**Background and rationale**

- Squamous cell carcinomas (SCCs) arise from epithelial tissues and share a common etiology.
- Environmental insults generate common genetic aberrations, such as amplification of Chr 3p, which are hallmarks of early oncogenesis in SCCs.

**Correlation of TP63 and NRG1 in squamous (2a) esophageal, (2b) lung, (2c) cutaneous skin, and (2d) head and neck cancer models**

- Percentage of squamous and non-squamous patient samples with PIK3CA, TP63 and SOX2 copy number amplification and loss of Chr 3p, which are hallmarks of early oncogenesis in SCCs.
- Inhibition of HER3 signaling, alone or in combination with EGFR Inhibitors, may therefore have broad applicability in SCCs.
- HMBD-001, a differentiated and potentially best-in-class HER3-targeting antibody that blocks HER3 heterodimers with EGFR to potently inhibit PI3K signaling, is currently being investigated in Phase I trials (NCI10557015).

**Conclusion**

- Common genetic alterations that increase HER3/NGR1 and EGFR signaling are frequently observed in squamous cell carcinomas.
- SCCs are more dependent on HER3 than EGFR, therefore inhibition of HER3, alone or in combination with EGFR inhibition, could have broad applicability in squamous cell carcinomas.

- Inhibition of HER3 signaling with a potentially best-in-class anti-HER3 antibody HMBD-001 results in potent monotherapy anti-tumor activity across various squamous cancers.
- HMBD-001 combination with EGFR inhibition could further improve efficacy in EGFR amplified SCCs.
- Hummingbird Bioscience will initiate Phase Ib studies in biomarker-selected populations of SCCs in the second half of 2023.

**References**


**Antibody therapy with HMBD-001 in combination with an EGFR inhibitor effectively inhibits tumor growth in biomarker selected preclinical models of squamous cell carcinomas**

- Anti-HER3 antibody, HMBD-001, in combination with an EGFR inhibitor effectively inhibits tumor growth in biomarker selected preclinical models of squamous cell carcinomas.

**Squamous models with TP63 amplification show robust monotherapy response to HMBD-001**

- In vivo efficacy studies of (6a) sqNSCLC (LU6432), (6b) ESCC (ES0199), and (6c) sqNSCLC (CTG-2558) models with TP63 amplification treated with HMBD-001 monotherapy.

**Combining HMBD-001 with cetuximab results in potent and sustained anti-tumor activity in TP63-positive and EGFR-amplified squamous models**

- In vivo efficacy studies of (7a) sqNSCLC (LU6432), (7b) ESCC (ES0199), and (7c) sqNSCLC (CTG-2558) models with TP63-positive and EGFR-amplified squamous models.