

Supplementary Table 2: Summary of the genetic mutations and tumour microenvironment alterations in non-small cell lung cancer.

|                   | Subcategory                      | Key finding/mechanism                                                | Resistance mechanism(s)                                             |
|-------------------|----------------------------------|----------------------------------------------------------------------|---------------------------------------------------------------------|
| Genetic mutations | EGFR                             | Common in NSCLC; targetable                                          | T790M mutation                                                      |
|                   | BRAF                             | V600E drives progression                                             | MAPK pathway activation                                             |
|                   | KRAS                             | Poor prognosis; constitutive proliferative signalling                | Resistance to direct KRAS inhibition is an active area of research. |
| TME               | Immune evasion                   | Immuno-suppressive cells (Tregs, MDSCs) inhibit anti-tumour immunity | Reduced immunotherapy efficacy                                      |
|                   | Cancer stem cells                | Promote persistence and recurrence                                   | Resistance to conventional therapies                                |
|                   | Hypoxia and nutrient deprivation | Induce metabolic adaptations                                         | Enhanced therapy resistance                                         |

MDSC: myeloid-derived suppressor cell; NSCLC: non-small cell lung cancer; TME: tumour microenvironment; Treg: regulatory T cell.