

## Regorafenib- a novel therapeutic approach for the treatment of experimental Pulmonary Hypertension

### Supplemental tables:

**Table 1. List of TKs and STKs upregulated in IPAH-PASMCs**

**(compared to donor-PASMCs)**

| Type | Kinase Uniprot ID | Kinase Name | Mean Specificity Score | Median Kinase Statistic |
|------|-------------------|-------------|------------------------|-------------------------|
| PTK  | Q08345            | DDR1        | 1,516460479            | 0,800631998             |
| PTK  | P43405            | Syk         | 1,392595087            | 0,379270616             |
| PTK  | P42680            | TEC         | 1,099043536            | 0,417297439             |
| PTK  | P51451            | BLK         | 1,06061171             | 0,440685869             |
| PTK  | P43403            | ZAP70       | 1,02124757             | 0,372014803             |
| PTK  | P30530            | Axl         | 1,009309564            | 0,372757928             |
| PTK  | P08069            | IGF1R       | 1,000245329            | 0,449679352             |
|      |                   |             |                        |                         |
| Type | Kinase Uniprot ID | Kinase Name | Mean Specificity Score | Median Kinase Statistic |
| STK  | Q13627            | DYRK1A      | 2,698970004            | 0,962910245             |
| STK  | P53779            | JNK3        | 2,579060977            | 0,350300442             |
| STK  | P45983            | JNK1        | 2,5456132              | 0,350300442             |
| STK  | P27361            | ERK1        | 2,434502089            | 0,389524176             |
| STK  | P28482            | ERK2        | 2,32536084             | 0,369860891             |
| STK  | P45984            | JNK2        | 2,311478759            | 0,354757298             |
| STK  | O14757            | CHK1        | 2,085766707            | 0,443626935             |
| STK  | Q16539            | MAPK14      | 1,865479292            | 0,316262218             |
| STK  | P06493            | CDC2/CDK1   | 1,808314474            | 0,321808683             |
| STK  | O43293            | DAPK3       | 1,765421042            | 0,702870446             |
| STK  | Q96GD4            | AurB/Aur1   | 1,693159591            | 0,619502918             |
| STK  | O15264            | p38[delta]  | 1,61851957             | 0,298487534             |
| STK  | Q16512            | PKN1/PRK1   | 1,610990368            | 0,57339075              |
| STK  | Q13164            | ERK5        | 1,551132042            | 0,36437315              |
| STK  | P48729            | CK1[alpha]  | 1,469267046            | 0,359477208             |
| STK  | P24941            | CDK2        | 1,344841317            | 0,294623954             |
| STK  | Q9UIK4            | DAPK2       | 1,327745908            | 0,409874906             |
| STK  | O76039            | CDKL5       | 1,237660956            | 0,411618105             |
| STK  | Q00535            | CDK5        | 1,150632344            | 0,327062551             |
| STK  | P50750            | CDK9        | 1,052904009            | 0,344364034             |
| STK  | Q15759            | p38[beta]   | 1,040196203            | 0,389016528             |
| STK  | Q8TD08            | ERK7        | 1,026872146            | 0,445531862             |

**Table 2. Kinases inhibited by regorafenib treatment in IPAH-PASMCs**

| Type | Kinase Uniprot ID | Kinase Name | Mean Specificity Score | Median Kinase Statistic |
|------|-------------------|-------------|------------------------|-------------------------|
| PTK  | P06239            | Lck         | 2,172763972            | 1,662272674             |
| PTK  | P00519            | Abl         | 1,890809981            | 1,429673187             |
| PTK  | P07947            | Yes         | 1,611653654            | 1,55896577              |
| PTK  | P42684            | Arg         | 1,33236283             | 1,374710113             |
| PTK  | P51451            | BLK         | 1,048701546            | 1,497320713             |
| PTK  | P43405            | Syk         | 1,01386118             | 1,238894683             |
|      |                   |             |                        |                         |
| Type | Kinase Uniprot ID | Kinase Name | Mean Specificity Score | Median Kinase Statistic |
| STK  | Q16512            | PKN1/PRK1   | 2,404383558            | 9,681785544             |
| STK  | P27361            | ERK1        | 1,833963679            | 4,138932992             |
| STK  | O14757            | CHK1        | 1,820464391            | 5,764893582             |
| STK  | P45984            | JNK2        | 1,680841712            | 4,04511258              |
| STK  | P16066            | ANP[alpha]  | 1,564359649            | 3,910785893             |
| STK  | O15264            | p38[delta]  | 1,508065307            | 3,915147527             |
| STK  | P24941            | CDK2        | 1,503467981            | 4,202821253             |
| STK  | P28482            | ERK2        | 1,373572076            | 3,865930586             |
| STK  | P06493            | CDC2/CDK1   | 1,303239493            | 4,060445271             |
| STK  | P53779            | JNK3        | 1,241408003            | 3,412545259             |
| STK  | P45983            | JNK1        | 1,201121141            | 3,412545259             |
| STK  | Q96GD4            | AurB/Aur1   | 1,193538602            | 5,516586485             |
| STK  | Q00535            | CDK5        | 1,138995923            | 4,47814888              |
| STK  | O96017            | CHK2        | 1,096549427            | 3,597653831             |
| STK  | Q96S38            | RSKL1       | 1,060491932            | 4,608102686             |
| STK  | Q16644            | MAPKAPK3    | 1,048248875            | 3,054903846             |
| STK  | O43293            | DAPK3       | 1,016240689            | 4,562227636             |

"The "mean specificity score" indicates the specificity of the predicted differential kinase activity with respect to the amount of peptides used for predicting the corresponding kinase. The higher the "mean specificity score", the less likely it is that the numerical value for the predicted kinase activity could have been generated using a random set of peptides (instead of the original substrates) from the present data set. The "mean specificity score" is calculated by the following equation:  $-\log_{10} p\text{-value}$ , where  $p < 0.05$  refers to the statistical significance for the changes of the phosphorylation for the substrate peptide sets between the two experimental conditions. For kinases with less stringent criteria during the upstream kinase prediction the p-value varies between 0.05 and 1 which results in a mean specificity score between "1 and 1.3."