NB-012: AKT-1 ASO for Hepatocellular Carcinoma

Clinical-stage antisense oligonucleotide (ASO) therapeutic targeting AKT-1, with potential across a range of cancer types.

NB-012: AKT-1 ASO for Hepatocellular Carcinoma

First-in-class clinical-stage ASO therapeutic targeting AKT-1

World's first clinical-stage ASO therapeutic targeting AKT-1, delivered via the QTsome™ LNP platform. With IND clearances in the US and China, active Phase I and Phase II trials, and FDA Orphan Drug Designation, NB-012 represents a differentiated and potentially practice-changing approach to hepatocellular carcinoma.

First-in-Class

The world's first clinical-stage ASO therapeutic targeting AKT-1, delivered via the QTsome™ LNP platform

Global Clinical Program

Active Phase I and Phase II trials with IND clearances in both the US and China; enrolling sites in Mainland China, Hong Kong and the US

FDA Orphan Drug Designation

Received FDA Orphan Drug Designation for hepatocellular carcinoma, underscoring unmet medical need

Combination Potential

Pre-clinical data shows superior tumor suppression in combination with TKIs (Sorafenib, Lenvatinib, Cabozantinib) and anti-PD-1 therapy

NB-012: Understanding AKT & the Mechanism

First-in-class clinical-stage ASO therapeutic targeting AKT-1

What is AKT?

AKT (Protein Kinase B) is a key intracellular kinase in the PI3K/AKT/mTOR signaling pathway, regulating cell survival, growth, proliferation, and metabolism. Dysregulation drives cancer progression.

Tumor Relevance

AKT is broadly relevant across multiple solid tumors, including hepatocellular carcinoma (HCC), NSCLC, breast, prostate and colorectal cancers driven by PI3K pathway dysregulation.

How the ASO Works

NB-012 is an antisense oligonucleotide (ASO) that binds specifically to AKT-1 mRNA, triggering its degradation and blocking translation, reducing AKT-1 protein expression to inhibit tumor growth and survival signaling.

QTsome™ LNP Platform

QTsome™ is a lipid nanoparticle (LNP) delivery system that encapsulates and protects the ASO, enabling efficient delivery into liver and tumor tissue with enhanced stability, uptake and therapeutic effect.

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Clinical Highlights

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No DLTs at 0.1, 0.3 or 0.6 mg/kg/week dose group. Infusion-related reactions (IRRs, Grade 2) occurred in 2 patients at 1.0 mg/kg/week, leading to a withdrawal.. MTD - 0.6 mg/kg/wk

9.4 mo

Median PFS across evaluable Phase I patients

15.9 mo

Median stable disease duration in Phase I

93.55%

Tumor Growth Inhibition with NB-012 + anti-PD-1 in pre-clinical models

3-Stage

Phase II design: monotherapy escalation → combo escalation → combo expansion

Phase I Takeaways

- MTD established at 0.6 mg/kg/week
- 1 confirmed partial response (11.5 months) in heavily pre-treated NSCLC patient
- Favorable tolerability; no withdrawals due to AEs

Phase II Status (as of Dec 2025)

- 10 subjects enrolled in monotherapy escalation (0.6–1.3 mg/kg/week)
- 3 subjects in combination cohort (0.6 mg/kg/week + Sorafenib)
- Zero DLTs; all Grade 1–2 TRAEs; no study terminations

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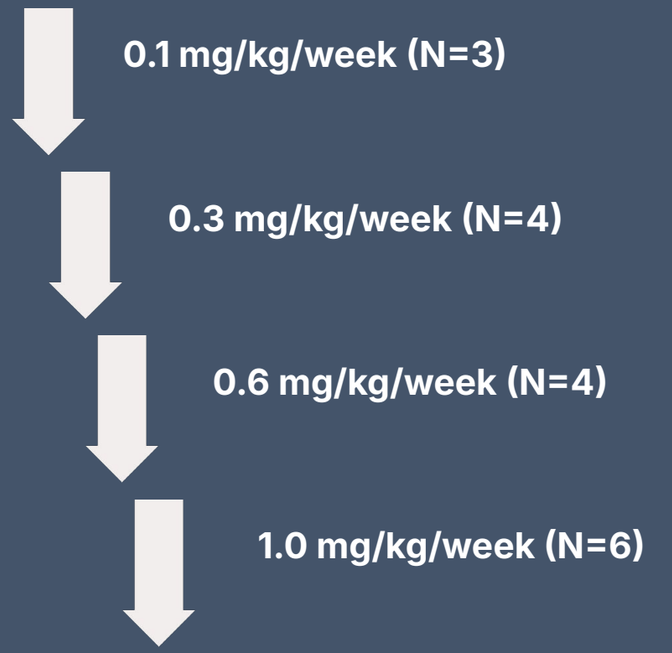
Phase I Trial: Study Design (NCT05267899)

A Phase I, first-in-human, open-label, dose-escalation study evaluating the safety, tolerability, and pharmacokinetics of NB-012 — an LNP suspension of AKT-1 antisense oligonucleotide — in patients with advanced solid tumors.

Dose Escalation Design (Traditional 3+3)



Primary: Safety and tolerability
Secondary: Pharmacokinetics and preliminary efficacy

Main Inclusion Criteria

- Advanced, histologically or cytologically confirmed solid tumors progressed from or relapsed after prior therapy, not candidates for curative therapy
- Measurable disease per RECIST 1.1
- ECOG Performance Status ≤ 2

Main Exclusion Criteria

- Anti-cancer therapy or investigational drugs within 4 weeks prior to first dose
- Pregnant, lactating, or planning to conceive during the trial
- Brain tumors or unstable brain metastases (stable for <3 months)

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Phase I Trial: Baseline Characteristics

The Phase I study enrolled 17 patients across 4 dose cohorts (0.1–1.0 mg/kg/week), representing a heavily pre-treated advanced solid tumor population — validating the real-world relevance of the safety and efficacy data generated.

Demographic Details	NB-012 0.1 mg/kg/week N=3 n (%)	NB-012 0.3 mg/kg/week N=4 n (%)	NB-012 0.6 mg/kg/week N=4 n (%)	NB-012 1.0 mg/kg/week N=6 n (%)	Total N=17 n (%)
Age (years)					
Mean (STD)	59.3 (1.53)	68.5 (5.07)	65.3 (15.28)	60.7 (11.25)	63.4 (10.09
Median (Min, Max)	59.0 (58, 61)	69.5 (62, 73)	63.0 (52, 83)	64.5 (39, 70)	63.0 (39, 83
Age Category					
<65 years	3 (100)	1 (25.0)	2 (50.0)	3 (50.0)	9 (52.9)
≥65 years	0	3 (75.0)	2 (50.0)	3 (50.0)	8 (47.1)
Sex					
Male	2 (66.7)	2 (50.0)	2 (50.0)	1 (16.7)	7 (41.2)
Female	1 (33.3)	2 (50.0)	2 (50.0)	5 (83.3)	10 (58.8)
Race					
White	1 (33.3)	2 (50.0)	3 (75.0)	2 (33.3)	8 (47.1)
Black or African American	2 (66.7)	1 (25.0)	0	2 (33.3)	5 (29.4)
Asian	0	0	1 (25.0)	1 (16.7)	2 (11.8)
Other[a]	0	1 (25.0)	0	1 (16.7)	2 (11.8)
BMI (kg/m²)					
Mean (STD)	29.50 (5.126)	24.50 (7.257)	23.00 (2.608)	25.93 (7.117)	25.54 (5.928
Median (Min, Max)	28.90 (24.7, 34.9)	25.35 (16.3, 31.0)	23.10 (20.2, 25.6)	26.15 (18.1, 36.3)	25.20 (16.3, 36.3

Baseline Characteristics	NB-012 0.1 mg/kg/week N=3 n (%)	NB-012 0.3 mg/kg/week N=4 n (%)	NB-012 0.6 mg/kg/week N=4 n (%)	NB-012 1.0 mg/kg/week N=6 n (%)	Total N=17 n (%)
Cancer Type					
Colon	0	2 (50.0)	1 (25.0)	2 (33.3)	5 (29.4)
Pancreas	0	1 (25.0)	1 (25.0)	1 (16.7)	3 (17.6)
Lung, Left	2 (66.7)	0	0	0	2 (11.8)
Rectum	0	0	2 (50.0)	0	2 (11.8)
Breast	0	0	0	1 (16.7)	1 (5.9)
Endometrial Cavity	0	0	0	1 (16.7)	1 (5.9)
Liver	1 (33.3)	0	0	0	1 (5.9)
Lung, Right	0	1 (25.0)	0	0	1 (5.9)
Other	0	0	0	1 (16.7)	1 (5.9)
Time from Initial Diagnosis Until Date of Enrolment (years)					
Mean (STD)	4.080 (1.566)	4.888 (3.187)	2.585 (1.285)	4.618 (4.670)	4.108 (3.188
Median	4.340	3.830	2.195	3.500	2.870
(Min, Max)	(2.40, 5.50)	(2.47, 9.42)	(1.57, 4.38)	(0.67, 12.59)	(0.67, 12.59
Stage at Study Entry					
II	1 (33.3)	0	0	0	1 (5.9)
IV	2 (66.7)	3 (75.0)	1 (25.0)	4 (66.7)	10 (58.8)
IVa	0	0	1 (25.0)	0	1 (5.9)
IVb	0	1 (25.0)	2 (50.0)	2 (33.3)	5 (29.4)
Current Tumor Stage at Study Entry					
TX	0	2 (50.0)	2 (50.0)	3 (50.0)	7 (41.2)
T1	1 (33.3)	0	0	1 (16.7)	2 (11.8)
T2	1 (33.3)	1 (25.0)	1 (25.0)	0	3 (17.6)
T3	1 (33.3)	1 (25.0)	0	2 (33.3)	4 (23.5)
T4	0	0	1 (25.0)	0	1 (5.9)
Current Node Stage at Study Entry					
NX	1 (33.3)	1 (25.0)	0	0	2 (11.8)
N0	0	1 (25.0)	3 (75.0)	2 (33.3)	6 (35.3)
N1	0	1 (25.0)	1 (25.0)	2 (33.3)	4 (23.5)
N1a	0	0	0	1 (16.7)	1 (5.9)
N2	2 (66.7)	1 (25.0)	0	1 (16.7)	4 (23.5)
Current Metastasis Stage at Study Entry					
M0	2 (66.7)	0	0	0	2 (11.8)
M1	0	1 (25.0)	1 (25.0)	4 (66.7)	6 (35.3)
M1a	0	2 (50.0)	1 (25.0)	0	3 (17.6)
M1b	1 (33.3)	1 (25.0)	2 (50.0)	1 (16.7)	5 (29.4)
M1c	0	0	0	1 (16.7)	1 (5.9)
Grade					
Moderately Differentiated	0	2 (50.0)	2 (50.0)	1 (16.7)	5 (29.4)
Poorly Differentiated	0	0	0	2 (33.3)	2 (11.8)
Not Applicable	1 (33.3)	0	0	0	1 (5.9)
Unknown	2 (66.7)	2 (50.0)	2 (50.0)	3 (50.0)	9 (52.9)
Time from Last Progression Until Date of Enrolment (years)[a]					
n	3	4	4	5	16
Mean (STD)	-0.017 (0.021)	0.155 (0.098)	0.038 (0.056)	0.054 (0.085)	0.062 (0.091
Median (Min, Max)	-0.010 (-0.04, 0.00)	0.150 (0.04, 0.28)	0.030 (-0.01, 0.10)	0.020 (-0.02, 0.18)	0.030 (-0.04, 0.28

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Phase I Trial: Safety Profile

NB-012 demonstrated a manageable and well-characterized safety profile across all dose levels in 17 evaluable patients. The MTD was established at 0.6 mg/kg/week, with no DLTs observed below this threshold.

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DLTs at ≤0.6 mg/kg

No dose-limiting toxicities at 0.1, 0.3, or 0.6 mg/kg/week cohorts

47%

TRAE Rate

8 of 17 patients experienced treatment-related AEs; most common were IRRs (29.4%) and arthralgia (11.8%)

29%

Grade ≥3 AEs

5 of 17 patients; only 1 Grade ≥3 event (Type 2 diabetes) was related to NB-012. All others were unrelated.

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Withdrawals Due to AEs

No patient withdrawals or study terminations attributable to adverse events across the entire trial

MedDRA Preferred Term	0.1 mg/kg (N=3)	0.3 mg/kg (N=4)	0.6 mg/kg (N=4)	1.0 mg/kg (N=6)	All (N=17)
Infusion related reaction	1 (33.3%) — 4 events	2 (50.0%) — 3 events	0	2 (33.3%) — 4 events	5 (29.4%) — 11 events
Arthralgia	0	1 (25.0%)	0	1 (16.7%)	2 (11.8%)
Type 2 diabetes mellitus (SAE)	1 (33.3%)	0	0	0	1 (5.9%)
Vomiting / Nausea / Fatigue / Other	—	Multiple Grade 1–2	—	—	≤1 patient each

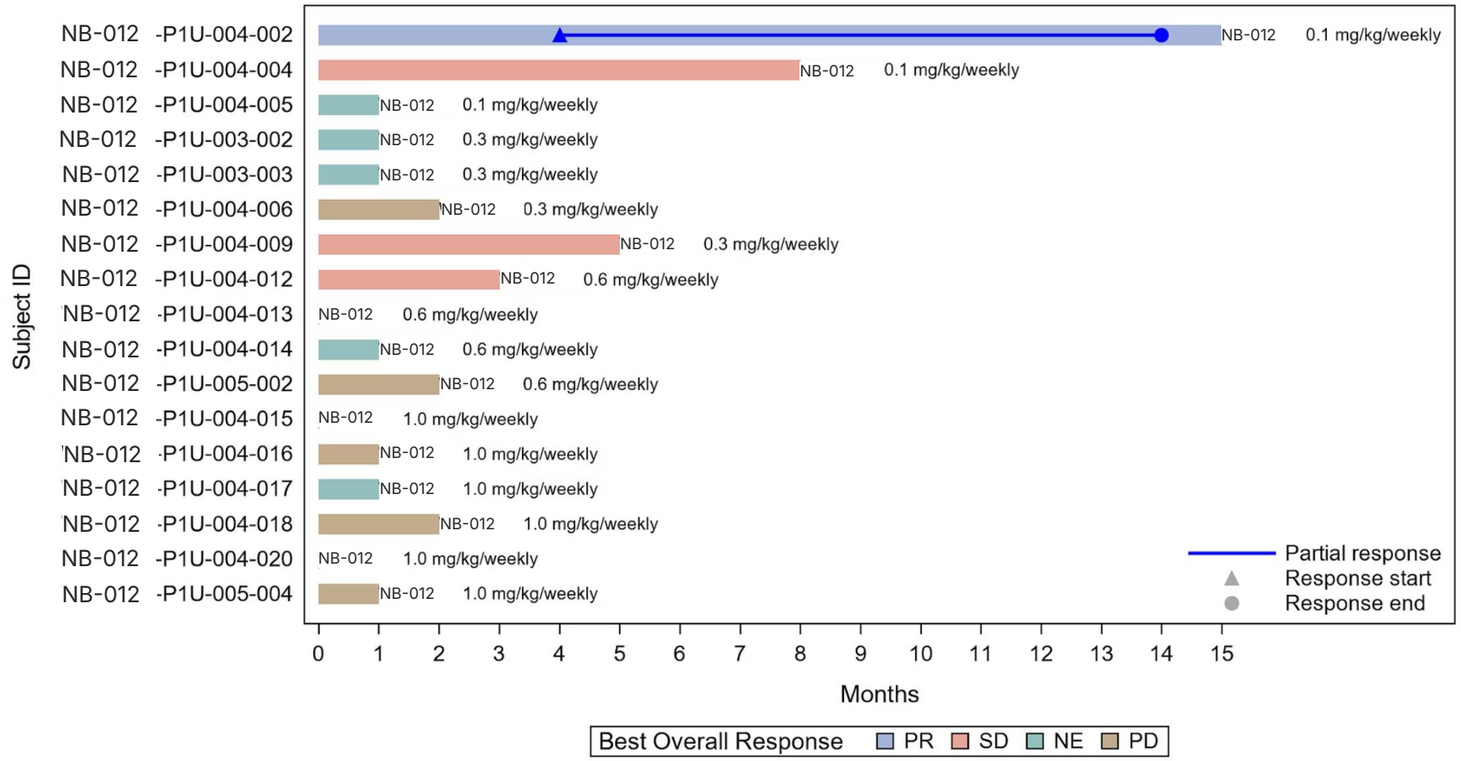
MTD established at 0.6 mg/kg/week. IRRs were managed by reducing infusion rate or pausing treatment; no Grade ≥3 IRRs reported. DLT definition has been optimized for Phase II based on principal investigator recommendations.

DLT: Dose Limiting Toxicity; MTD: Maximal Tolerable Dose; SAE: Serious Adverse Event; TRAE: Treatment-Related Adverse Event.

NB-012: AKT-1 ASO for Hepatocellular Carcinoma

Phase I Trial: Swimmer Plot of Response

The swimmer plot below illustrates individual patient treatment durations and best overall responses across dose cohorts of NB-012 (0.1–1.0 mg/kg/weekly). Preliminary signs of efficacy included one confirmed partial response (PR) lasting 11.5 months, prolonged stable disease (SD) with a median duration of 15.9 months, and a median PFS of 9.4 months across evaluable participants.



Partial Response

1 confirmed PR with 11.5-month duration at 0.1 mg/kg/weekly

Stable Disease

Median SD duration of 15.9 months across dose groups

Median PFS

9.4 months across the evaluable patient population

These findings suggest that NB-012 has promising potential as a safe and effective treatment for advanced solid tumors, warranting continued dose exploration and combination strategies in subsequent trials.

NB-012: AKT-1 ASO for Hepatocellular Carcinoma

Phase 1 Trial: Efficacy Profile Summary

Key Efficacy Endpoints

BOR

PR in 1 participant; SD in 3 participants across dose groups

ORR

5.9% (1/17; 95% CI: [0.8, 90.6])

DOR

11.5 months for the confirmed partial responder

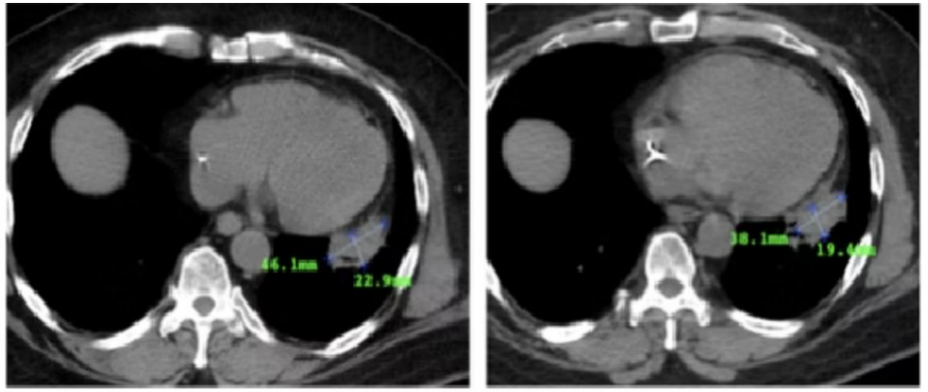
The ongoing Phase 2 clinical trial is expected to deliver critical efficacy data for **NB-012 combined with Sorafenib (TKI)** as a second-line treatment for advanced HCC.

Notable Case Report: Confirmed PR

M/62y, advanced NSCLC — 7 prior treatment lines. Monotherapy with NB-012 at 0.1 mg/kg/week yielded a PR by RECIST 1.1 criteria after 4 cycles, maintained for **11.5 months**.

CT imaging confirmed measurable tumor reduction after 2 cycles:

- Baseline: 46.1 mm × 22.9 mm (25 AUG 2022)
- Post-treatment: 38.1 mm × 19.4 mm (24 OCT 2022)



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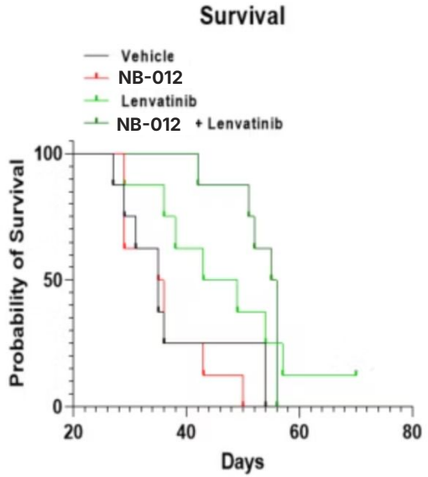
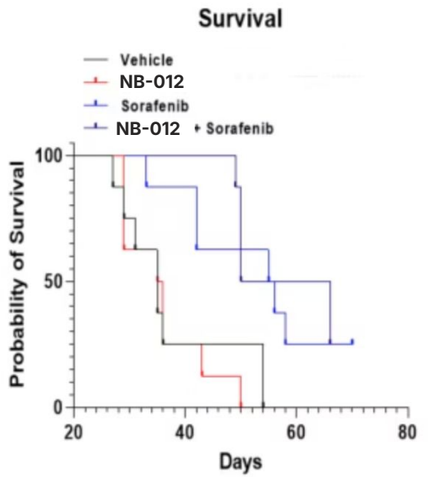
Pre-Clinical Data: TKI Combination Shows Superior Efficacy

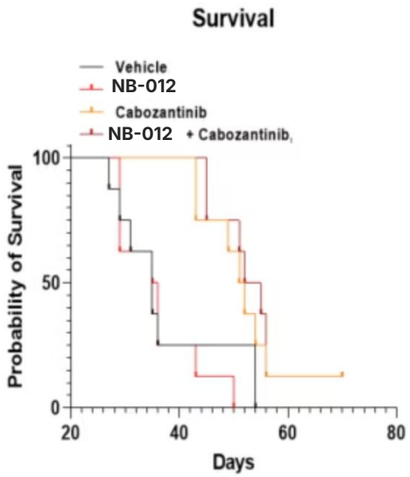
In multiple pre-clinical tumor models, NB-012 combined with TKIs (Lenvatinib, Sorafenib, and Cabozantinib) demonstrated markedly enhanced tumor suppression compared to TKI monotherapy alone. Survival benefits were also observed across combination arms versus vehicle control.

Tumor Growth Inhibition (TGI)

Combination	Combo TGI	Mono TGI
NB-012 + Lenvatinib	66.05%	50.84%
NB-012 + Sorafenib	86.81%	55.68%
NB-012 + Cabozantinib	75.89%	47.84%







Median Survival Benefit

NB-012 + Lenvatinib extended median survival to **55.5 days vs. 46 days** for Lenvatinib monotherapy — a statistically significant improvement. Sorafenib and Cabozantinib combinations showed numerical improvement over vehicle but no significant difference vs. their monotherapy arms.

Kaplan-Meier survival curves across three TKI combination arms confirm that NB-012 enhances and extends the survival benefit conferred by TKI therapy, with the Lenvatinib combination showing the most pronounced and statistically significant improvement.

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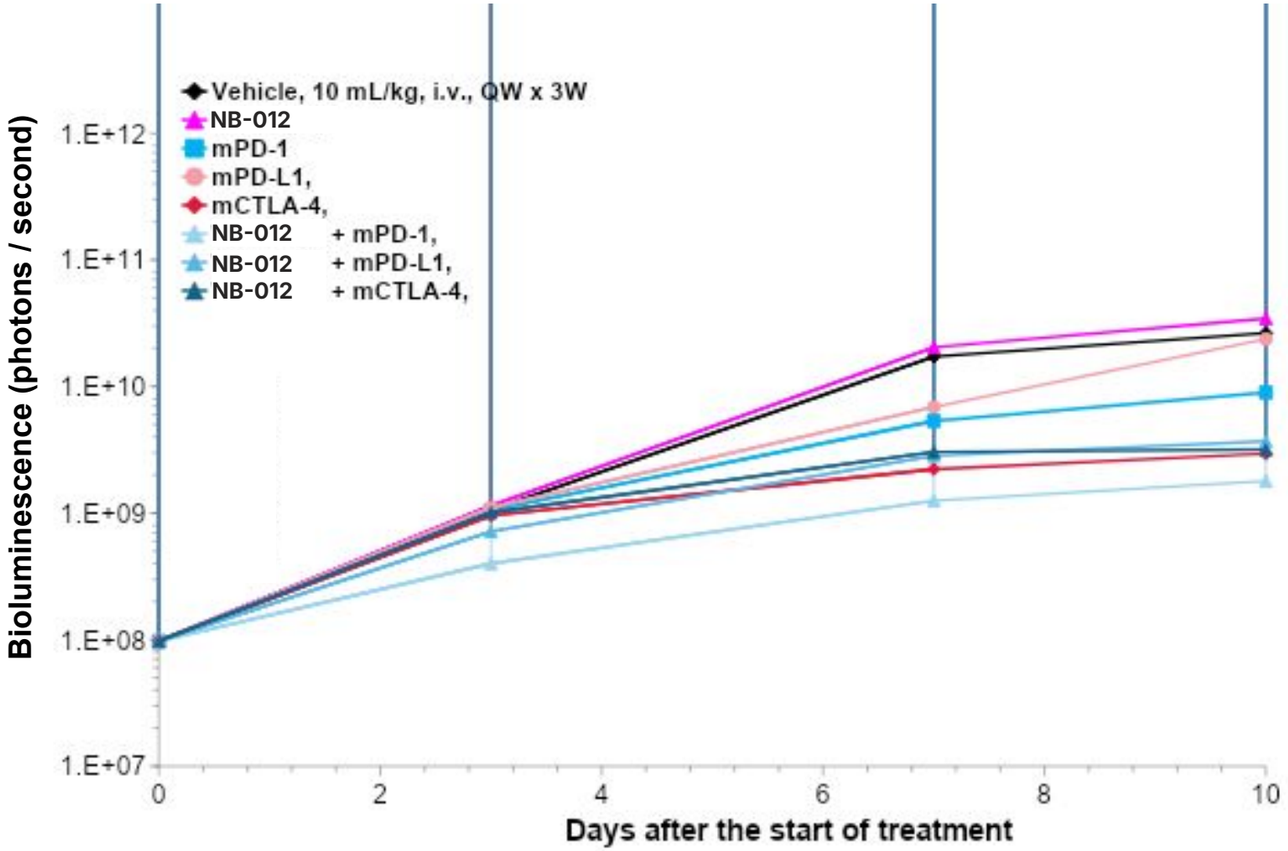
NB-012+ PD-1 Combination Drives Markedly Stronger Tumor Suppression



Tumor Growth Inhibition

NB-012 + mPD-1

TGI: 93.55% — substantially higher than mPD-1 monotherapy

mPD-1 Monotherapy

TGI: 66.28% — meaningful but inferior to the combination arm

The bioluminescence tumor volume curves demonstrate that combining NB-012 with anti-PD-1 delivers a **27-percentage-point improvement in TGI**, underscoring the synergistic potential of this combination approach. These results support continued investigation of NB-012 as an immunotherapy enhancer in combination regimens.

NB-012: AKT-1 ASO for Hepatocellular Carcinoma

Phase II Trial: Study Design (NCT06309485)

This global multi-center Phase II study evaluates NB-012 monotherapy and combination therapy with sorafenib across three sequential stages in patients with advanced HCC, enrolling sites in Mainland China, Hong Kong and the United States.

1 | 2 | 3

Stage 1 — Monotherapy Escalation

~9–24 subjects (China only). Traditional 3+3 design to determine MTD/RP2D of single-agent NB-012 in advanced, subsequent-line HCC.

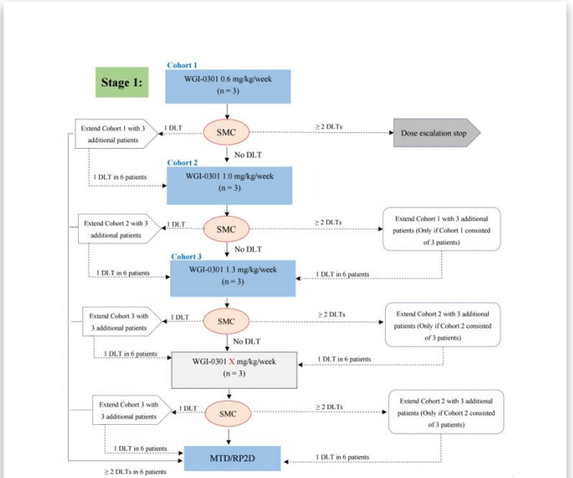
Stage 2 — Combo Escalation + Expansion

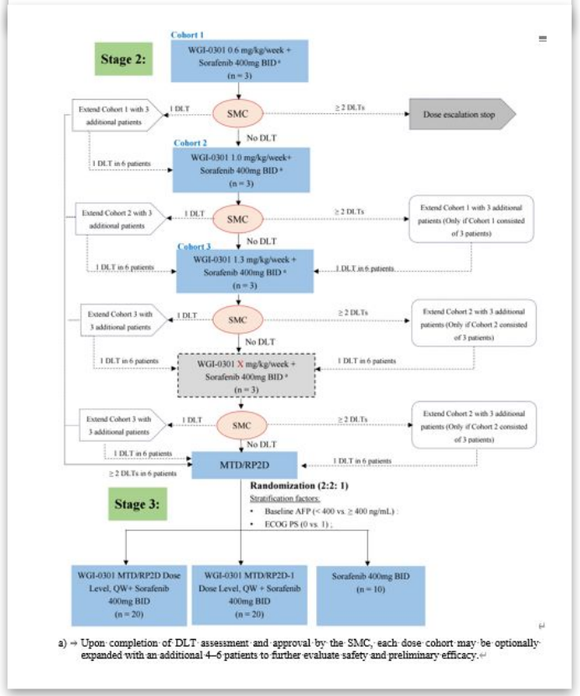
~9–48 subjects (China, HK, US). Determine MTD/RP2D of NB-012 + Sorafenib in advanced HCC with ≥1st line failure/intolerance. US sites enroll up to 20% of patients.

Stage 3 — Combo Dose Expansion

~50 subjects (China, HK, US). Evaluate preliminary efficacy and safety of NB-012+ Sorafenib in advanced HCC with only 1st-line systemic immunotherapy failure/intolerance.

In Stages 2 and 3, US sites will enroll up to 20% of total patients, reflecting a true global multi-center registration strategy.





NB-012: AKT-1 ASO for Hepatocellular Carcinoma

Phase II Trial: Safety Profile Update (NCT06309485)

As of December 15, 2025, the Phase II trial has demonstrated an encouraging safety profile across all dose levels, with no dose-limiting toxicities observed in either monotherapy or combination cohorts.

Enrollment Status

10 subjects enrolled in single-agent dose escalation (0.6 / 1.0 / 1.3 mg/kg/week groups). 3 subjects enrolled in the 0.6 mg/kg/week combination dose group. All completed the DLT observation period.

No DLTs Observed

Zero dose-limiting toxicities across all monotherapy dose levels and in the combination cohort — a key indicator of a manageable and favorable tolerability profile.

TRAE Profile

Common TRAEs included infusion-related reactions, elevated AST, thrombocytopenia, diarrhea, and anorexia — **all Grade 1–2**. No Grade ≥3 events were related to NB-012 per investigator assessment.

No Withdrawals

No patient withdrawals or study terminations due to adverse events. 2 SAEs (spontaneous pneumothorax and obstructive pneumonia) both assessed as unrelated to NB-012.

Overall, NB-012 monotherapy has demonstrated good safety and tolerability in patients with advanced HCC in China, supporting continued dose escalation and combination evaluation.

Accelerating Innovation to Improve Patients' Lives

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For more information about partnership opportunities and to join us on this exciting journey of bringing transformative therapies to patents worldwide, please reach out to:

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