TPS8663 **Poster Session**

A phase 1/2 open-label, multicenter, first-in-human study of the safety, tolerability, pharmacokinetics, and antitumor activity of BH-30643 in adult subjects with locally advanced or metastatic NSCLC harboring EGFR and/or HER2 mutations (SOLARA).

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Background: Clinical outcomes for patients with metastatic *EGFR*-mutant NSCLC have steadily improved with successive generations of EGFR tyrosine kinase inhibitors (TKIs). However, there remains significant need for further advancement in progression-free survival (PFS) and overall survival (OS), as these outcomes still fall short when compared to the remarkable benefits observed with newer TKIs in *ALK* and *ROS1* driven NSCLC. BH-30643 is a first-in-class EGFR TKI with a novel macrocyclic structure offering potent, reversible, mutant selective inhibition of classical and atypical *EGFR* activating mutations without vulnerability to common on-target resistance mutations. Cellular activity of BH-30643 was recently described (AACR 2025) demonstrating sub-nanomolar potency for EGFR exon 19del and L858R classical mutations which are maintained in the presence of T790M +/- C797S. High potency was also observed against atypical *EGFR* mutations (e.g., G719X, L861Q, S768I) and exon 20 insertions, as well as mutant *HER2*. Such an OMNI-EGFR inhibitor may have the potential to overcome some of the limitations of earlier agents. **Methods:** SOLARA (NCT06706076, BH-30643-01) is a Phase 1/2, multicenter, open-label, dose escalation, first-in-human study to determine the safety, tolerability, pharmacokinetics, and antitumor activity of BH-30643, in adult subjects with locally advanced or metastatic NSCLC harboring *EGFR* and/or *HER2* mutations. Enrollment based on local molecular testing and/or liquid biopsy is permitted. Asymptomatic brain metastases (treated or untreated) are eligible. BH-30643 is administered orally twice daily until disease progression or intolerable toxicity. The study consists of an initial dose escalation part using a Bayesian optimal interval design to identify Recommended Dose(s) for Evaluation (RDE). Dose-limiting toxicities (DLTs) are evaluated for the first 21 days of treatment. A subsequent expansion part will further evaluate the RDE(s) to identify a Recommended Phase 2 Dose (RP2D), studying cohorts with or without prior systemic therapy across a range of *EGFR*/*HER2* driver mutations. Efficacy will be evaluated by RECIST 1.1 criteria and toxicity by CTCAE V5.0. Plasma is collected for circulating tumor DNA (ctDNA) analysis at baseline and on treatment. Enrollment is underway, with planned enrollment across ~35 sites in multiple continents. Clinical trial information: NCT06706076. Research Sponsor: BlossomHill Therapeutics, Inc.