

P1.272: First-in-Human Phase 1 Study of TXN10128 (ENPP1i) plus Irinotecan: Durable Responses in TKI-Refractory EGFR-Mutated NSCLC



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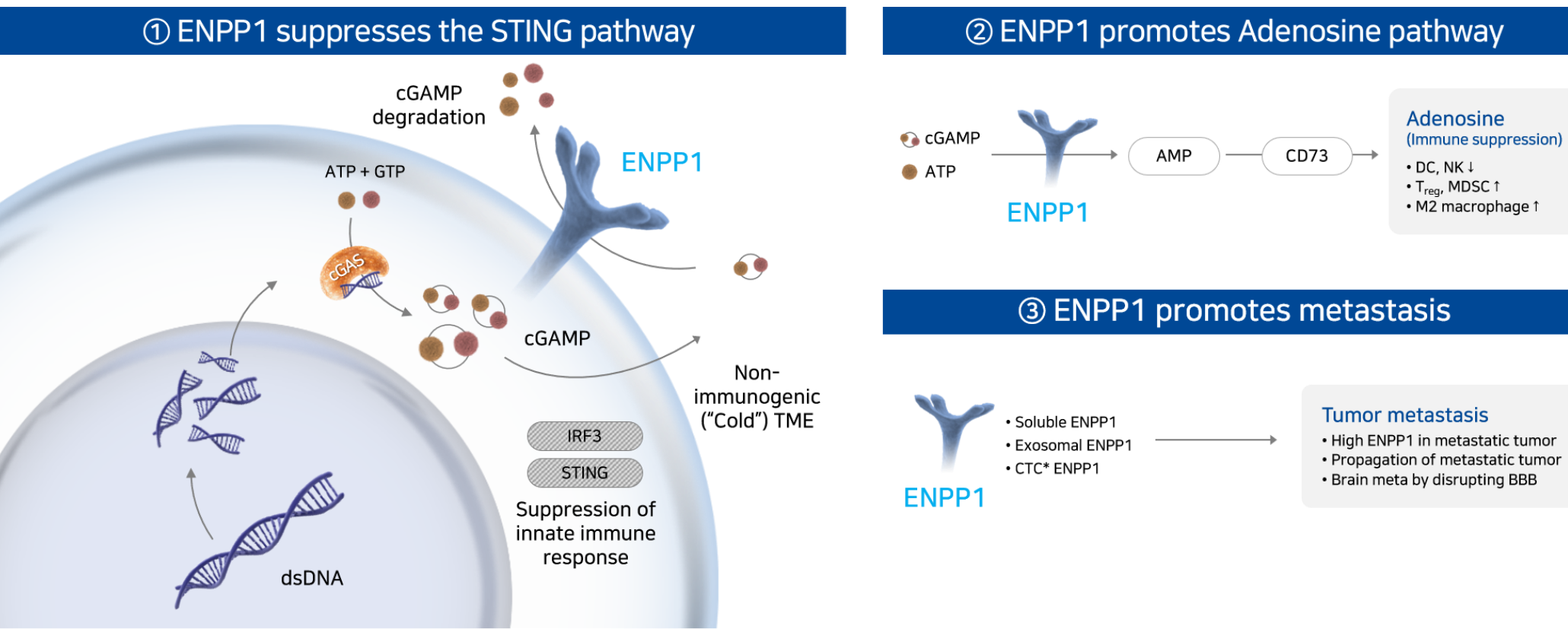


**IASLC 2026 World
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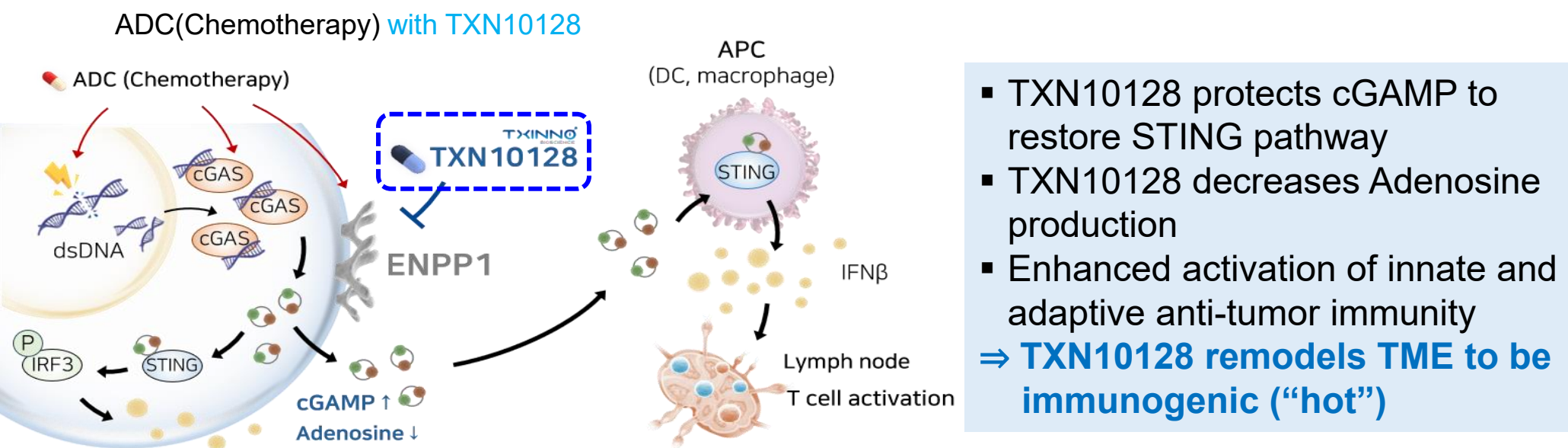
**SEPTEMBER 12 – 15, 2026
SEOUL, REPUBLIC OF KOREA**

INTRODUCTION

ENPP1 is an innate immune checkpoint that suppresses STING signaling and increases immune-suppressive Adenosine.



TXN10128 inhibits ENPP1 to restore STING pathway and remodel TME from "cold" to "hot".



METHODS

- Title: *A Multicenter, Open-label, Phase 1 Dose escalation and Expansion Study of TXN10128, an Inhibitor of ENPP1 as monotherapy and combination therapy with Irinotecan or Paclitaxel in Subjects with Locally Advanced (Unresectable) or Metastatic Solid Tumors (NCT05978492).*
- This ongoing Phase 1 dose-escalation and expansion study evaluated TXN10128 alone and in rational combinations. The present analysis focused on patients with EGFR-mutated NSCLC treated with TXN10128 in combination with irinotecan who had progressed on prior EGFR TKI therapies.
- The primary endpoints were safety, tolerability, and determination of the recommended Phase 2 dose (RP2D). Secondary endpoints included objective response rate (ORR) and progression-free survival (PFS), assessed according to RECIST v1.1.

RESULTS: All tumors

Baseline characteristics

Heavily pretreated patients with EGFRm NSCLC (median 3 prior lines; 89% post-3rd-gen TKI, 100% post-platinum)

Table 2. Baseline Characteristics

Characteristics	Safety Dataset	Efficacy Dataset (EGFRm NSCLC)
	n=19	n=9
Age, median (range), years	63 (43–81)	66 (58–76)
Sex, Male / Female, n	13 / 6	5 / 4
ECOG PS 1, n (%)	17 (90)	9 (100)
Prior lines of therapy, median (range)	2 (1–8)	3 (2–6)
Prior 3rd-gen EGFR TKI, n (%)	8 (42)	8 (89)
Prior platinum-based chemotherapy, n (%)	19 (100)	9 (100)
Brain metastases at baseline, n (%)	7 (37)	4 (44)
Liver metastases at baseline, n (%)	5 (26)	1 (11)
Tumor types enrolled		
NSCLC – EGFRm	8 (42)	9 (100)
NSCLC – WT	3 (16)	—
NSCLC – SQ	4 (21)	—
NSCLC – ALKm	1 (5)	—
BTC/HNSCC/Pancreatic	1/1/1	—

Safety

Well tolerated across 700~1,500 mg QD, with Grade ≥ 3 TRAEs (5.3%) and no new safety signals.

Table 3. Safety Summary of TXN10128 plus Irinotecan

AEs	TXN10128 + Irinotecan (n=19), n (%)
any TEAE	18 (94.7)
Grade ≥3 TEAEs	12 (63.2)
any TRAE	9 (47.4)
Grade ≥3 TRAEs	1 (5.3)
SAEs	5 (26.3)
AEs leading to dose interruption	6 (31.6)
ADRs leading to dose interruption	2 (10.5)

Abbreviations: TEAE, treatment-emergent adverse event; TRAE, treatment-related adverse event; SAE, serious adverse event; ADR, adverse drug reaction.

Table 4. Most Common Treatment-Related Adverse Events (TRAEs ≥ 10%)

TRAEs	TXN10128 + Irinotecan (n=19), n (%)
Nausea	4 (21.1)
Decreased appetite	2 (10.5)
Fatigue	2 (10.5)
Vomiting	2 (10.5)
Pyrexia	2 (10.5)

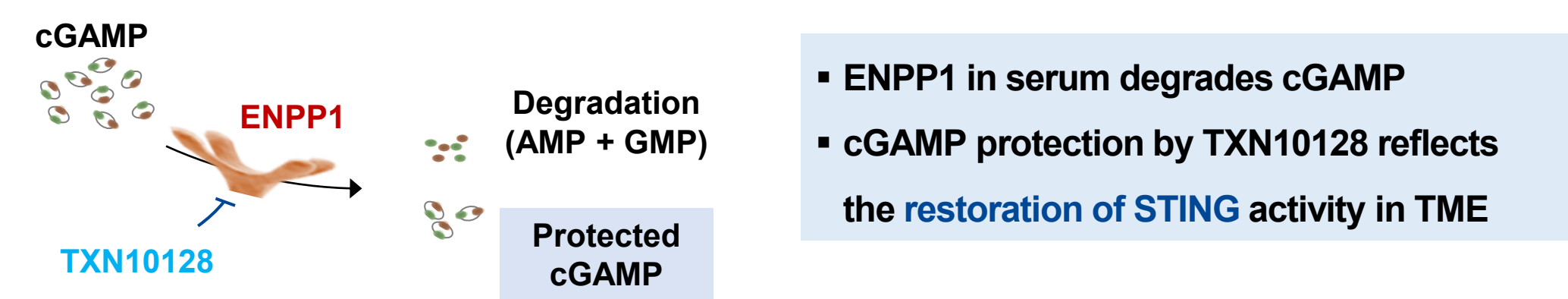
Footnote: Immune-related TRAEs were reported in 4 patients(15.8%), all of which were Grade 1.

Pharmacokinetics

Pharmacokinetic analysis demonstrated a dose-dependent increase in systemic exposure, supporting a favorable once-daily (QD) dosing profile of TXN10128.

RESULTS: EGFRm NSCLC

PD Biomarker: cGAMP protection



PK–PD correlation

Target engagement was demonstrated by robust cGAMP protection in blood, observed across all evaluated dose levels in TXN10128-treated patients.

Data are omitted for confidentiality and will be available on-site

Efficacy: Tumor assessment & Treatment duration/PFS (EGFRm NSCLC, n = 9)

Preliminary efficacy demonstrated durable responses in a subset of patients. The median PFS was 6.7 months (95% CI, 2.5–NR) by Kaplan-Meier estimation.

Data are omitted for confidentiality and will be available on-site

Efficacy: Case study — Tumor response and durable disease control

Data are omitted for confidentiality and will be available on-site

Efficacy: Case study — Immune modulation

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DISCUSSION AND CONCLUSION

- TXN10128 plus irinotecan demonstrated a favorable safety profile and promising durable clinical efficacy in TKI-refractory EGFR-mutated NSCLC.
- These proof-of-concept findings support the biological rationale for combining ENPP1 inhibition with DNA damage induction to remodel the immunosuppressive TME.
- Further development of TXN10128 in combination with TOP1 inhibitor-based ADCs is warranted.
- These data establish proof-of-concept for ENPP1 inhibition in TKI-refractory EGFRm NSCLC. Following MFDS Phase 2 approval (1 Jul 2026), ENRISE study (TXN10128-02) will open enrollment in Q4 2026.

Acknowledgement

The authors thank the patients, their families, and all investigators, coordinators, and site staff for their contributions. This study was sponsored by Txinno Bioscience Inc. and supported by the Korea Drug Development Fund (RS-2023-00282830, Republic of Korea).

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