**ΔS (CDK9 - CDK2)** ΔΔG CDK2 Selectivity (CDK9 - CDK2) CDK9 MUE:  $0.88_{0.54}^{1.29}$ MUE: 1.71<sub>1.10</sub><sup>2.34</sup> MUE: 1.17<sup>1:53</sup><sub>0:82</sub> RMSE: 1.15<sup>1.59</sup><sub>0.67</sub> RMSE: 2.10<sup>2.65</sup><sub>1.47</sub> RMSE: 1.37<sup>1.66</sup><sub>1.04</sub> Predicted  $\Delta\Delta G$  (kcal/mol) ∆∆G (kcal/mol) Predicted AS (kcal/mol) Predicted -2 -2 Experimental  $\Delta S$  (kcal/mol) Experimental ΔΔG (kcal/mol) Experimental ΔΔG (kcal/mol) **ΔS (ERK2 - CDK2)**  $\Delta\Delta G$ CDK2 ERK2 Selectivity (ERK2 - CDK2) MUE:  $0.76^{1.04}_{0.52}$ MUE: 0.83<sup>1.07</sup><sub>0.59</sub> MUE: 1.22<sup>1.55</sup><sub>0.91</sub>

