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A Phase 1 Study of BGB-B2033 (GPC3x4-1BB Bispecific Antibody) Monotherapy in Patients With Selected Advanced or Metastatic Solid Tumors: First Disclosure of Clinical Data

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Key Takeaway Points

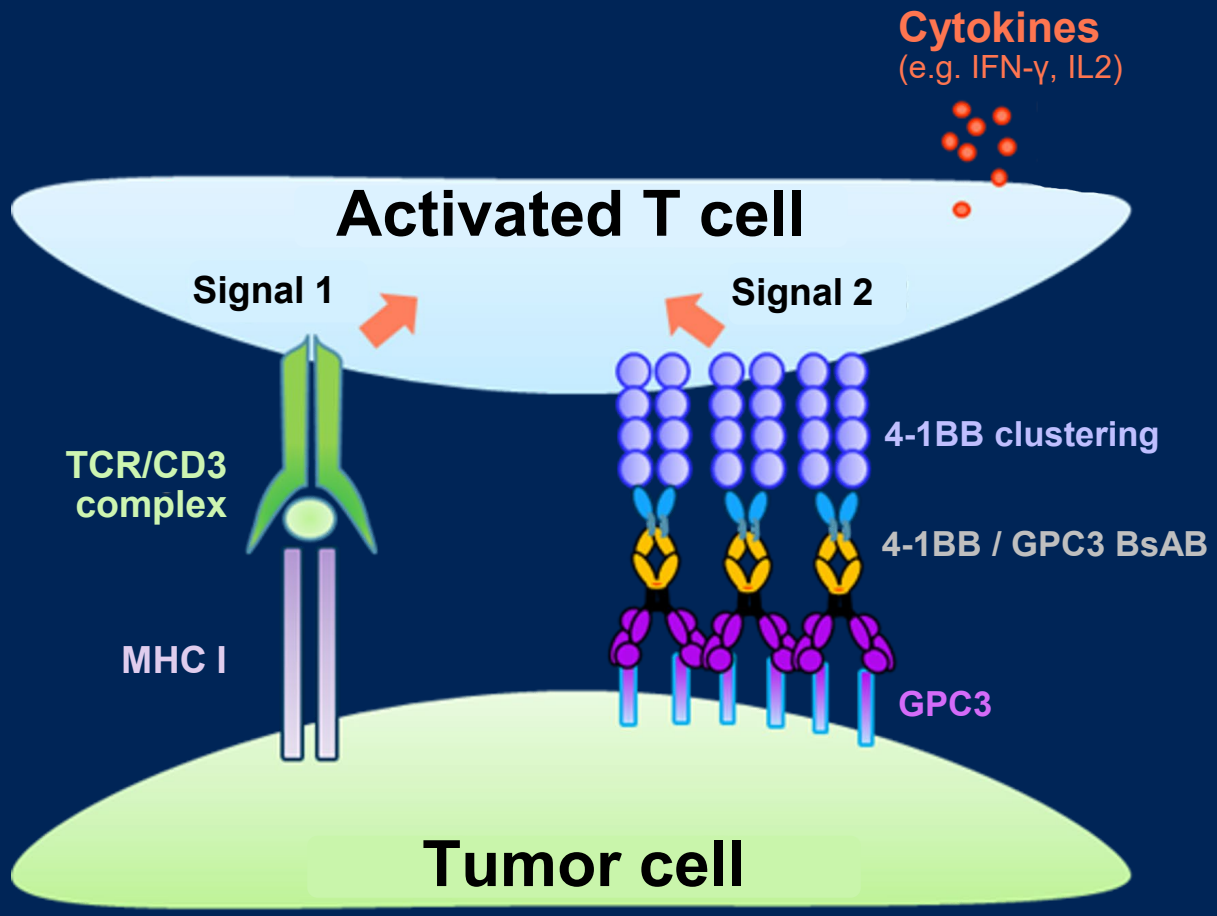
1. BGB-B2033, a first-in-class bispecific antibody targeting GPC3 and 4-1BB, was rationally designed to induce intra-tumoral T cell activation

2. BGB-B2033 demonstrates unprecedented antitumor activity in a heavily pretreated HCC population

3. BGB-B2033 exhibited a highly favorable safety profile with excellent tolerability, particularly in late-line HCC; MTD has not been determined

Background

- **Glypican-3 (GPC3)**: tumor-associated antigen highly expressed in multiple tumors, including in ~90% of HCC with any staining[1]
- **4-1BB (CD137):** key costimulatory receptor of T cells and a promising therapeutic target in cancer
- **BGB-B2033** is a novel, rationally designed IgG-based GPC3 x 4-1BB bispecific antibody
  - Activates 4-1BB on CD8+ T-cells only in the presence of GPC3-expressing tumor cells, enabling targeted tumor activity
  - Engineered Fc region designed to extend PK exposure while maintaining localized immune activation[2]



1. Ishiguro et al, *Sci. Transl. Med*. 9, eaal4291 (2017) 2. Li et al. Poster #6009 AACR 2025

Study Design (NCT06427941)

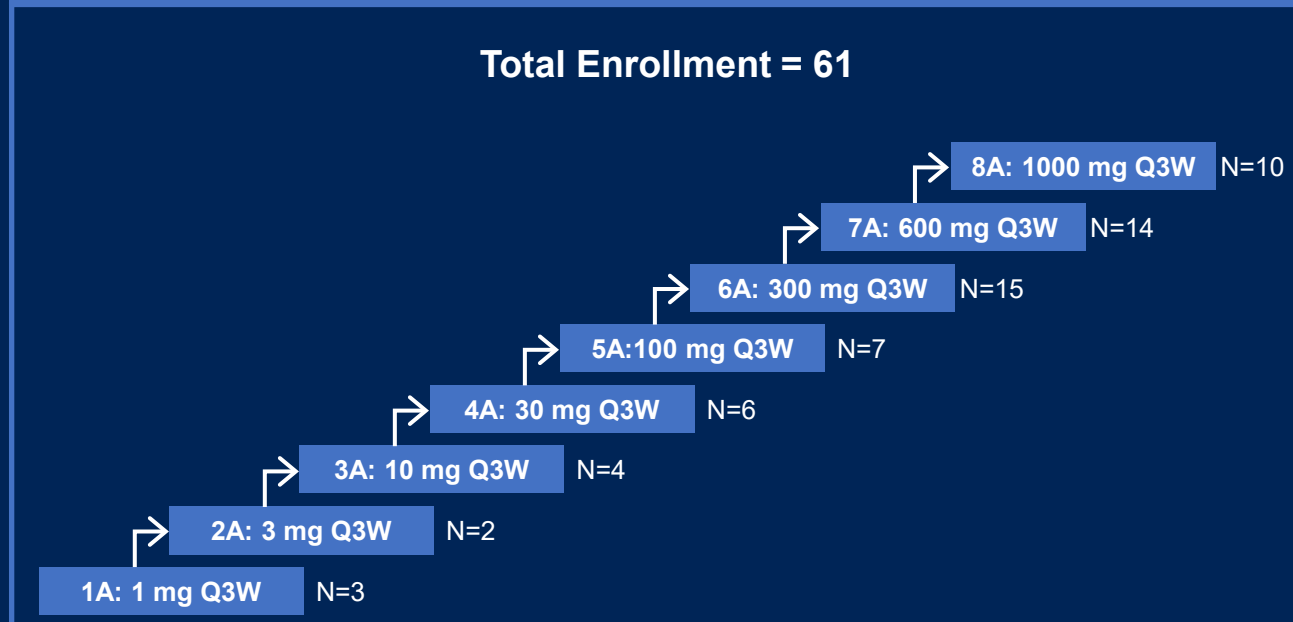
Phase 1 study of BGB-B2033 alone or in combination with tislelizumab with or without bevacizumab in patients with advanced solid tumors

KEY ELIGIBILITY CRITERIA

- Pretreated advanced HCC
  - Child Pugh A
- GPC3 expressing tumors having received at least 1 prior therapy including:
  - Squamous NSCLC
  - AFP+ GC
- ECOG 0-1
- At least 1 measurable lesion by RECIST 1.1
- Archival tissue or fresh biopsy for GPC3 testing

MONOTHERAPY DOSE ESCALATION

BGB-B2033 Q3W



DCO: April 15, 2026; median study follow-up was 4.8 (range, 0.3-15.5) months

ENDPOINTS

Primary

- Safety
- Recommended dose for expansion
- MTD

Secondary

- Objective response rate by investigator per RECISTv1.1
- Pharmacokinetics/ pharmacodynamics
- Immunogenicity

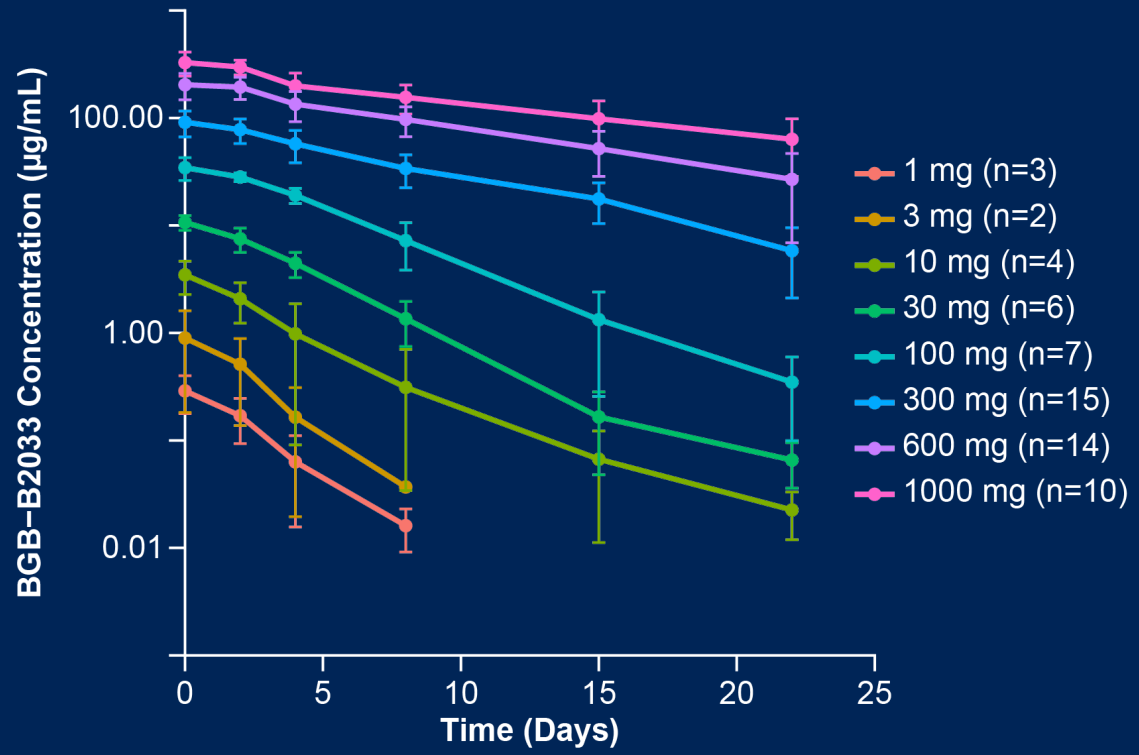
AFP, alpha-fetoprotein; CPI, checkpoint inhibitors; DCO, data cut-off; ECOG, Eastern Cooperative Oncology Group; GC, gastric cancer; GPC3, Glypican-3; HCC, hepatocellular carcinoma; Q3W, every 3 weeks; RECIST, Response Evaluation Criteria in Solid Tumors

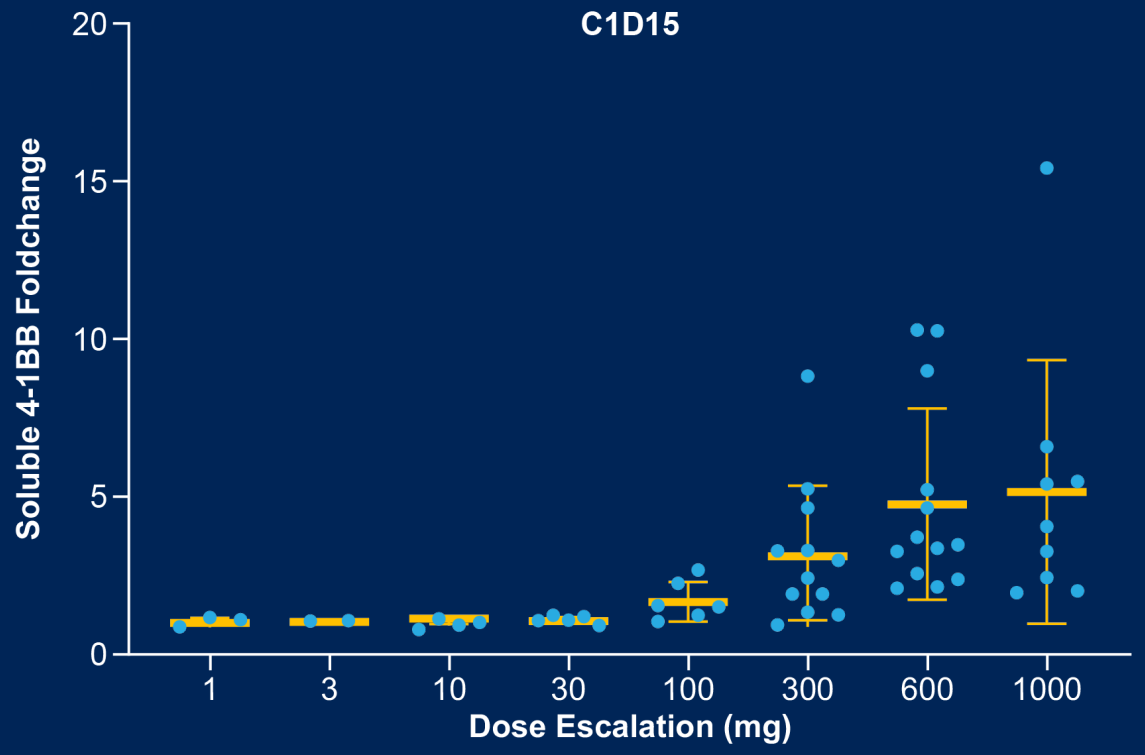
Baseline Demographics and Disease Characteristics

		Total (N=61)
Male , n (%)		54 (88.5)
Race, n (%)	Asian	56 (91.8)
	Black or African American	1 (1.6)
	Native Hawaiian/Pacific Islander	3 (4.9)
	White	1 (1.6)
ECOG PS, n (%)	0	32 (52.5)
	1	29 (47.5)
Type of Cancer, n (%)	Gastric	1 (1.6)
	HCC	60 (98.4)
Etiology of Hepatitis, n (%)	HBV	53 (86.9)
	HCV	2 (3.3)
	Other	6 (9.8)
Number of Prior Lines, median (range)		2.0 (1-6)
Prior Lines of Systemic Therapy, n (%)	Prior PD(L)-1	59 (96.7)
	Prior TKI	48 (78.7)
	Prior PD(L)-1 and TKI	46 (75.4)

ECOG PS, European Cooperative Oncology Group Performance Score; HBV, Hepatitis B; HCV, Hepatitis C; HCC, hepatocellular carcinoma; PD-1, programmed cell death protein 1;PD-L1, programmed death-ligand 1; TKI, tyrosine kinase inhibitor

Doses of >300 mg Exhibit Linear PK and Increased Soluble 4-1BB



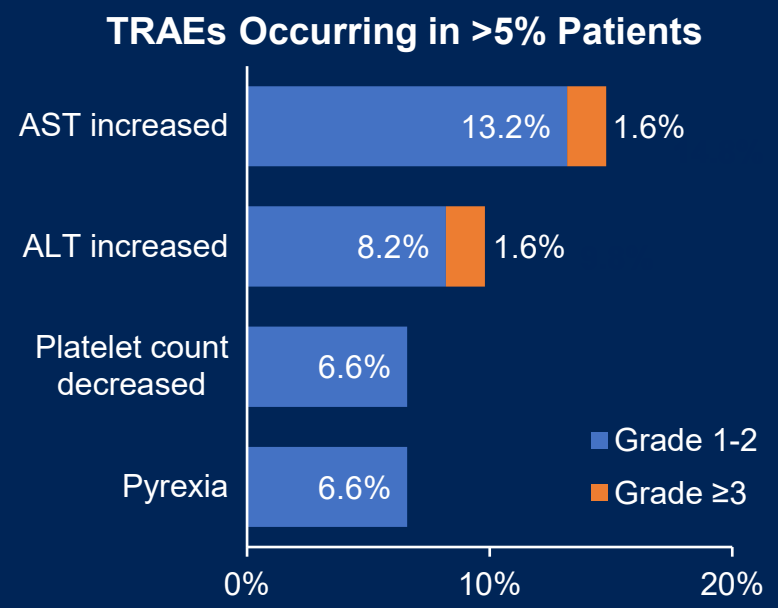


- Mean $t_{1/2}$ range of 5-11 days at doses >300 mg

Data cut-off: 15 April 2026

BGB-B2033 Was Well Tolerated, With Limited AEs

n, (%)	1-100 mg N=22	300 mg N=15	600 mg N=14	1000 mg N=10	Total N=61
Any TEAE	15 (68.2)	9 (60.0)	9 (64.3)	9 (90.0)	42 (68.9)
Grade ≥3 TEAEs	5 (22.7)	4 (26.7)	0	5 (50.0)	14 (23.0)
Any TRAEs	8 (36.4)	9 (60.0)	7 (50.0)	5 (50.0)	29 (47.5)
Grade ≥3 TRAEs	2 (9.1)	2 (13.3)	0	1 (10.0)	5 (8.2)
Any Serious TEAEs	1 (4.5)	0	2 (14.3)	4 (40.0)	7 (11.5)
TEAEs Leading to Discontinuation	0	0	0	2 (20.0)	2 (3.3)
DLT, n	0	1	0	0	1



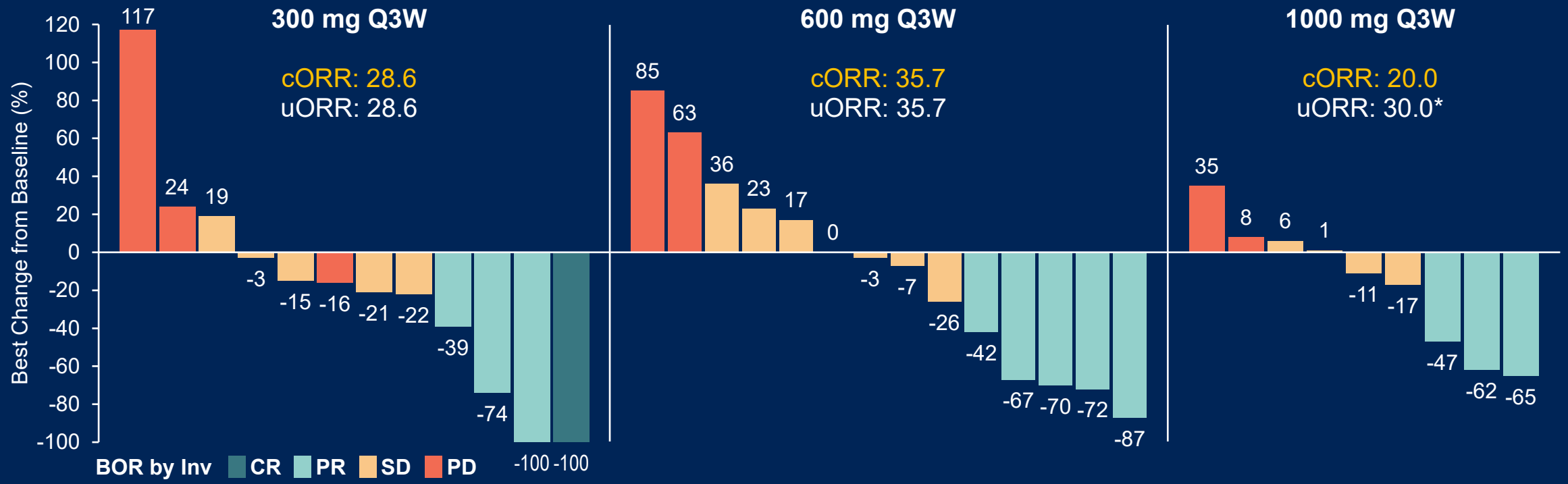
- IMAEs occurred in 4 (6.6%)[a] patients, none of which were Grade ≥3
- Two patients discontinued treatment due to AEs, only 1 due to TRAE (Grade 3 drug eruption)
- One DLT (Grade 3 ALT increased) occurred and resolved after dose interruption

Data cut-off: 15 April 2026

[a]Two hypothyroidism and two rash.

AE, adverse event; ALT, alanine aminotransferase; AST, aspartate aminotransferase; DLT, dose-limiting toxicity; IMAE, immune-mediated adverse events; TEAE, treatment emergent adverse event; TRAE, treatment-related treatment emergent adverse event

Promising Antitumor Activity in Heavily Pretreated HCC



- At doses ≥300 mg, confirmed ORR was 28.9% and unconfirmed ORR was 31.6%

Data cut-off: 15 April 2026

*A PR at week 36 was reported at 1000 mg, with patient on treatment, pending for confirmation in the next tumor assessment.

BOR, best overall response; c, confirmed; CR, complete response; HCC, hepatocellular carcinoma; Inv, investigator; ORR, objective response; PD, progressive disease; PR, partial response; SD, stable disease; u, unconfirmed

Conclusions

- The first-in-class GPC3x4-1BB bispecific antibody, BGB-B2033, demonstrated a favorable safety and tolerability profile in heavily pretreated patients with HCC
  - Frequency and severity of AEs were low (8% Grade ≥3 TRAEs; no Grade ≥3 IMAEs)
- BGB-B2033 demonstrated approximately linear PK and a prominent PD effect, with an increase in soluble 4-1BB at dose levels ≥300 mg
- Unprecedented antitumor activity was observed in heavily pretreated advanced HCC
  - Confirmed ORR of 28.6, 35.7, and 20% at 300, 600 and 1000 mg, respectively
  - At doses ≥300 mg, confirmed ORR was 28.9% and unconfirmed ORR was 31.6%
- Given the compelling antitumor activity and favorable safety profile, registration-enabling studies are in active development

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