NB-011: Tumor MicroEnvironment Activated (TMEA) - Legubicin

Innovative Platform and Pipeline — Transforming cancer treatment through tumor-specific activation technology.

NB-011: Tumor MicroEnvironment Activated

Validated Platform

The Tumor MicroEnvironment Activated (TMEA) platform addresses a fundamental challenge in oncology: conventional drugs exert less than 1% of their effects in tumors, causing systemic toxicity including cardiotoxicity, hematotoxicity and immunotoxicity. Legumain-activated drugs accumulate and activate selectively in the tumor microenvironment, dramatically reducing systemic toxicity.

Biologics

Conditionally activated antibodies releasing active biologics to engage immune cells

ADC

Antibody-drug conjugates activated only in the tumor microenvironment

Albumin-Drug

Albumin conjugates delivering active payloads selectively to tumors

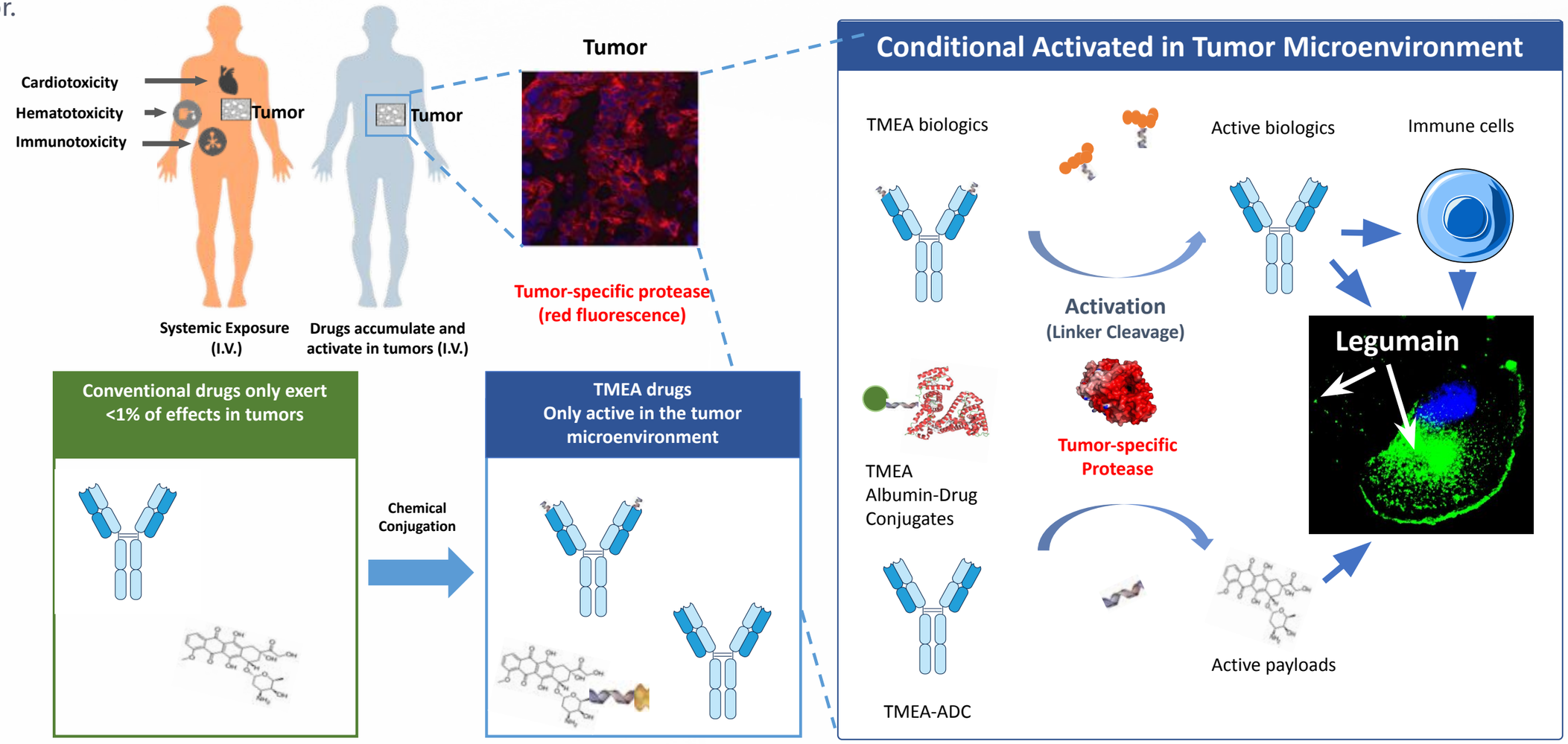
De-Risked Asset

Legubicin has completed a Phase II/III trial vs. doxorubicin, demonstrating superior PFS, OS, ORR, and DCR, with >20-fold reduction in Grade ≥3 cardiac toxicity and 43.8% vs. 1.9% treatment discontinuation due to cardiotoxicity. NDA filing underway in China.

NB-011: Tumor MicroEnvironment Activated

The Problem: Systemic Toxicity vs. Tumor Targeting

TMEA biologics and TMEA-ADCs are conditionally activated in the tumor microenvironment by tumor-specific proteases such as Legumain. Linker cleavage releases active biologics that engage immune cells, and active payloads that exert cytotoxic effects, all localized within the tumor.



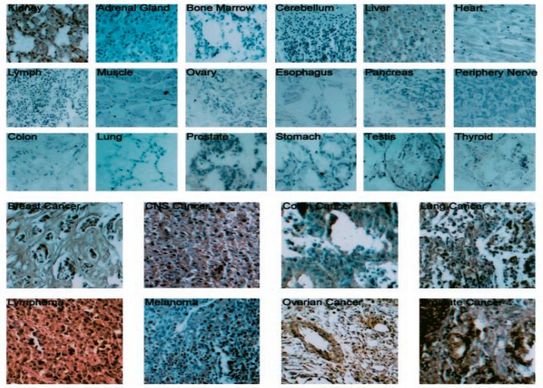
NB-011: Tumor MicroEnvironment Activated

Employing Legumain As a Novel Therapeutic Strategy

Highlights

- Highly expressed in cancer (TME & tumor cells) compared with normal tissues
- Pan-solid tumor expression and associated with tumor progression, angiogenesis, metastasis, and poor prognosis
- Activities are milieu (acidic pH, redox potential, cofactor, substrate) dependent
- Localized to the endo/lysosome, cell surface, cytosol or nucleus

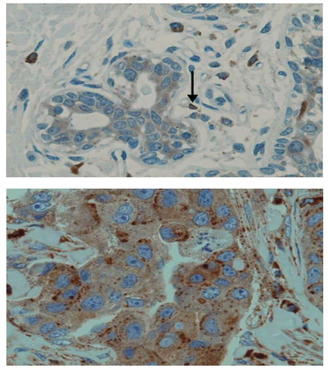
Normal tissues



Cancer tissues

"Overexpression of Legumain in Tumors Is Significant for Invasion/Metastasis and a Candidate Enzymatic Target for Prodrug Therapy" *Cancer Research* **2003,** *63*, 2957–2964

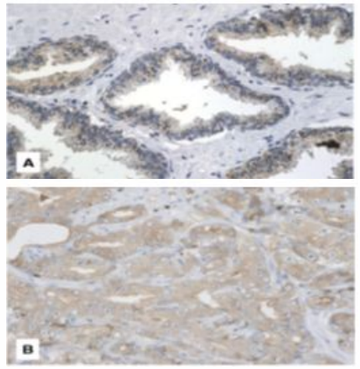
Normal breast tissue



Breast cancer

"Legumain expression as a prognostic factor in breast cancer patients" *Breast Cancer Research and Treatment* **2007,** *102(1)*:1–6

Normal prostate tissue



Prostate cancer

Association of Legumain expression pattern with prostate cancer invasiveness and aggressiveness, *World J Urol.* **2013**, *31(2)*:359–364

Table 1 Legumain detection in human solid tumors

Carcinoma type	Number analyzed	Number positive	Percentage positive	Degree of positivity
Breast carcinoma	43	43	100%	+++
Colon carcinoma	34	32	95%	+++
Lung carcinoma	24	14	58%	+++
Prostate carcinoma	56	42	75%	++++
Ovarian carcinoma	23	17	73%	++
Central nervous system tumors	8	8	100%	++
Lymphoma	14	8	57%	+
Melanoma		5	41%	+

Review article:"Structure and function of legumain in health and disease" Elfriede Dall, Hans Brandstetter, *Biochimie* (2015) 1-25

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Overview of Legumain expression data in solid tumors

Lung Cancer
- 165 samples
- 100% positive;
- >65% strongly positive

Breast Cancer
- 110 samples
- 95% positive;
- >70% strongly positive

Colorectal Cancer
- 100 samples
- 100% positive;
- >100% strongly positive

Liver Cancer
- 109 samples
- 100% positive;
- >40% strongly positive

Bladder Cancer
- 116 samples
- 95% positive
- >70% strongly positive

Gastric Cancer
- 106 samples
- 100% positive
- >88% strongly positive

Lyphoma (DLBCL)
- 192 samples
- 100% positive
- >16% strongly positive

Soft Tissue Sarcoma
- 105 samples
- 100% positive
- >45% strongly positive

Ovarian Cancer
- 100 samples
- 100% positive;
- >72% strongly positive

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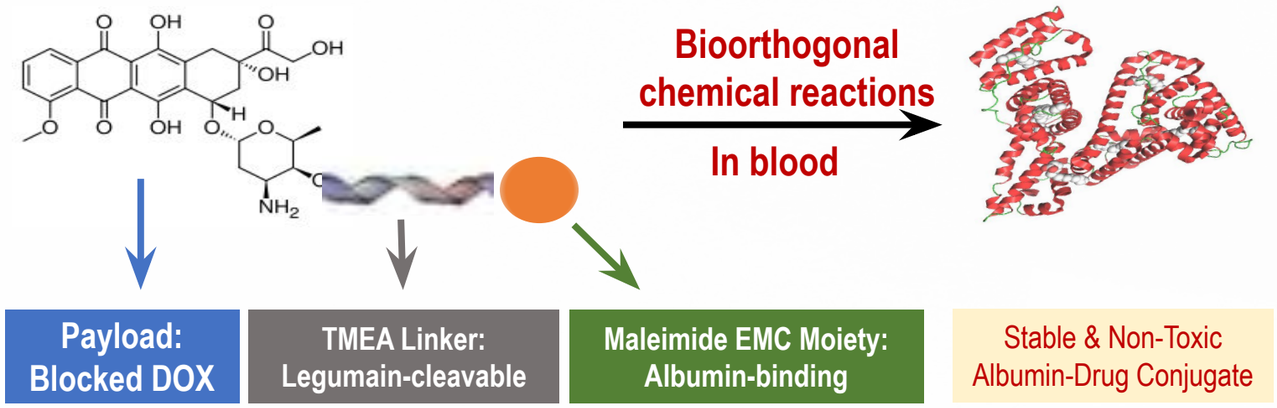
Legumain: A Novel Therapeutic Target



Legubicin is a **first-in-class (FIC) albumin-drug conjugate (XDC)** activated by legumain, a tumor-specific protease highly expressed in various human cancers.

Diagram shows the chemical structure of Legubicin, its components, and its activation in blood.

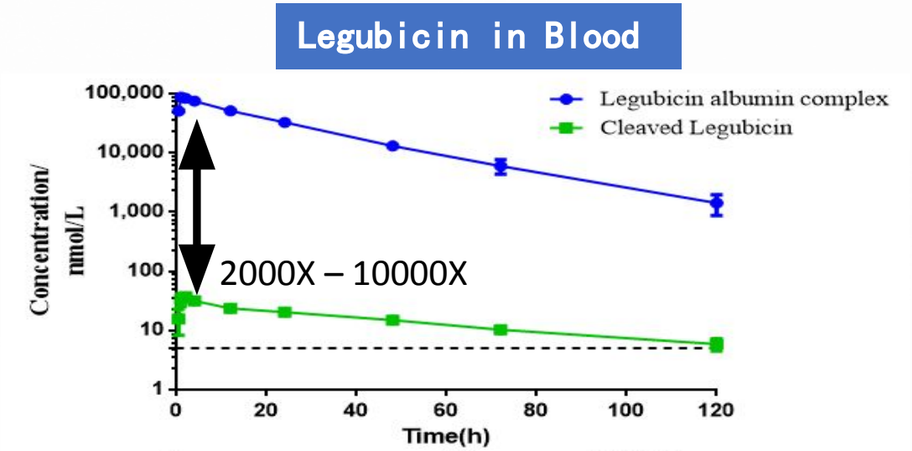
Payload: Blocked DOX

TMEA Linker: Legumain-cleavable

Maleimide EMC Moiety: Albumin-binding

Bioorthogonal chemical reactions In blood

Stable & Non-Toxic Albumin-Drug Conjugate



PK data (avg. 6 patients): Legubicin albumin complex maintains 2,000–10,000× higher concentration than cleaved (free) Legubicin in blood, confirming stable, non-toxic systemic circulation.

Key Advantages

Low Systemic Toxicity
In normal tissues, DOX payload is inactivated by the conjugated linker, reducing cardio- and hematotoxicity

Tumor-Targeted Activation
Localized DOX release in TME via legumain activation under acidic pH and EPR effect of serum albumin

Robust IP Protection
Composition of matter and linker-payload patents authorized in US, Australia, and China; follow-on applications in progress

NB-011: Tumor MicroEnvironment Activated - Legubicin

Legubicin Phase II/III – Study Design

A Randomized, Double-blind, Positive Control, Pivotal Trial of Legubicin vs Doxorubicin in Advanced STS

Key eligibility criteria:

- Unresectable/recurring/metastatic STS;
- ECOG PS 0-2;
- Exclude ASPS, CCS, GIST, CS, EES, ARMS and ERMS subtypes;
- Previous cumulative anthracycline dose ≤100 mg/m2 of DOX or its equivalent.

Stratification:

- Histology;
- Anthracycline treatment history;
- Legumain expression (≥40% vs 20%-40% vs not evaluable/indeterminate);

Arm 1 Legubicin:
270 mg/m^2 Q3W

~1.9x equimolar dose of DOX

Arm 2 Doxorubicin:
75 mg/m^2 Q3W
(1L advanced/metastatic STS regimen)

Primary endpoint:
PFS by IRC;

Secondary endpoints:
OS, ORR, DCR;
Safety and % of patients reaching cardiotoxicity indicators by Cardiotoxicity IRC;

Clinical trial identification: CTR20212527
Abbreviations: STS: soft tissue sarcoma; ECOG PS: Eastern Cooperative Oncology Group performance status; Q3W: once every 3 weeks; 1L: first-line treatment; ASPS: alveolar soft part sarcoma; CCS: clear cell sarcoma; GIST: gastrointestinal stromal tumor; CS: chondrosarcoma; EES: extraosseous Ewing sarcoma; ARMS: alveolar rhabdomyosarcoma; ERMS: embryonal rhabdomyosarcoma; PFS: progression-free survival; IRC: Independent Review Committee; ORR: objective response rate; OS: overall survival; DCR: disease control rate;

NB-011: Tumor MicroEnvironment Activated - Legubicin

Legubicin Phase II/III - Demographics and Baseline Characteristics

	Legubicin arm (N=157)	Doxorubicin arm (N=144)	Total (N=301)
Median age (range), years	58.0 (18-74)	54.0 (20-75)	55.0 (18-75)
Male sex, n (%)	81 (51.6)	65 (45.1)	146 (48.5)
Asian race, n (%)	157 (100.0)	144 (100.0)	301 (100.0)
ECOG PS, n (%)			
0	48 (30.6)	43 (29.9)	91 (30.2)
1	105 (66.9)	96 (66.7)	201 (66.8)
2	4 (2.5)	5 (3.5)	9 (3.0)
Histology, n (%)			
Undifferentiated pleomorphic sarcoma	15 (9.6)	20 (13.9)	35 (11.6)
Synovial sarcoma	15 (9.6)	15 (10.4)	30 (10.0)
Liposarcoma	22 (14.0)	18 (12.5)	40 (13.3)
Leiomyosarcoma	28 (17.8)	22 (15.3)	50 (16.6)
Other	76 (48.4)	69 (47.9)	145 (48.2)
Missing	1 (0.6)	0	1(0.3)
Treatment lines, n (%)			
First-line	133 (84.7)	119 (82.6)	252 (83.7)
Second-line and above	24 (15.3)	25 (17.4)	49 (16.3)
• Previously treated with anthracyclines	7 (4.5)	12 (8.3)	19 (6.3)
• No previous treatment of anthracyclines	17 (10.8)	13 (9.0)	30 (10.0)
State of cancer at enrollment, n (%)			
Recurrence/ metastasis	135 (86.0)	108 (75.0)	243 (80.7)
No recurrence/ metastasis	22 (14.0)	36 (25.0)	57 (18.9)
Legumain expression, n (%)			
Strongly positive	18 (11.5)	12 (8.3)	30 (10.0)
Weakly positive	45 (28.7)	34 (23.6)	79 (26.2)
Unknown	94 (59.9)	98 (68.1)	192 (63.8)

*A total of 306 patients were randomized and treated in the trial, of whom 5 patients were incorrectly enrolled with non–soft tissue sarcoma indications and were subsequently excluded from the ITT analysis set. Abbreviations: ECOG PS: Eastern Cooperative Oncology Group performance status; ITT: intention-to-treat;

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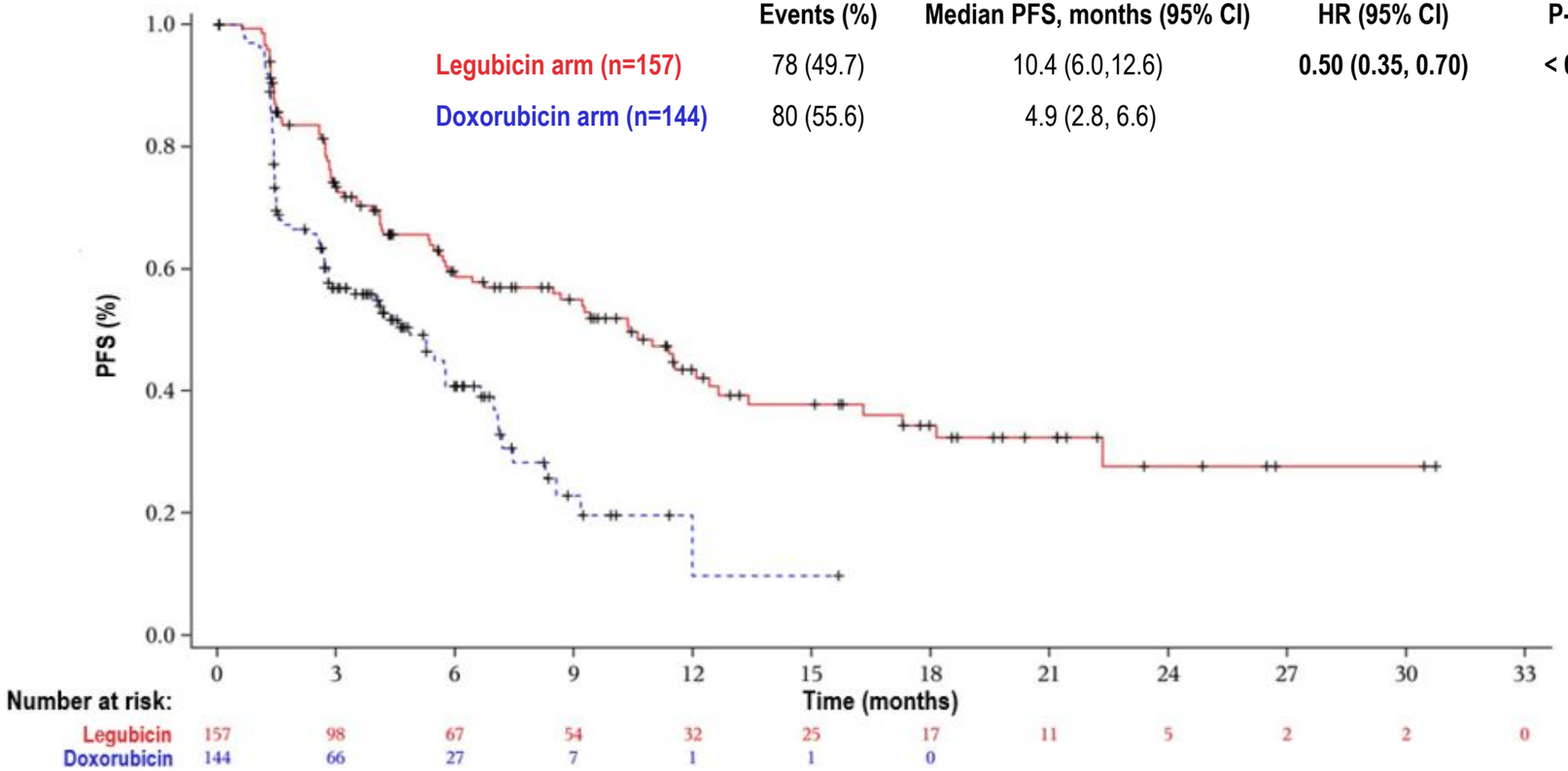
Legubicin Phase II/III - Primary End Point: Progression-Free Survival

Per IRC (ITT Analysis Set)

	Events (%)	Median PFS, months (95% CI)	HR (95% CI)	P-value
Legubicin arm (n=157)	78 (49.7)	10.4 (6.0,12.6)	**0.50 (0.35, 0.70)**	**< 0.0001**
Doxorubicin arm (n=144)	80 (55.6)	4.9 (2.8, 6.6)		



Statistically significant PFS improvement (HR=0.50 [95% CI: 0.35, 0.70]; one-sided P< 0.0001) was observed favoring legubicin over doxorubicin

*A total of 306 patients were randomized and treated in the trial, of whom 5 patients were incorrectly enrolled with non–soft tissue sarcoma indications and were subsequently excluded from the ITT analysis set. Abbreviations: PFS: progression-free survival; IRC: Independent Review Committee; ITT: intention-to-treat; CI: confidence interval; HR, hazard ratio;

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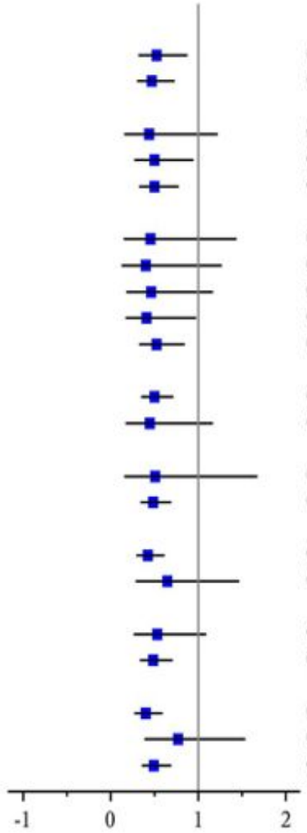
Legubicin Phase II/III - Progression-Free Survival by Subgroups

Significant OS benefit (HR=0.49 [95% CI: 0.30, 0.79]) was observed favoring legubicin over doxorubicin;
Higher ORR and DCR were observed with legubicin vs doxorubicin, consistent with other efficacy results;

Per IRC (ITT Analysis Set) - Univariate Analysis

	Legubicin arm		Doxorubicin arm		
Subgroups	**Number/ Events**	**mPFS (95% CI)**	**Number/ Events**	**mPFS (95% CI)**	**HR(95%CI)**
Sum of diameters of target lesions					
≥ 10cm	71/35	10.3(4.1, 17.3)	63/33	4.9(2.9, 7.0)	0.53(0.31, 0.88)
< 10cm	86/43	11.0(6.0, 13.4)	81/47	4.4(2.6, 7.1)	0.47(0.30, 0.73)
Legumain expression					
Strongly positive	18/10	11.5(4.2, NA)	12/7	2.6(1.3, NA)	0.44(0.16, 1.23)
Weakly positive	45/24	6.4(4.1, 18.1)	34/21	4.4(2.6, 7.5)	0.50(0.27, 0.94)
Unknown	94/44	10.6(5.7, 16.3)	98/52	5.3(2.8, 7.0)	0.50(0.32, 0.77)
Histology					
Undifferentiated pleomorphic sarcoma	15/6	NA(2.7, NA)	20/10	2.8(1.5, NA)	0.46(0.14, 1.44)
Synovial sarcoma	15/9	6.4(4.1, NA)	15/9	6.6(1.3, NA)	0.40(0.13, 1.27)
Liposarcoma	22/10	11.5(1.4, NA)	18/12	2.6(1.4, 9.2)	0.46(0.18, 1.17)
Leiomyosarcoma	28/16	10.3(2.7, 16.3)	22/12	5.1(1.4, 7.5)	0.41(0.17, 0.98)
Other	76/37	10.6(5.6, 22.3)	69/37	5.5(2.8, 7.2)	0.52(0.32, 0.85)
Treatment lines					
First-line	133/65	10.4(5.7, 13.4)	119/68	4.4(2.7, 6.6)	0.50(0.35, 0.71)
Second-line and above	24/13	11.5(3.0, 22.3)	25/12	4.9(2.7, NA)	0.45(0.17, 1.17)
Prior anthracycline treatment *					
Yes	18/10	12.1(3.5, 22.3)	18/6	NA(2.6, NA)	0.51(0.16, 1.68)
No	139/68	10.3(5.8, 12.6)	126/74	4.4(2.7, 5.7)	0.49(0.34, 0.69)
Recurrent/metastatic STS					
Yes	135/68	10.6(6.0, 12.6)	108/64	4.1(2.7, 5.5)	0.42(0.29, 0.62)
No	22/10	9.4(2.9, NA)	36/16	7.1(4.4, 12.0)	0.64(0.28, 1.47)
Prior radiotherapy					
Yes	32/16	6.7(4.1, 12.6)	32/20	4.9(2.7, 7.5)	0.53(0.26, 1.09)
No	125/62	10.6(6.0, 16.3)	112/60	5.3(2.6, 6.6)	0.48(0.33, 0.71)
Prior tumor surgery					
Yes	126/61	11.5(6.0, 16.3)	100/61	4.0(2.2, 5.5)	0.40(0.27, 0.59)
No	31/17	8.5(3.5, NA)	44/19	5.7(4.4, 12.0)	0.77(0.38, 1.54)
Total	157/78	10.4(6.0, 12.6)	144/80	4.9(2.8, 6.6)	0.50(0.35, 0.69)



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Secondary Endpoints – OS, ORR & DCR Results

Significant OS benefit (HR=0.49 [95% CI: 0.30, 0.79]) was observed favoring legubicin over doxorubicin.
Higher ORR and DCR were observed with legubicin vs doxorubicin, consistent with other efficacy results.

Overall Survival

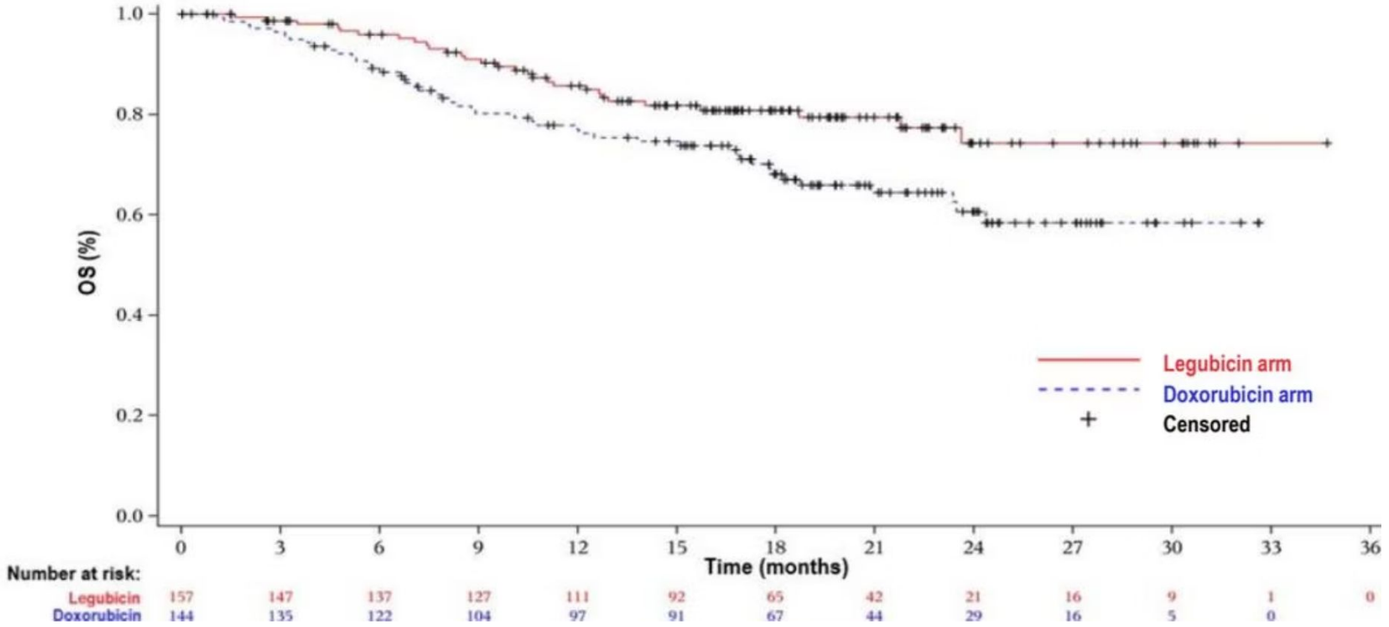
HR=0.49 (95% CI: 0.30–0.79) favoring legubicin; OS P25: 23.6 months (Legubicin) vs. 13.8 months (Doxorubicin)

ORR

Legubicin: 23.6% (95% CI: 17.2–31.0) vs. Doxorubicin: 18.1% (95% CI: 12.2–25.3)

DCR

Legubicin: 80.9% (95% CI: 73.9–86.7) vs. Doxorubicin: 63.9% (95% CI: 55.5–71.7)



OS (ITT Analysis Set)

	Events (%)	Median OS, months (95% CI)	OS P25, months (95% CI)	HR (95% CI)
Legubicin arm (n=157)	29 (18.5)	NA (NA, NA)	23.6	0.49 (0.30, 0.79)
Doxorubicin arm (n=144)	47 (32.6)	NA (24.3, NA)	13.8	

ORR & DCR

	ORR (%), 95%CI	DCR (%), 95%CI
Legubicin arm (n=157)	37 (23.6) (17.2, 31.0)	127 (80.9) (73.9, 86.7)
Doxorubicin arm (n=144)	26 (18.1) (12.2, 25.3)	92 (63.9) (55.5, 71.7)

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Safety Profile: Dramatically Reduced Toxicity

Legubicin demonstrated a markedly superior safety profile vs. doxorubicin across cardiac, hematologic, gastrointestinal, and other toxicities — supporting long-term maintenance treatment potential.

Toxicity Category	Legubicin (N=160)	Doxorubicin (N=146)	Key Difference
Treatment discontinuation due to cardiotoxicity	3 (1.9%)	64 (43.8%)	−42.0% (95% CI: −50.2, −33.4)
Grade ≥3 cardiac TRAEs (total)	3 (1.9%)	58 (39.7%)	>20-fold reduction
Grade ≥3 hematologic TRAEs	49 (30.6%)	135 (92.5%)	−61.9%
Grade ≥3 GI TRAEs	0 (0%)	5 (3.4%)	Complete elimination
Treatment-related alopecia	22 (13.8%)	108 (74.0%)	−60.2%

The major DOX-related dose-limiting toxicity — cardiotoxicity — was reduced over **20-fold** in grade ≥3 cardiac TRAEs, resulting in significantly fewer treatment discontinuations.

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Legubicin Phase II/III — Conclusions

Significant PFS & OS Benefit

HR=0.50 for PFS (P<0.0001) and HR=0.49 for OS, consistent across all predefined subgroups; higher ORR (23.6% vs. 18.1%) and DCR (80.9% vs. 63.9%)

Favorable Safety Profile

Clear reduction in cardiac, hematologic, and GI toxicities enables longer cumulative treatment and overcomes DOX dose limitations

Paradigm-Shifting Potential

Supports legubicin as a promising STS therapy that may replace DOX across multiple subtypes and provides clinical proof for legumain-activated ALDC, reshaping chemotherapy paradigms

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Legubicin Clinical Development Path

Indication	Combo	Phase	Line	Dose	Status	Location
STS	Mono	Ph2/3	1L	270 mg/m² Q3W	NDA application	China
NSCLC	Mono	Ph2b	3L+	270 mg/m² Q2W	IND application	China
NSCLC	PD-1 inhibitor	Ph1b/2	2L	270 mg/m² Q2W	Patient recruitment	China
NSCLC	3rd EGFR TKI	Ph1b/2	2/3L	270 mg/m² Q2W	IND approval	China
Breast cancer	Combo	Ph2	TNBC & HER2+ MBC	270 mg/m² Q2W	Patient recruitment	China
Ovarian cancer	Combo	Ph2	PS/PR	270 mg/m² Q2W	Patient recruitment	China
STS	Mono	Ph1 bridging	ROC	TBD	IND application	US

Overcome Toxicity
Eliminate on-target/off-tumor toxicity

Enhance Efficacy
Lead to significant enhancement of anti-tumor efficacy

Enable Combinations
Allow for powerful synergistic combination therapies

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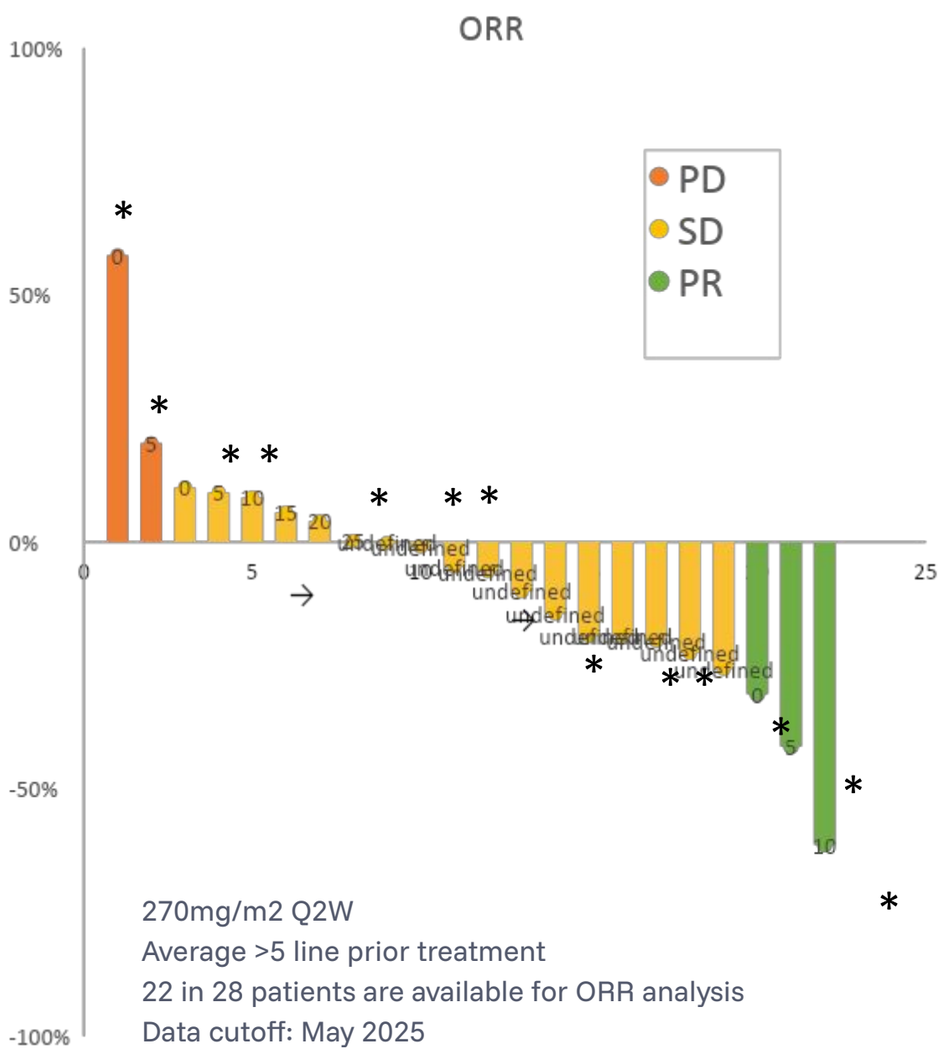
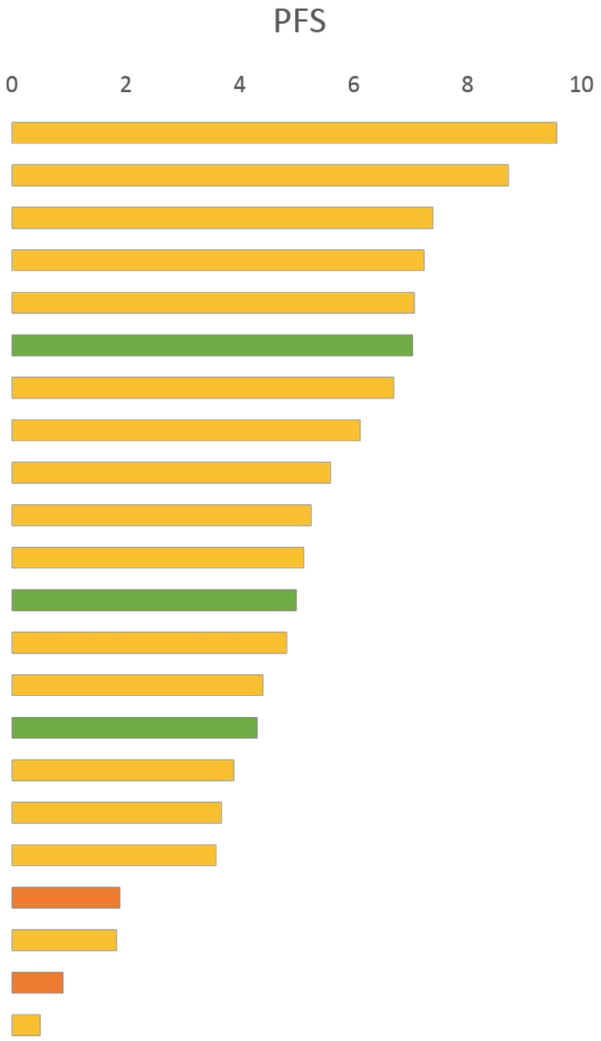
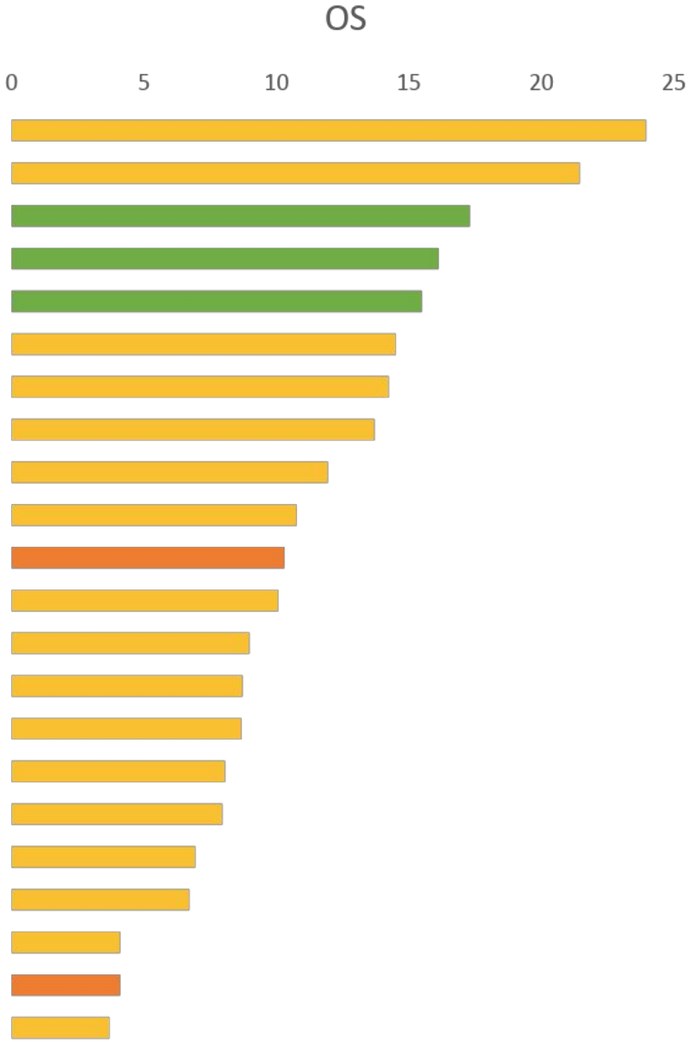
Legubicin as Monotherapy for 3L+ Lung Adenocarcinoma







270mg/m2 Q2W
Average >5 line prior treatment
22 in 28 patients are available for ORR analysis
Data cutoff: May 2025

*: EGFR mutation +

Through Sept 2025, the latest PFS and OS are 5.16 and 15.15 months respectively from 33 NSCLC patients.

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Mechanism of Combination of Legubicin and Osimertinib

Legubicin, a Topoisomerase II (TOPO II) inhibitor, exploits a critical vulnerability in both sensitive and osimertinib-resistant EGFRm NSCLC cells. By inducing transient DNA strand breaks and inhibiting religation, it amplifies DNA damage and cell death — a mechanism that remains active even when EGFR-TKI resistance has emerged via the GSK3/FBXW7 degradation axis.

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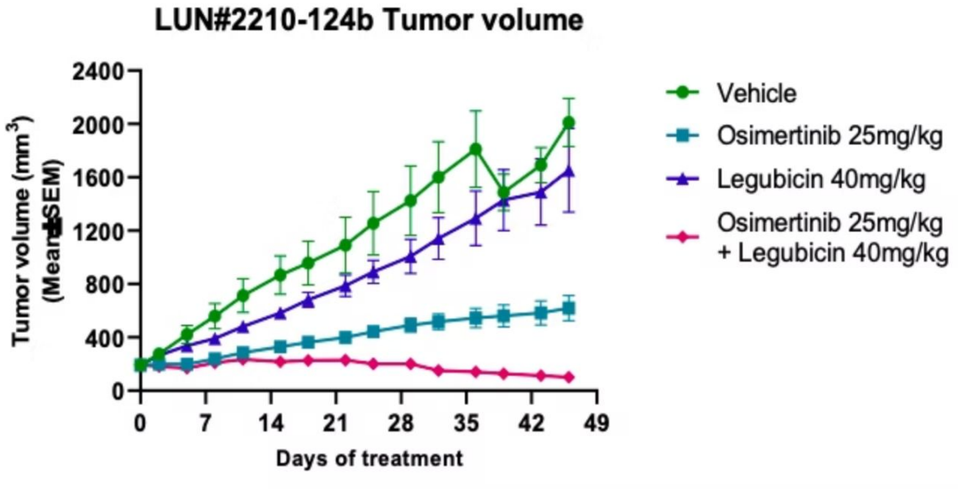
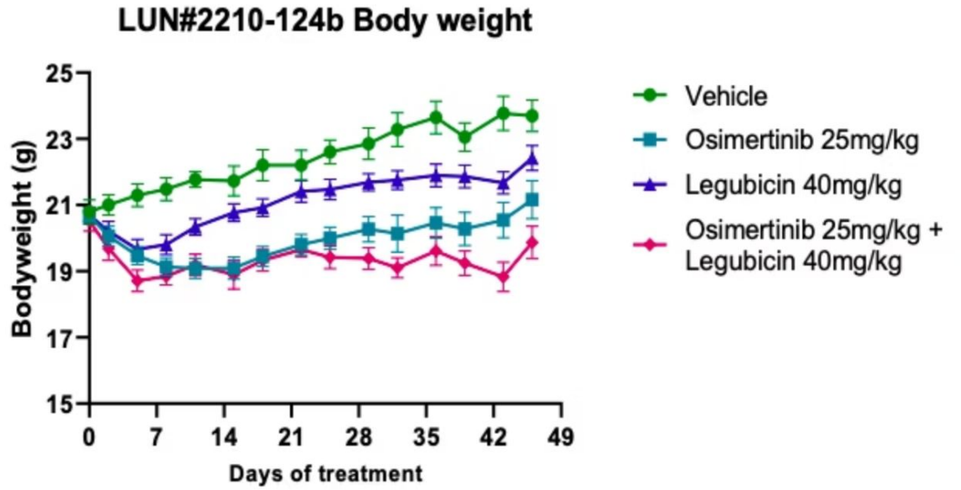
Legubicin + Osimertinib: Overcoming EGFR-Independent Resistance

A central challenge in EGFRm NSCLC management is acquired resistance that arises through EGFR-independent pathways — such as ERBB2 amplification, FGFR alterations, and PI3K/PTEN pathway dysregulation. The LUN#2210-4a-124b osimertinib-resistant PDX model harbors L858R with concurrent ERBB2 amplification, providing a clinically relevant system to evaluate bypass resistance mechanisms.





Resistant Model Profile

LUN#2210-4a-124b PDX model carrying EGFR L858R with ERBB2 amplification — representing a classic bypass resistance mechanism not addressable by EGFR-TKI re-challenge alone.

Resistance Genomic Landscape

Alterations assessed across EGFR, ERBB2, FGFR1, FGFR2, PTEN, and PIK3CA loci, highlighting the complexity of EGFR-independent resistance pathways targeted by the combination strategy.

Combination Strategy

Osimertinib QD combined with Legubicin targets TOPO II-mediated DNA damage independent of EGFR signaling, providing a mechanistically orthogonal approach to overcome bypass resistance.

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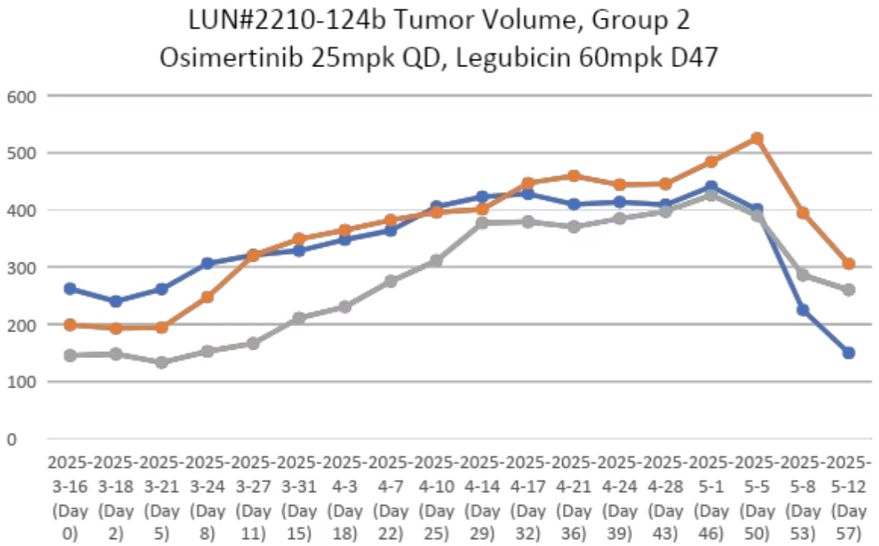
In Vivo Efficacy in EGFR-Independent Resistance PDX Model

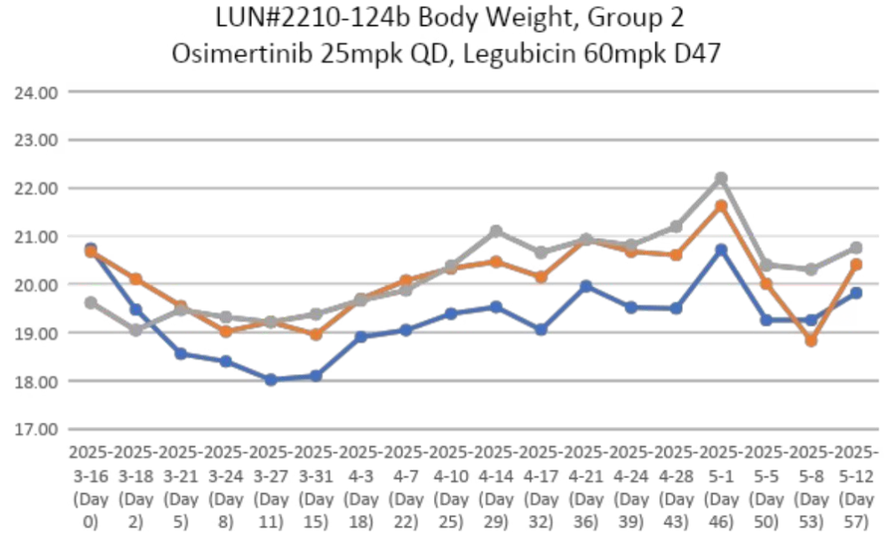
Building on mechanistic evidence, in vivo experiments in the LUN#2210-4a-124b osimertinib-resistant PDX model (EGFR L858R + ERBB2 amplification) evaluated Legubicin at 60 mg/kg as monotherapy and in combination with osimertinib. These data directly assess the ability of the combination to overcome non-EGFR bypass resistance mechanisms.

Tumor Growth Inhibition



Legubicin at 60 mg/kg demonstrates meaningful single-agent tumor growth inhibition in the osimertinib-resistant model, establishing monotherapy activity as a foundation for the combination regimen.

Combination Efficacy



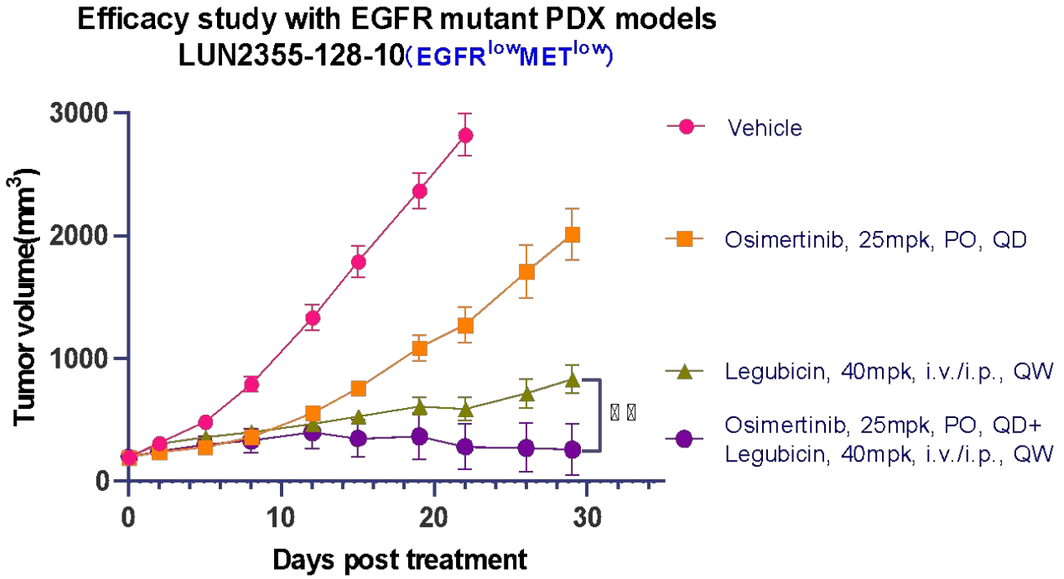
The Legubicin + osimertinib combination produced superior tumor control compared to either monotherapy arm, underscoring the additive-to-synergistic potential in EGFR-independent resistant settings driven by ERBB2 amplification.

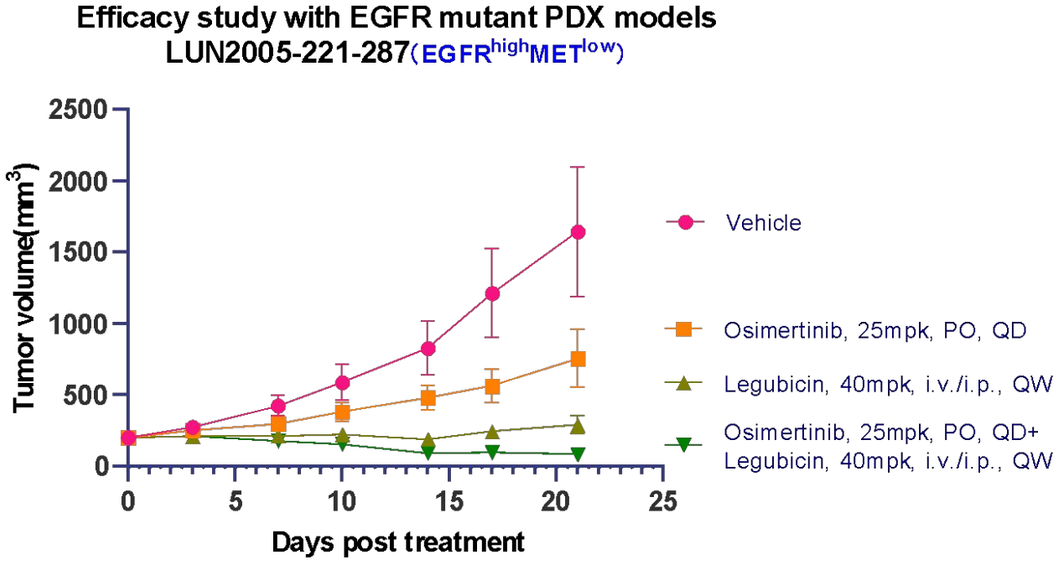
Model: LUN#2210-4a-124b | Mutations: EGFR L858R + ERBB2 Amplification | Legubicin dose: 60 mg/kg

NB-011: Tumor MicroEnvironment Activated - Legubicin

In Vivo Efficacy Across Two Additional Osimertinib-Resistant PDX Models

To confirm that combination benefit extends beyond a single resistance phenotype, Legubicin efficacy was evaluated in two additional osimertinib-resistant PDX models — each carrying EGFR L858R with distinct co-occurring molecular features and differing EGFR and MET expression profiles. This multi-model approach strengthens translational confidence.





Model	Mutant	EGFR RNA (FPKM)	MET RNA (FPKM)
LUN2355-128-10	L858R	7.029	5.332
LUN2005-221-287	L858R	363.235	11.393

Model: LUN#2210-4a-124b | Mutations: EGFR L858R + ERBB2 Amplification | Legubicin dose: 60 mg/kg

Slide 22:
Is this study underway? The slide says that it is planned for 3Q 2025, it is now 2Q 2026.

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Legubicin + 3rd-Gen EGFR TKI for nsq NSCLC: Ph1b/2 Study Design (China)

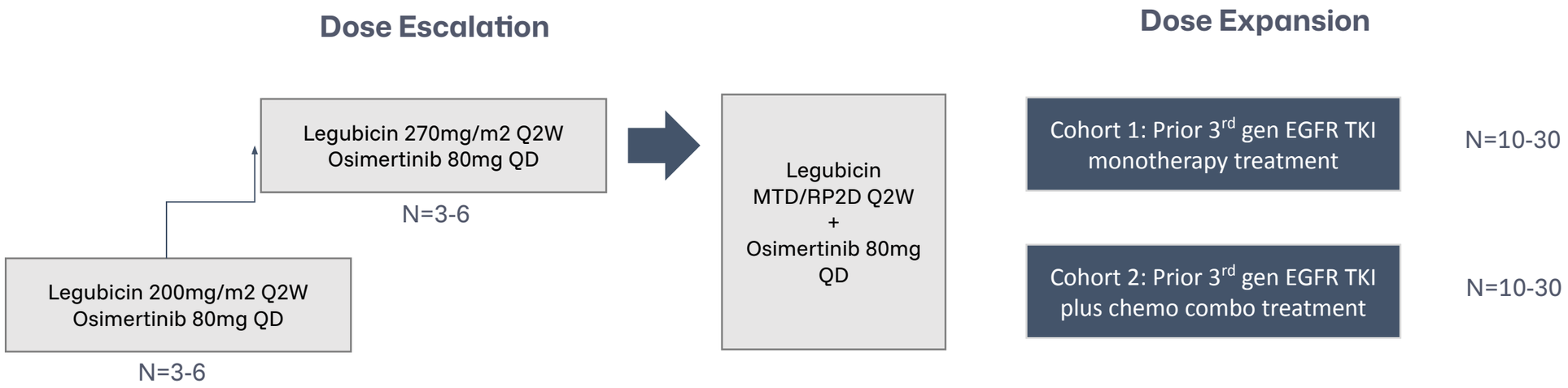
Study Type: Phase 1b/2, single-arm, open-label, multicenter
Status: Under protocol development CTP
Registration: Future FDA/China NDA submission planned

Key Inclusion

- Locally advanced or metastatic nsq NSCLC
- EGFR exon 19 del or L858R, G719X, S768I, or L861Q (alone or in combination)
- Previously treated with osimertinib or other 3rd-gen EGFR-TKIs

Key Exclusion

- History of non-infectious ILD/pneumonitis requiring steroids
- Lung-specific intercurrent clinically significant illness
- EGFR C797X mutation or MET amp/OE detected from tumor tissue



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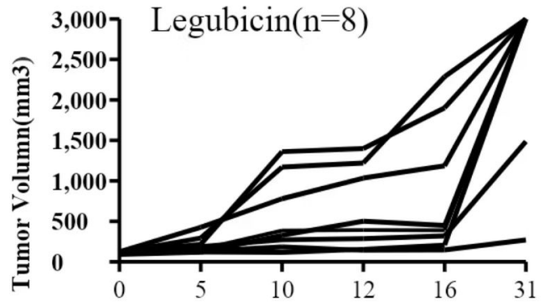
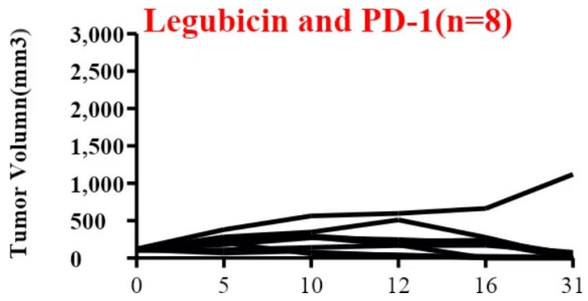
Synergistic Effect of Legubicin in Combination with PD-1 Antibody

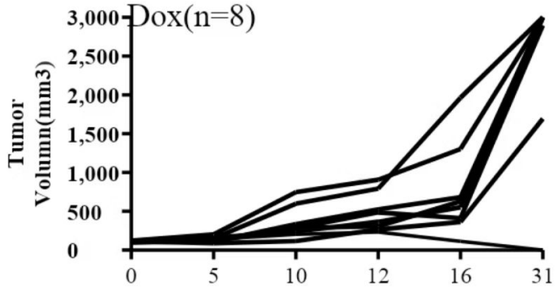
In the immunocompetent CT26 syngeneic mouse model, Legubicin at just 20 mg/kg (1/4 MTD) combined with anti-PD-1 antibody (10 mg/kg) achieved a complete response (CR) rate of 87.5% (7/8) — dramatically outperforming doxorubicin + PD-1 (CR: 12.5%, 1/8), PD-1 monotherapy (CR: 1/8), and Legubicin monotherapy (CR: 1/8). This potent immunogenic synergy distinguishes Legubicin from conventional anthracyclines.

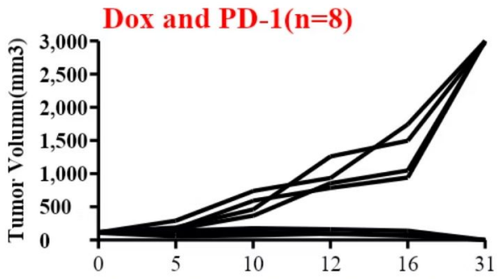
Legubicin + PD-1 (CR: 7/8 — 87.5%)



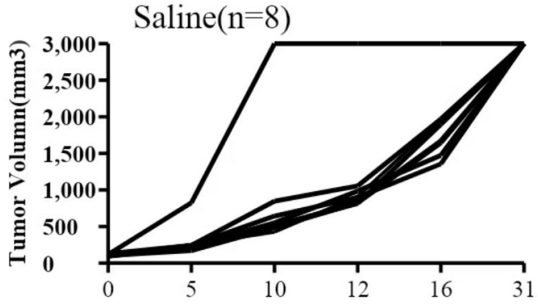


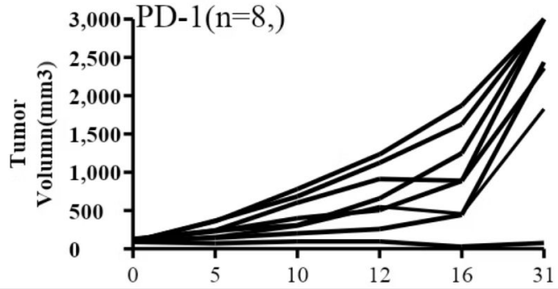
Doxorubicin + PD-1 (CR: 1/8 — 12.5%)





Monotherapy Arms (CR: 0–1/8)





Bottom graphs are ~0–12.5% CR, with the displayed/typical value being 12.5% (1/8) per arm.
CT26 syngeneic model | Legubicin dose: 20 mg/kg (1/4 MTD) | PD-1 antibody: 10 mg/kg | Legubicin + PD-1 achieves 7× higher CR rate vs. doxorubicin + PD-1

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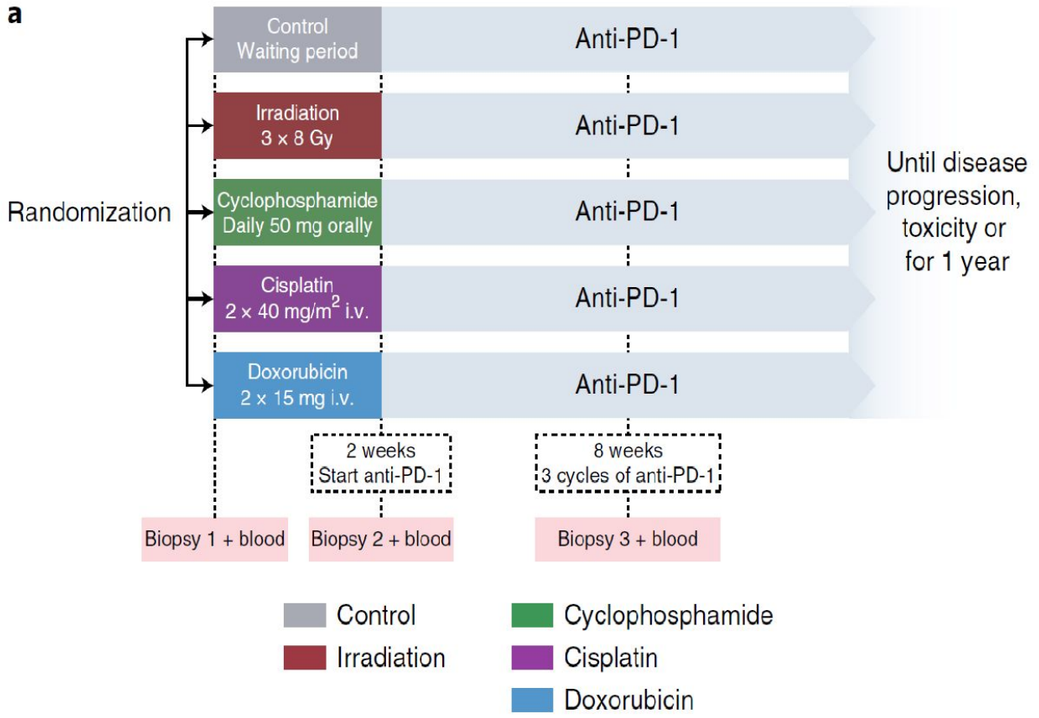
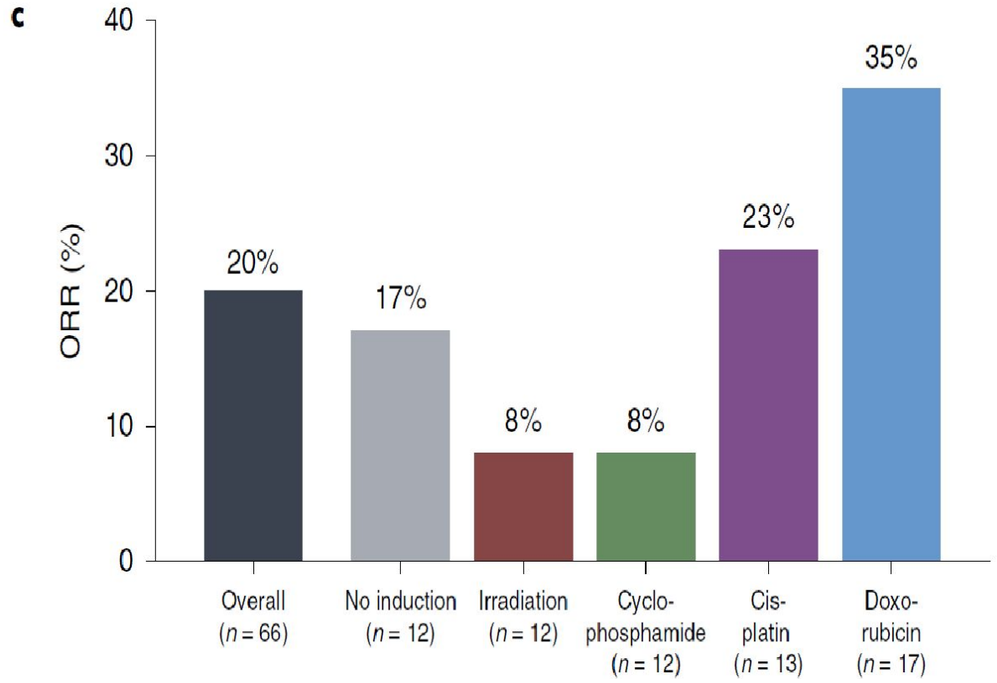
Clinical evidence of doxorubicin combo with PD-1 inhibitor

The TONIC trial (NCT02499367) provides pivotal clinical proof-of-concept that anthracycline induction can potentiate anti-PD-1 checkpoint blockade. Doxorubicin was administered at a low dose of 15 mg per patient (9.4 mg/m^2), followed by nivolumab (3 mg/kg Q2W). Post-induction biopsies revealed significant upregulation of immune-related genes in the PD-1/PD-L1 and T cell cytotoxicity pathways, suggesting that anthracycline-mediated immunogenic cell death primes the tumor microenvironment for checkpoint inhibitor response.



Study design: Patients randomized to 1 of 4 induction cohorts (doxorubicin, cyclophosphamide, cisplatin, or irradiation) or no induction, all followed by nivolumab.



ORR per cohort (iRECIST, investigator-assessed). The doxorubicin + nivolumab cohort demonstrated one of the highest ORR signals, supporting immune priming as a key mechanism and the clinical rationale for Legubicin + PD-1 combination development.

Reference: TONIC Trial — Nivolumab After Induction in TNBC (NCT02499367) | Nature Medicine 2019 | https://doi.org/10.1038/s41591-019-04324

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Legubicin combo with PD-1 inhibitor for nsq NSCLC: a Ph1b/2 study in China

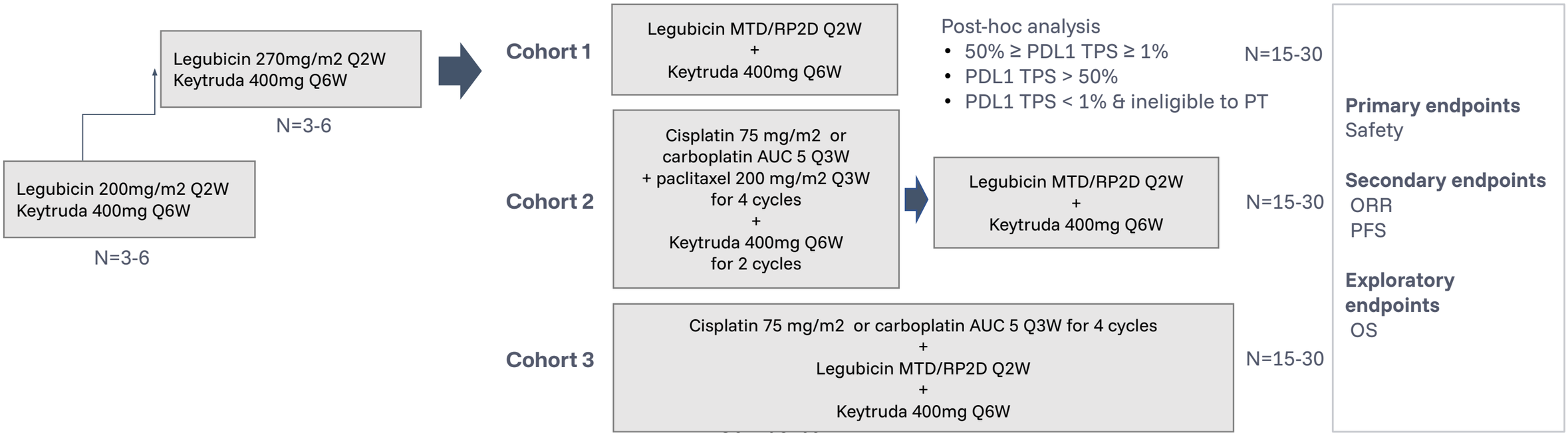
Legubicin demonstrated a markedly superior safety profile vs. doxorubicin across cardiac, hematologic, gastrointestinal, and other toxicities — supporting long-term maintenance treatment potential.

Key Inclusion

- Locally advanced or metastatic nsq NSCLC
- EGFR- or ALK-directed therapy not indicated
- No prior systemic treatment for advanced/metastatic disease

Key Exclusion

- Predominantly squamous cell histology NSCLC
- Prior anti-PD-1, anti-PD-L1, or anti-PD-L2 therapy
- Prior systemic cytotoxic chemotherapy or antineoplastic biologics for metastatic disease



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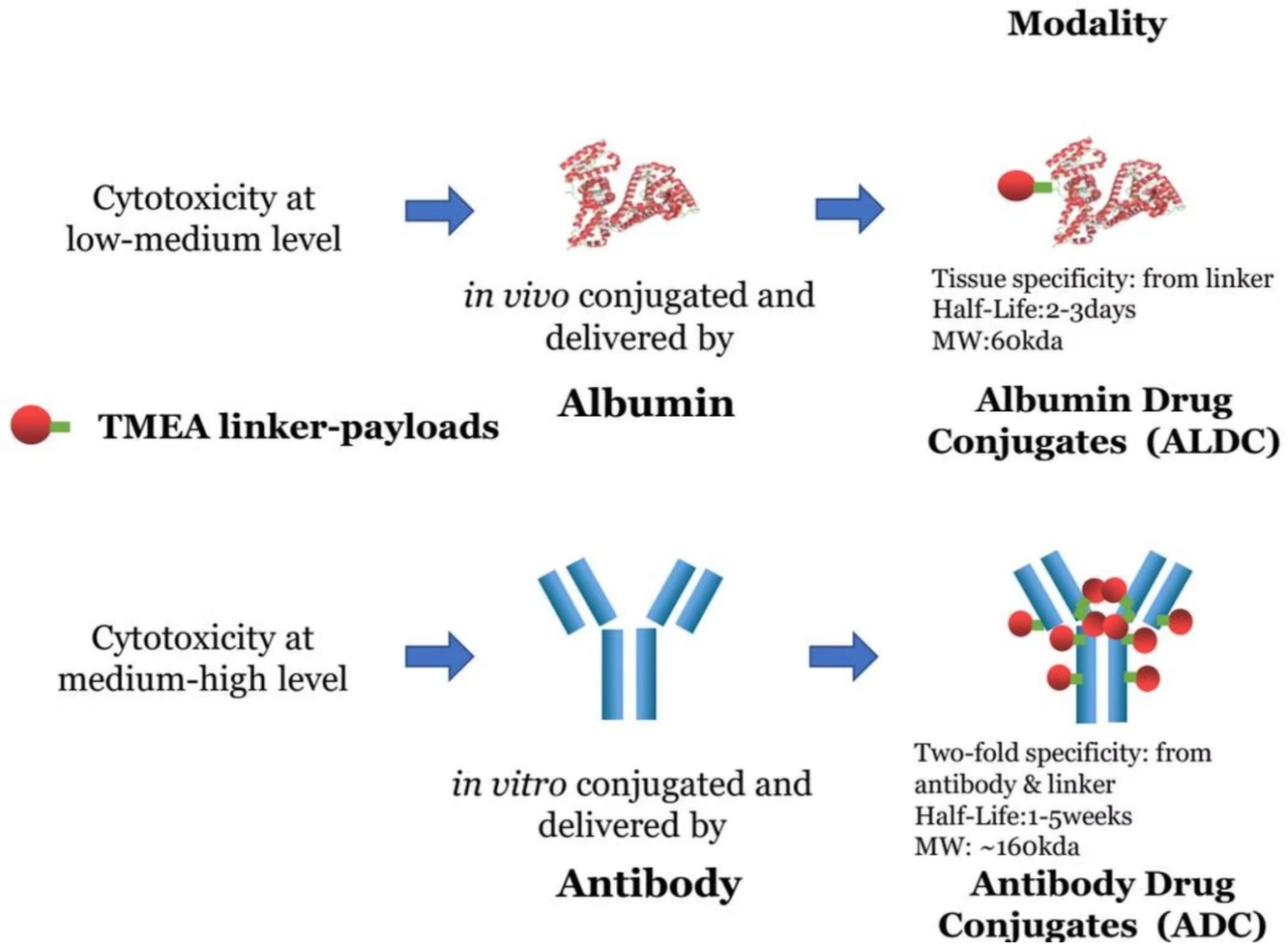
TMEA-XDC: TMEA linker-payload delivered by albumin and antibody



Payloads	Stage
Doxorubicin	NDA
DXd	Phase 1
AXL/VEGFRi	IND filing
TLR7/8 agonist	IND filing
pan-RASi	...
Eribulin	...
PARPi	...
...	

Dual Payloads	Stage
DXd&TLR7/8A	GMP level
DXd&pan-RASi	
PARPi&pan-RASi	
...	
Other combinations	

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