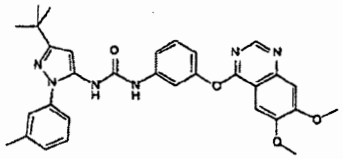
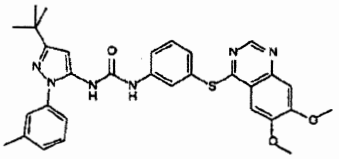
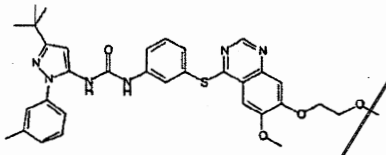
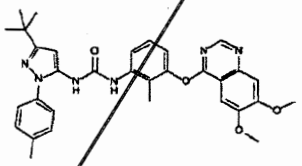
	Name	pMEK IC50 (nM)	A375 Viability EC50 (nM)	BRAF V600E Kd (nM)	BRAF WT Kd nM	RAF 1 Kd nM	S35
	(trifluoromethyl)-1H-pyrazol-3-yl]urea						
	Ex 245 1-(3-(2-fluoropropan-2-yl)isoxazol-5-yl)-3-(3-(7-methoxy-6-(4,4-dioxo-3-thiomorpholinopropoxy)quinazolin-4-ylthio)phenyl)urea	A	D	A	A	B	C*
	Ex 246 1-(4-methoxy-3-(trifluoromethyl)phenyl)-3-(3-(7-methoxy-6-(3-(4,4-dioxothiomorpholino)propoxy)quinazolin-4-ylthio)phenyl)urea	A	C	A	B	B	C*
	Ex 247 1-(3-(6,7-bis(2-Methoxyethoxy)quinazolin-4-ylthio)phenyl)-3-(3-tert-butylisoxazol-5-yl)urea	A	D	A	B	B	C
	Ex 248 1-(3-(2-fluoropropan-2-yl)isoxazol-5-yl)-3-(3-(6-methoxy-7-(2-morpholinoethoxy)quinazolin-4-ylthio)phenyl)urea	B	D	A	B	B	C*
	Ex 249 1-(4-methoxy-3-(trifluoromethyl)phenyl)-3-(3-(6-methoxy-7-(2-morpholinoethoxy)quinazolin-4-ylthio)phenyl)	C	D	B	C	C	C*

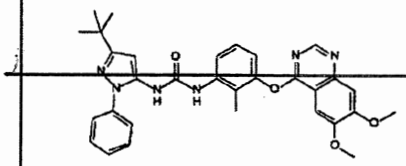
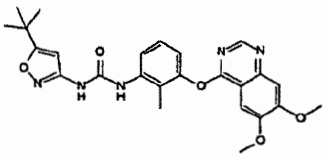
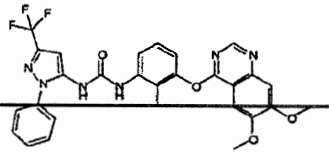
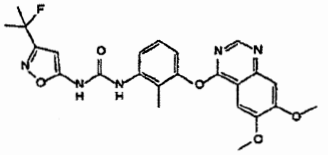
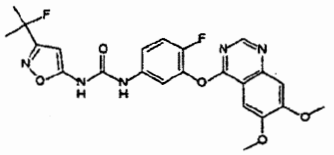
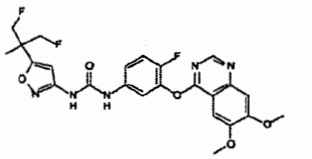
	Name	pMEK IC50 (nM)	A375 Viability EC50 (nM)	BRAF V600E Kd (nM)	BRAF WT Kd nM	RAF 1 Kd nM	S35
	urea						
	Ex 250 1-(4-methoxy-3-(trifluoromethyl)phenyl)-3-(3-(6-methoxy-7-(2-morpholinoethoxy)quinazolin-4-yloxy)phenyl) urea	B	D	A	A	A	C*
	Ex 251 1-(3-(2-fluoropropan-2-yl)isoxazol-5-yl)-3-(3-(6-methoxy-7-(2-morpholinoethoxy)quinazolin-4-yloxy)phenyl) urea	B	D	A	A	B	C*
	Ex 252 1-(1-tert-butyl-1H-pyrazol-4-yl)-3-(3-(6,7-dimethoxyquinazolin-4-yloxy)phenyl) urea	D	D	A	B	B	C
	Ex 253 1-(5-tert-butylisoxazol-3-yl)-3-(3-(6,7-dimethoxyquinazolin-4-ylsulfinyl) phenyl)urea	C	D	D	D	D	C
	Ex 254 1-(3-(6,7-dimethoxyquinazolin-4-yloxy)phenyl)-3-(3-(trifluoromethyl)isoxazol-5-yl)urea	D	D	A	B	A	C*
	Ex 255 1-(3-(6,7-dimethoxyquinazolin-4-yloxy)phenyl)-3-(3-(1-hydroxy-2-methylpropan-2-yl)isoxazol-5-yl)urea	D	D	A	B	B	C

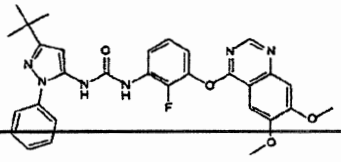
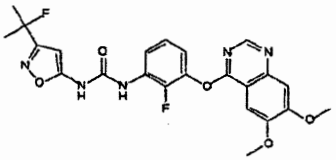
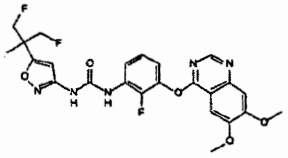
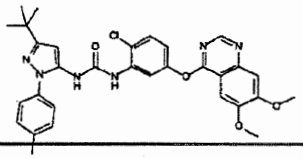
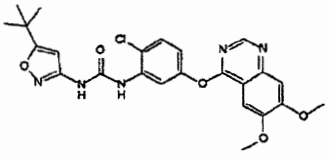
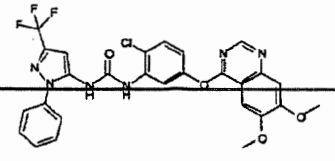
	Name	pMEK IC50 (nM)	A375 Viability EC50 (nM)	BRAF V600E Kd (nM)	BRAF WT Kd nM	RAF 1 Kd nM	S35
	Ex 266 1-(3-(6,7-dimethoxyquinazolin-4-yloxy)-4-fluorophenyl)-3-(5-(1,1,1-trifluoro-2-methylpropan-2-yl)isoxazol-3-yl)urea	A	ND	A	A	A	C
	Ex 267 1-(3-(6,7-dimethoxyquinazolin-4-yloxy)phenyl)-3-(3-(1,1,1-trifluoro-2-methylpropan-2-yl)isoxazol-5-yl)urea	A	C	A	A	A	C
	Ex 268 1-(3-(6,7-dimethoxyquinazolin-4-ylthio)phenyl)-3-(3-(1,1,1-trifluoro-2-methylpropan-2-yl)isoxazol-5-yl)urea	A	C	A	A	A	C
	Ex 269 1-(5-(6,7-dimethoxyquinazolin-4-yloxy)-2,4-difluorophenyl)-3-(3-(2-fluoropropan-2-yl)isoxazol-5-yl)urea	A	A	A	A	A	D
	Ex 270 1-(5-tert-butylisoxazol-3-yl)-3-(5-(6,7-dimethoxyquinazolin-4-yloxy)-2,4-difluorophenyl)urea	A	A	A	A	A	D
	Ex 271 1-(5-(6,7-dimethoxyquinazolin-4-yloxy)-2,4-difluorophenyl)-3-(1-phenyl-3-(trifluoromethyl)-1H-pyrazol-5-yl)urea	A	B	B	D	D	D

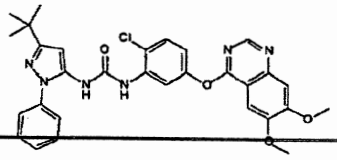
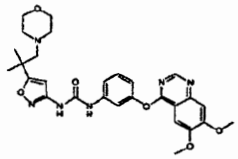
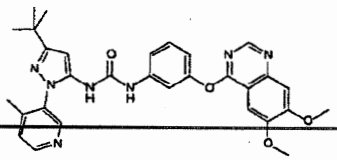
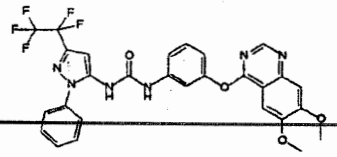
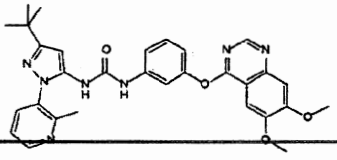
	Name	pMEK IC50 (nM)	A375 Viability EC50 (nM)	BRAF V600E Kd (nM)	BRAF WT Kd nM	RAF 1 Kd nM	S35
	Ex 272 1-(3-tert-butyl-1-p-tolyl-1H-pyrazol-5-yl)-3-(5-(6,7-dimethoxyquinazolin-4-yloxy)-2,4-difluorophenyl)urea	A	ND	C	D	D	D
	Ex 273 1-(3-tert-butyl-1-phenyl-1H-pyrazol-5-yl)-3-(5-(6,7-dimethoxyquinazolin-4-yloxy)-2,4-difluorophenyl)urea	A	ND	C	D	D	D
	Ex 274 1-(3-tert-butyl-1-p-tolyl-1H-pyrazol-5-yl)-3-(3-(6,7-dimethoxyquinazolin-4-yloxy)phenyl)urea	A	ND	B	D	D	D
	Ex 275 1-(3-tert-Butyl-1-p-tolyl-1H-pyrazol-5-yl)-3-(3-(6,7-dimethoxyquinazolin-4-ylthio)phenyl)urea	A	ND	B	D	D	D
	Ex 276 1-(3-tert-butyl-1-p-tolyl-1H-pyrazol-5-yl)-3-(3-(6-methoxy-7-(2-methoxyethoxy)quinazolin-4-yloxy)phenyl)urea	A	ND	A	D	D	D
	Ex 277 1-(3-tert-Butyl-1-p-tolyl-1H-pyrazol-5-yl)-3-(3-(6-methoxy-7-(2-methoxyethoxy)quinazolin-4-ylthio)phenyl	A	ND	B	D	D	D

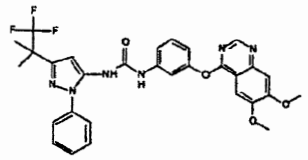
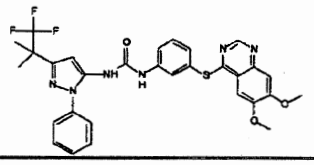
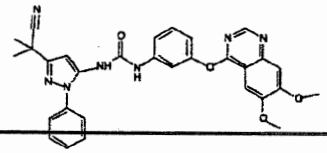
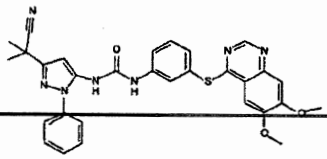
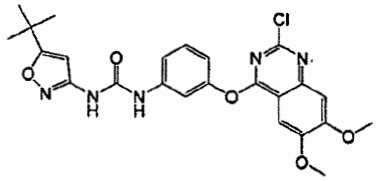
	Name	pMEK IC50 (nM)	A375 Viability EC50 (nM)	BRAF V600E Kd (nM)	BRAF WT Kd nM	RAF 1 Kd nM	S35
	)urea						
	Ex 278 1-(3-(2-cyanopropan-2-yl)phenyl)-3-(3-(6,7-dimethoxyquinazolin-4-yloxy)phenyl)urea	B	C	A	A	A	C
	Ex 279 1-(3-(2-cyanopropan-2-yl)phenyl)-3-(3-(6,7-dimethoxyquinazolin-4-ylthio)phenyl)urea	B	D	A	A	A	C
	Ex 280 1-(3-(2-cyanopropan-2-yl)phenyl)-3-(3-(6-methoxy-7-(2-methoxyethoxy)quinazolin-4-yloxy)phenyl)urea	C	D	A	A	A	ND
	Ex 281 1-(3-(2-cyanopropan-2-yl)phenyl)-3-(3-(6-methoxy-7-(2-methoxyethoxy)quinazolin-4-ylthio)phenyl)urea	B	D	A	A	A	ND
	Ex 282 1-(3-tert-butyl-1-(2,4-dimethylphenyl)-1H-pyrazol-5-yl)-3-(3-(6,7-dimethoxyquinazolin-4-yloxy)phenyl)urea	A	ND	C	D	D	C
	Ex 283 1-(3-tert-butyl-1-(2,4-dimethylphenyl)-1H-pyrazol-5-yl)-3-(3-(6-methoxy-7-(2-methoxyethoxy)quinazoli	A	D	C	D	D	C

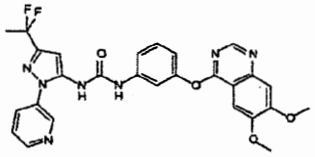
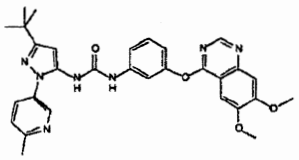
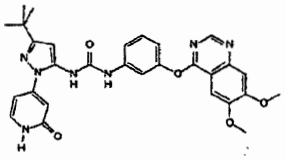
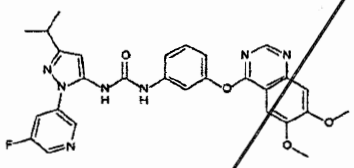
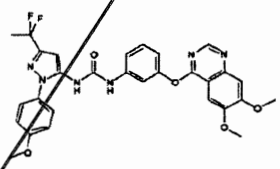
	Name	pMEK IC50 (nM)	A375 Viability EC50 (nM)	BRAF V600E Kd (nM)	BRAF WT Kd nM	RAF 1 Kd nM	S35
	n-4-ylthio)phenyl)urea						
	Ex 284 1-(3-tert-butyl-1-(2,4-dimethylphenyl)-1H-pyrazol-5-yl)-3-(3-(6,7-dimethoxyquinazolin-4-ylthio)phenyl)urea	A	D	D	D	D	C
	Ex 285 1-(3-tert-butyl-1-m-tolyl-1H-pyrazol-5-yl)-3-(3-(6,7-dimethoxyquinazolin-4-yloxy)phenyl)urea	A	ND	B	D	D	D
	Ex 286 Preparation of 1-(3-tert-butyl-1-m-tolyl-1H-pyrazol-5-yl)-3-(3-(6,7-dimethoxyquinazolin-4-ylthio)phenyl)urea	A	ND	B	D	D	D
	Ex 287 1-(3-tert-butyl-1-m-tolyl-1H-pyrazol-5-yl)-3-(3-(6-methoxy-7-(2-methoxyethoxy)quinazolin-4-ylthio)phenyl)urea	A	ND	C	D	D	D
	Ex 288 1-(3-tert-butyl-1-p-tolyl-1H-pyrazol-5-yl)-3-(3-(6,7-dimethoxyquinazolin-4-yloxy)-2-methylphenyl)urea	A	ND	B	D	D	C
	Ex 289 1-(3-tert-butyl-1-phenyl-1H-pyrazol-5-yl)-3-(3-(6,7-dimethoxyqu	A	C	A	D	C	C

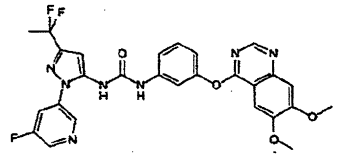
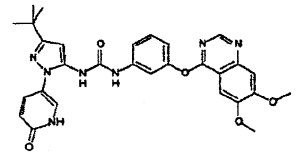
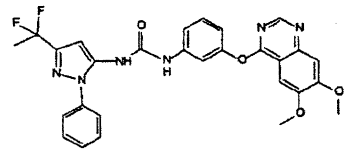
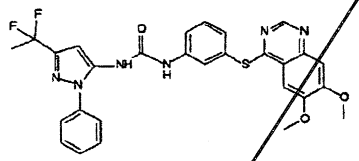
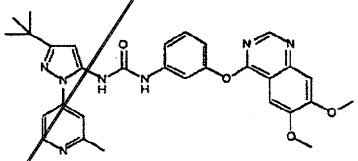
	Name	pMEK IC50 (nM)	A375 Viability EC50 (nM)	BRAF V600E Kd (nM)	BRAF WT Kd nM	RAF 1 Kd nM	S35
	inazolin-4-yloxy)-2-methylphenyl)urea						
	Ex290 1-(5-tert-butylisoxazol-3-yl)-3-(3-(6,7-dimethoxyquinazolin-4-yloxy)-2-methylphenyl)urea	A	B	A	A	A	C
	Ex 291 1-(3-(6,7-Dimethoxyquinazolin-4-yloxy)-2-methylphenyl)-3-(1-phenyl-3-(trifluoromethyl)-1H-pyrazol-5-yl)urea	C	D	A	C	B	B
	Ex292 1-(3-(6,7-dimethoxyquinazolin-4-yloxy)-2-, methylphenyl)-3-(5-(2-fluoropropan-2-yl)isoxazol-3-yl)urea	C	D	A	A	A	C
	Ex293 1-(3-(6,7-dimethoxyquinazolin-4-yloxy)-4-fluorophenyl)-3-(3-(2-fluoropropan-2-yl)isoxazol-5-yl)urea	A	B	A	A	A	C
	Ex 294 1-(5-(1,3-difluoro-2-methylpropan-2-yl)isoxazol-3-yl)-3-(3-(6,7-dimethoxyquinazolin-4-yloxy)-4-fluorophenyl)urea	A	ND	A	A	A	D

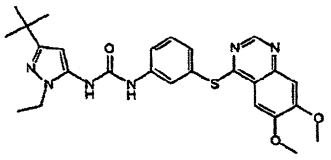
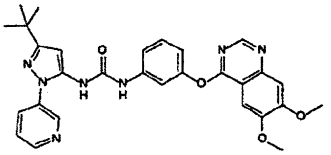
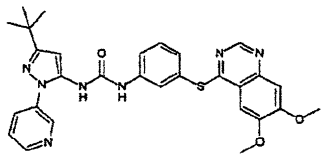
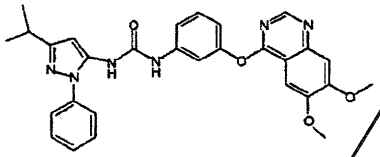
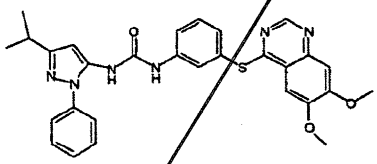
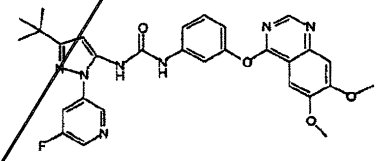
	Name	pMEK IC50 (nM)	A375 Viability EC50 (nM)	BRAF V600E Kd (nM)	BRAF WT Kd nM	RAF 1 Kd nM	S35
	Ex 295 1-(3-tert-butyl-1-phenyl-1H-pyrazol-5-yl)-3-(3-(6,7-dimethoxyquinazolin-4-yloxy)-2-fluorophenyl)urea	C	D	A	D	C	C
	Ex 296 1-(3-(6,7-dimethoxyquinazolin-4-yloxy)-2-fluorophenyl)-3-(3-(2-fluoropropan-2-yl)isoxazol-5-yl)urea	D	D	A	A	A	B
	Ex 297 1-(5-(1,3-difluoro-2-methylpropan-2-yl)isoxazol-3-yl)-3-(3-(6,7-dimethoxyquinazolin-4-yloxy)-2-fluorophenyl)urea	B	B	A	A	A	C
	Ex 298 1-(3-tert-butyl-1-p-tolyl-1H-pyrazol-5-yl)-3-(2-chloro-5-(6,7-dimethoxyquinazolin-4-yloxy)phenyl)urea	A	A	D	D	D	D
	Ex 299 1-(5-tert-butylisoxazol-3-yl)-3-(2-chloro-5-(6,7-dimethoxyquinazolin-4-yloxy)phenyl)urea	A	ND	A	B	A	C
	Ex 300 1-(2-chloro-5-(6,7-dimethoxyquinazolin-4-yloxy)phenyl)-3-(1-phenyl-3-(trifluoromet	B	D	C	D	D	C

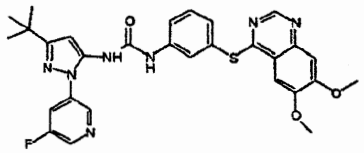
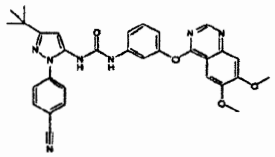
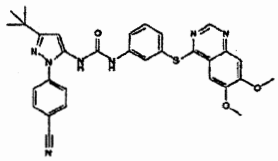
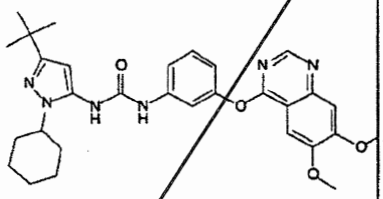
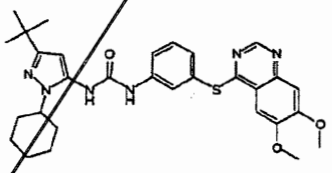
	Name	pMEK IC50 (nM)	A375 Viability EC50 (nM)	BRAF V600E Kd (nM)	BRAF WT Kd nM	RAF 1 Kd nM	S35
	hyl)-1H-pyrazol-5-yl)urea						
	Ex 301 1-(3-tert-butyl-1-phenyl-1H-pyrazol-5-yl)-3-(2-chloro-5-(6,7-dimethoxyquinazolin-4-yloxy)phenyl)urea	A	B	D	D	D	D
	Ex 302 Preparation of 1-(3-(6,7-dimethoxyquinazolin-4-yloxy)phenyl)-3-(5-(2-methyl-1-morpholinopropan-2-yl)isoxazol-3-yl)urea	D	D	B	D	D	B
	Ex 303 1-(3-tert-butyl-1-(4-methylpyridin-3-yl)-1H-pyrazol-5-yl)-3-(3-(6,7-dimethoxyquinazolin-4-yloxy)phenyl)urea	A	A	A	C	B	D
	Ex 304 1-(3-(6,7-dimethoxyquinazolin-4-yloxy)phenyl)-3-(3-(perfluoroethyl)-1-phenyl-1H-pyrazol-5-yl)urea	B	A	B	D	D	C
	Ex 305 1-(3-tert-butyl-1-(2-methylpyridin-3-yl)-1H-pyrazol-5-yl)-3-(3-(6,7-dimethoxyquinazolin-4-yloxy)phenyl)urea	A	A	A	C	B	D

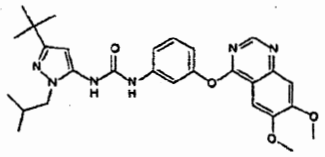
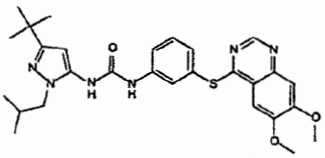
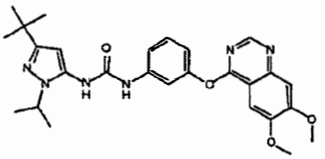
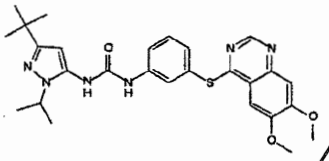
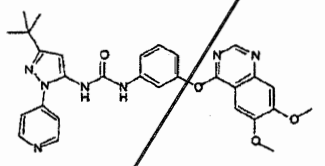
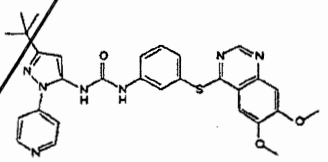
	Name	pMEK IC50 (nM)	A375 Viability EC50 (nM)	BRAF V600E Kd (nM)	BRAF WT Kd nM	RAF1 Kd nM	S35
	Ex 306 1-(3-(6,7-dimethoxyquinazolin-4-yloxy)phenyl)-3-(1-phenyl-3-(1,1,1-trifluoro-2-methylpropan-2-yl)-1H-pyrazol-5-yl)urea	A	ND	B	D	D	D
	Ex 307 1-(3-(6,7-dimethoxyquinazolin-4-ylthio)phenyl)-3-(1-phenyl-3-(1,1,1-trifluoro-2-methylpropan-2-yl)-1H-pyrazol-5-yl)urea	A	ND	B	D	D	D
	Ex 308 1-(3-(2-cyanopropan-2-yl)-1-phenyl-1H-pyrazol-5-yl)-3-(3-(6,7-dimethoxyquinazolin-4-yloxy)phenyl)urea	A	B	A	B	B	D
	Ex 309 1-(3-(2-cyanopropan-2-yl)-1-phenyl-1H-pyrazol-5-yl)-3-(3-(6,7-dimethoxyquinazolin-4-ylthio)phenyl)urea	A	ND	A	C	C	C
	Ex 310 1-(5-tert-butylisoxazol-3-yl)-3-(3-(2-chloro-6,7-dimethoxyquinazolin-4-yloxy)phenyl)urea	D	D	C	D	C	A

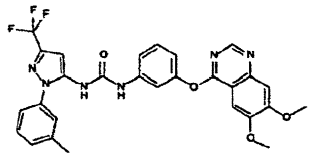
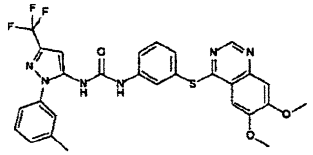
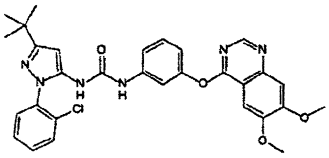
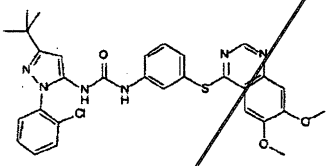
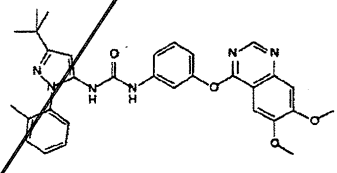
	Name	pMEK IC50 (nM)	A375 Viability EC50 (nM)	BRAF V600E Kd (nM)	BRAF WT Kd nM	RAF 1 Kd nM	S35
	Ex 311 1-(3-(1,1-difluoroethyl)-1-(pyridin-3-yl)-1H-pyrazol-5-yl)-3-(3-(6,7-dimethoxyquinazolin-4-yloxy)phenyl)urea	B	B	A	A	A	C
	Ex 312 1-(3-tert-butyl-1-(6-methylpyridin-3-yl)-1H-pyrazol-5-yl)-3-(3-(6,7-dimethoxyquinazolin-4-yloxy)phenyl)urea	A	A	A	C	B	D
	Ex 313 Preparation of 1-(3-tert-butyl-1-(2-oxo-1,2-dihydropyridin-4-yl)-1H-pyrazol-5-yl)-3-(3-(6,7-dimethoxyquinazolin-4-yloxy)phenyl)urea	B	C	A	B	B	D
	Ex 314 1-(3-(6,7-dimethoxyquinazolin-4-yloxy)phenyl)-3-(1-(5-fluoropyridin-3-yl)-3-isopropyl-1H-pyrazol-5-yl)urea	B	A	A	C	B	D
	Ex 315 1-(3-(1,1-difluoroethyl)-1-(4-methoxyphenyl)-1H-pyrazol-5-yl)-3-(3-(6,7-dimethoxyquinazolin-4-yloxy)phenyl)urea	A	A	A	D	C	D

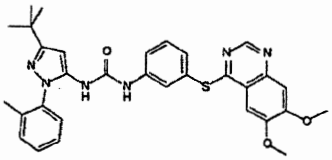
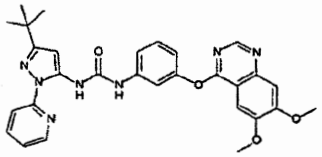
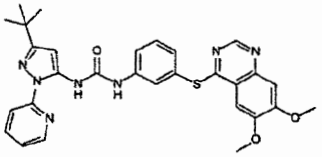
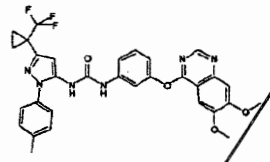
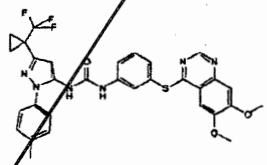
	Name	pMEK IC50 (nM)	A375 Viability EC50 (nM)	BRAF V600E Kd (nM)	BRAF WT Kd nM	RAF 1 Kd nM	S35
	Ex 316 1-(3-(1,1-difluoroethyl)-1-(5-fluoropyridin-3-yl)-1H-pyrazol-5-yl)-3-(3-(6,7-dimethoxyquinazolin-4-yloxy)phenyl)urea	B	C	A	B	A	C
	Ex 317 1-(3-tert-butyl-1-(6-oxo-1,6-dihydropyridin-3-yl)-1H-pyrazol-5-yl)-3-(3-(6,7-dimethoxyquinazolin-4-yloxy)phenyl)urea	D	D	A	D	C	D
	Ex 318 1-(3-(1,1-difluoroethyl)-1-phenyl-1H-pyrazol-5-yl)-3-(3-(6,7-dimethoxyquinazolin-4-yloxy)phenyl)urea	A	A	A	B	B	C
	Ex 319 Preparation of 1-(3-(1,1-difluoroethyl)-1-phenyl-1H-pyrazol-5-yl)-3-(3-(6,7-dimethoxyquinazolin-4-ylthio)phenyl)urea	A	A	A	C	B	C
	Ex 320 1-(3-tert-butyl-1-(2-methylpyridin-4-yl)-1H-pyrazol-5-yl)-3-(3-(6,7-dimethoxyquinazolin-4-yloxy)phenyl)urea	A	ND	A	D	D	D

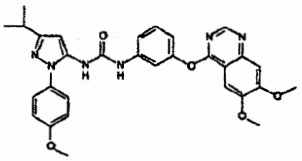
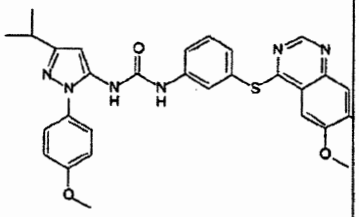
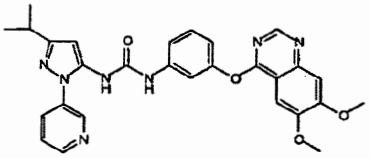
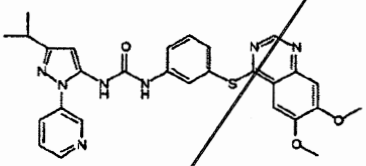
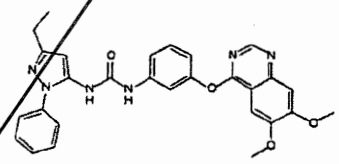
	Name	pMEK IC50 (nM)	A375 Viability EC50 (nM)	BRAF V600E Kd (nM)	BRAF WT Kd nM	RAF 1 Kd nM	S75
	Ex 321 1-(3-tert-butyl-1-ethyl-1H-pyrazol-5-yl)-3-(3-(6,7-dimethoxyquinazolin-4-ylthio)phenyl)urea	B	C	A	B	A	C
	Ex 322 1-(3-tert-butyl-1-(pyridin-3-yl)-1H-pyrazol-5-yl)-3-(3-(6,7-dimethoxyquinazolin-4-yloxy)phenyl)urea	A	ND	A	B	B	D
	Ex 323 1-(3-tert-butyl-1-(pyridin-3-yl)-1H-pyrazol-5-yl)-3-(3-(6,7-dimethoxyquinazolin-4-ylthio)phenyl)urea	A	B	A	C	C	D
	Ex 324 Preparation of 1-(3-(6,7-dimethoxyquinazolin-4-yloxy)phenyl)-3-(3-isopropyl-1-phenyl-1H-pyrazol-5-yl)urea	A	A	A	B	B	D
	Ex 325 1-(3-(6,7-dimethoxyquinazolin-4-ylthio)phenyl)-3-(3-isopropyl-1-phenyl-1H-pyrazol-5-yl)urea	A	A	A	B	B	C
	Ex 326 Preparation of 1-(3-tert-butyl-1-(5-fluoropyridin-3-yl)-1H-pyrazol-5-yl)-3-(3-(6,7-dimethoxyqu	A	ND	A	C	C	D

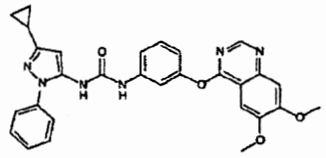
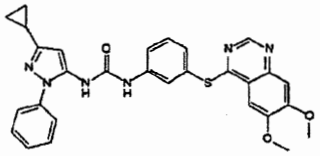
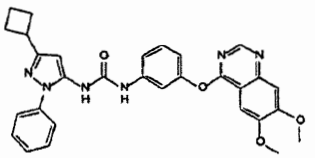
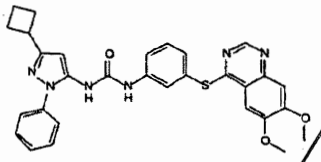
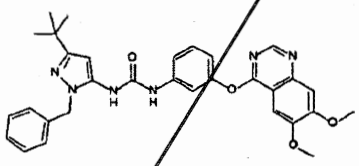
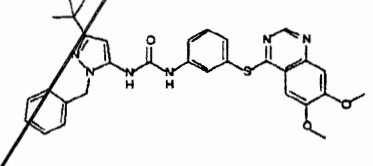
	Name	pMEK IC50 (nM)	A375 Viability EC50 (nM)	BRAF V600E Kd (nM)	BRAF WT Kd nM	RAF 1 Kd nM	S35
	inazolin-4-yloxy)phenyl)urea						
	Ex 327 1-(3-tert-butyl-1-(5-fluoropyridin-3-yl)-1H-pyrazol-5-yl)-3-(3-(6,7-dimethoxyquinazolin-4-ylthio)phenyl)urea	A	ND	A	C	C	D
	Ex 328 1-(3-tert-butyl-1-(4-cyanophenyl)-1H-pyrazol-5-yl)-3-(3-(6,7-dimethoxyquinazolin-4-yloxy)phenyl)urea	A	ND	A	B	B	D
	Ex 329 Preparation of 1-(3-tert-butyl-1-(4-cyanophenyl)-1H-pyrazol-5-yl)-3-(3-(6,7-dimethoxyquinazolin-4-ylthio)phenyl)urea	A	ND	B	B	C	D
	Ex 330 1-(3-tert-butyl-1-cyclohexyl-1H-pyrazol-5-yl)-3-(3-(6,7-dimethoxyquinazolin-4-yloxy)phenyl)urea	D	D	A	D	D	C
	Ex 331 1-(3-tert-butyl-1-cyclohexyl-1H-pyrazol-5-yl)-3-(3-(6,7-dimethoxyquinazolin-4-ylthio)phenyl)urea	A	D	B	C	C	B

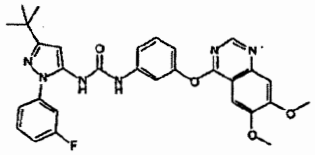
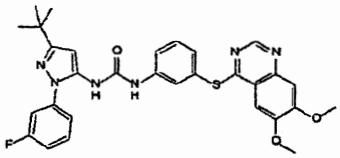
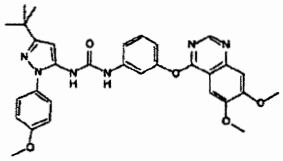
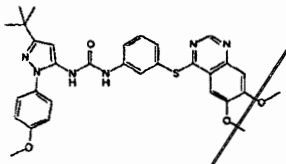
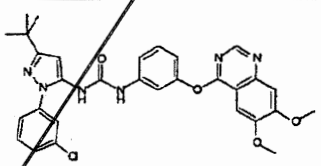
	Name	pMEK IC50 (nM)	A375 Viability EC50 (nM)	BRAF V600E Kd (nM)	BRAF WT Kd nM	RAF 1 Kd nM	S35
	Ex 332 1-(3-tert-butyl-1-isobutyl-1H-pyrazol-5-yl)-3-(3-(6,7-dimethoxyquinazolin-4-yloxy)phenyl)urea	C	D	A	B	B	C
	Ex 333 1-(3-tert-butyl-1-isobutyl-1H-pyrazol-5-yl)-3-(3-(6,7-dimethoxyquinazolin-4-ylthio)phenyl)urea	C	ND	A	B	B	C
	Ex 334 1-(3-tert-butyl-1-isopropyl-1H-pyrazol-5-yl)-3-(3-(6,7-dimethoxyquinazolin-4-yloxy)phenyl)urea	C	C	A	B	B	C
	Ex 335 1-(3-tert-butyl-1-isopropyl-1H-pyrazol-5-yl)-3-(3-(6,7-dimethoxyquinazolin-4-ylthio)phenyl)urea	B	D	A	B	B	C
	Ex336 1-(3-tert-butyl-1-(pyridin-4-yl)-1H-pyrazol-5-yl)-3-(3-(6,7-dimethoxyquinazolin-4-yloxy)phenyl)urea	A	ND	A	C	C	D
	Ex 337 1-(3-tert-butyl-1-(pyridin-4-yl)-1H-pyrazol-5-yl)-3-(3-(6,7-dimethoxyqu	A	ND	A	C	C	D

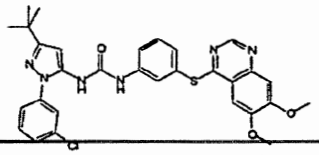
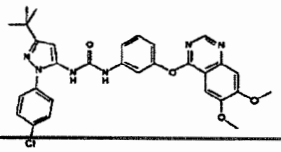
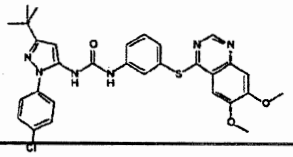
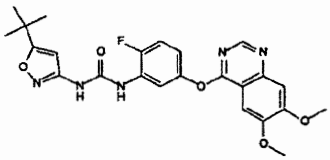
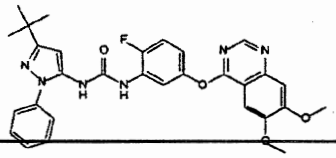
	Name	pMEK IC50 (nM)	A375 Viability EC50 (nM)	BRAF V600E Kd (nM)	BRAF WT Kd nM	RAF 1 Kd nM	S35
	inazolin-4-ylthio)phenyl)urea						
	Ex 338 1-(3-(6,7-dimethoxyquinazolin-4-yloxy)phenyl)-3-(1-m-tolyl-3-(trifluoromethyl)-1H-pyrazol-5-yl)urea	A	A	A	C	B	C
	Ex 339 1-(3-(6,7-dimethoxyquinazolin-4-ylthio)phenyl)-3-(1-m-tolyl-3-(trifluoromethyl)-1H-pyrazol-5-yl)urea	A	ND	B	D	C	C
	Ex 340 1-(3-tert-butyl-1-(2-chlorophenyl)-1H-pyrazol-5-yl)-3-(3-(6,7-dimethoxyquinazolin-4-yloxy)phenyl)urea	A	ND	B	D	D	D
	Ex 341 1-(3-tert-butyl-1-(2-chlorophenyl)-1H-pyrazol-5-yl)-3-(3-(6,7-dimethoxyquinazolin-4-ylthio)phenyl)urea	A	ND	B	D	D	C
	Ex 342 1-(3-tert-butyl-1-o-tolyl-1H-pyrazol-5-yl)-3-(3-(6,7-dimethoxyquinazolin-4-yloxy)phenyl)urea	A	ND	B	D	D	D

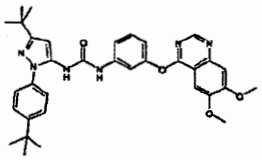
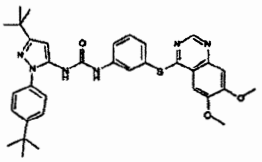
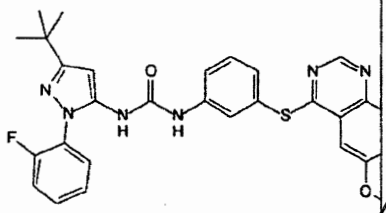
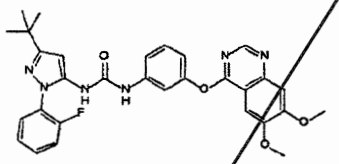
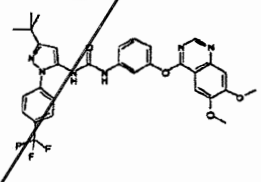
	Name	pMEK IC50 (nM)	A375 Viability EC50 (nM)	BRAF V600E Kd (nM)	BRAF WT Kd nM	RAF 1 Kd nM	S35
	Ex 343 1-(3-tert-butyl-1-o-tolyl-1H-pyrazol-5-yl)-3-(3-(6,7-dimethoxyquinazolin-4-ylthio)phenyl)urea	A	ND	B	D	D	C
	Ex 344 1-(3-tert-Butyl-1-(pyridin-2-yl)-1H-pyrazol-5-yl)-3-(3-(6,7-dimethoxyquinazolin-4-yloxy)phenyl)urea	C	ND	C	D	D	C
	Ex 345 1-(3-tert-butyl-1-(pyridin-2-yl)-1H-pyrazol-5-yl)-3-(3-(6,7-dimethoxyquinazolin-4-ylthio)phenyl)urea	C	D	D	D	D	B
	Ex 346 1-(3-(6,7-dimethoxyquinazolin-4-yloxy)phenyl)-3-(1-p-tolyl-3-(1-(trifluoromethyl)cyclopropyl)-1H-pyrazol-5-yl)urea	A	ND	A	D	D	D
	Ex 347 1-(3-(6,7-dimethoxyquinazolin-4-ylthio)phenyl)-3-(1-p-tolyl-3-(1-(trifluoromethyl)cyclopropyl)-1H-pyrazol-5-yl)urea	A	ND	B	D	D	D

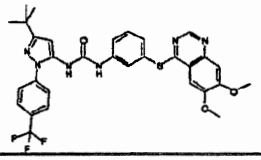
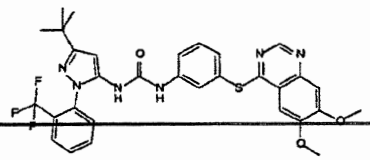
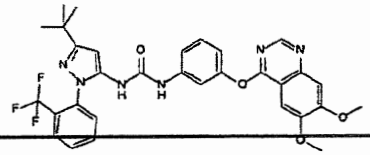
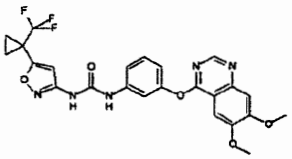
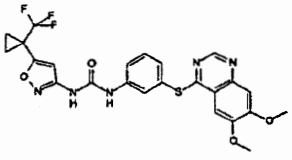
	Name	pMEK IC50 (nM)	A375 Viability EC50 (nM)	BRAF V600E Kd (nM)	BRAF WT Kd nM	RAF 1 Kd nM	S35
	Ex 348 1-(3-(6,7-dimethoxyquinazolin-4-yloxy)phenyl)-3-(3-isopropyl-1-(4-methoxyphenyl)-1H-pyrazol-5-yl)urea	A	A	A	D	C	D
	Ex 349 1-(3-(6,7-dimethoxyquinazolin-4-ylthio)phenyl)-3-(3-isopropyl-1-(4-methoxyphenyl)-1H-pyrazol-5-yl)urea	A	A	A	D	C	C
	Ex 350 1-(3-(6,7-dimethoxyquinazolin-4-yloxy)phenyl)-3-(3-isopropyl-1-(pyridin-3-yl)-1H-pyrazol-5-yl)urea	B	B	A	A	A	D
	Ex 351 1-(3-(6,7-dimethoxyquinazolin-4-ylthio)phenyl)-3-(3-isopropyl-1-(pyridin-3-yl)-1H-pyrazol-5-yl)urea	A	B	A	C	A	C
	Ex 352 1-(3-(6,7-dimethoxyquinazolin-4-yloxy)phenyl)-3-(3-ethyl-1-phenyl-1H-pyrazol-5-yl)urea	C	B	A	A	A	C

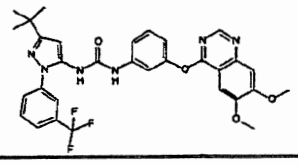
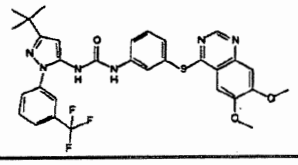
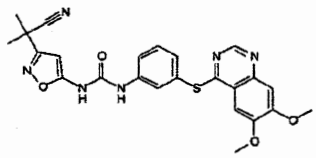
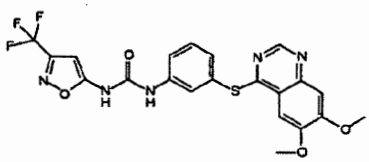
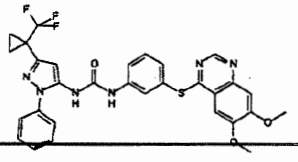
	Name	pMEK IC50 (nM)	A375 Viability EC50 (nM)	BRAF V600E Kd (nM)	BRAF WT Kd nM	RAF 1 Kd nM	S35
	Ex 353 1-(3-cyclopropyl-1-phenyl-1H-pyrazol-5-yl)-3-(3-(6,7-dimethoxyquinazolin-4-yloxy)phenyl)urea	B	B	A	B	A	C
	Ex 354 1-(3-cyclopropyl-1-phenyl-1H-pyrazol-5-yl)-3-(3-(6,7-dimethoxyquinazolin-4-ylthio)phenyl)urea	B	B	A	A	A	C
	Ex 355 Preparation of 1-(3-cyclobutyl-1-phenyl-1H-pyrazol-5-yl)-3-(3-(6,7-dimethoxyquinazolin-4-yloxy)phenyl)urea	A	A	A	C	C	C
	Ex 356 1-(3-cyclobutyl-1-phenyl-1H-pyrazol-5-yl)-3-(3-(6,7-dimethoxyquinazolin-4-ylthio)phenyl)urea	B	A	A	D	C	C
	Ex 357 1-(1-benzyl-3-tert-butyl-1H-pyrazol-5-yl)-3-(3-(6,7-dimethoxyquinazolin-4-yloxy)phenyl)urea	B	D	A	C	D	C
	Ex 358 1-(1-benzyl-3-tert-butyl-1H-pyrazol-5-yl)-3-(3-(6,7-dimethoxyquinazolin-4-ylthio)phenyl)urea	B	ND	A	D	D	C

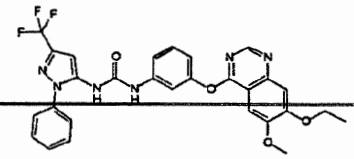
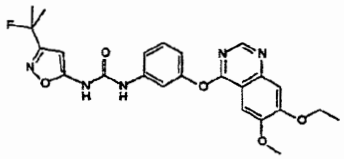
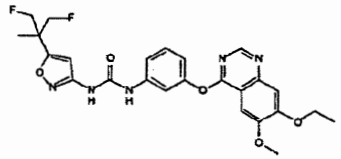
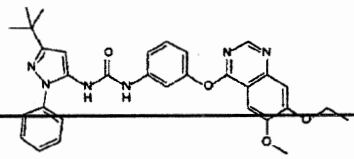
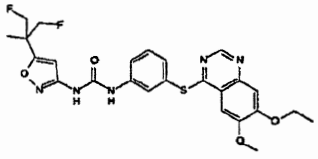
	Name	pMEK IC50 (nM)	A375 Viability EC50 (nM)	BRAF V600E Kd (nM)	BRAF WT Kd nM	RAF 1 Kd nM	S35
	Ex 359 1-(3-tert-butyl-1-(3-fluorophenyl)-1H-pyrazol-5-yl)-3-(3-(6,7-dimethoxyquinazolin-4-yloxy)phenyl)urea	A	ND	A	D	D	D
	Ex 360 1-(3-tert-butyl-1-(3-fluorophenyl)-1H-pyrazol-5-yl)-3-(3-(6,7-dimethoxyquinazolin-4-ylthio)phenyl)urea	A	ND	B	D	D	D
	Ex 361 1-(3-tert-butyl-1-(4-methoxyphenyl)-1H-pyrazol-5-yl)-3-(3-(6,7-dimethoxyquinazolin-4-yloxy)phenyl)urea	A	D	A	B	C	C
	Ex 362 Preparation of 1-(3-tert-butyl-1-(4-methoxyphenyl)-1H-pyrazol-5-yl)-3-(3-(6,7-dimethoxyquinazolin-4-ylthio)phenyl)urea	A	ND	C	D	D	D
	Ex 363 1-(3-tert-butyl-1-(3-chlorophenyl)-1H-pyrazol-5-yl)-3-(3-(6,7-dimethoxyquinazolin-4-yloxy)phenyl)urea	A	ND	A	B	D	D

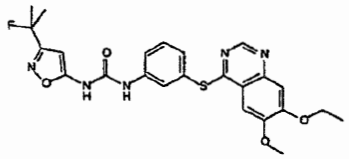
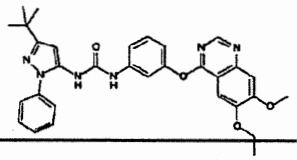
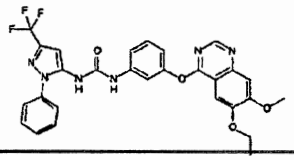
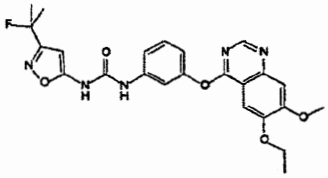
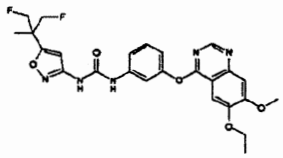
	Name	pMEK IC50 (nM)	A375 Viability EC50 (nM)	BRAF V600E Kd (nM)	BRAF WT Kd nM	RAF 1 Kd nM	S35
	Ex 364 1-(3-tert-butyl-1-(3-chlorophenyl)-1H-pyrazol-5-yl)-3-(3-(6,7-dimethoxyquinazolin-4-ylthio)phenyl)urea	A	ND	A	C	D	D
	Ex 365 1-(3-tert-butyl-1-(4-chlorophenyl)-1H-pyrazol-5-yl)-3-(3-(6,7-dimethoxyquinazolin-4-yloxy)phenyl)urea	A	ND	B	D	D	D
	Ex 366 1-(3-tert-butyl-1-(4-chlorophenyl)-1H-pyrazol-5-yl)-3-(3-(6,7-dimethoxyquinazolin-4-ylthio)phenyl)urea	A	ND	B	D	D	D
	Ex 367 1-(5-tert-butylisoxazol-3-yl)-3-(5-(6,7-dimethoxyquinazolin-4-yloxy)-2-fluorophenyl)urea	A	B	A	A	A	D
	Ex 368 1-(3-tert-butyl-1-phenyl-1H-pyrazol-5-yl)-3-(5-(6,7-dimethoxyquinazolin-4-yloxy)-2-fluorophenyl)urea	A	ND	C	D	D	D

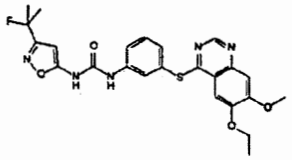
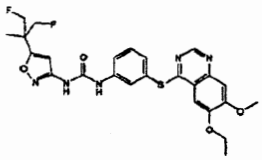
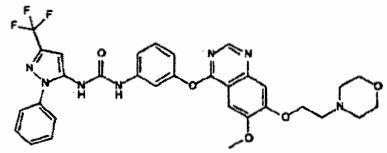
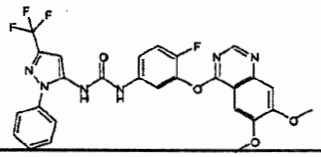
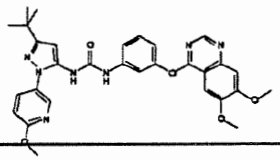
	Name	pMEK IC50 (nM)	A375 Viability EC50 (nM)	BRAF V600E Kd (nM)	BRAF WT Kd nM	RAF 1 Kd nM	S35
	Ex 369 1-(3-tert-butyl-1-(4-tert-butylphenyl)-1H-pyrazol-5-yl)-3-(3-(6,7-dimethoxyquinazolin-4-yloxy)phenyl)urea	A	D	A	C	D	C
	Ex 370 1-(3-tert-butyl-1-(4-tert-butylphenyl)-1H-pyrazol-5-yl)-3-(3-(6,7-dimethoxyquinazolin-4-ylthio)phenyl)urea	A	ND	A	D	D	D
	Ex 371 1-(3-tert-butyl-1-(2-fluorophenyl)-1H-pyrazol-5-yl)-3-(3-(6,7-dimethoxyquinazolin-4-ylthio)phenyl)urea	A	ND	B	D	D	D
	Ex 372 1-(3-tert-butyl-1-(2-fluorophenyl)-1H-pyrazol-5-yl)-3-(3-(6,7-dimethoxyquinazolin-4-yloxy)phenyl)urea	A	ND	A	C	C	D
	Ex 373 1-(3-tert-butyl-1-(4-(trifluoromethyl)phenyl)-1H-pyrazol-5-yl)-3-(3-(6,7-dimethoxyquinazolin-4-yloxy)phenyl)urea	A	ND	C	D	D	C

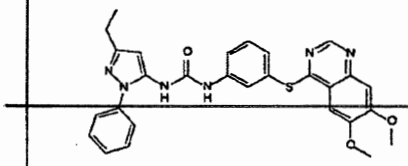
	Name	pMEK IC50 (nM)	A375 Viability EC50 (nM)	BRAF V600E Kd (nM)	BRAF WT Kd nM	RAF 1 Kd nM	S35
	Ex 374 1-(3-tert-butyl-1-(4-(trifluoromethyl)phenyl)-1H-pyrazol-5-yl)-3-(3-(6,7-dimethoxyquinazolin-4-ylthio)phenyl)urea	A	ND	B	D	D	C
	Ex 375 1-(3-tert-butyl-1-(2-(trifluoromethyl)phenyl)-1H-pyrazol-5-yl)-3-(3-(6,7-dimethoxyquinazolin-4-ylthio)phenyl)urea	A	ND	C	D	D	C
	Ex 376 1-(3-tert-butyl-1-(2-(trifluoromethyl)phenyl)-1H-pyrazol-5-yl)-3-(3-(6,7-dimethoxyquinazolin-4-yloxy)phenyl)urea	A	ND	C	D	D	D
	Ex 377 1-(3-(6,7-dimethoxyquinazolin-4-yloxy)phenyl)-3-(5-(1-(trifluoromethyl)cyclopropyl)isoxazol-3-yl)urea	A	A	A	A	A	C
	Ex 378 1-(3-(6,7-dimethoxyquinazolin-4-ylthio)phenyl)-3-(5-(1-(trifluoromethyl)cyclopropyl)isoxazol-3-yl)urea	B	A	A	A	A	C

	Name	pMEK IC50 (nM)	A375 Viability EC50 (nM)	BRAF V600E Kd (nM)	BRAF WT Kd nM	RAF 1 Kd nM	S35
	Ex 379 1-(3-tert-butyl-1-(3-(trifluoromethyl)phenyl)-1H-pyrazol-5-yl)-3-(3-(6,7-dimethoxyquinazolin-4-yloxy)phenyl)urea	A	ND	B	D	D	D
	Ex 380 1-(3-tert-butyl-1-(3-(trifluoromethyl)phenyl)-1H-pyrazol-5-yl)-3-(3-(6,7-dimethoxyquinazolin-4-ylthio)phenyl)urea	A	ND	B	D	D	C
	Ex 381 1-(3-(2-cyanopropan-2-yl)isoxazol-5-yl)-3-(3-(6,7-dimethoxyquinazolin-4-ylthio)phenyl)urea	A	ND	A	A	A	C
	Ex 382 1-(3-(6,7-dimethoxyquinazolin-4-ylthio)phenyl)-3-(3-(trifluoromethyl)isoxazol-5-yl)urea	D	D	A	A	A	C
	Ex 383 1-(3-(6,7-dimethoxyquinazolin-4-ylthio)phenyl)-3-(1-phenyl-3-(1-(trifluoromethyl)cyclopropyl)-1H-pyrazol-5-yl)urea	A	ND	B	D	D	C
	Example 384 Preparation of 1-(3-(7-ethoxy-6-	C	B	A	C	B	C

	Name	pMEK IC50 (nM)	A375 Viability EC50 (nM)	BRAF V600E Kd (nM)	BRAF WT Kd nM	RAF 1 Kd nM	S35
	methoxyquinazolin-4-yloxy)phenyl)-3-(1-phenyl-3-(trifluoromethyl)-1H-pyrazol-5-yl)urea						
	Ex 385 1-(3-(7-ethoxy-6-methoxyquinazolin-4-yloxy)phenyl)-3-(3-(2-fluoropropan-2-yl)isoxazol-5-yl)urea	B	B	A	A	A	C
	Ex 386 1-(5-(1,3-difluoro-2-methylpropan-2-yl)isoxazol-3-yl)-3-(3-(7-ethoxy-6-methoxyquinazolin-4-yloxy)phenyl)urea	A	A	A	A	A	C
	Ex 387 1-(3-tert-butyl-1-phenyl-1H-pyrazol-5-yl)-3-(3-(7-ethoxy-6-methoxyquinazolin-4-yloxy)phenyl)urea	A	ND	A	C	C	D
	Example 388 Preparation of 1-(5-(1,3-difluoro-2-methylpropan-2-yl)isoxazol-3-yl)-3-(3-(7-ethoxy-6-methoxyquinazolin-4-ylthio)phenyl)urea	B	B	A	A	A	C

	Name	pMEK IC50 (nM)	A375 Viability EC50 (nM)	BRAF V600E Kd (nM)	BRAF WT Kd nM	RAF1 Kd nM	S35
	Ex 389 1-(3-(7-ethoxy-6-methoxyquinazolin-4-ylthio)phenyl)-3-(3-(2-fluoropropan-2-yl)isoxazol-5-yl)urea	C	B	A	A	A	C
	Ex 390 1-(3-tert-butyl-1-phenyl-1H-pyrazol-5-yl)-3-(3-(6-ethoxy-7-methoxyquinazolin-4-yloxy)phenyl)urea	A	ND	A	B	C	D
	Ex 391 1-(3-(6-ethoxy-7-methoxyquinazolin-4-yloxy)phenyl)-3-(1-phenyl-3-(trifluoromethyl)-1H-pyrazol-5-yl)urea	A	A	A	B	B	C
	Ex 392 1-(3-(6-ethoxy-7-methoxyquinazolin-4-yloxy)phenyl)-3-(3-(2-fluoropropan-2-yl)isoxazol-5-yl)urea	A	A	A	A	A	C
	Ex 393 1-(5-(1,3-difluoro-2-methylpropan-2-yl)isoxazol-3-yl)-3-(3-(6-ethoxy-7-methoxyquinazolin-4-yloxy)phenyl)urea	A	A	A	A	A	C

	Name	pMEK IC50 (nM)	A375 Viability EC50 (nM)	BRAF V600E Kd (nM)	BRAF WT Kd nM	RAF 1 Kd nM	S35
	Ex 394 1-(3-(6-ethoxy-7-methoxyquinazolin-4-ylthio)phenyl)-3-(3-(2-fluoropropan-2-yl)isoxazol-5-yl)urea	A	B	A	A	A	C
	Ex 395 1-(5-(1,3-difluoro-2-methylpropan-2-yl)isoxazol-3-yl)-3-(3-(6-ethoxy-7-methoxyquinazolin-4-ylthio)phenyl)urea	A	A	A	A	A	C
	Ex 396 (1-(3-(6-methoxy-7-(2-morpholinoethoxy)quinazolin-4-yloxy)phenyl)-3-(1-phenyl-3-(trifluoromethyl)-1H-pyrazol-5-yl)urea	C	C	A	C	C	C
	Ex 397 1-(3-(6,7-dimethoxyquinazolin-4-yloxy)-4-fluorophenyl)-3-(1-phenyl-3-(trifluoromethyl)-1H-pyrazol-5-yl)urea	A	B	A	D	C	C
	Ex 398 1-(3-tert-butyl-1-(4-methoxyphenyl)-1H-pyrazol-5-yl)-3-(3-(6,7-dimethoxyquinazolin-4-yloxy)phenyl)urea	A	ND	A	C	C	D

	Name	pMEK IC50 (nM)	A375 Viability EC50 (nM)	BRAF V600E Kd (nM)	BRAF WT Kd nM	RAF1 Kd nM	S35
	Ex 399 1-(3-(6,7-dimethoxyquinazolin-4-ylthio)phenyl)-3-(3-ethyl-1-phenyl-1H-pyrazol-5-yl)urea	B	B	A	A	A	C

pMEK IC_{50} and A375 Viability EC_{50}: A ≤250, 250<B≤500, 500<C≤1000, D>1000, BRAF V600E Kd, BRAF WT Kd and RAF1 Kd: A ≤250, 250<B≤500, 500<C≤1000, D>1000
S35: A ≤0.10, 0.10<B≤0.20, 0.20<C≤0.40, D>0.40 (Asterisk indicates an S35 score calculated using a panel of 321 distinct kinases, no asterisk indicates an S35 score calculated using a panel of 290 distinct kinases); and
ND= no data.

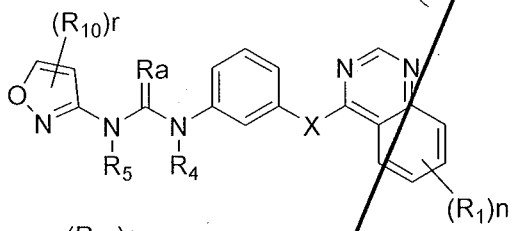
[00536] Also provided herein are isotopically enriched analogs of the compounds provided herein. Isotopic enrichment (for example, deuteration) of pharmaceuticals to improve pharmacokinetics ("PK"), pharmacodynamics ("PD"), and toxicity profiles, has been demonstrated previously with some classes of drugs. See, for example, Lijinsky *et. al.*, *Food Cosmet. Toxicol.*, 20: 393 (1982); Lijinsky *et. al.*, *J. Nat. Cancer Inst.*, 69: 1127 (1982); Mangold *et. al.*, *Mutation Res.* 308: 33 (1994); Gordon *et. al.*, *Drug Metab. Dispos.*, 15: 589 (1987); Zello *et. al.*, *Metabolism*, 43: 487 (1994); Gately *et. al.*, *J. Nucl. Med.*, 27: 388 (1986); Wade D, *Chem. Biol. Interact.* 117: 191 (1999).

[00537] Isotopic enrichment of a drug can be used, for example, to (1) reduce or eliminate unwanted metabolites, (2) increase the half-life of the parent drug, (3) decrease the number of doses needed to achieve a desired effect, (4) decrease the amount of a dose necessary to achieve a desired effect, (5) increase the formation of active metabolites, if any are formed, and/or (6) decrease the production of deleterious metabolites in specific tissues and/or create a more effective drug and/or a safer drug for combination therapy, whether the combination therapy is intentional or not.

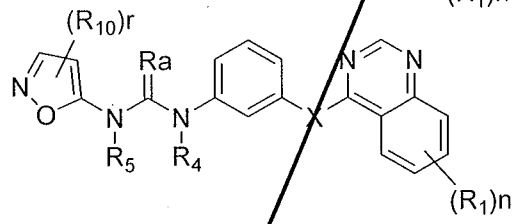
[00538] Replacement of an atom for one of its isotopes often will result in a change in the reaction rate of a chemical reaction. This phenomenon is known as the Kinetic Isotope Effect ("KIE"). For example, if a C–H bond is broken during a rate-determining step in a chemical reaction (*i.e.* the step with the highest transition state

What is claimed is:

1. A compound having formula VA or VB:



VA



VB

or a pharmaceutically acceptable salt, solvate, or hydrate thereof, wherein
r is 0, 1 or 2;
X is O or S;
n is 1 to 4
R^a is O;
R^4 and R^5 are each independently hydrogen or methyl;
R^{10} is independently selected from halo, haloalkyl, alkyl, cycloalkyl, aryl, heterocyclyl, and heteroaryl where the alkyl group is optionally substituted with 1 or 2 groups selected from halo and cyano, and where the cycloalkyl, aryl and heteroaryl group is optionally substituted with 1 or 2 groups selected from halo, cyano, alkyl and haloalkyl; and
each R^1 is absent, or is independently selected from
halo, nitro, alkyl, cycloalkylalkyl, heterocyclylalkyl, aralkyl, heteroaryl, heteroaralkyl, cycloalkylcarbonylamino, $—R^6OR^7$, $—R^6OR^9OR^7$, $—R^6OR^9N(R^7)_2$, or
any two adjacent R^1 groups together form an alkylenedioxy group;
each R^6 is independently a direct bond, alkylene chain or alkenylene chain;
each R^7 is independently selected from hydrogen, alkyl, alkenyl, alkynyl, cycloalkyl, cycloalkylalkyl, aryl, aralkyl, heterocyclyl, heterocyclylalkyl, heteroaryl and heteroaralkyl, or
two R^7 groups together with the N atom to which they are attached form a heterocyclyl or heteroaryl; or
each R^9 is independently an alkylene chain or an alkenylene chain.

2. The compound of claim 1, or a pharmaceutically acceptable salt thereof, wherein R^4 and R^5 are each hydrogen.

3. The compound of claim 1, or a pharmaceutically acceptable salt thereof, wherein each R^1 is selected from the group consisting of $—R^6OR^7$, $—R^6OR^9OR^7$, $—R^6OR^9N(R^7)_2$; and

each R^6 is independently a direct bond, alkylene chain or alkenylene chain;

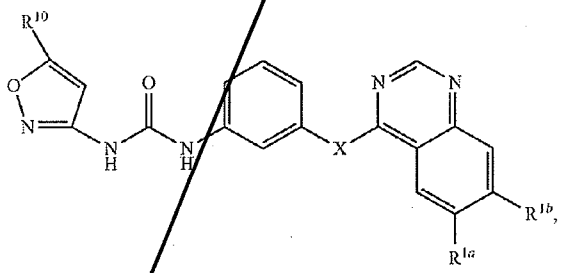
each R^7 is independently selected from hydrogen, alkyl, alkenyl, alkynyl, cycloalkyl, cycloalkylalkyl, aryl, aralkyl, heterocyclyl, heterocyclylalkyl, heteroaryl and heteroaralkyl, or

two R^7 groups together with the N atom to which they are attached form a heterocyclyl or heteroaryl; and

each R^9 is independently an alkylene chain or an alkenylene chain.

4. The compound of claim 1 having formula XVII:

XVII



or a pharmaceutically acceptable salt, solvate or hydrate thereof,

wherein X is O or S;

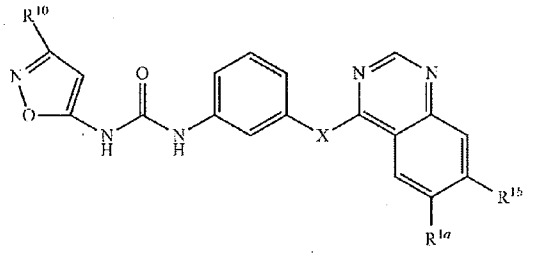
R^{1a} and R^{1b} are independently selected from alkoxy, alkoxyalkoxy, or alkylsulfonylalkoxy; or

two R^{1a} and R^{1b} groups together form an alkylenedioxy group; and

R^{10} is hydrogen, halo, alkyl, haloalkyl, aryl, heterocyclyl, heteroaryl, cycloalkyl or cycloalkylalkyl.

5. The compound of claim 1 having formula XIX:

XIX



or a pharmaceutically acceptable salt, solvate or hydrate thereof,

wherein X is O or S;

R^{1a} and R^{1b} are independently selected from methoxy, methoxyethoxy, or methylsulfonylpropyloxy; or

two R^{1a} and R^{1b} groups together with the carbon atoms on which they are substituted form an ethylenedioxy group; and

R^{10} is hydrogen, halo, alkyl, haloalkyl, aryl, heterocyclyl, heteroaryl, cycloalkyl or cycloalkylalkyl.

6. The compound selected from
1-(5-tert-butylisoxazol-3-yl)-3-(3-(6, 7-dimethoxyquinazolin-4-yloxy)phenyl)urea;
1-(5-tert-butylisoxazol-3-yl)-3-(3-(6-methoxyquinazolin-4-yloxyphenyl)urea;
1-(5-tert-butylisoxazol-3-yl)-3-(3-(7-methoxyquinazolin-4-yloxy)phenyl)urea;
1-(5-tert-butylisoxazol-3-yl)-3-(3-(6,7-difluoroquinazolin-4-yloxy)phenyl)urea;
1-(5-tert-butylisoxazol-3-yl)-3-(3-(5-methylquinazolin-4-yloxy)phenyl)urea;
1-(5-tert-butylisoxazol-3-yl)-3-[3-(7-ethoxy-6-methoxyquinazolin-4-yloxy)phenyl]urea hydrochloride;
1-(5-tert-butylisoxazol-3-yl)-3-{3-[6-methoxy-7-(2-methoxyethoxy)quinazolin-4-yloxy]phenyl}urea hydrochloride;
1-(5-tert-butylisoxazol-3-yl)-3-(3-(6-methylquinazolin-4-yloxy)phenyl)urea;
1-(5-tert-butylisoxazol-3-yl)-3-(3-(6,7-dimethoxyquinazolin-4-yloxy)-4-fluorophenyl)urea;
1-(5-tert-butylisoxazol-3-yl)-3-(4-chloro-3-(6, 7-dimethoxyquinazolin-4-yloxy)phenyl)urea;
1-(5-tert-butylisoxazol-3-yl)-3-(3-(6-ethoxy-7-methoxyquinazolin-4-yloxy)phenyl)urea;
1-{3-[6,7-bis(2-methoxyethoxy)quinazolin-4-yloxy]phenyl}-3-(5-tert-butylisoxazol-3-yl)urea hydrochloride;
1-(5-tert-Butylisoxazol-3-yl)-3-[3-(6, 7-diethoxyquinazolin-4-yloxy)phenyl]urea hydrochloride;
1-(5-tert-butylisoxazol-3-yl)-3-[3-(7,8-dihydro-[1,4]dioxino[2,3-g] quinazolin-4-yloxy)phenyl]urea hydrochloride;
1-(5-tert-butylisoxazol-3-yl)-3-{3-[7-methoxy-6-(2-methoxyethoxy)quinazolin-4-yloxy]phenyl}urea hydrochloride;
1-(5-tert-butylisoxazol-3-yl)-3-(3-(6-(2-methoxyethoxy)quinazolin-4-yloxy)phenyl)urea
1-(5-tert-Butylisoxazol-3-yl)-3-(3-(7-methoxy-6-(3-(methylsulfonyl)propoxy)quinazolin-4-ylthio)phenyl)urea;
1-(3-(2-fluoropropan-2-yl)isoxazol-5-yl)-3-(3-(7-methoxy-6-(3-(methylsulfonyl)propoxy) quinazolin-4-yloxy)phenyl)urea;
1-(5-tert-butylisoxazol-3-yl)-3-(3-(7-(2-methoxyethoxy)quinazolin-4-yloxy)phenyl)urea;
1-(5-tert-butylisoxazol-3-yl)-3-(3-(7-methoxy-6-(3-(methylsulfonyl)propoxy)quinazolin-4-ylthio)phenyl)urea;
1-(5-tert-butylisoxazol-3-yl)-3-(3-(7-methoxy-6-(2-methoxyethoxy)quinazolin-4-ylthio)phenyl)urea;
1-(5-tert-butylisoxazol-3-yl)-3-(3-(6, 7-dimethoxyquinazolin-4-ylthio)phenyl)urea;
1-(5-tert-butylisoxazol-3-yl)-3-(3-(6, 7-difluoroquinazolin-4-ylthio)phenyl)urea;
1-(5-tert-butylisoxazol-3-yl)-3-(3-(7-methoxyquinazolin-4-ylthio)phenyl)urea;
1-(5-tert-butylisoxazol-3-yl)-3-(3-(6-methoxyquinazolin-4-ylthio)phenyl)urea;

1-(5-tert-Butylisoxazol-3-yl)-3-[3-(7-ethoxy-6-methoxyquinazolin-4-ylthio)phenyl]urea;
1-(5-tert-butylisoxazol-3-yl)-3-[3-(6, 7-diethoxyquinazolin-4-ylthio)phenyl]urea;
1-(5-tert-butylisoxazol-3-yl)-3-{3-[6-methoxy-7-(2-methoxyethoxy)quinazolin-4-ylthio]phenyl}urea hydrochloride;
1-{3-[6,7-bis(2-methoxyethoxy)quinazolin-4-ylthio]phenyl}-3-(5-tert-butylisoxazol-3-yl)urea hydrochloride;
1-(5-tert-butylisoxazol-3-yl)-3-[3-(7,8-dihydro-[1,4]dioxino[2,3-g]quinazolin-4-ylthio) phenyl]urea hydrochloride;
1-(5-tert-butylisoxazol-3-yl)-3-{3-[7-methoxy-5-(tetrahydro-2H-pyran-4-ylthio)quinazolin-4-yloxy]phenyl}urea;
1-(5-tert-butylisoxazol-3-yl)-3-(3-(6-ethoxy-7-methoxyquinazolin-4-ylthio)phenyl)urea;
1-(5-tert-butylisoxazol-3-yl)-3-(3-(7-methoxy-6-(3-(methylsulfonyl)propoxy)quinazolin-4-ylthio)phenyl)urea;
1-(5-tert-butylisoxazol-3-yl)-3-(3-(6-(2-methoxyethoxy)quinazolin-4-ylthio)phenyl)urea;
1-(5-tert-butylisoxazol-3-yl)-3-(3-(7-methoxy-6-(2-(methylsulfonyl)ethoxy)quinazolin-4-ylthio)phenyl)urea;
1-(5-tert-butylisoxazol-3-yl)-3-{3-[6-(5-{[2-(methylsulfonyl)ethylamino]methyl}furan-2-yl)quinazolin-4-yloxy]phenyl}urea;
1-(5-tert-butylisoxazol-3-yl)-3-{3-[7-methoxy-5-(tetrahydro-2H-pyran-4-yloxy)quinazolin-4-yloxy]phenyl}urea;
1-(5-tert-butylisoxazol-3-yl)-3-(3-(7-hydroxy-6-methoxyquinazolin-4-yloxy)phenyl)urea;
1-(5-tert-butylisoxazol-3-yl)-3-(3-(6-hydroxy-7-methoxyquinazolin-4-yloxy)phenyl)urea;
1-(3-(6, 7-dimethoxyquinazolin-4-yloxy)phenyl)-3-(5-phenylisoxazol-3-yl)urea;
1-(3-(6, 7-dimethoxyquinazolin-4-yloxy)phenyl)-3-(3-isopropylisoxazo1-5-yl)urea;
1-(3-(6, 7-dimethoxyquinazolin-4-yloxy)phenyl)-3-(3-(tetrahydro-2H-pyran-4-yl)isoxazol-5-yl)urea;
1-(3-cyclopropylisoxazol-5-yl)-3-(3-(6, 7-dimethoxyquinazolin-4-yloxy)phenyl)urea;
1-(3-(2-cyanopropan-2-yl)isoxazol-5-yl)-3-(3-(6,7-dimethoxyquinazolin-4-yloxy)phenyl)urea;
1-(3-(6, 7-dimethoxyquinazolin-4-yloxy)phenyl)-3-(3-(2-fluoropropan-2-yl)isoxazol-5-yl)urea;
1-(3-(6, 7-dimethoxyquinazolin-4-yloxy)phenyl)-3-(5-(1-methylcyclopropyl)isoxazol-3-yl)urea;
1-(3-(6, 7-dimethoxyquinazolin-4-yloxy)phenyl)-3-(5-(1-hydroxy-2-methylpropan-2-yl)isoxazol-3-yl)urea;
1-(3-tert-butylisoxazol-5-yl)-3-(3-(6,7-dimethoxyquinazolin-4-yloxy)phenyl)urea;
1-(3-(6, 7-dimethoxyquinazolin-4-yloxy)phenyl)-3-(5-isopropylisoxazo1-3-yl)urea;
1-(3-(6, 7-dimethoxyquinazolin-4-ylthio)phenyl)-3-(5-isopropylisoxazo1-3-yl)urea;
1-(5-cyclopentylisoxazol-3-yl)-3-(3-(6,7-dimethoxyquinazolin-4-yloxy)phenyl)urea;
1-(3-(6, 7-dimethoxyquinazolin-4-yloxy)phenyl)-3-(5-(2-fluoropropan-2-yl)isoxazol-3-yl)urea;

1-(3-(1, 1-difluoroethyl)isoxazol-5-yl)-3-(3-(6,7-dimethoxyquinazolin-4-yloxy)phenyl)urea;
1-(3-(6, 7-dimethoxyquinazolin-4-yloxy)phenyl)-3-(3-(1-(trifluoromethyl)cyclobutyl)isoxazol-5-yl)urea;
1-(3-(6, 7-dimethoxyquinazolin-4-ylthio)phenyl)-3-(3-(1-(trifluoromethyl)cyclobutyl)isoxazol-5-yl)urea;
1-[3-(1,3-difluoro-2-methylpropan-2-yl)isoxazol-5-yl]-3-[3-(6, 7-dimethoxyquinazolin-4-yloxy]phenyl)urea;
1-[3-(1,3-difluoro-2-methylpropan-2-yl)isoxazol-5-yl]-3-[3-(6, 7-dimethoxyquinazolin-4-ylthio]phenyl)urea;
1-[5-(1,3-difluoro-2-methylpropan-2-yl)isoxazol-3-yl]-3-[3-(6, 7-dimethoxyquinazolin-4-yloxy)phenyl]urea;
1-(3-cyclopentylisoxazol-5-yl)-3-(3-(6,7-dimethoxyquinazolin-4-yloxy)phenyl)urea;
1-(3-(6, 7-dimethoxyquinazolin-4-ylthio)phenyl)-3-(3-(2-fluoropropan-2-yl)isoxazol-5-yl)urea;
1-[5-(1,3-difluoro-2-methylpropan-2-yl)isoxazol-3-yl]-3-[3-(6, 7-dimethoxyquinazolin-4-ylthio)phenyl]urea;
1-(5-cyclopentylisoxazol-3-yl)-3-(3-(6,7-dimethoxyquinazolin-4-ylthio)phenyl)urea;
1-(3-tert-butylisoxazol-5-yl)-3-(3-(6-methoxy-7-(2-methoxyethoxy)quinazolin-4-yloxy)phenyl)urea;
1-(3-(6-Methoxy-7-(2-methoxyethoxy)quinazolin-4-yloxy)phenyl)-3-(5-phenylisoxazol-3-yl)urea;
1-(5-isopropylisoxazol-3-yl)-3-(3-(6-methoxy-7-(2-methoxyethoxy)quinazolin-4-yloxy)phenyl)urea;
1-(3-cyclopentylisoxazol-5-yl)-3-(3-(6-methoxy-7-(2-methoxyethoxy)quinazolin-4-yl oxy)phenyl)urea;
1-(3-(1, 1-difluoroethyl)isoxazol-5-yl)-3-(3-(6-methoxy-7-(2-methoxyethoxy)quinazolin-4-yloxy)phenyl)urea;
1-[5-(1,3-difluoro-2-methylpropan-2-yl)isoxazol-3-yl]-3-{3-[6-methoxy-7-(2-methoxyethoxy)quinazolin-4-yloxy]phenyl}urea;
1-(3-cyclopropylisoxazol-5-yl)-3-(3-(6-methoxy-7-(2-methoxyethoxy)quinazolin-4-yl oxy)phenyl)urea;
1-(3-isopropylisoxazol-5-yl)-3-(3-(6-methoxy-7-(2-methoxyethoxy)quinazolin-4-yloxy)phenyl)urea;
1-(3-(6-methoxy-7-(2-methoxyethoxy)quinazolin-4-yloxy)phenyl)-3-(3-(tetrahydro-2H-pyran-4-yl)isoxazol-5-yl)urea;
1-(3-(2-fluoropropan-2-yl)isoxazol-5-yl)-3-(3-(6-methoxy-7-(2-methoxyethoxy)quinazolin-4-yloxy)phenyl)urea;
1-(5-cyclopentylisoxazol-3-yl)-3-(3-(6-methoxy-7-(2-methoxyethoxy)quinazolin-4-yloxy)phenyl)urea;

1-(3-(6-methoxy-7-(2-methoxyethoxy)quinazolin-4-yloxy)phenyl)-3-(3-(trifluoromethyl)isoxazol-5-yl)urea;
1-[5-(1,3-difluoro-2-methylpropan-2-yl)isoxazol-3-yl]-3-{3-[6-methoxy-7-(2-methoxyethoxy)quinazolin-4-ylthio]phenyl}urea;
1-(5-isopropylisoxazol-3-yl)-3-(3-(6-methoxy-7-(2-methoxyethoxy)quinazolin-4-ylthio)phenyl)urea;
1-(3-(2-fluoropropan-2-yl)isoxazol-5-yl)-3-(3-(6-methoxy-7-(2-methoxyethoxy)quinazolin-4-ylthio)phenyl)urea;
1-(5-cyclopentylisoxazol-3-yl)-3-(3-(6-methoxy-7-(2-methoxyethoxy)quinazolin-4-ylthio)phenyl)urea;
1-(3-(6, 7-dimethoxyquinazolin-4-yloxy)phenyl)-3-(3-(trifluoromethyl)isoxazol-5-yl)urea;
1-(3-(6,7-dimethoxyquinazolin-4-yloxy)phenyl)-3-(3-(1-hydroxy-2-methylpropan-2-yl)isoxazol-5-yl)urea;
1-(3-(2-fluoropropan-2-yl)isoxazol-5-yl)-3-(3-(7-hydroxy-6-methoxyquinazolin-4-yloxy)phenyl)urea;
1-(3-(2-fluoropropan-2-yl)isoxazol-5-yl)-3-(3-(6-hydroxy-7-methoxyquinazolin-4-yloxy)phenyl)urea;
1-(3-(6,7-dimethoxyquinazolin-4-yloxy)phenyl)-3-(5-(1,1, 1-trifluoro-2-methylpropan-2-yl)isoxazol-3-yl)urea;
1-(3-(6-ethoxy-7-methoxyquinazolin-4-yloxy)phenyl)-3-(5-(1, 1, 1-trifluoro-2-methylpropan-2-yl)isoxazol-3-yl)urea;
1-(3-(6,7-dimethoxyquinazolin-4-ylthio)phenyl)-3-(5-(1, 1, 1-trifluoro-2-methylpropan-2-yl)isoxazol-3-yl)urea;
1-(3-(6-ethoxy-7-methoxyquinazolin-4-ylthio)phenyl)-3-(5-(1, 1, 1-trifluoro-2-methylpropan-2-yl)isoxazol-3-yl)urea;
1-(3-(7-hydroxy-6-methoxyquinazolin-4-yloxy)phenyl)-3-(5-(1,1, 1-trifluoro-2-methylpropan-2-yl)isoxazol-3-yl)urea;
1-(3-(6-hydroxy-7-methoxyquinazolin-4-yloxy)phenyl)-3-(5-(1, 1, 1-trifluoro-2-methylpropan-2-yl)isoxazol-3-yl)urea;
1-(3-(6,7-dimethoxyquinazolin-4-yloxy)-2-fluorophenyl)-3-(5-(1, 1,1-trifluoro-2-methylpropan-2-yl)isoxazo1-3-yl)urea;
1-(3-(6, 7-dimethoxyquinazolin-4-yloxy)-4-fluorophenyl)-3-(5-(1, 1, 1-trifluoro-2-methylpropan-2-yl)isoxazol-3-yl)urea;
1-(3-(6, 7-dimethoxyquinazolin-4-yloxy)phenyl)-3-(3-(1, 1, 1-trifluoro-2-methylpropan-2-yl)isoxazol-5-yl)urea;
1-(3-(6, 7-dimethoxyquinazolin-4-ylthio)phenyl)-3-(3-(1, 1, 1-trifluoro-2-methylpropan-2-yl)isoxazol-5-yl)urea; and
1-(5-(6, 7-dimethoxyquinazolin-4-yl oxy)-2, 4-difluorophenyl)-3-(3-(2-fluoropropan-2-yl)isoxazol-5-yl)urea;

1-(5-tert-butylisoxazol-3-yl)-3-(5-(6, 7-dimethoxyquinazolin-4-yloxy)-2,4-difluorophenyl)urea;
1-(5-tert-butylisoxazol-3-yl)-3-(3-(6, 7-dimethoxyquinazolin-4-yloxy)-2-methylphenyl)urea;
1-(3-(6, 7-dimethoxyquinazolin-4-yloxy)-2-methylphenyl)-3-(5-(2-fluoropropan-2-yl)isoxazol-3-yl)urea;
1-(3-(6, 7-dimethoxyquinazolin-4-yloxy)-4-fluorophenyl)-3-(3-(2-fluoropropan-2-yl)isoxazol-5-yl)urea;
1-(5-(1,3-difluoro-2-methylpropan-2-yl)isoxazol-3-yl)-3-(3-(6, 7-dimethoxyquinazolin-4-yloxy)-4-fluorophenyl)urea;
1-(3-(6, 7-dimethoxyquinazolin-4-yloxy)-2-fuorophenyl)-3-(3-(2-fluoropropan-2-yl)isoxazol-5-yl)urea;
1-(5-(1,3-difluoro-2-methylpropan-2-yl)isoxazol-3-yl)-3-(3-(6, 7-dimethoxyquinazolin-4-yloxy)-2-fluorophenyl)urea;
1-(5-tert-butylisoxazol-3-yl)-3-(2-chloro-5-(6, 7-dimethoxyquinazolin-4-yloxy)phenyl)urea;
1-(5-tert-butylisoxazol-3-yl)-3-(5-(6,7-dimethoxyquinazolin-4-yloxy)-2-fluorophenyl)urea;
1-(3-(6, 7-dimethoxyquinazolin-4-yloxy)phenyl)-3-(5-(1-(trifluoromethyl)cyclopropyl)isoxazol-3-yl)urea;
1-(3-(6, 7-dimethoxyquinazolin-4-ylthio)phenyl)-3-(5-(1-(trifluoromethyl)cyclopropyl)isoxazol-3-yl)urea;
1-(3-(2-cyanopropan-2-yl)isoxazol-5-yl)-3-(3-(6,7-dimethoxyquinazolin-4-ylthio)phenyl)urea;
1-(3-(6, 7-dimethoxyquinazolin-4-ylthio)phenyl)-3-(3-(trifluoromethyl)isoxazol-5-yl)urea;
1-(3-(7-ethoxy-6-methoxyquinazolin-4-yloxy)phenyl)-3-(3-(2-fluoropropan-2-yl)isoxazol-5-yl)urea;
1-(5-(1,3-difluoro-2-methylpropan-2-yl)isoxazol-3-yl)-3-(3-(7-ethoxy-6-methoxyquinazolin-4-yloxy)phenyl)urea;
1-(5-(1, 3-difluoro-2-methylpropan-2-yl)isoxazol-3-yl)-3-(3-(7-ethoxy-6-methoxyquinazolin-4-ylthio)phenyl)urea;
1-(3-(7-ethoxy-6-methoxyquinazolin-4-ylthio)phenyl)-3-(3-(2-fluoropropan-2-yl)isoxazol-5-yl)urea;
1-(3-(6-ethoxy-7-methoxyquinazolin-4-yloxy)phenyl)-3-(3-(2-fluoropropan-2-yl)isoxazol-5-yl)urea;
1-(5-(1,3-difluoro-2-methylpropan-2-yl)isoxazol-3-yl)-3-(3-(6-ethoxy-7-methoxyquinazolin-4-yloxy)phenyl)urea·
1-(3-(6-ethoxy-7-methoxyquinazolin-4-ylthio)phenyl)-3-(3-(2-fluoropropan-2-yl)isoxazol-5-yl)urea;

1-(5-(1,3-difluoro-2-methylpropan-2-yl)isoxazol-3-yl)-3-(3-(6-ethoxy-7-methoxyquinazolin-4-ylthio)phenyl)urea;

or a pharmaceutically acceptable salt, solvate or hydrate thereof.

7. The compound of claim 1, or a pharmaceutically acceptable salt thereof, wherein n is 2;

each R^1 is independently $-R^6OR^7$ or $-R^6OR^9OR^7$;

each R^6 is independently a direct bond, alkylene chain or alkenylene chain;

each R^7 is selected from the group consisting of hydrogen, alkyl, alkenyl, alkynyl, cycloalkyl, cycloalkylalkyl, aryl, aralkyl, heterocyclyl, heterocyclylalkyl, heteroaryl and heteroaralkyl, and

each R^9 is independently an alkylene chain or an alkenylene chain.

8. The compound of claim 1, or a pharmaceutically acceptable salt thereof, wherein X is O.

9. The compound of claim 1, or a pharmaceutically acceptable salt thereof, wherein X is S.

10. The compound of claim 1, or a pharmaceutically acceptable salt thereof, wherein R^{10} is selected from hydrogen, halo, alkyl, cyanoalkyl, haloalkyl or cycloalkyl.

11. The compound of claim 10, or a pharmaceutically acceptable salt thereof, wherein R^{10} is alkyl or haloalkyl.

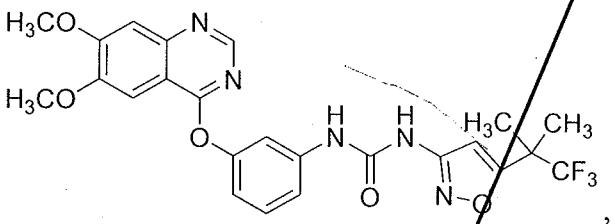
12. The compound of any of claim 11, or a pharmaceutically acceptable salt thereof, wherein R^{10} is C_4 alkyl or C_4 haloalkyl.

13. The compound of claim 1, or a pharmaceutically acceptable salt thereof, wherein R^{10} is $-C(CH_3)_3$, $-CH(CH_3)_2$, $-C(CH_3)_2CN$, $-C(CH_3)_2CF_3$, $-CF(CH_3)_2$, $-CF_2(CH_3)$, $-C(CH_3)_2CH_2OH$, $-C(CH_3)(CH_2F)_2$, $-C(CH_3)_2CH_2OCH_3$, or CF_3.

14. The compound of claim 1, or a pharmaceutically acceptable salt thereof, where n is 2 and each R^{1a} and R^{1b} are independently selected from methoxy and methoxyethoxy; or

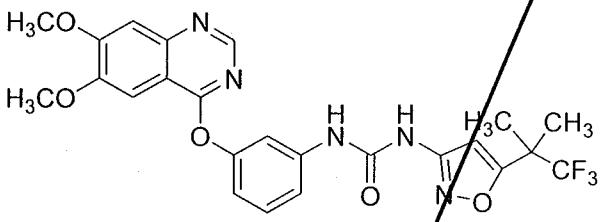
R^{1a} and R^{1b} together with the carbon atoms on which they are substituted form an ethylenedioxy group.

15. A compound which is



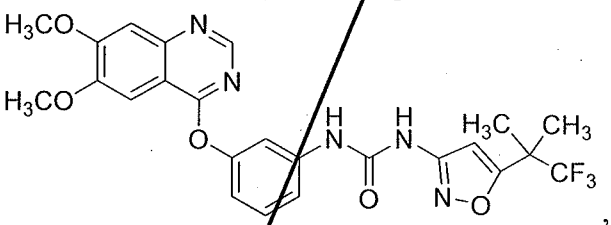
or a pharmaceutically acceptable salt thereof.

16. A pharmaceutical composition, comprising from about 1 mg to about 2000 mg of a compound that is



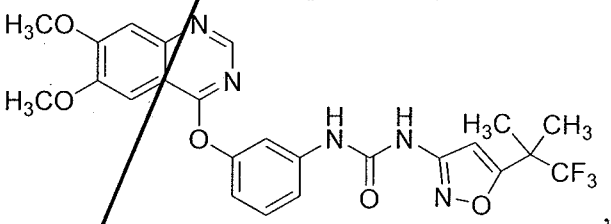
or a pharmaceutically acceptable salt thereof, and at least one pharmaceutically acceptable carrier, excipient or diluent.

17. (New) A pharmaceutical composition according to claim 16, comprising from about 10 mg to about 1000 mg of a compound that is



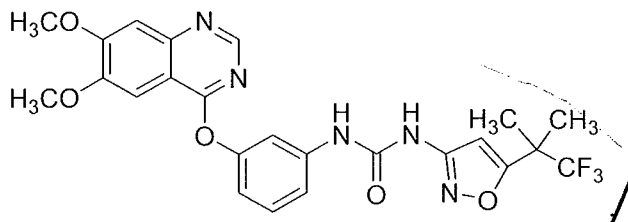
or a pharmaceutically acceptable salt thereof.

18. A pharmaceutical composition according to claim 16, comprising from about 20 mg to about 500 mg of a compound that is



or a pharmaceutically acceptable salt thereof.

19. A pharmaceutical composition according to claim 16, comprising from about 25 mg to about 250 mg of a compound that is



or a pharmaceutically acceptable salt thereof.

20. A pharmaceutical composition according to claim 16, wherein said pharmaceutical composition is in a dosage form suitable for oral administration to a patient.

21. A pharmaceutical composition according to claim 20, wherein said dosage form is a tablet, capsule, troche, lozenge, pastille, cachet, pellet, gum, bulk powder, effervescent powder, non-effervescent powder, solution, emulsion, suspension, wafer, sprinkle, elixir, or syrup.

22. A pharmaceutical composition according to claim 21 wherein said dosage form is a tablet, capsule, cachet, effervescent powder, non-effervescent powder, solution, emulsion, suspension, or syrup.

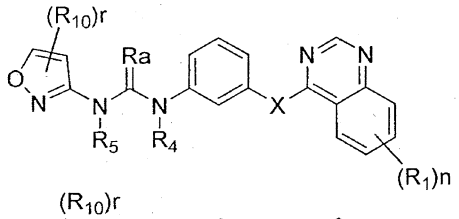
23. A pharmaceutical composition according to claim 22, wherein said dosage form is a tablet, capsule, solution, emulsion, suspension, or syrup.

24. A pharmaceutical composition according to claim 22, wherein said dosage form is a tablet or capsule.

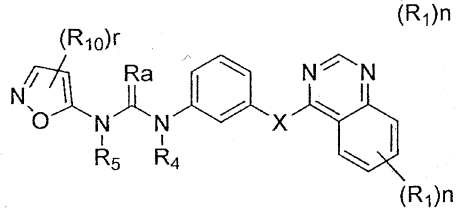
25. A pharmaceutical composition according to claim 22, wherein said dosage form is a tablet.

CLAIMS

1. A compound having formula VA or VB:



VA



VB

or a pharmaceutically acceptable salt, solvate, or hydrate thereof, wherein
r is 0, 1 or 2;
X is O or S;
n is 1 to 4
R^a is O;
R^4 and R^5 are each hydrogen;
R^{10} is independently selected from halo, haloalkyl, alkyl, cycloalkyl, aryl, heterocyclyl, and heteroaryl where the alkyl group is optionally substituted with 1 or 2 groups selected from halo and cyano, and where the cycloalkyl, aryl and heteroaryl group is optionally substituted with 1 or 2 groups selected from halo, cyano, alkyl and haloalkyl; and
each R^1 is absent, or is independently selected from
halo, nitro, alkyl, cycloalkylalkyl, heterocyclylalkyl, aralkyl, heteroaryl, heteroaralkyl, cycloalkylcarbonylamino, $—R^6OR^7$, $—R^6OR^9OR^7$, $—R^6OR^9N(R^7)_2$, or
any two adjacent R^1 groups together form an alkylenedioxy group;
each R^6 is independently a direct bond, alkylene chain or alkenylene chain;
each R^7 is independently selected from hydrogen, alkyl, alkenyl, alkynyl, cycloalkyl, cycloalkylalkyl, aryl, aralkyl, heterocyclyl, heterocyclylalkyl, heteroaryl and heteroaralkyl, or
two R^7 groups together with the N atom to which they are attached form a heterocyclyl or heteroaryl; or
each R^9 is independently an alkylene chain or an alkenylene chain; and wherein
a cycloalkyl group is a monovalent monocyclic or bicyclic hydrocarbon radical consisting solely of carbon and hydrogen atoms, having from three to ten carbon

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atoms, and which is saturated and attached to the rest of the molecule by a single bond;

a heterocyclyl group is a 3 to 15 membered non-aromatic ring which consists of at least one carbon atom and from one to five heteroatoms selected from a group consisting of nitrogen, oxygen and sulfur; and

a heteroaryl group is a monocyclic or multicyclic 5 to 20 membered aromatic ring system, where 1 to 5 of the atoms in the ring system is nitrogen, oxygen or sulfur.

2. The compound of claim 1, or a pharmaceutically acceptable salt thereof, wherein each R^1 is selected from the group consisting of $—R^6OR^7$, $—R^6OR^9OR^7$, $—R^6OR^9N(R^7)_2$; and

each R^6 is independently a direct bond, alkylene chain or alkenylene chain;

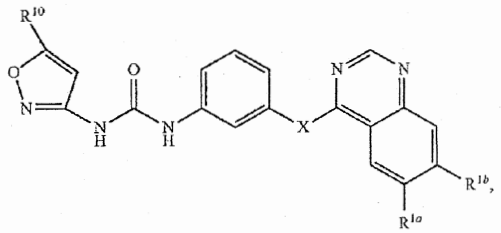
each R^7 is independently selected from hydrogen, alkyl, alkenyl, alkynyl, cycloalkyl, cycloalkylalkyl, aryl, aralkyl, heterocyclyl, heterocyclylalkyl, heteroaryl and heteroaralkyl, or

two R^7 groups together with the N atom to which they are attached form a heterocyclyl or heteroaryl; and

each R^9 is independently an alkylene chain or an alkenylene chain.

3. The compound of claim 1 having formula XVII:

XVII



or a pharmaceutically acceptable salt, solvate or hydrate thereof,

wherein X is O or S;

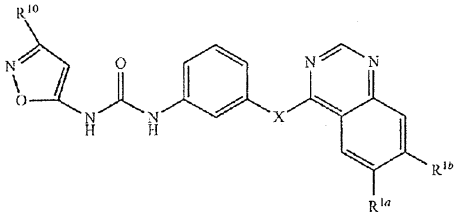
R^{1a} and R^{1b} are independently selected from alkoxy, alkoxyalkoxy, or alkylsulfonylalkoxy; or

two R^{1a} and R^{1b} groups together form an alkylenedioxy group; and

R^{10} is hydrogen, halo, alkyl, haloalkyl, aryl, heterocyclyl, heteroaryl, cycloalkyl or cycloalkylalkyl.

4. The compound of claim 1 having formula XIX:

XIX



or a pharmaceutically acceptable salt, solvate or hydrate thereof,

wherein X is O or S;

R^{1a} and R^{1b} are independently selected from methoxy, methoxyethoxy, or methylsulfonylpropyloxy; or

two R^{1a} and R^{1b} groups together with the carbon atoms on which they are substituted form an ethylenedioxy group; and

R^{10} is hydrogen, halo, alkyl, haloalkyl, aryl, heterocyclyl, heteroaryl, cycloalkyl or cycloalkylalkyl.

5. The compound selected from

1-(5-tert-butylisoxazol-3-yl)-3-(3-(6, 7-dimethoxyquinazolin-4-yloxy)phenyl)urea;
1-(5-tert-butylisoxazol-3-yl)-3-(3-(6-methoxyquinazolin-4-yloxyphenyl)urea;
1-(5-tert-butylisoxazol-3-yl)-3-(3-(7-methoxyquinazolin-4-yloxy)phenyl)urea;
1-(5-tert-butylisoxazol-3-yl)-3-(3-(6,7-difluoroquinazolin-4-yloxy)phenyl)urea;
1-(5-tert-butylisoxazol-3-yl)-3-(3-(5-methylquinazolin-4-yloxy)phenyl)urea;
1-(5-tert-butylisoxazol-3-yl)-3-[3-(7-ethoxy-6-methoxyquinazolin-4-yloxy)phenyl]urea hydrochloride;
1-(5-tert-butylisoxazol-3-yl)-3-{3-[6-methoxy-7-(2-methoxyethoxy)quinazolin-4-yloxy]phenyl}urea hydrochloride;
1-(5-tert-butylisoxazol-3-yl)-3-(3-(6-methylquinazolin-4-yloxy)phenyl)urea;
1-(5-tert-butylisoxazol-3-yl)-3-(3-(6,7-dimethoxyquinazolin-4-yloxy)-4-fluorophenyl)urea;
1-(5-tert-butylisoxazol-3-yl)-3-(4-chloro-3-(6, 7-dimethoxyquinazolin-4-yloxy)phenyl)urea;
1-(5-tert-butylisoxazol-3-yl)-3-(3-(6-ethoxy-7-methoxyquinazolin-4-yloxy)phenyl)urea;
1-{3-[6,7-bis(2-methoxyethoxy)quinazolin-4-yloxy]phenyl}-3-(5-tert-butylisoxazol-3-yl)urea hydrochloride;
1-(5-tert-Butylisoxazol-3-yl)-3-[3-(6, 7-diethoxyquinazolin-4-yloxy)phenyl]urea hydrochloride;
1-(5-tert-butylisoxazol-3-yl)-3-[3-(7,8-dihydro-[1,4]dioxino[2,3-g] quinazolin-4-yloxy)phenyl]urea hydrochloride;
1-(5-tert-butylisoxazol-3-yl)-3-{3-[7-methoxy-6-(2-methoxyethoxy)quinazolin-4-yloxy]phenyl}urea hydrochloride;
1-(5-tert-butylisoxazol-3-yl)-3-(3-(6-(2-methoxyethoxy)quinazolin-4-yloxy)phenyl)urea

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1-(5-tert-Butylisoxazol-3-yl)-3-(3-(7-methoxy-6-(3-(methylsulfonyl)propoxy)quinazolin-4-ylthio)phenyl)urea;
1-(3-(2-fluoropropan-2-yl)isoxazol-5-yl)-3-(3-(7-methoxy-6-(3-(methylsulfonyl)propoxy) quinazolin-4-yloxy)phenyl)urea;
1-(5-tert-butylisoxazol-3-yl)-3-(3-(7-(2-methoxyethoxy)quinazolin-4-yloxy)phenyl)urea;
1-(5-tert-butylisoxazol-3-yl)-3-(3-(7-methoxy-6-(3-(methylsulfonyl)propoxy)quinazolin-4-ylthio)phenyl)urea;
1-(5-tert-butylisoxazol-3-yl)-3-(3-(7-methoxy-6-(2-methoxyethoxy)quinazolin-4-ylthio)phenyl)urea;
1-(5-tert-butylisoxazol-3-yl)-3-(3-(6, 7-dimethoxyquinazolin-4-ylthio)phenyl)urea;
1-(5-tert-butylisoxazol-3-yl)-3-(3-(6, 7-difluoroquinazolin-4-ylthio)phenyl)urea;
1-(5-tert-butylisoxazol-3-yl)-3-(3-(7-methoxyquinazolin-4-ylthio)phenyl)urea;
1-(5-tert-butylisoxazol-3-yl)-3-(3-(6-methoxyquinazolin-4-ylthio)phenyl)urea;
1-(5-tert-Butylisoxazol-3-yl)-3-[3-(7-ethoxy-6-methoxyquinazolin-4-ylthio)phenyl]urea;
1-(5-tert-butylisoxazol-3-yl)-3-[3-(6, 7-diethoxyquinazolin-4-ylthio)phenyl]urea;
1-(5-tert-butylisoxazol-3-yl)-3-{3-[6-methoxy-7-(2-methoxyethoxy)quinazolin-4-ylthio]phenyl}urea hydrochloride;
1-{3-[6,7-bis(2-methoxyethoxy)quinazolin-4-ylthio]phenyl}-3-(5-tert-butylisoxazol-3-yl)urea hydrochloride;
1-(5-tert-butylisoxazol-3-yl)-3-[3-(7,8-dihydro-[1,4]dioxino[2,3-g]quinazolin-4-ylthio) phenyl]urea hydrochloride;
1-(5-tert-butylisoxazol-3-yl)-3-{3-[7-methoxy-5-(tetrahydro-2H-pyran-4-ylthio)quinazolin-4-yloxy]phenyl}urea;
1-(5-tert-butylisoxazol-3-yl)-3-(3-(6-ethoxy-7-methoxyquinazolin-4-ylthio)phenyl)urea;
1-(5-tert-butylisoxazol-3-yl)-3-(3-(7-methoxy-6-(3-(methylsulfonyl)propoxy)quinazolin-4-ylthio)phenyl)urea;
1-(5-tert-butylisoxazol-3-yl)-3-(3-(6-(2-methoxyethoxy)quinazolin-4-ylthio)phenyl)urea;
1-(5-tert-butylisoxazol-3-yl)-3-(3-(7-methoxy-6-(2-(methylsulfonyl)ethoxy)quinazolin-4-ylthio)phenyl)urea;
1-(5-tert-butylisoxazol-3-yl)-3-{3-[6-(5-{[2-(methylsulfonyl)ethylamino]methyl}furan-2-yl)quinazolin-4-yloxy]phenyl}urea;
1-(5-tert-butylisoxazol-3-yl)-3-{3-[7-methoxy-5-(tetrahydro-2H-pyran-4-yloxy)quinazolin-4-yloxy]phenyl}urea;
1-(5-tert-butylisoxazol-3-yl)-3-(3-(7-hydroxy-6-methoxyquinazolin-4-yloxy)phenyl)urea;
1-(5-tert-butylisoxazol-3-yl)-3-(3-(6-hydroxy-7-methoxyquinazolin-4-yloxy)phenyl)urea;
1-(3-(6, 7-dimethoxyquinazolin-4-yloxy)phenyl)-3-(5-phenylisoxazol-3-yl)urea;
1-(3-(6, 7-dimethoxyquinazolin-4-yloxy)phenyl)-3-(3-isopropylisoxazol-5-yl)urea;
1-(3-(6, 7-dimethoxyquinazolin-4-yloxy)phenyl)-3-(3-(tetrahydro-2H-pyran-4-yl)isoxazol-5-yl)urea;

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1-(3-cyclopropylisoxazol-5-yl)-3-(3-(6, 7-dimethoxyquinazolin-4-yloxy)phenyl)urea;
1-(3-(2-cyanopropan-2-yl)isoxazol-5-yl)-3-(3-(6,7-dimethoxyquinazolin-4-yloxy)phenyl)urea;
1-(3-(6, 7-dimethoxyquinazolin-4-yloxy)phenyl)-3-(3-(2-fluoropropan-2-yl)isoxazol-5-yl)urea;
1-(3-(6, 7-dimethoxyquinazolin-4-yloxy)phenyl)-3-(5-(1-methylcyclopropyl)isoxazol-3-yl)urea;
1-(3-(6, 7-dimethoxyquinazolin-4-yloxy)phenyl)-3-(5-(1-hydroxy-2-methylpropan-2-yl)isoxazol-3-yl)urea;
1-(3-tert-butylisoxazol-5-yl)-3-(3-(6,7-dimethoxyquinazolin-4-yloxy)phenyl)urea;
1-(3-(6, 7-dimethoxyquinazolin-4-yloxy)phenyl)-3-(5-isopropylisoxazo1-3-yl)urea;
1-(3-(6, 7-dimethoxyquinazolin-4-ylthio)phenyl)-3-(5-isopropylisoxazo1-3-yl)urea;
1-(5-cyclopentylisoxazol-3-yl)-3-(3-(6,7-dimethoxyquinazolin-4-yloxy)phenyl)urea;
1-(3-(6, 7-dimethoxyquinazolin-4-yloxy)phenyl)-3-(5-(2-fluoropropan-2-yl)isoxazol-3-yl)urea;
1-(3-(1, 1-difluoroethyl)isoxazol-5-yl)-3-(3-(6,7-dimethoxyquinazolin-4-yloxy)phenyl)urea;
1-(3-(6, 7-dimethoxyquinazolin-4-yloxy)phenyl)-3-(3-(1-(trifluoromethyl)cyclobutyl)isoxazol-5-yl)urea;
1-(3-(6, 7-dimethoxyquinazolin-4-ylthio)phenyl)-3-(3-(1-(trifluoromethyl)cyclobutyl)isoxazol-5-yl)urea;
1-[3-(1,3-difluoro-2-methylpropan-2-yl)isoxazol-5-yl]-3-[3-(6, 7-dimethoxyquinazolin-4-yloxy]phenyl)urea;
1-[3-(1,3-difluoro-2-methylpropan-2-yl)isoxazol-5-yl]-3-[3-(6, 7-dimethoxyquinazolin-4-ylthio]phenyl)urea;
1-[5-(1,3-difluoro-2-methylpropan-2-yl)isoxazol-3-yl]-3-[3-(6, 7-dimethoxyquinazolin-4-yloxy)phenyl]urea;
1-(3-cyclopentylisoxazol-5-yl)-3-(3-(6,7-dimethoxyquinazolin-4-yloxy)phenyl)urea;
1-(3-(6, 7-dimethoxyquinazolin-4-ylthio)phenyl)-3-(3-(2-fluoropropan-2-yl)isoxazol-5-yl)urea;
1-[5-(1,3-difluoro-2-methylpropan-2-yl)isoxazol-3-yl]-3-[3-(6, 7-dimethoxyquinazolin-4-ylthio)phenyl]urea;
1-(5-cyclopentylisoxazol-3-yl)-3-(3-(6,7-dimethoxyquinazolin-4-ylthio)phenyl)urea;
1-(3-tert-butylisoxazol-5-yl)-3-(3-(6-methoxy-7-(2-methoxyethoxy)quinazolin-4-yloxy)phenyl)urea;
1-(3-(6-Methoxy-7-(2-methoxyethoxy)quinazolin-4-yloxy)phenyl)-3-(5-phenylisoxazol-3-yl)urea;
1-(5-isopropylisoxazol-3-yl)-3-(3-(6-methoxy-7-(2-methoxyethoxy)quinazolin-4-yloxy)phenyl)urea;
1-(3-cyclopentylisoxazol-5-yl)-3-(3-(6-methoxy-7-(2-methoxyethoxy)quinazolin-4-yl oxy)phenyl)urea;
1-(3-(1, 1-difluoroethyl)isoxazol-5-yl)-3-(3-(6-methoxy-7-(2-methoxyethoxy)quinazolin-4-yloxy)phenyl)urea;
1-[5-(1,3-difluoro-2-methylpropan-2-yl)isoxazol-3-yl]-3-{3-[6-methoxy-7-(2-methoxyethoxy)quinazolin-4-yloxy]phenyl}urea;

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1-(3-cyclopropylisoxazol-5-yl)-3-(3-(6-methoxy-7-(2-methoxyethoxy)quinazolin-4-yl oxy)phenyl)urea;
1-(3-isopropylisoxazol-5-yl)-3-(3-(6-methoxy-7-(2-methoxyethoxy)quinazolin-4-yloxy)phenyl)urea;
1-(3-(6-methoxy-7-(2-methoxyethoxy)quinazolin-4-yloxy)phenyl)-3-(3-(tetrahydro-2H-pyran-4-yl)isoxazol-5-yl)urea;
1-(3-(2-fluoropropan-2-yl)isoxazol-5-yl)-3-(3-(6-methoxy-7-(2-methoxyethoxy)quinazolin-4-yloxy)phenyl)urea;
1-(5-cyclopentylisoxazol-3-yl)-3-(3-(6-methoxy-7-(2-methoxyethoxy)quinazolin-4-yloxy)phenyl)urea;
1-(3-(6-methoxy-7-(2-methoxyethoxy)quinazolin-4-yloxy)phenyl)-3-(3-(trifluoromethyl)isoxazol-5-yl)urea;
1-[5-(1,3-difluoro-2-methylpropan-2-yl)isoxazol-3-yl]-3-{3-[6-methoxy-7-(2-methoxyethoxy)quinazolin-4-ylthio]phenyl}urea;
1-(5-isopropylisoxazol-3-yl)-3-(3-(6-methoxy-7-(2-methoxyethoxy)quinazolin-4-ylthio)phenyl)urea;
1-(3-(2-fluoropropan-2-yl)isoxazol-5-yl)-3-(3-(6-methoxy-7-(2-methoxyethoxy)quinazolin-4-ylthio)phenyl)urea;
1-(5-cyclopentylisoxazol-3-yl)-3-(3-(6-methoxy-7-(2-methoxyethoxy)quinazolin-4-ylthio)phenyl)urea;
1-(3-(6, 7-dimethoxyquinazolin-4-yloxy)phenyl)-3-(3-(trifluoromethyl)isoxazol-5-yl)urea;
1-(3-(6,7-dimethoxyquinazolin-4-yloxy)phenyl)-3-(3-(1-hydroxy-2-methylpropan-2-yl)isoxazol-5-yl)urea;
1-(3-(2-fluoropropan-2-yl)isoxazol-5-yl)-3-(3-(7-hydroxy-6-methoxyquinazolin-4-yloxy)phenyl)urea;
1-(3-(2-fluoropropan-2-yl)isoxazol-5-yl)-3-(3-(6-hydroxy-7-methoxyquinazolin-4-yloxy)phenyl)urea;
1-(3-(6,7-dimethoxyquinazolin-4-yloxy)phenyl)-3-(5-(1,1, 1-trifluoro-2-methylpropan-2-yl)isoxazol-3-yl)urea;
1-(3-(6-ethoxy-7-methoxyquinazolin-4-yloxy)phenyl)-3-(5-(1, 1, 1-trifluoro-2-methylpropan-2-yl)isoxazol-3-yl)urea;
1-(3-(6,7-dimethoxyquinazolin-4-ylthio)phenyl)-3-(5-(1, 1, 1-trifluoro-2-methylpropan-2-yl)isoxazol-3-yl)urea;
1-(3-(6-ethoxy-7-methoxyquinazolin-4-ylthio)phenyl)-3-(5-(1, 1, 1-trifluoro-2-methylpropan-2-yl)isoxazol-3-yl)urea;
1-(3-(7-hydroxy-6-methoxyquinazolin-4-yloxy)phenyl)-3-(5-(1,1, 1-trifluoro-2-methylpropan-2-yl)isoxazol-3-yl)urea;
1-(3-(6-hydroxy-7-methoxyquinazolin-4-yloxy)phenyl)-3-(5-(1, 1, 1-trifluoro-2-methylpropan-2-yl)isoxazol-3-yl)urea;

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1-(3-(6,7-dimethoxyquinazolin-4-yloxy)-2-fluorophenyl)-3-(5-(1, 1,1-trifluoro-2-methylpropan-2-yl)isoxazo1-3-yl)urea;
1-(3-(6, 7-dimethoxyquinazolin-4-yloxy)-4-fluorophenyl)-3-(5-(1, 1, 1-trifluoro-2-methylpropan-2-yl)isoxazol-3-yl)urea;
1-(3-(6, 7-dimethoxyquinazolin-4-yloxy)phenyl)-3-(3-(1, 1, 1-trifluoro-2-methylpropan-2-yl)isoxazol-5-yl)urea;
1-(3-(6, 7-dimethoxyquinazolin-4-ylthio)phenyl)-3-(3-(1, 1, 1-trifluoro-2-methylpropan-2-yl)isoxazol-5-yl)urea; and
1-(5-(6, 7-dimethoxyquinazolin-4-yl oxy)-2, 4-difluoropheny1)-3-(3-(2-fluoropropan-2-yl)isoxazol-5-yl)urea;
1-(5-tert-butylisoxazol-3-yl)-3-(5-(6, 7-dimethoxyquinazolin-4-yloxy)-2,4-difluorophenyl)urea;
1-(5-tert-butylisoxazol-3-yl)-3-(3-(6, 7-dimethoxyquinazolin-4-yloxy)-2-methylphenyl)urea;
1-(3-(6, 7-dimethoxyquinazolin-4-yloxy)-2-methylphenyl)-3-(5-(2-fluoropropan-2-yl)isoxazol-3-yl)urea;
1-(3-(6, 7-dimethoxyquinazolin-4-yloxy)-4-fluoropheny1)-3-(3-(2-fluoropropan-2-yl)isoxazol-5-yl)urea;
1-(5-(1,3-difluoro-2-methylpropan-2-yl)isoxazol-3-yl)-3-(3-(6, 7-dimethoxyquinazolin-4-yloxy)-4-fluorophenyl)urea;
1-(3-(6, 7-dimethoxyquinazolin-4-yloxy)-2-fuorophenyl)-3-(3-(2-fluoropropan-2-yl)isoxazol-5-yl)urea;
1-(5-(1,3-difluoro-2-methylpropan-2-yl)isoxazol-3-yl)-3-(3-(6, 7-dimethoxyquinazolin-4-yloxy)-2-fluorophenyl)urea;
1-(5-tert-butylisoxazol-3-yl)-3-(2-chloro-5-(6, 7-dimethoxyquinazolin-4-yloxy)phenyl)urea;
1-(5-tert-butylisoxazol-3-yl)-3-(5-(6,7-dimethoxyquinazolin-4-yloxy)-2-fluorophenyl)urea;
1-(3-(6, 7-dimethoxyquinazolin-4-yloxy)phenyl)-3-(5-(1-(trifluoromethyl)cyclopropyl)isoxazol-3-yl)urea;
1-(3-(6, 7-dimethoxyquinazolin-4-ylthio)phenyl)-3-(5-(1-(trifluoromethyl)cyclopropyl)isoxazol-3-yl)urea;
1-(3-(2-cyanopropan-2-yl)isoxazol-5-yl)-3-(3-(6,7-dimethoxyquinazolin-4-ylthio)phenyl)urea;
1-(3-(6, 7-dimethoxyquinazolin-4-ylthio)phenyl)-3-(3-(trifluoromethyl)isoxazol-5-yl)urea;
1-(3-(7-ethoxy-6-methoxyquinazolin-4-yloxy)phenyl)-3-(3-(2-fluoropropan-2-yl)isoxazol-5-yl)urea;
1-(5-(1,3-difluoro-2-methylpropan-2-yl)isoxazol-3-yl)-3-(3-(7-ethoxy-6-methoxyquinazolin-4-yloxy)phenyl)urea;
1-(5-(1, 3-difluoro-2-methylpropan-2-yl)isoxazol-3-yl)-3-(3-(7-ethoxy-6-methoxyquinazolin-4-ylthio)phenyl)urea;
1-(3-(7-ethoxy-6-methoxyquinazolin-4-ylthio)phenyl)-3-(3-(2-fluoropropan-2-yl)isoxazol-5-yl)urea;

1-(3-(6-ethoxy-7-methoxyquinazolin-4-yloxy)phenyl)-3-(3-(2-fluoropropan-2-yl)isoxazol-5-yl)urea;
1-(5-(1,3-difluoro-2-methylpropan-2-yl)isoxazol-3-yl)-3-(3-(6-ethoxy-7-methoxyquinazolin-4-yloxy)phenyl)urea·
1-(3-(6-ethoxy-7-methoxyquinazolin-4-ylthio)phenyl)-3-(3-(2-fluoropropan-2-yl)isoxazol-5-yl)urea;
1-(5-(1,3-difluoro-2-methylpropan-2-yl)isoxazol-3-yl)-3-(3-(6-ethoxy-7-methoxyquinazolin-4-ylthio)phenyl)urea;
or a pharmaceutically acceptable salt, solvate or hydrate thereof.

6. The compound of claim 1, or a pharmaceutically acceptable salt thereof, wherein n is 2;
each R^1 is independently $-R^6OR^7$ or $-R^6OR^9OR^7$;
each R^6 is independently a direct bond, alkylene chain or alkenylene chain;
each R^7 is selected from the group consisting of hydrogen, alkyl, alkenyl, alkynyl, cycloalkyl, cycloalkylalkyl, aryl, aralkyl, heterocyclyl, heterocyclylalkyl, heteroaryl and heteroaralkyl, and
each R^9 is independently an alkylene chain or an alkenylene chain.

7. The compound of claim 1, or a pharmaceutically acceptable salt thereof, wherein X is O.

8. The compound of claim 1, or a pharmaceutically acceptable salt thereof, wherein X is S.

9. The compound of claim 1, or a pharmaceutically acceptable salt thereof, wherein R^{10} is selected from hydrogen, halo, alkyl, cyanoalkyl, haloalkyl or cycloalkyl.

10. The compound of claim 1, or a pharmaceutically acceptable salt thereof, wherein R^{10} is alkyl or haloalkyl.

11. The compound of any of claim 10, or a pharmaceutically acceptable salt thereof, wherein R^{10} is C_4 alkyl or C_4 haloalkyl.

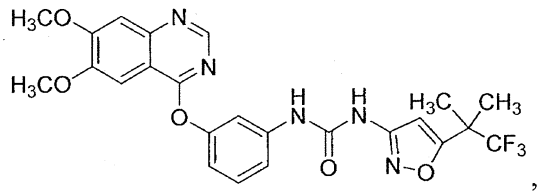
12. The compound of claim 1, or a pharmaceutically acceptable salt thereof, wherein R^{10} is $-C(CH_3)_3$, $-CH(CH_3)_2$, $-C(CH_3)_2CN$, $-C(CH_3)_2CF_3$, $-CF(CH_3)_2$, $-CF_2(CH_3)$, $-C(CH_3)_2CH_2OH$, $-C(CH_3)(CH_2F)_2$, $-C(CH_3)_2CH_2OCH_3$, or CF_3.

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13. The compound of claim 1, or a pharmaceutically acceptable salt thereof, where n is 2 and each R^{1a} and R^{1b} are independently selected from methoxy and methoxyethoxy; or

R^{1a} and R^{1b} together with the carbon atoms on which they are substituted form an ethylenedioxy group.

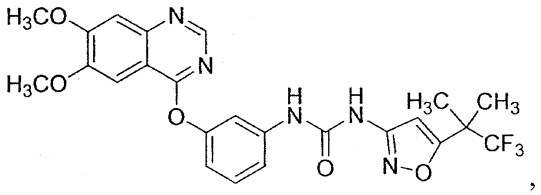
14. A compound which is



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or a pharmaceutically acceptable salt thereof.

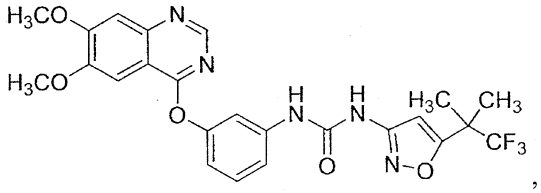
15. A pharmaceutical composition, comprising from about 1 mg to about 2000 mg of a compound that is



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or a pharmaceutically acceptable salt thereof, and at least one pharmaceutically acceptable carrier, excipient or diluent.

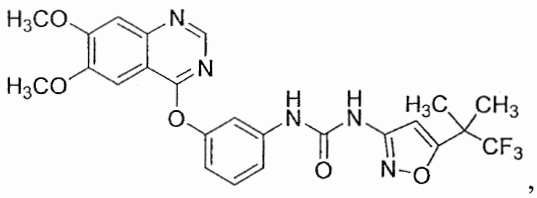
16. (New) A pharmaceutical composition according to claim 15, comprising from about 10 mg to about 1000 mg of a compound that is



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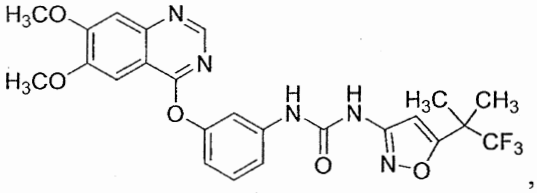
or a pharmaceutically acceptable salt thereof.

17. A pharmaceutical composition according to claim 15, comprising from about 20 mg to about 500 mg of a compound that is



or a pharmaceutically acceptable salt thereof.

18. A pharmaceutical composition according to claim 15, comprising from about 25 mg to about 250 mg of a compound that is



or a pharmaceutically acceptable salt thereof.

19. A pharmaceutical composition according to claim 15, wherein said pharmaceutical composition is in a dosage form suitable for oral administration to a patient.

20. A pharmaceutical composition according to claim 19, wherein said dosage form is a tablet, capsule, troche, lozenge, pastille, cachet, pellet, gum, bulk powder, effervescent powder, non-effervescent powder, solution, emulsion, suspension, wafer, sprinkle, elixir, or syrup.

21. A pharmaceutical composition according to claim 20 wherein said dosage form is a tablet, capsule, cachet, effervescent powder, non-effervescent powder, solution, emulsion, suspension, or syrup.

22. A pharmaceutical composition according to claim 21, wherein said dosage form is a tablet, capsule, solution, emulsion, suspension, or syrup.

23. A pharmaceutical composition according to claim 21, wherein said dosage form is a tablet or capsule.

24. A pharmaceutical composition according to claim 21, wherein said dosage form is a tablet.