Discovery of 2-(1*H*-indol-5-ylamino)-6-(2,4,-difluorophenylsulfonyl)-8-methylpyrido[2,3-*d*] pyrimidin-7(8*H*)-one (7ao) as a Potent Selective Inhibitor of Polo Like Kinase 2 (PLK2)

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Author Contributions

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Contents:

Table 1. Kinase inhibition profile of **7ao** (Reaction Biology Corp)

Kinase:	**7ao** IC50 (μM)
ABL1	>10
ABL2/ARG	>10
ACK1	>10
AKT1	>10
AKT2	>10
AKT3	>10
ALK	>10
ALK1/ACVRL1	>10
ALK3/BMPR1A	>10
ALK5/TGFBR1	>10
ARAF	>10
ARK5/NUAK1	>10
ASK1/MAP3K5	>10
Aurora A	>10
Aurora B	>10
Aurora C	>10
AXL	>10
BLK	>10
BMPR2	>10
BMX/ETK	>10
BRAF	>10
BRK	>10
BRSK1	>10
BRSK2	>10
BTK	>10
c-Kit	>10
c-MER	>10
c-MET	>10
c-Src	>10
CAMK1a	>10
CAMK1b	>10
CAMK1d	>10
CAMK1g	>10
CAMK2a	>10
CAMK2b	>10
CAMK2d	>10
CAMK2g	>10
CAMK4	>10
CAMKK1	>10
CAMKK2	>10
CDC7/DBF4	>10
CDK1/cyclin A	>10

CDK1/cyclin B	>10
CDK1/cyclin E	>10
CDK16/cyclin Y (PCTAIRE)	>10
CDK2/cyclin A	>10
CDK2/Cyclin A1	>10
CDK2/cyclin E	>10
CDK3/cyclin E	>10
CDK4/cyclin D1	>10
CDK4/cyclin D3	>10
CDK5/p25	>10
CDK5/p35	>10
CDK6/cyclin D1	>10
CDK6/cyclin D3	>10
CDK7/cyclin H	>10
CDK9/cyclin K	>10
CDK9/cyclin T1	>10
CHK1	>10
CHK2	>10
CK1a1	>10
CK1d	>10
CK1epsilon	>10
CK1g1	>10
CK1g2	>10
CK1g3	>10
CK2a	>10
CK2a2	>10
CLK1	>10
CLK2	>10
CLK3	>10
CLK4	>10
COT1/MAP3K8	>10
CSK	>10
CTK/MATK	>10
DAPK1	>10
DAPK2	>10
DCAMKL1	>10
DCAMKL2	>10
DDR1	>10
DDR2	>10
DLK/MAP3K12	>10
DMPK	>10
DMPK2	>10
DRAK1/STK17A	>10
DYRK1/DYRK1A	>10
DYRK1B	>10

DYRK2	>10
DYRK3	>10
DYRK4	>10
EGFR	>10
EPHA1	>10
EPHA2	>10
EPHA3	>10
EPHA4	>10
EPHA5	>10
EPHA6	>5.0
EPHA7	>10
EPHA8	>10
EPHB1	>10
EPHB2	>10
EPHB3	>10
EPHB4	>10
ERBB2/HER2	>10
ERBB4/HER4	>10
ERK1	>10
ERK2/MAPK1	>10
ERK5/MAPK7	>10
ERK7/MAPK15	>10
FAK/PTK2	>10
FER	>10
FES/FPS	>10
FGFR1	>5.0
FGFR2	>10
FGFR3	>5.0
FGFR4	>10
FGR	>10
FLT1/VEGFR1	>10
FLT3	>5.0
FLT4/VEGFR3	>10
FMS	>10
FRK/PTK5	>10
FYN	>10
GCK/MAP4K2	>10
GLK/MAP4K3	>10
GRK1	>10
GRK2	>10
GRK3	>10
GRK4	>10
GRK5	>10
GRK6	>10
GRK7	>10

GSK3a	>5.0
GSK3b	NC
Haspin	>10
HCK	>10
HGK/MAP4K4	>10
HIPK1	>10
HIPK2	>10
HIPK3	>10
HIPK4	>10
HPK1/MAP4K1	>10
IGF1R	>10
IKKa/CHUK	>10
IKKb/IKBKB	>10
IKKe/IKBKE	>10
IR	>10
IRAK1	>10
IRAK4	>10
IRR/INSRR	>10
ITK	>10
JAK1	>10
JAK2	>10
JAK3	>10
JNK1	>10
JNK2	>10
JNK3	>10
KDR/VEGFR2	>10
KHS/MAP4K5	>10
LATS1	>10
LATS2	>10
LCK	>10
LCK2/ICK	>10
LIMK1	>10
LIMK2	>10
LKB1	>10
LOK/STK10	>10
LRRK2	>10
LYN	>10
LYN B	>10
MAPKAPK2	>10
MAPKAPK3	>10
MAPKAPK5/PRAK	>10
MARK1	>10
MARK2/PAR-1Ba	>10
MARK3	>10
MARK4	>10

MEK1	>10
MEK2	>10
MEK3	>10
MEKK1	>10
MEKK2	>10
MEKK3	>10
MELK	>10
MINK/MINK1	>10
MKK4	>10
MKK6	>10
MLCK/MYLK	>10
MLCK2/MYLK2	>10
MLK1/MAP3K9	>10
MLK2/MAP3K10	>10
MLK3/MAP3K11	>10
MNK1	>10
MNK2	>10
MRCKa/CDC42BPA	>10
MRCKb/CDC42BPB	>10
MSK1/RPS6KA5	>10
MSK2/RPS6KA4	>10
MSSK1/STK23	>10
MST1/STK4	>10
MST2/STK3	>10
MST3/STK24	>10
MST4	>10
MUSK	>10
MYLK3	>10
MYO3b	>10
NEK1	0.63
NEK11	>10
NEK2	1.83
NEK3	>10
NEK4	>10
NEK5	4.42
NEK6	>10
NEK7	>10
NEK9	>5.0
NLK	>10
OSR1/OXSR1	>10
P38a/MAPK14	>10
P38b/MAPK11	>10
P38d/MAPK13	>10
P38g	>10
p70S6K/RPS6KB1	>10

p70S6Kb/RPS6KB2	>10
PAK1	>10
PAK2	>10
PAK3	>10
PAK4	>10
PAK5	>10
PAK6	>10
PASK	>10
PBK/TOPK	>10
PDGFRa	>10
PDGFRb	>10
PDK1/PDPK1	>10
PHKg1	>10
PHKg2	>10
PIM1	>10
PIM2	>10
PIM3	>10
PKA	>10
PKAcb	>10
PKAcg	>10
PKCa	>10
PKCb1	>10
PKCb2	>10
PKCd	>10
PKCepsilon	>10
PKCeta	>10
PKCg	>10
PKCiota	>10
PKCmu/PRKD1	>10
PKCnu/PRKD3	>10
PKCtheta	>10
PKCzeta	>10
PKD2/PRKD2	>10
PKG1a	>10
PKG1b	>10
PKG2/PRKG2	>10
PKN1/PRK1	>10
PKN2/PRK2	>10
PKN3/PRK3	>10
PLK1	>10
PLK2	0.374
PLK3	>10
PLK4/SAK	>10
PRKX	>10
PYK2	>10

RAF1	>10
RET	>10
RIPK2	>10
RIPK3	>10
RIPK5	>10
ROCK1	>10
ROCK2	>10
RON/MST1R	>10
ROS/ROS1	>10
RSK1	>5.0
RSK2	>10
RSK3	>10
RSK4	>10
SGK1	>10
SGK2	>10
SGK3/SGKL	>10
SIK1	>10
SIK2	>10
SIK3	>10
SLK/STK2	>10
SNARK/NUAK2	>10
SRMS	>10
SRPK1	>10
SRPK2	>10
SSTK/TSSK6	>10
STK16	>10
STK22D/TSSK1	>10
STK25/YSK1	>10
STK32B/YANK2	>10
STK32C/YANK3	>10
STK33	>10
STK38/NDR1	>10
STK38L/NDR2	>10
STK39/STLK3	>10
SYK	>10
TAK1	>10
TAOK1	>10
TAOK2/TAO1	>10
TAOK3/JIK	>10
TBK1	>10
TEC	>10
TESK1	>10
TGFBR2	>10
TIE2/TEK	>10
TLK1	>10

TLK2	>10
TNIK	>5.0
TNK1	>10
TRKA	>5.0
TRKB	>10
TRKC	>10
TSSK2	>10
TSSK3/STK22C	>5.0
TTBK1	>10
TTBK2	>10
TXK	>10
TYK1/LTK	>10
TYK2	>10
TYRO3/SKY	>10
ULK1	>10
ULK2	>10
ULK3	>10
VRK1	>10
VRK2	>10
WEE1	>10
WNK1	>10
WNK2	>10
WNK3	>10
YES/YES1	>10
ZAK/MLTK	>10
ZAP70	>10
ZIPK/DAPK3	>10

Figure 1. Kinome map for **7ao**

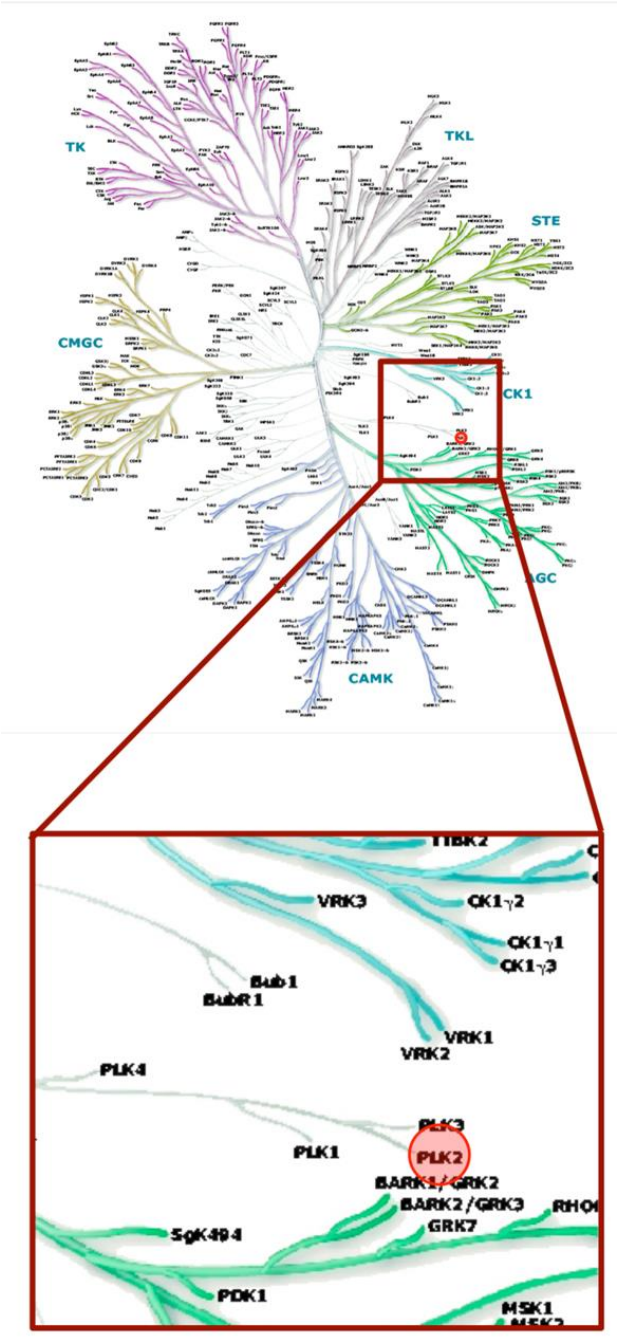

Figure 1: Kinase profiling of compound **7ao** was performed using biochemical kinase assays against a panel of 355 functional human kinases (Reaction Biology Corporation). The kinome

tree maps PLK2 as the sole target of **7ao** amongst the kinases tested with an IC_{50} value of 287 nM.