

**Supplementary Figure 1: Osimertinib monotherapy induce tumor growth inhibition in a NSCLC EGFR G719A;S768I mutation PDX model *in vivo*.**

(A) Tumor growth inhibition following daily dosing of vehicle or osimertinib 25 mg/kg in the subcutaneous, LC-F-29 PDX model in nude mice. (B) Waterfall plot representing tumor volume of individual mice at the end of the treatment period (C) No significant body weight loss (less than 10% of starting body weight) is observed at these efficacious doses. Data expressed as percentage change in nude mouse body weight relative to start size on day 0.

Data are represented as mean ± SEM (n=10 per group).



**Supplementary Figure 2: Osimertinib as monotherapy induce a stronger inhibition of the level of pEGFR and the downstream signalling pathways than afatinib.**

Individual quantification of the level of (A) p-EGFR or (B) pERK1/2 or (C) pS6 or (D) pAKT determined by immunoblot on tumors collected 1, 6, 16 and 24h following one dose of either vehicle, osimertinib or afatinib. Data are represented as mean ± SEM (n=4 for vehicle and treated groups).



**Supplementary Figure 3: MET amplification induces resistance to osimertinib treatment in a NSCLC EGFR G719A mutation PDX model *in vivo*.**

(A) Tumor growth inhibition following daily dosing of vehicle or osimertinib 25 mg/kg, in the subcutaneous LU1901 PDX models in nude mice. (B) Waterfall plot representing tumor volume of individual mice at the end of the treatment period (C) No significant body weight loss (less than 10% of starting body weight) is observed at these efficacious doses. Data expressed as percentage change in nude mouse body weight relative to start size on day 0.

Data are represented as mean ± SEM (n=10 per group).