SUPPLEMENTARY ONLINE DATA

Effects of acutely inhibiting PI3K isoforms and mTOR on regulation of glucose metabolism in vivo

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Figure S1 Levels of drug in mouse blood after administration

I.P. Intraperitoneal.

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### Table S1  Effect of compounds on enzyme activities

Results are the percentage enzyme activity remaining after treatment with 10 μM of the drug. Enzyme assays were performed by the National Centre for Protein Kinase Profiling, University of Dundee, Dundee, U.K. Results are means of duplicate determinations. AMPK, AMP-activated protein kinase; ASK1, apoptosis signal regulating kinase 1; BRSK, BR serine/threonine kinase; BTK, Bruton agammaglobulinemia tyrosine kinase; CAMK, calcium/calmodulin-dependent protein kinase; CAMKK, CAMK kinase; CHK, checkpoint kinase; CDK, cyclin-dependent kinase; CK, casein kinase; CLK2, CDC-like kinase 2; CSK, c-Src tyrosine kinase; DAPK1, death-associated protein kinase 1; DYRK, dual-specificity tyrosine-(Y)-phosphorylation-regulated kinase; E2F2, eukaryotic elongation factor-2 kinase; EPH, Ephrin type receptor; ERK, extracellular-signal-regulated kinase; FGF, fibroblast growth factor receptor 1; GCK, glucokinase (hexokinase 4); GSK3, glycogen synthase kinase 3; HIPK1, homeodomain interacting protein kinase 1; IGF-1R, insulin-like growth factor 1 receptor; IR, insulin receptor; IRR, insulin receptor-related receptor; IRAK4, interleukin-1 receptor-associated kinase 4; JAK2, Janus kinase 2; JNK, c-Jun N-terminal kinase; Lck, lymphocyte-specific protein tyrosine kinase; LKB1, liver kinase B1; MAPK, mitogen-activated protein kinase; MKK, MKK kinase; MNK, MAPK-interacting serine/threonine kinase; MAPKAP, MAPK-associated protein; MARK, microtubule affinity-regulating kinase; MEKK1, MAPK/ERK kinase kinase 1; MELK, maternal embryonic leucine zipper kinase; MINK1, misshapen-like kinase 1; MLK, mixed lineage kinase; MSK1, mitogen- and stress-activated kinase 1; MST, mammalian STE20-like protein kinase; NEK, NIMA (never in mitosis gene a)-related kinase; PAK, p21 protein (Cdc42/Rac)-activated kinase; PKB, protein kinase B; PKD1, protein kinase D; PLK1, polo-like kinase 1; PRAK, p38-regulated/activated protein kinase; PRR2, protein kinase G-C-related kinase 2; RIPK2, receptor-interacting serine/threonine kinase 2; ROCK2, Rho-associated coiled-coil-containing protein kinase 2; RSK, ribosomal S6 kinase; SGK1, serum/glucocorticoid regulated kinase 1; S6K1, S6 kinase 1; SmMLCK, smooth muscle myosin light chain kinase; Src, v-src sarcoma (Schmidt-Ruppin A-2) viral oncogene homologue; SRPK1, SRSF protein kinase 1; SYK, spleen tyrosine kinase; TAK1, transforming growth factor-β-activated kinase 1; TAO1, TAO kinase 1; TBK1, TANK [TRAF (tumour-necrosis-factor-receptor-associated factor)-binding kinase 1; TRKA, TRK1-transforming tyrosine kinase protein; TTK, TTK protein kinase; YES1, v-yes-1 Yamaguchi sarcoma viral oncogene homologue 1; VEGFR, vascular endothelial growth factor receptor.

| Enzyme | PI-103 (10 μM) | AS252424 (10 μM) | BE2235 (10 μM) | ZSTK474 (10 μM) |
|--------|----------------|------------------|----------------|-----------------|
| MKK1   | 105            | 70               | 116            | 83              |
| MKK2   | 115            | 77               | 86             | 95              |
| MKK6   | 107            | 99               | 93             | 83              |
| ERK1   | 112            | 85               | 106            | 106             |
| ERK2   | 106            | 104              | 114            | 105             |
| JNK1   | 102            | 99               | 105            | 93              |
| JNK2   | 100            | 85               | 89             | 87              |
| JNK3   | 101            | 90               | 93             | 88              |
| p38α MAPK | 109       | 86               | 111            | 89              |
| p38β MAPK | 100       | 74               | 96             | 95              |
| p38γ MAPK | 76      | 65               | 101            | 92              |
| ERK8   | 87             | 10               | 94             | 92              |
| RSK1   | 101            | 88               | 97             | 95              |
| RSK2   | 96             | 40               | 81             | 83              |
| PDK1   | 107            | 97               | 98             | 92              |
| PKBα   | 78             | 97               | 126            | 123             |
| PKBβ   | 114            | 40               | 106            | 84              |
| SGK1   | 92             | 59               | 98             | 98              |
| SGK2   | 43             | 109              | 98             | 98              |
| PKA    | 100            | 66               | 82             | 76              |
| ROK1   | 91             | 70               | 84             | 85              |
| PRK2   | 71             | 88               | 74             | 82              |
| PKCβ   | 93             | 102              | 87             | 86              |
| PKCδ   | 98             | 123              | 87             | 87              |
| PKD1   | 120            | 55               | 107            | 96              |
| MSK1   | 105            | 54               | 102            | 89              |
| MNK1   | 97             | 48               | 101            | 96              |
| MNK2   | 90             | 62               | 94             | 101             |
| MAPKAP-K2 | 90       | 80               | 99             | 91              |
| MAPKAP-K3 | 100     | 63               | 110            | 97              |
| PRAK   | 77             | 64               | 93             | 82              |
| CAMKkb | 114            | 51               | 61             | 87              |
| CAMK1  | 99             | 46               | 100            | 114             |
| SmMLCK | 48             | 37               | 109            | 91              |
| PHK    | 84             | 61               | 95             | 94              |
| DAPK1  | 30             | 8                | 107            | 75              |
| CHK1   | 115            | 87               | 146            | 90              |
| CHK2   | 85             | 53               | 80             | 88              |
| GSK3b  | 48             | 10               | 76             | 79              |
| CDK2-Cyclin A | 94     | 89               | 74             | 77              |
| PLK1   | 93             | 90               | 95             | 75              |
| Aurora A | 92            | 95               | 104            | 99              |
| Aurora B | 95            | 71               | 101            | 94              |
| LKB1   | 62             | 52               | 105            | 103             |
| AMPK   | 99             | 39               | 99             | 92              |
| MARK1  | 107            | 90               | 86             | 87              |
| MARK2  | 88             | 67               | 100            | 94              |
| MARK3  | 108            | 63               | 81             | 89              |
| MARK4  | 109            | 56               | 85             | 161             |
| BRSK1  | 99             | 44               | 89             | 88              |
### Table S1 Continued

| Enzyme   | PI-103 (10 μM) | AS-252424 (10 μM) | BEZ235 (10 μM) | ZSTK474 (10 μM) |
|----------|----------------|-------------------|----------------|-----------------|
| MELK     | 104            | 91                | 91             | 91              |
| NUAK1    | 98             | 73                | 44             | 90              |
| CK1      | 100            | 85                | 96             | 76              |
| CK2      | 102            | 25                | 79             | 54              |
| Dyrk1A   | 59             | 3                 | 93             | 78              |
| Dyrk2    | 83             | 20                | 79             | 93              |
| Dyrk3    | 64             | 18                | 56             | 87              |
| Nek2α    | 86             | 136               | 145            | 106             |
| Nek6     | 87             | 94                | 95             | 83              |
| Ikkβ     | 74             | 73                | 92             | 94              |
| Ikkε     | 85             | 40                | 86             | 84              |
| Tbk1     | 91             | 70                | 107            | 102             |
| Pim1     | 72             | 7                 | 92             | 97              |
| Pim2     | 90             | 7                 | 94             | 92              |
| Pim3     | 41             | 7                 | 87             | 76              |
| Srryk1   | 116            | 39                | 106            | 92              |
| Etk      | 99             | 91                | 110            | 96              |
| Hipk1    | 63             | 29                | 89             | 100             |
| Hipk2    | 18             | 3                 | 101            | 63              |
| Hipk3    | 82             | 23                | 102            | 98              |
| Clk2     | 25             | 16                | 53             | 85              |
| Pak2     | 106            | 89                | 87             | 100             |
| Pak4     | 70             | 65                | 87             | 92              |
| Pak5     | 112            | 49                | 90             | 84              |
| Pak6     | 108            | 71                | 105            | 93              |
| Mst2     | 115            | 60                | 89             | 92              |
| Mst4     | 114            | 45                | 100            | 88              |
| Gck      | 91             | 53                | 12             | 104             |
| Mnk1     | 116            | 24                | 75             | 102             |
| Mek1     | 97             | 56                | 67             | 92              |
| Mlk1     | 65             | 53                | 67             | 86              |
| Mlk3     | 57             | 32                | 62             | 97              |
| Tao1     | 84             | 18                | 81             | 93              |
| Ask1     | 101            | 110               | 106            | 90              |
| Tak1     | 79             | 48                | 67             | 97              |
| IraK4    | 119            | 114               | 78             | 102             |
| Ripp2    | 72             | 19                | 28             | 89              |
| Ttk      | 66             | 56                | 91             | 88              |
| Src      | 99             | 96                | 121            | 104             |
| Ltk      | 85             | 110               | 54             | 89              |
| Csk      | 101            | 100               | 100            | 84              |
| Yes1     | 92             | 36                | 69             | 72              |
| Btk      | 82             | 45                | 20             | 98              |
| Jak2     | 93             | 60                | 24             | 79              |
| Syk      | 69             | 55                | 72             | 85              |
| Eph-A2   | 113            | 51                | 110            | 106             |
| Eph-A4   | 103            | 74                | 105            | 87              |
| Eph-B1   | 131            | 94                | 133            | 96              |
| Eph-B2   | 105            | 100               | 77             | 106             |
| Eph-B3   | 127            | 52                | 117            | 113             |
| Eph-B4   | 86             | 89                | 99             | 105             |
| Fgf-r1   | 118            | 42                | 106            | 102             |
| Her4     | 114            | 68                | 117            | 103             |
| IGF-1r   | 54             | 75                | 72             | 87              |
| Ir       | 80             | 94                | 99             | 104             |
| Ir    | 89             | 36                | 80             | 88              |
| Trk-a    | 93             | 79                | 59             | 83              |
| Vgrf     | 92             | 22                | 80             | 87              |