ORIC-114 is a highly selective, brain penetrant, orally bioavailable, irreversible inhibitor designed to selectively target EGFR and HER2 with high potency against exon 20 insertion mutations, making it a promising therapeutic candidate to address the unmet medical need of having both meaningful systemic as well as CNS antitumor activity.

PATIENT POPULATION
- **Any advanced solid tumor with locally documented**:
  - EGFR exon 20 insertion mutation
  - HER2 amplification or overexpression
  - Applicable EGF mutation (NSCLC only)
- **Prior chemotherapies**
- **All other prior therapies allowed**, including prior exon 20 targeted therapies
- **RECIST v1.1**
- **All other prior therapies allowed**, including prior exon 20 targeted therapies

PATIENT CHARACTERISTICS
- **Age, years, median (range)**: 63 (25,86) to 63 (25,86)
- **CNS metastases at baseline, n (%)**: 86% presented with CNS metastases at baseline
- **HER2 targeted agents** – 7 (30) to 3 (60)
- **ESMO 2023 Annual Meeting Poster 1333P**
- **ORIC-114 is a highly selective, brain penetrant, orally bioavailable, irreversible inhibitor that selectively targets EGFR and HER2 with high potency against exon 20 insertion mutations and atypical EGFR mutations (Poster #1345P)**

ORIC-114 SAFETY PROFILE
- **Treatment Related Adverse Events (TRAEs)** occurring in ≥10% of patients
  - **Grade 1-2 TRAEs**
    - Vomiting
    - Decreased appetite
    - Nausea
    - Diarrhea
    - Hematologic
    - Dose Reductions: 2 (18) to 3 (13)
    - Dose Discontinuations: 1 (9) to 1 (4)
- **Grade ≥4 TRAEs**
  - Nausea
  - Hematologic
  - Other

PATIENT VIGNETTES
- **Confirmed Complete Intraocular and Systemic Response in Patient with EGFR Exon 20 Mutated NSCLC and Active CNS Metastases that Progressed on Prior EGFR Exon 20 Therapy**
- **Confirmed 100% Regression of Target Lesions in Patient with HER2 Exon 20 Mutated NSCLC**

CONCLUSIONS
- **ORIC-114 is a highly selective, brain penetrant, orally bioavailable, irreversible inhibitor that selectively targets EGFR and HER2 with high potency against exon 20 insertion mutations and atypical EGF mutations (Poster #1345P)**
- **ORIC-114 has a clinical half-life that supports QD dosing and is well tolerated across all doses**
- **The safety profile of ORIC-114 consists mainly of Grade 1 and 2 adverse events with low evidence of off-target toxicities**
- **The most common TRAEs were low grade rash and diarrhea, with only 6% G3 diarrhea and no ≥G3 rash**
- **Multiple responses were observed in patients with HER2 exon 20 mutated NSCLC in a Phase 1b study**
- **Multiple responses were observed in additional patients with EGFR exon 20 mutated NSCLC, most previously treated with 20 targeted therapies**
- **Multiple responses were observed in patients with HER2 exon 20 mutated NSCLC**
- **Given the observed side therapeutic index, dose escalation continues with higher QD and BID doses to select provisional RP2Ds for dose optimization**