

The Reversible and Selective FGFR2/3 inhibitor CGT4859 has Superior Target Coverage of Resistance Mutations Missed by Leading FGFR Inhibitors

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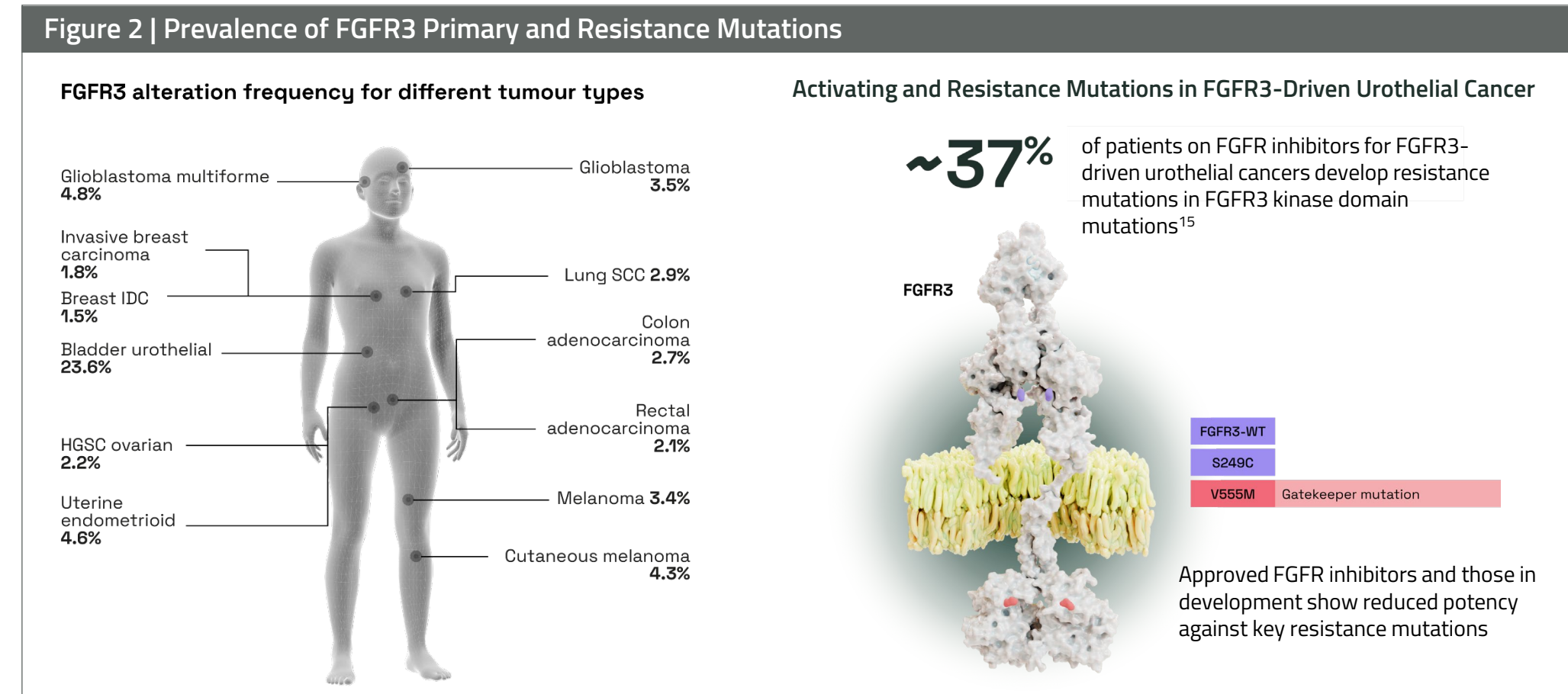
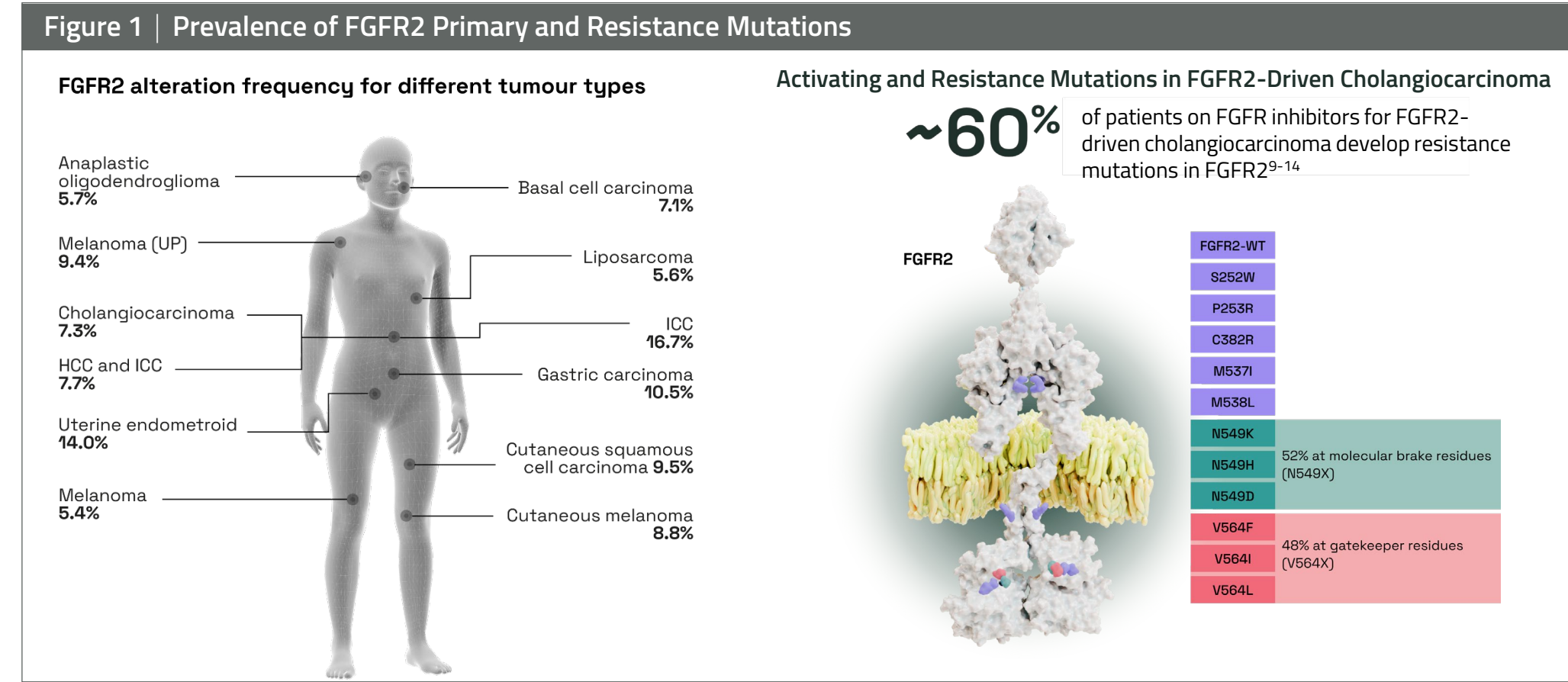
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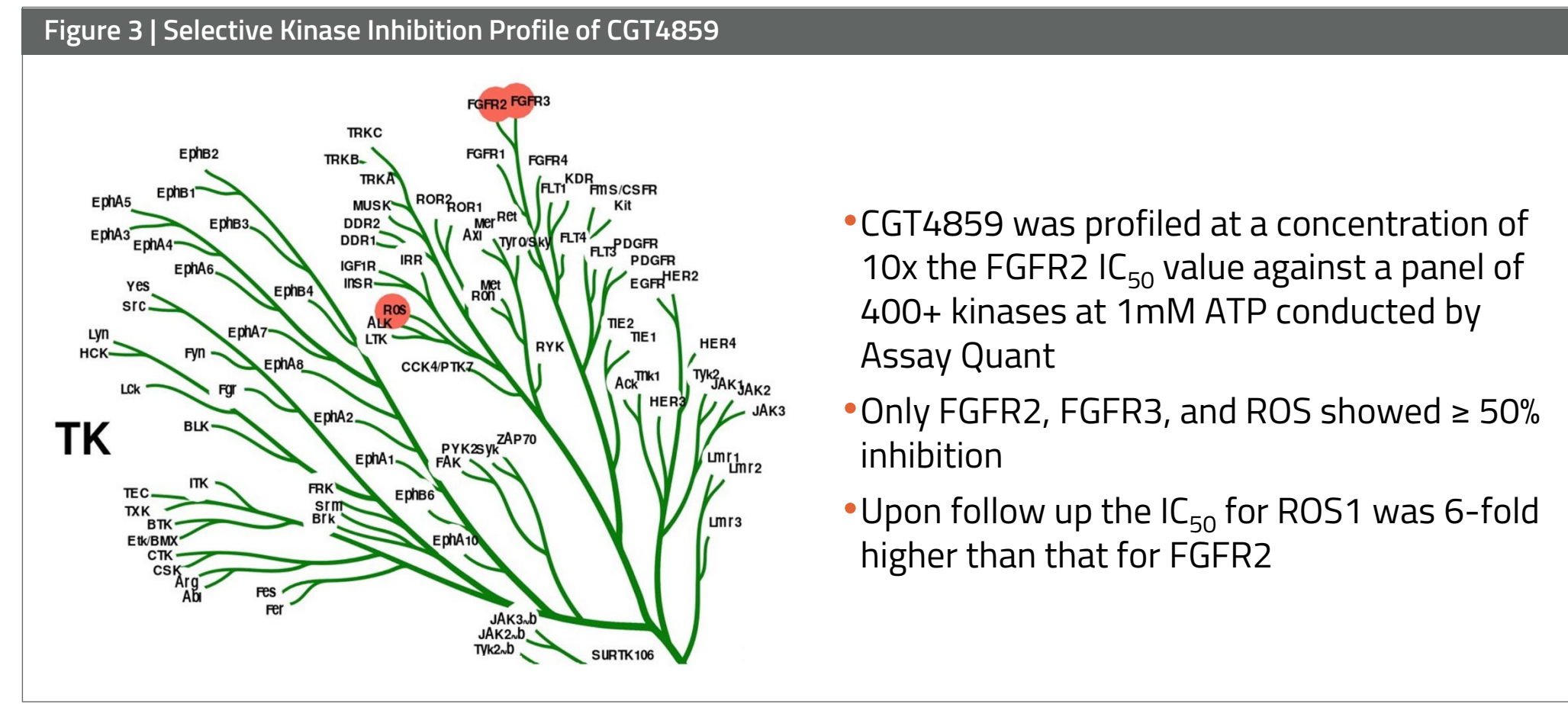
Poster #27
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BACKGROUND

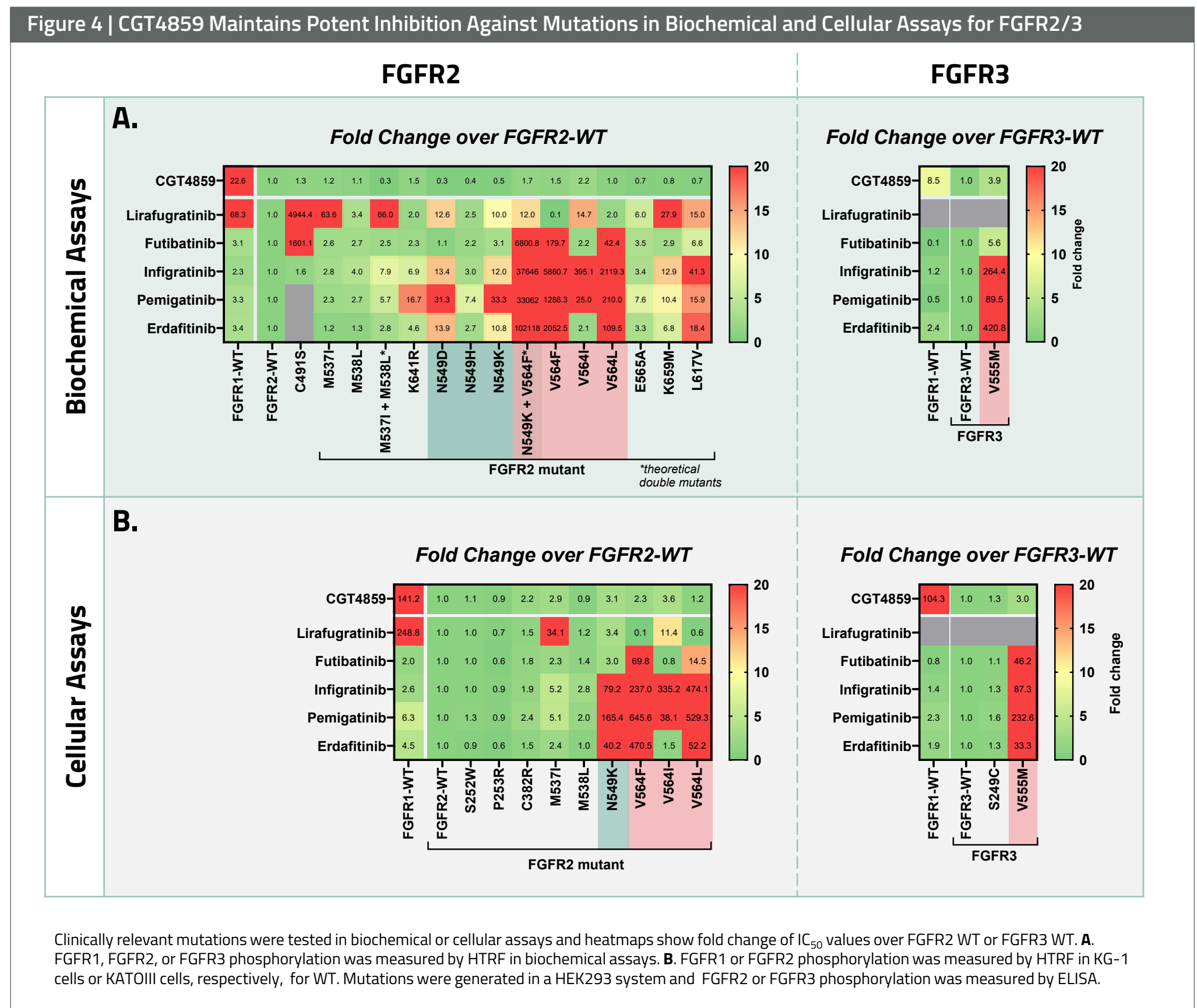
- The family of fibroblast growth factor receptors (FGFRs) consists of four transmembrane receptor tyrosine kinases, FGFR1-FGFR4¹
- FGFR2/3 alterations account for 4.1% of all cancers²
- Approved pan-FGFR inhibitors show on-target , dose-limiting toxicities with >75% of patients experiencing FGFR1-mediated hyperphosphatemia³⁻⁸



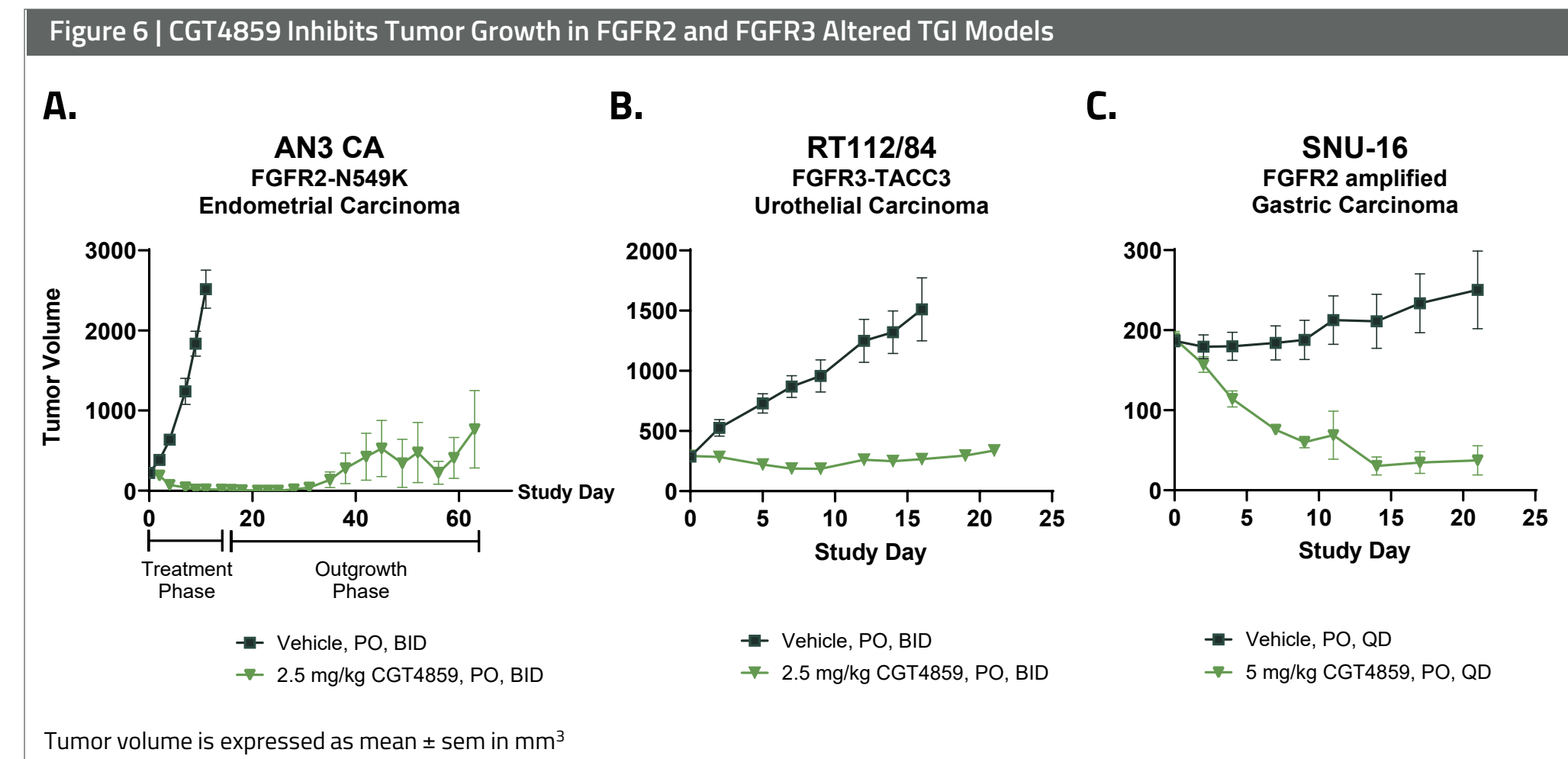
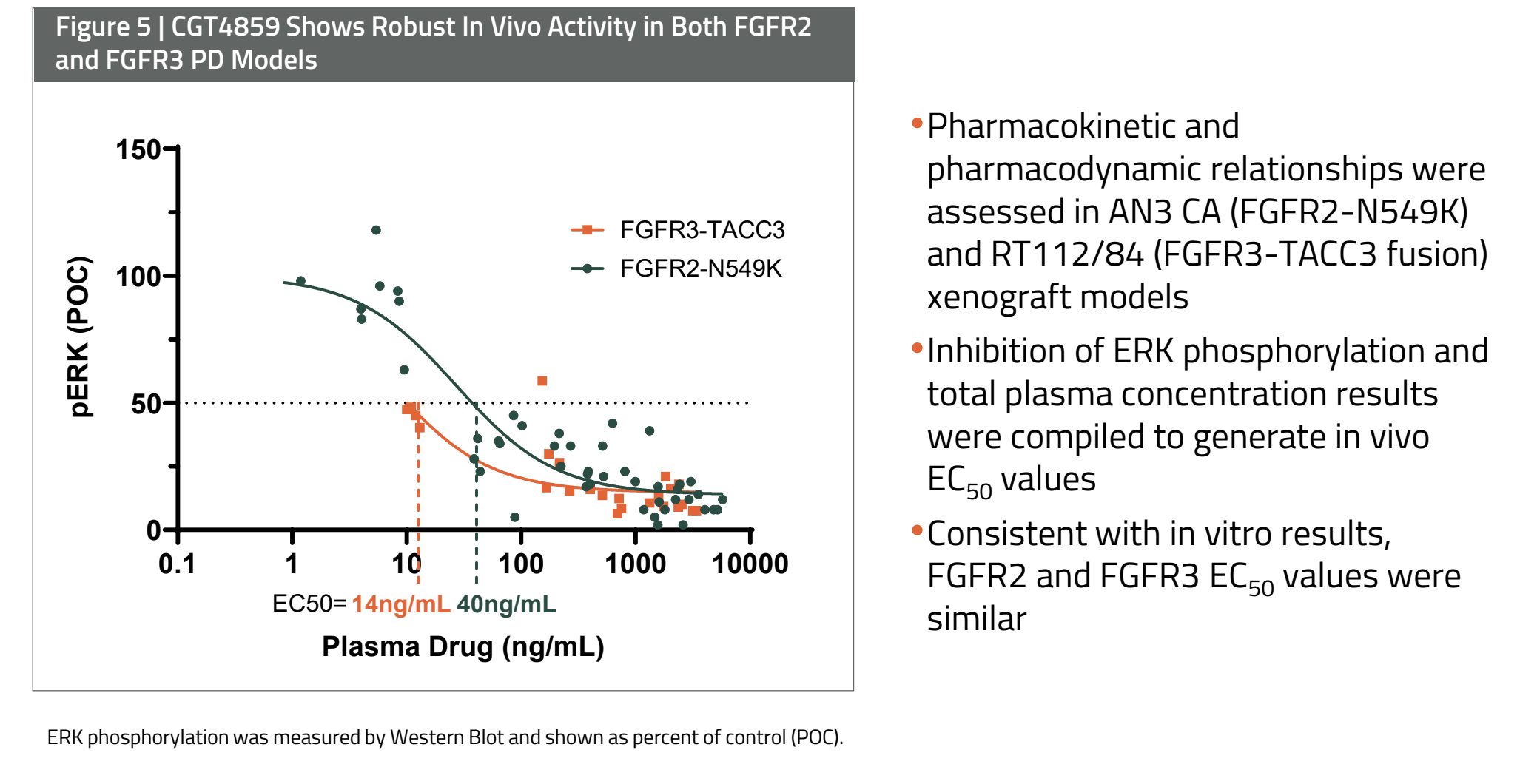
RESULTS



RESULTS, continued



- CGT4859 retains potency against primary mutations as well as acquired resistance mutations in FGFR2 and FGFR3 including the gatekeeper and molecular brake mutations – key clinical vulnerabilities of other FGFR inhibitors
- Patients can develop multiple FGFR2 or FGFR3 mutations, CGT4859 retains potency against theoretical in cis FGFR2 double mutants in biochemical assays



- Tumor growth inhibition was assessed in xenograft models with FGFR2/3 alterations including FGFR2-N549K mutation, FGFR3-TACC3 fusion, and FGFR2 amplification. CGT4859 was orally administered either BID or QD for 14–21 days in tumors staged to ~200 mm³.
- CGT4859 demonstrated complete tumor regression at a dose of 2.5 mg/kg BID with durable tumor response in the AN3CA TGI model, where animals were treated for 14 days and subsequently monitored for outgrowth (Panel A).
- Maximal activity was observed across all models at ≥2.5 mg/kg QD or BID and there were no drug-related deaths or early terminations.

CONCLUSIONS

- CGT4859 is an FGFR2/3 inhibitor that addresses an unmet medical need in the FGFR inhibitor class**
- CGT4859 spares FGFR1 to avoid hyperphosphatemia-related dose modifications
 - CGT4859 retains potency on clinically relevant FGFR2 and FGFR3 acquired resistance mutations
 - CGT4859 has robust efficacy at tolerated exposures in nonclinical models

CGT4859, a highly potent and selective FGFR2 and FGFR3 inhibitor¹

Covers activating and resistance mutations

FGFR1 FGFR2 FGFR3 FGFR4

Pan-inhibitors associated with FGFR1-mediated dose limiting toxicities¹

A multicenter Phase 1/2 trial of CGT4859 has been initiated in the United States and will enroll patients with intrahepatic cholangiocarcinoma or other advanced solid tumors harboring FGFR2 and/or FGFR3 genetic alterations (NCT06777316)