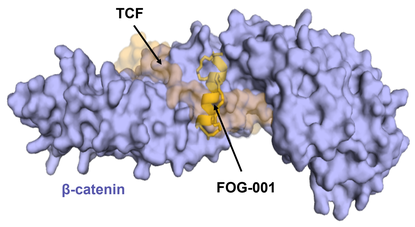
# A phase 1/2 trial of FOG-001, a first-in-class direct β-catenin:TCF inhibitor – Safety and preliminary antitumor activity in patients with adamantinomatous craniopharyngioma

Kyriakos P. Papadopoulos[1], Priscilla K. Brastianos[2], Michael Cecchini[3], Moh'd Khushman[4], Shivaani Kummar[5], Meredith Pelster[6], Jordi Rodon[7], Sunil Sharma[8], Rona Yaeger[9], Jonathan Rojo[10], Amber L. Wells[10], Megan Tipps[10], Laura Strong[10], Wade Berry[10], Amanda Garofalo[10], Lalith Akella[10], Ziyang Yu[10], Jorge D. Ramos[10], Marie Huong Nguyen[10], Keith Orford[10], Samuel J. Klempner[2]

*[1]START San Antonio, San Antonio, TX, USA; [2]Massachusetts General Hospital, Boston, MA, USA; [3]Yale University School of Medicine, New Haven, CT, USA; [4]Washington University School of Medicine, St. Louis, MO, USA; [5]Oregon Health and Science University, Portland, OR, USA; [6]Sarah Cannon Research Institute, Nashville, TN, USA; [7]The University of Texas MD Anderson Cancer Center, Houston, TX, USA; [8]Honor Health, Scottsdale, AZ, USA; [9]Memorial Sloan Kettering Cancer Center, New York, NY, USA; [10]Parabilis Medicines, Cambridge, MA, USA*

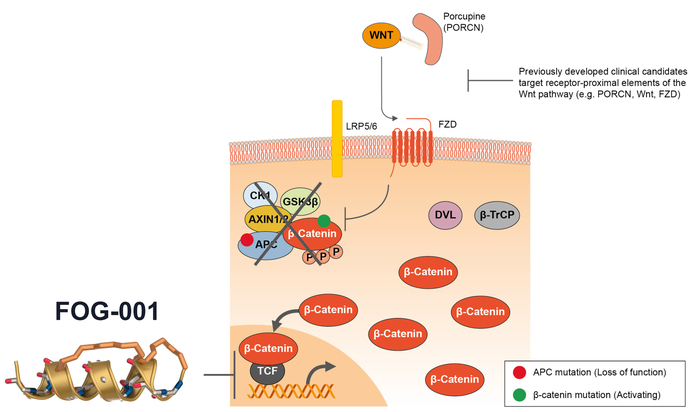
## Background

**Figure 1.** FOG-001 – A novel β-catenin:TCF inhibitor




- Adamantinomatous craniopharyngiomas (ACPs) are rare brain tumors that most often arise in the suprasellar region and are associated with substantial morbidity.
- There are no approved systemic therapies and both surgical and radiation treatments are often complex and associated with a significant risk of complications.
- ACPs are almost always associated with mutations in the *CTNNB1* gene leading to abnormal activation of the Wnt/β-catenin signaling pathway.[1,2]
- As of the data cut-off (11-Aug-2025), a total of 3 patients with ACP have been enrolled across FOG-001 dose levels 3 and 5.

**Figure 2.** FOG-001 – mechanism of action



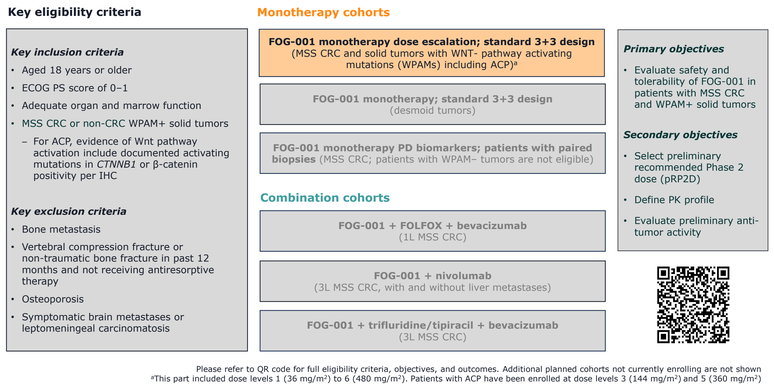

- FOG-001 is a first-in-class and only direct inhibitor of β-catenin that competitively inhibits the interaction between β-catenin and the T-cell factor (TCF) family of transcription factors, the most downstream node in the Wnt/β-catenin signaling pathway.
- By directly targeting the β-catenin:TCF protein–protein interaction, FOG-001 is downstream of, and thereby targets, virtually all mutations that activate canonical Wnt signaling.
- Preclinical data demonstrate good tolerability of FOG-001 with a clear therapeutic window.

## Objectives

- In this poster we present the safety and preliminary efficacy findings from the FOG-001-101 study of FOG-001 in patients with ACP.

## Methods

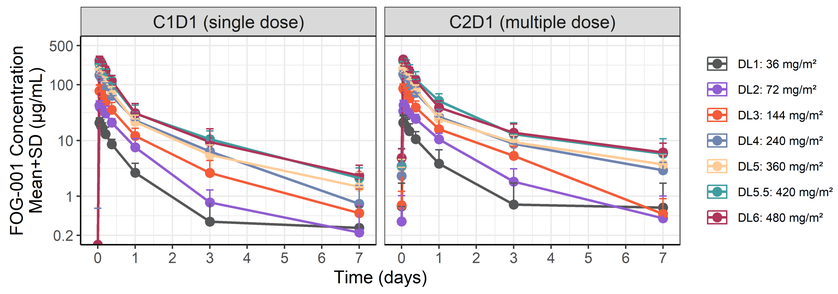
**Figure 3.** FOG-001-101 study cohorts (NCT05919264)




Please refer to QR code for full eligibility criteria, objectives, and outcomes. Additional planned cohorts not currently enrolling are not shown
[a]This part included dose levels 1 (36 mg/m²) to 6 (480 mg/m²). Patients with ACP have been enrolled at dose levels 3 (144 mg/m²) and 5 (360 mg/m²)

## Results

**Figure 4.** FOG-001 pharmacokinetic characteristics




- FOG-001 has favorable pharmacokinetic characteristics:
  - Extensive distribution.
  - Dose-proportional exposure.
  - Low inter-patient variability.

### Baseline characteristics

- As of August 11, 2025, 3 patients with ACP have received FOG-001 monotherapy at doses of 144 mg/m² (n=1) and 360 mg/m² (n=2).
- Key characteristics:
  - All patients are male.
  - Median age is 42 years (range 19–62 years).
  - All had prior surgery and 1 received radiation.
  - All have tumors with evidence of Wnt pathway activation (2 had *CTNNB1* mutations and 1 was positive for nuclear β-catenin expression (IHC)).

### Efficacy

- Tumor size has decreased in all patients.
- Two patients achieved partial responses (PR) with 56.0% and 48.0% reduction in tumor size.
- One patient has stable disease with a 19.2% decrease in tumor size.

### Safety

- The most commonly reported TRAEs were low-grade and reversible.
- The most common TRAE was platelet count decreased (n=2).
- No treatment-related serious adverse events, dose reductions or treatment discontinuations have been reported.

## FOG-001-101 sites open for enrollment

- START – San Antonio
- Massachusetts General Cancer Center
- Sarah Cannon Research Institute
- University of Texas – MD Anderson Cancer Center
- Yale School of Medicine
- Memorial Sloan Kettering Cancer Center
- Washington University School of Medicine
- Honor Health
- University of Minnesota
- Oregon Health & Science University
- Stanford Cancer Center
- University of Pittsburgh Hillman Cancer Center
- University of Wisconsin
- Johns Hopkins
- University Hospitals Seidman Cancer Center
- Florida Cancer Specialists
- University of California San Francisco

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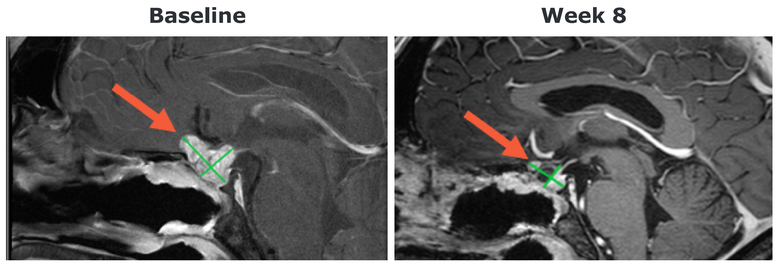
## References

1. Sekine S, et al. Am J Pathol 2002;161:1997–2001.
2. Brastianos PK, et al. Nat Genet 2014;46:161–5.

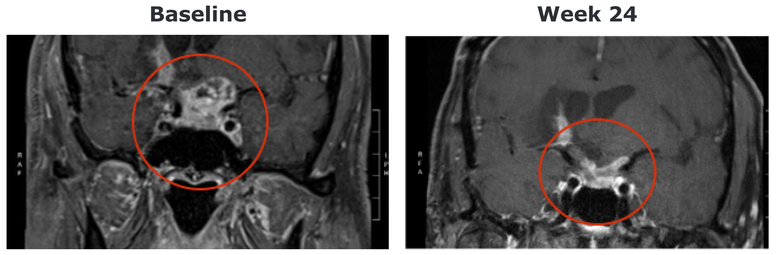
**Patient Cases:** Tumor reductions seen in all 3 patients with ACP

**Figure 5.** Patient 1 – Dose Level 5 (360 mg/m²)



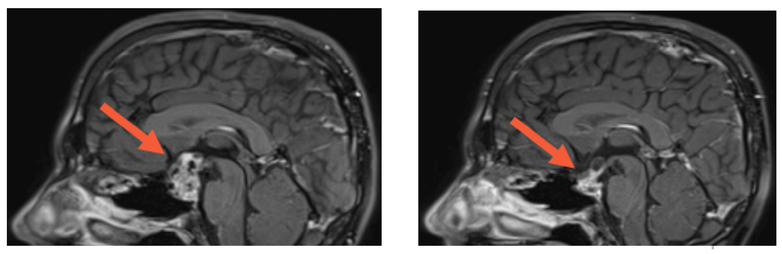

- 42-year-old male diagnosed with ACP in 2021.
- Mass was elevating the optic chiasm, leading to a visual field cut.
- Showed significant tumor reduction at Week 8 (–24%).
- Achieved a PR at Week 16 (–56%).

**Figure 6.** Patient 2 – Dose Level 5 (360 mg/m²)




- 62-year-old male with ACP symptomatic since 2023, including bi-temporal visual field defects.
- Has maintained stable disease for 48 weeks, with a 19.2% tumor reduction.

**Figure 7.** Patient 3 – Dose Level 3 (144 mg/m²)




- 19-year-old male with ACP diagnosed in 2019.
- FOG-001 treatment improved headaches and visual field deficits.
- Despite missed doses, maintained a PR (–48%) out to ~1 year.

## Conclusions

- FOG-001 is a stabilized Helicon™ peptide that selectively inhibits the β-catenin/TCF interaction.
- All patients have had tumor size reductions, with two PRs, suggesting that the Wnt/β-catenin signaling pathway is an actionable target in ACP.
- FOG-001 has a well-managed safety and tolerability profile.
- These findings provide a strong foundation for continued advancement of FOG-001 and highlight its promising potential to meaningfully impact disease by specifically targeting the underlying mechanism through inhibition of Wnt/β-catenin.

**Enrollment is currently ongoing: NCT05919264**

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