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BeyondSpring

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By attending this presentation, you acknowledge that you will be solely responsible for your own assessment of the market and our market position and that you will conduct your own analysis and be solely responsible for forming your own view of the potential future performance of our business.

Investment Highlights

Plinabulin Favorable Safety Profile	> 700 Cancer Patients Treated with Good Tolerability
Anti-cancer Efficacy	Positive Phase 3 study in 2L/3L NSCLC with Overall Survival Benefit: 1. durable anti-cancer benefit in doubling 2-year, 3-year OS rate 2. enables more chemo doses by reducing chemotherapy-associated TRAE
Target IO Failure	Promising efficacy data in triple IO combo (Plinabulin + PD-1/PD-L1 + radiation/chemotherapy) in patients with various cancers after IO-failure
SEED: Novel TPD Platform & Pipeline	SEED: 9 Disclosed Pipeline Assets with 1 expected to enter First Human Dose in 2025; Investments and R&D Collaborations from Eli Lilly and Company and Eisai
Intellectual Property	Strong Global Patent Protection for Plinabulin and SEED TPD Platform and Pipeline
Regulatory Strategy	Multiple Phase 1/2 studies reading out in 2024 that will inform potentially pivotal clinical studies in 2025

Pipeline

	Indication/Target	Program	Preclinical	Phase 1	Phase 2	Phase 3	Registration	Trial Name / Collaborator
Late stage	**NSCLC (2nd/3rd line)**	Plinabulin + Docetaxel						Study 103 (DUBLIN-3) - Presented at ISLAC, ESMO 2024 Published in "LANCET Respiratory Medicine" 09/2024
Late stage	**CIN Prevention**	Plinabulin + Pegfilgrastim						Studies 105 & 106 (PROTECTIVE-1 & PROTECTIVE-2)
Investigator Initiated Trials	**ES-SCLC (2nd/3rd line)**	Plinabulin + Nivolumab + Ipilimumab						Presented at SITC 2023
Investigator Initiated Trials	**NSCLC (2nd/3rd line PD-1/L1 progressed)**	Plinabulin + Pembrolizumab + Docetaxel						Study 303 Presented at ESMO 2024, SITC 2024
Investigator Initiated Trials	**ES-SCLC (1st line)**	Plinabulin + Pembrolizumab + Etoposide / Platinum						Study 302
Investigator Initiated Trials	**Multiple cancers (PD-1/PD-L1 failed)**	Plinabulin + PD-1/PD-L1 + Radiation						Presented at SITC 2023
Early Stage	**Preclinical assets**	BPI-002, BPI-003, BPI-004						
SEED	**9 Targets in Oncology, Neurodegeneration, Immunology and Antiviral**	Targeted Protein Degradation Molecular Glue Platform						

1) Dalian Wanchunbulin Pharmaceuticals Ltd., a BeyondSpring subsidiary, owns Greater China rights to Plinabulin
2) BeyondSpring is an equity investor of SEED Therapeutics, a targeted protein degradation company

Sale of a Portion of Equity Interest in SEED to Advance Lead Asset Plinabulin in Anti-Cancer Clinical Development

- **$35.4 M gross proceeds for non-diluting financing by selling a portion of SEED A-1 shares**
  - Strategically positioned to advance our 303 and 302 studies in Plinabulin combination with immune checkpoint inhibitors to registrational trials
  - Explore business development partnerships to bring Plinabulin to cancer patients with limited treatment options

- **Win-win for both BeyondSpring and SEED**
  - BeyondSpring will be strategically positioned to advance its late-stage clinical trials for Plinabulin without diluting shareholder equity.
  - BeyondSpring will retain 14.4% equity stake in SEED and remain part of SEED's continued success in revolutionizing drug discovery.
  - SEED will diversify its shareholder base while continue to drive success in Targeted Protein Degradation innovation.

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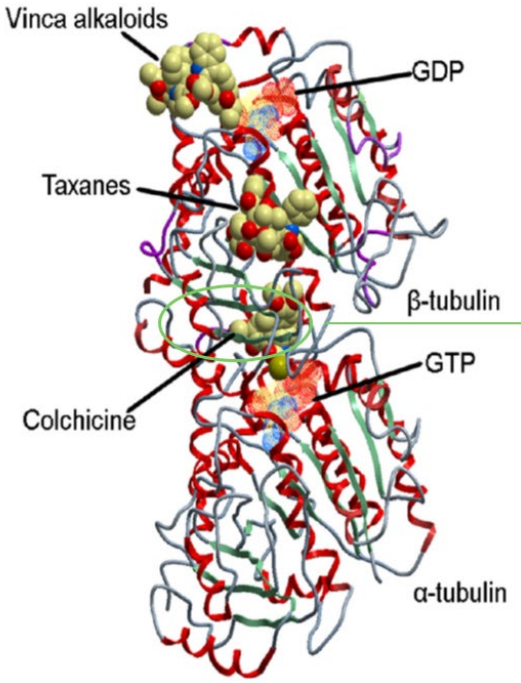
Plinabulin: First-in-class Late-Stage Clinical Asset for Cancer Treatment

Plinabulin: Induces Innate and Adaptive Immunity via Dendritic Cell (DC) Maturation

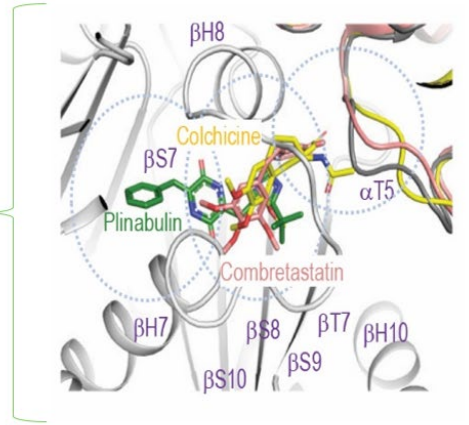
By depolymerizing microtubules, plinabulin releases and activates immune-defense protein GEF-H1

Plinabulin is a unique tubulin binder and does not change tubulin dynamics

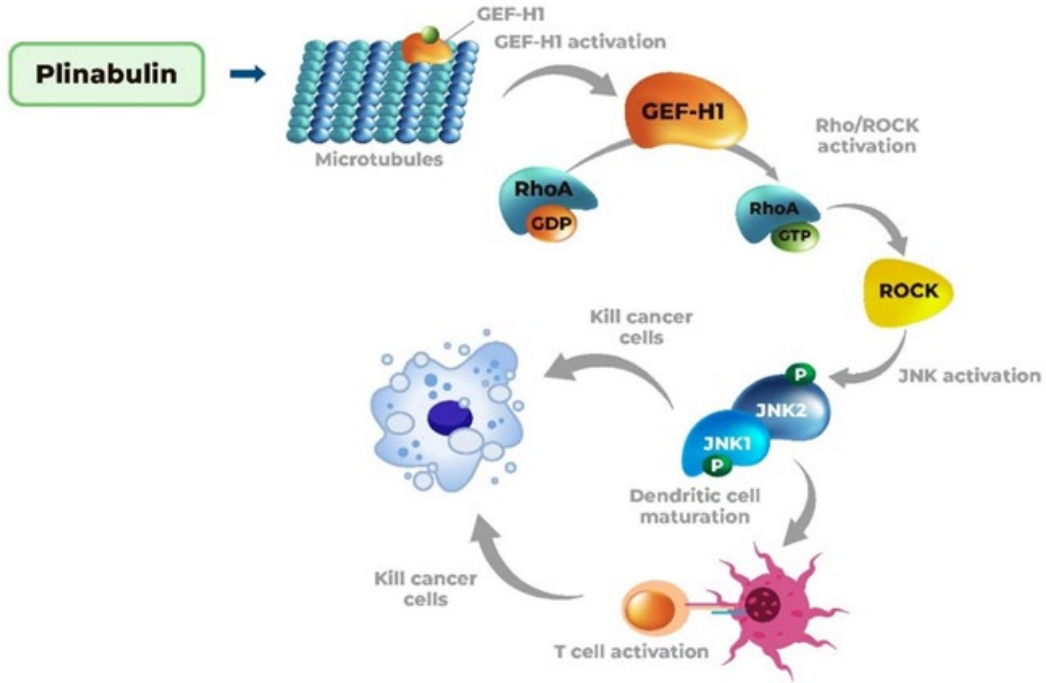
Tubulin Binding Sites



Plinabulin Binds to β-Tubulin, Near the Colchicine Site[1]



Plinabulin Novel Target GEF-H1 activates RhoA/ROCK pathway, leading to DC Maturation[2]



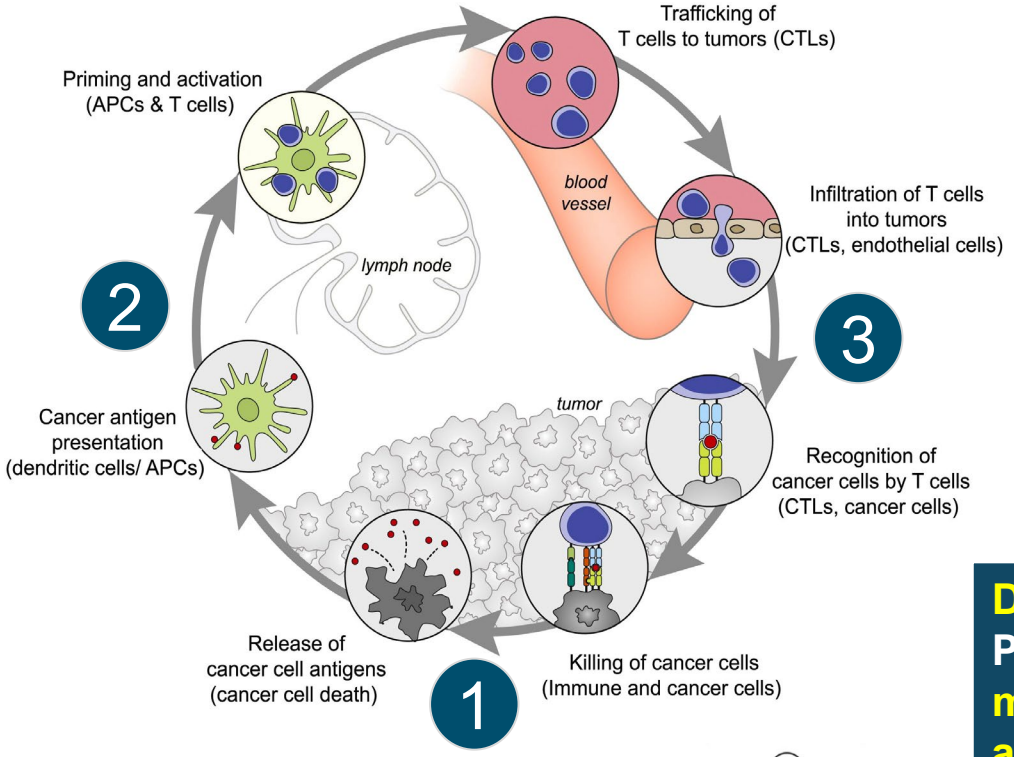
[1] La Sala et al., Chem 5(11): 2969-2986 (2019) [2] Kashyap et al., Cell Reports 28(13): 3367-3380 (2019)

Triple IO combo: Plinabulin+PD-1/L1+Chemo/RT's Potential in **Re-sensitizing** Patients who Failed Prior Immunotherapies, a High Unmet Medical Need

Acquired resistance to PD-1/L1: "T cell exhaustion" or "antigen presenting cell pathway mutation"[1].

② Plinabulin (DC Maturation)

Improved antigen presentation
Stimulate maturation of dendritic cells to increase antigen presentation;
DC sustains anti-tumor immunity[2]



③ Checkpoint Inhibitors

Anti-tumor T cell activation
Optimize T cell response

DC is the most potent Antigen Presenting Cell (APC), which is the missing link between real-time tumor antigen generated from chemo/radiation to Tumor-antigen specific T cells.

① Radiation (RT)/Chemotherapy

Release tumor antigens
For more potent anti-cancer effect

① Chemotherapy
Radiation Therapy
Oncolytic Viruses
Antibody Drug Conjugates
Targeted Therapy

1. Memon et al. Cancer Cell 42, 209–224 (2024).
2. Graph adapted from Mellman I, et al. Immunity 2023

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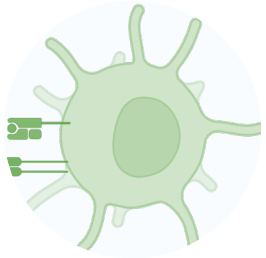
Plinabulin's Immunomodulation and Neutropenia-Mitigating Activities Position it as a Valuable Addition for Immuno-Chemotherapy Combination Regimens

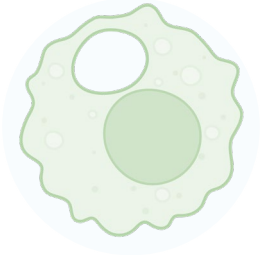
These aspects result in an optimal scenario of added efficacy with potentially reduced toxicity.



Dendritic Cells

Plinabulin induces **dendritic cell maturation**

Enhanced antigen presentation and T cell priming



Tumor Vasculature

Plinabulin Targets **tumor vasculature**

Limits blood flow to tumor

Improves safety*

Plinabulin **reduces chemotherapy-induced neutropenia**

Improved therapeutic index of chemotherapy-based regimens

Enhances PD-1/PD-L1 targeting agents to boost T cell function, kill tumor cells, and Normalize vasculature

Extends therapeutic duration and improves anti-cancer benefit

*To date, over 700 cancer patients have been treated with good tolerability.

Plinabulin Clinical Studies in Multiple Cancers

>700 cancer patients treated with Plinabulin with good tolerability

	Indication/Target	Program	Preclinical	Phase 1	Phase 2	Phase 3	Registration	Trial Name / Collaborator
Late stage	**NSCLC (2nd/3rd line)**	Plinabulin + Docetaxel						Study 103 (DUBLIN-3) - OS, PFS, ORR benefit [1]
Late stage	**CIN Prevention**	Plinabulin alone or + Pegfilgrastim						Studies 105 & 106 [2, 3] (PROTECTIVE-1 & PROTECTIVE-2)
	NSCLC (2L/3L, progressed on PD-1 / PD-L1)	Plinabulin + Pembrolizumab + Docetaxel						**Study 303**
	ES-SCLC (1L)	Plinabulin + Pembrolizumab + Etoposide / Platinum						Study 302
	Multiple cancers (PD-1/PD-L1 failed)	Plinabulin + PD-1/PD-L1 + Radiation						THE UNIVERSITY OF TEXAS MD Anderson Cancer Center

Plinabulin's MOA is not restricted to Lung Cancer; other solid tumors may benefit in combination with I/O

- ✓ Promising clinical efficacy has been observed a number of cancers, including head and neck cancer, and Hodgkin's lymphoma.

1. Han et al., **Lancet Resp Med** 12(10): 775-786 (2024), 2. Blaney et al. **JAMA Oncol** 6(11): e204429 (2020); 3. Blaney et al. **JAMA Network Open** 5(1): e2145446 (2022)

Plinabulin Improves Overall Survival and Enhances Safety in 2L/3L NSCLC (Dublin-3 Study)

- The Lancet Respiratory Medicine (Sept 9, 2024)
- BeyondSpring Delivers Oral Presentation at ISLAC 2024 World (globenewswire.com)
- BeyondSpring Presents Final Data Analysis of DUBLIN-3 (globenewswire.com)

2L/3L NSCLC (No Driver Mutation) Has Been a Historically Difficult Space in Which to Develop

Treatment options in 2L/3L NSCLC are limited

- Docetaxel-based therapies remains the standard of care in 2L/3L NSCLC (EGFR wild type). **No new therapy approved in the last 10 years.**
- However, **docetaxel-based therapies (SOC) demonstrate limited efficacy and are associated with >40% severe (grade 3/4) neutropenia.**
- Other approved agents:
  - **Ramucirumab + Docetaxel vs. Docetaxel**: OS HR=0.86, severe neutropenia 49% vs. 40%;[1]
  - **Pemetrexed vs. Docetaxel**: OS HR=0.99, severe neutropenia 5% vs. 40%.[2]
- Additionally, with immunotherapies moving to first line NSCLC, **there is a growing population of 2L/3L patients that are refractory to immunotherapy.**

2L, second line; 3L, third line; ADC, antibody drug conjugate; EGFR; epidermal growth factor receptor; HR, hazard ratio; ITT, intention-to-treat; NSCLC, non-small cell lung cancer; ORR, overall response rate; OS, overall survival, PD-(L)1, programmed death (ligand)-1; PFS, progression-free survival; SOC, standard of care; TKI, tyrosine kinase inhibitor; TTfields, tumor treating fields.

1. Garon et al. *Lancet*. 2014;384:665–673; 2. Hanna et al. *J Clin Oncol*. 2004;22:1589–1597.

Plinabulin Has Been Successfully Evaluated with Docetaxel in a Phase 3 Study with Advanced and Metastatic, Pre-treated NSCLC EGFR Wild Type Patients

Docetaxel + Plinabulin vs. Docetaxel + Placebo in Patients with EGFR Wild-Type NSCLC

Study Plan

- Global, randomized, single-blinded (patients only)
- Stratified by region (Asia/non-Asia), prior line (2L or 3L), ECOG (0-1/2), Prior PD-1/PD-L1 (yes/no)

Primary endpoint

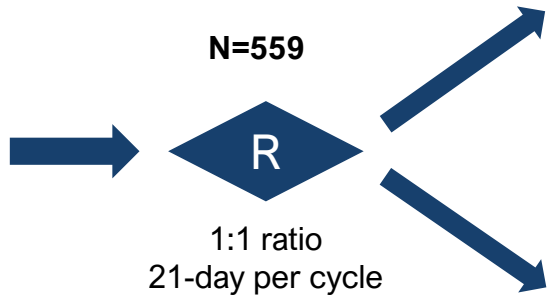
Overall survival (OS)

Secondary endpoints

- ORR, PFS
- Percent of patients without severe neutropenia (Day 8, cycle 1)
- Month 24 and 36 OS rate
- DoR
- Q-TWiST; QoL
- Proportion of patients who received docetaxel >8 cycles, >10 cycles and >12 cycles

Inclusion Criteria:

- Non-squamous or squamous NSCLC
- Stage IIIb/IV
- ECOG ≤ 2
- Progression during or after treatment with one or two treatment regimens containing a platinum
- Must have at least one measurable lung lesion
- **Prior checkpoint inhibitor therapy allowed**[1]



Plinabulin IV Infusion: 1 or 2 dose per cycle

DP:
Docetaxel
(75 mg/m2, day 1)
+ **Plinabulin**
(30 mg/m2, day 1, 8)

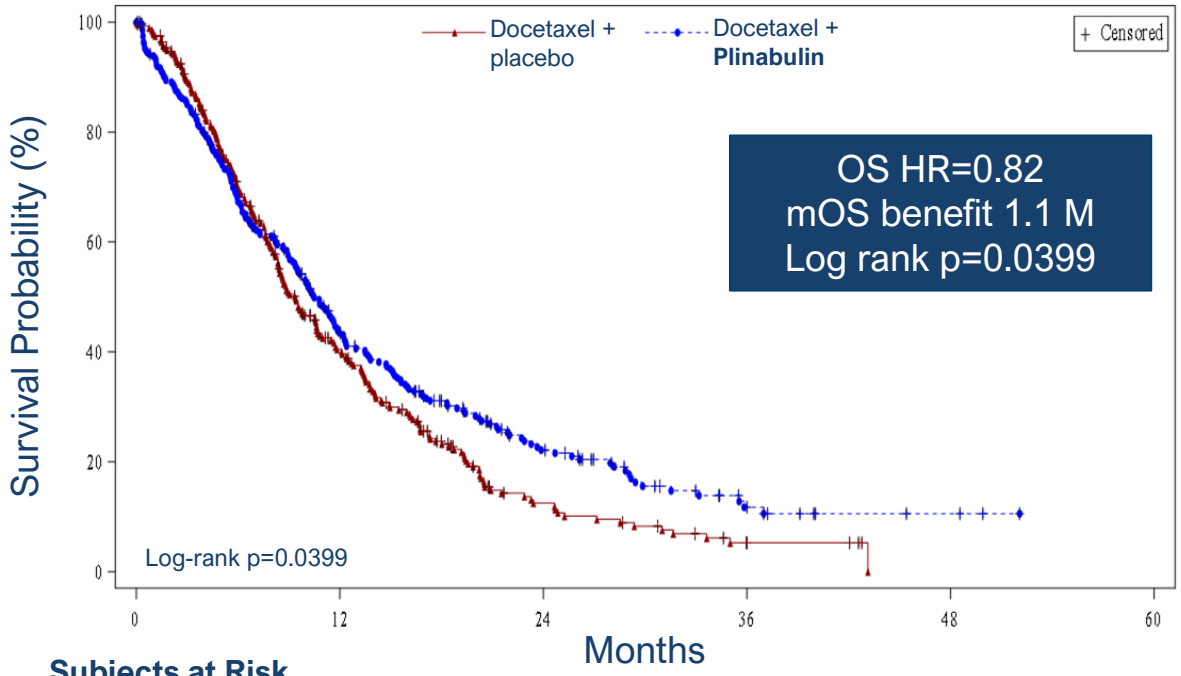
D:
Docetaxel
(75 mg/m2, day 1)
+ Placebo (day 1, 8)

[1] 85% CPI naïve; **15% failed PD-(L)1 blockade**

Balanced Baseline Characteristics

	Docetaxel + Placebo (n=281)	Docetaxel + Plinabulin (n=278)
Median age, y (range)	60 (25, 85)	61 (37, 82)
Sex, n (%)		
Male	207 (73.7)	199 (71.6)
Female	74 (26.3)	79 (28.4)
Tumor histology, n (%)		
Non-squamous	178 (63.3)	154 (55.4)
Squamous	100 (35.6)	120 (43.2)
Missing	3 (1.1)	4 (1.4)
ECOG, n (%)		
0	44 (15.7)	40 (14.4)
1	225 (80.1)	229 (82.4)
2 & missing	12 (4.3)	9 (3.2)
Regional distribution, n (%)		
Asian	245 (87.2)	243 (87.4)
Non-Asian	36 (12.8)	35 (12.6)
Cancer Stage, n (%)		
IIIB	41 (14.6)	50 (18.0)
IV	236 (84.0)	224 (80.6)
Prior PD-1/PD-L1 therapy received, n (%)		
Yes	57 (20.3)	49 (17.6)
No	224 (79.7)	229 (82.4)
Lines of prior therapy, n (%)		
First-line	212 (75.4)	204 (73.4)
Second-line	69 (24.6)	74 (26.6)

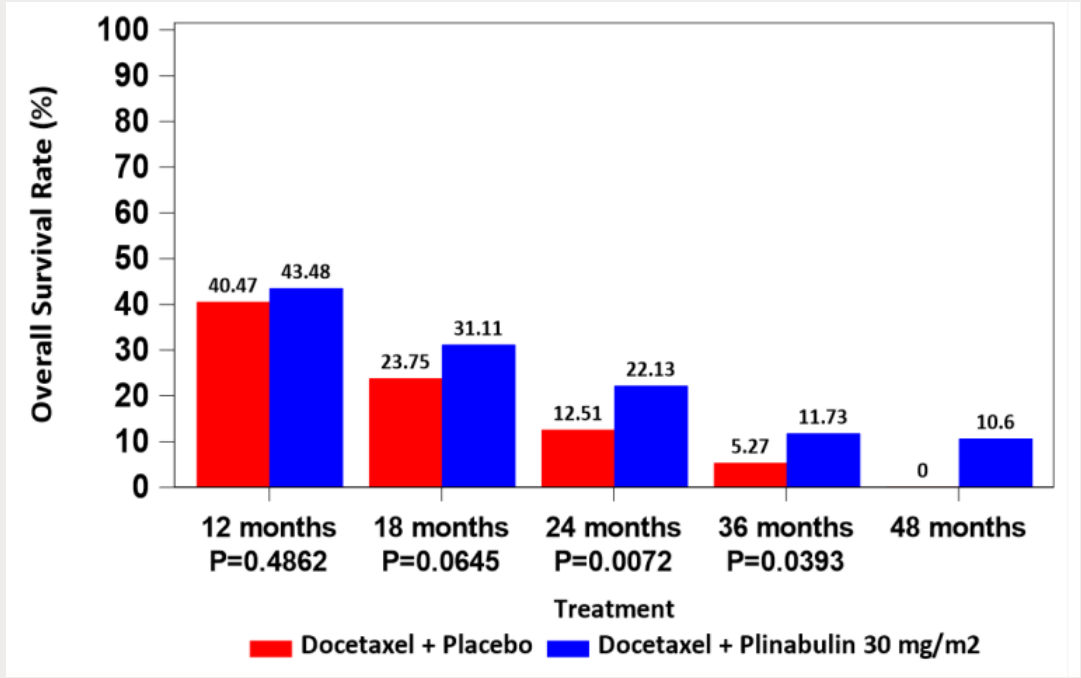
Plinabulin + Docetaxel Met its Primary Endpoint (OS) and Showed Significant Improvement in Long-term OS Rate



Subjects at Risk

Docetaxel (75mg/m2) + placebo					
281	97	21	4	0	0
Docetaxel (75mg/m2) + Plinabulin (30mg/m2)					
278	108	41	10	3	0

	Mean OS (SE)	Median OS (95% CI)	HR
Docetaxel	12.77 (0.676)	9.4 (8.4, 10.7)	
Plinabulin + Docetaxel	15.05 (0.848)	10.5 (9.3, 11.9)	0.82 (0.68, 0.99)



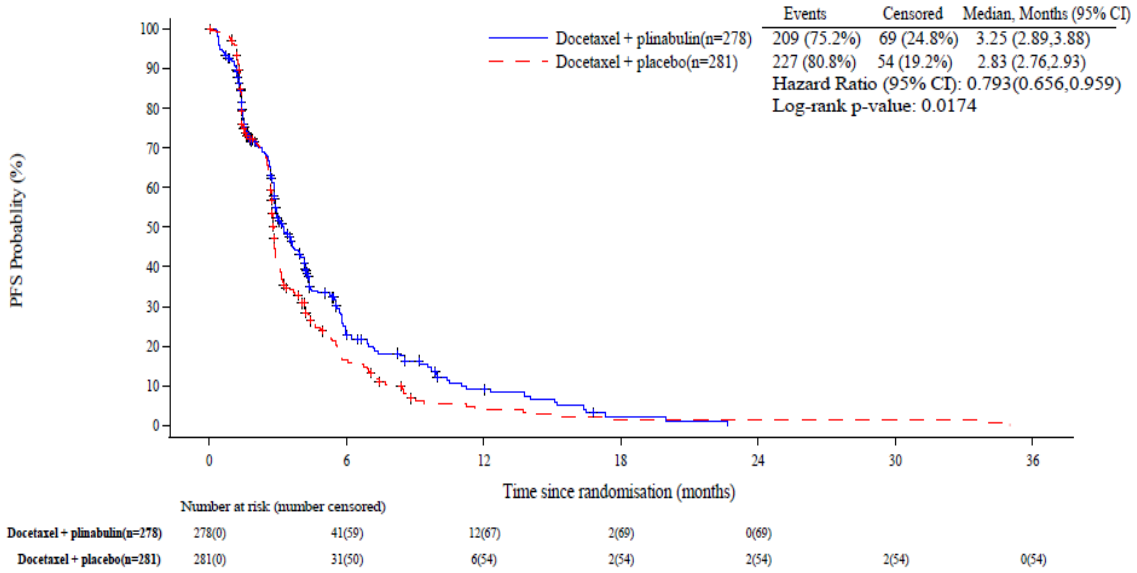
OS Rate Increase Results

- Significantly increased OS rate in 24 months, and 36 months (doubling benefit)
- 48m OS rate: D + Product X (10.6%) vs D (0%)

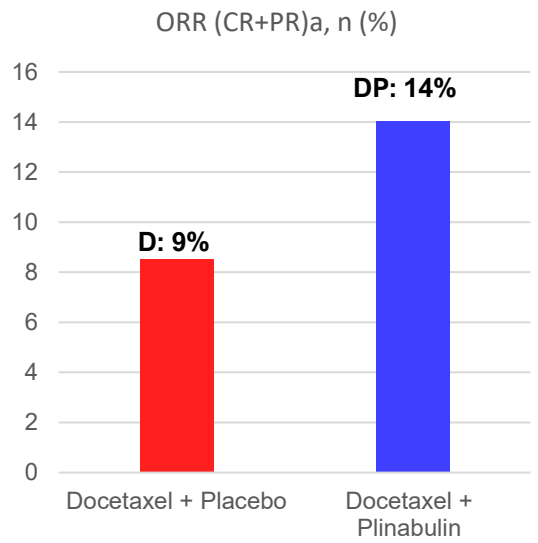
2L/3L EGFRwt NSCLC SOC at time of trial: Docetaxel

Plinabulin + Docetaxel Significantly Improved PFS and ORR

PFS



ORR



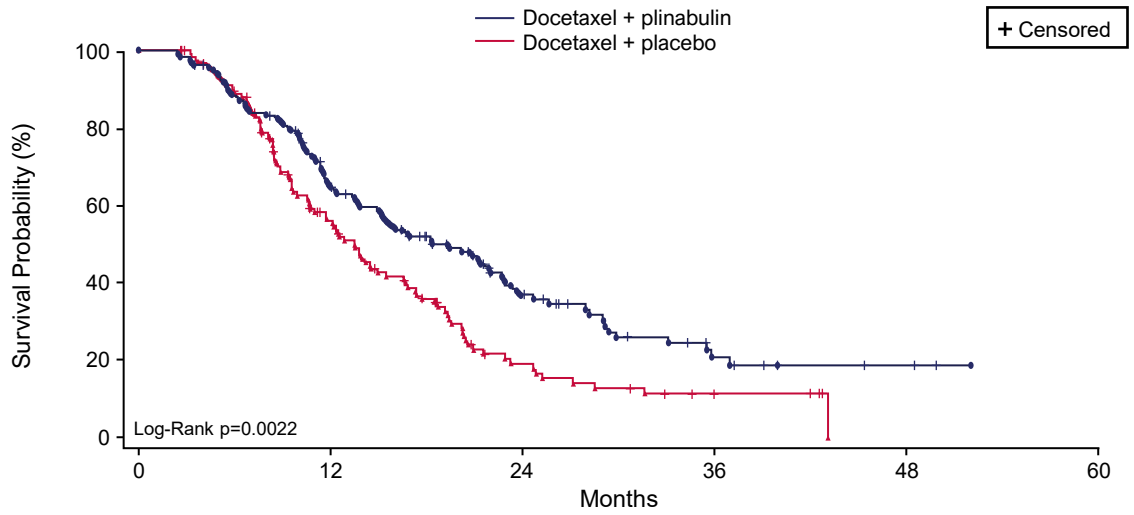
ITT	N	Median PFS Month (95% CI)	HR	Log rank P value
Docetaxel (D)	281	2.8 (2.76, 2.93)		
Plinabulin + Docetaxel (DP)	278	3.3 (2.89, 3.88)	0.79 (0.66, 0.96)	**p = 0.0174**

P value = 0.0404

2L/3L EGFRwt NSCLC SOC at time of trial: Docetaxel

Plinabulin Increases Cycles of Treatment and Improved OS Benefit with More Cycles of Treatment

OS K-M Graph for treatment cycles ≥4 cycles

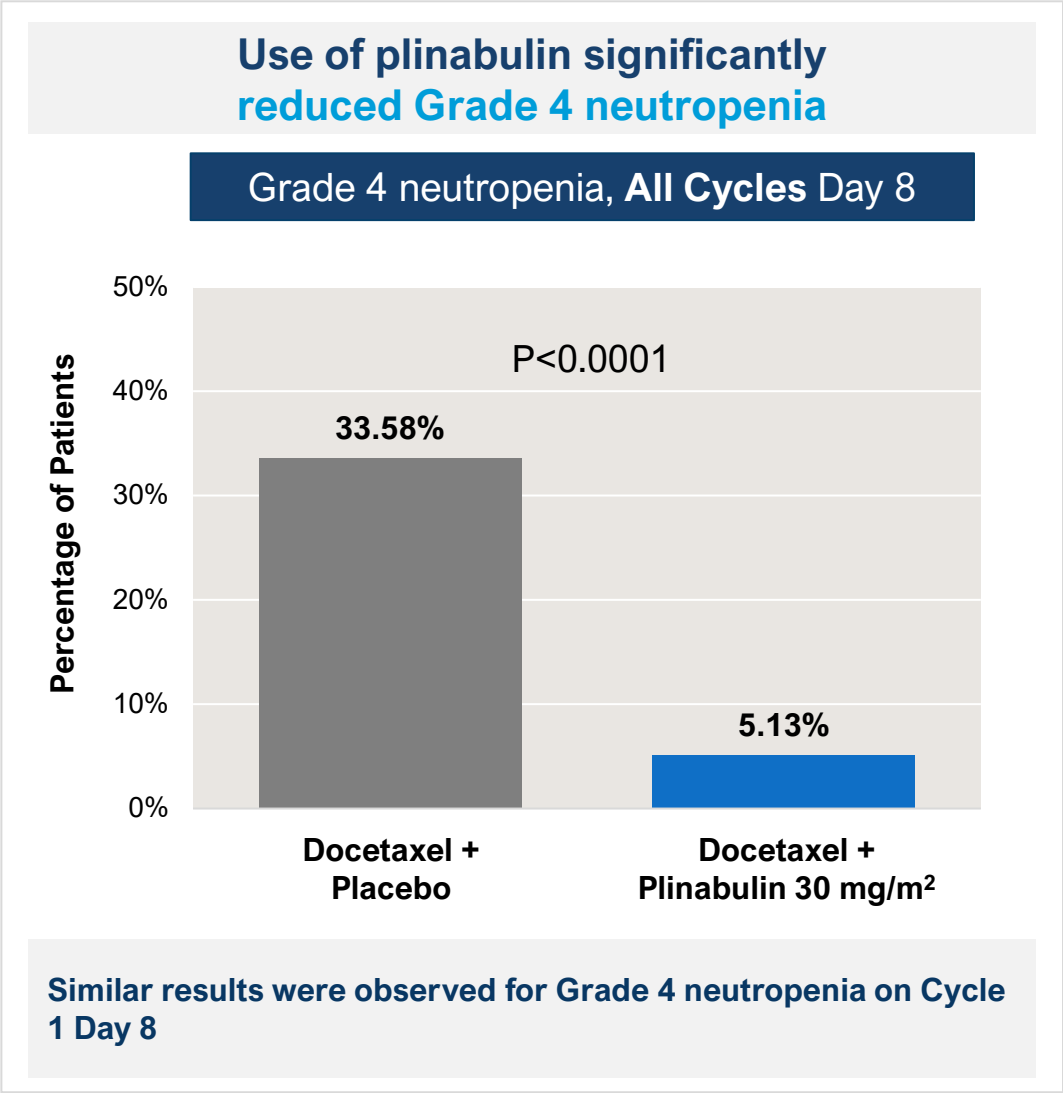


	N	Median OS	HR	P value
Docetaxel	128	13.5 (10.68, 16.54)		
Plinabulin + Docetaxel	133	18.3 (14.96, 22.88)	**0.634**	**P = 0.0022**

Consistently improved median OS observed with more treatment cycles

Number of cycles	Median OS in Months (95% CI)		p-value	HR (95% CI)
	Docetaxel + Plinabulin	Docetaxel + Placebo		
≥4 cycles	18·3 (14·96, 22·88) n=133	13·5 (10·98, 16·54) n=127	0·0027	0·639 (0·476, 0·858)
≥6 cycles	22·9 (19·40, 29·42) n=70	17·3 (12·36, 19·56) n=64	0·0021	0·507 (0·326, 0·788)
≥8 cycles	28·2 (21·99, NA) n=45	19·3 (13·77, 24·85) n=31	0·0121	0·453 (0·240, 0·854)
≥10 cycles	35·5 (22·72, NA) n=27	19·2 (12·39, 20·55) n=18	0·0001	0·174 (0·064, 0·473)
≥12 cycles	NA n=21	20·5 (12·39, NA) n=9	0·0142	0·155 (0·028, 0·855)

Plinabulin Significantly Reduce Grade 4 Neutropenia (>80% reduction) with less use of G-CSF

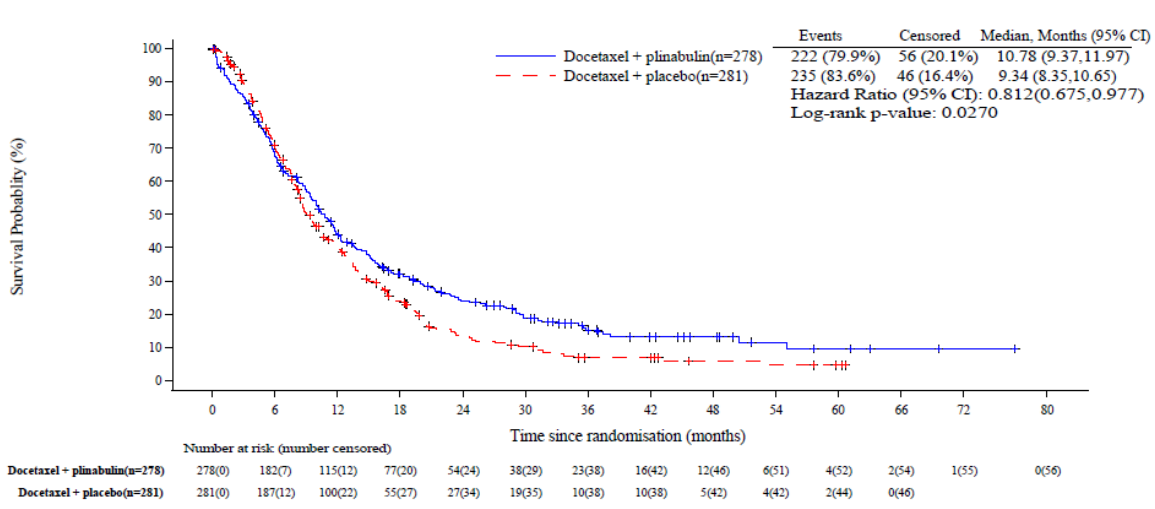


Less Use of G-CSF use in each treatment cycle for Plinabulin Arm

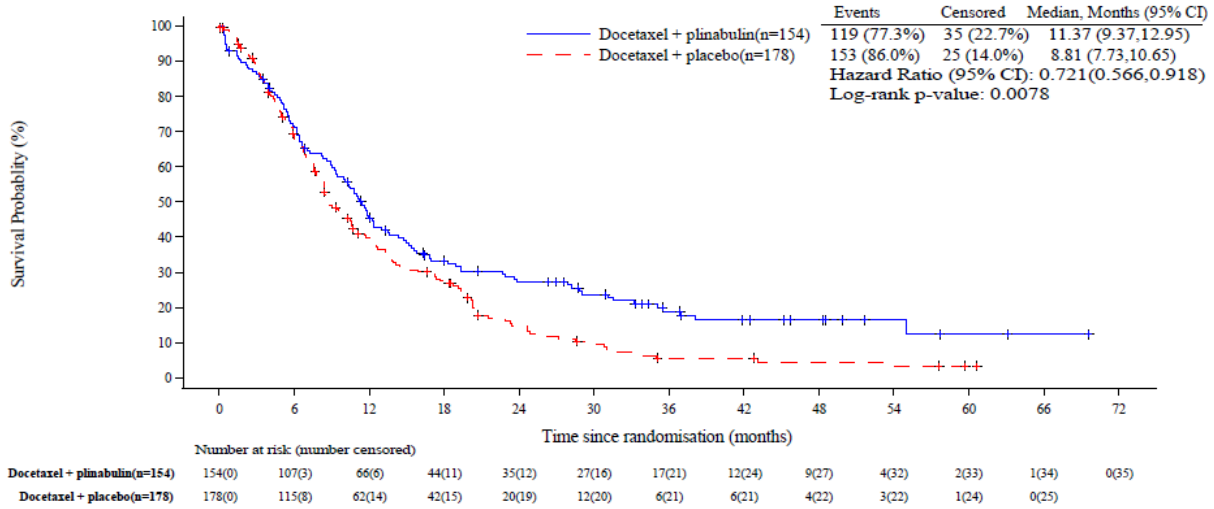
Treatment cycle	Docetaxel + plinabulin n/N (%)	Docetaxel + placebo n/N (%)
Any cycle	152/274 (55·5)	182/278 (65·5)
Cycle 1	111/274 (40·5)	141/278 (50·7)
Cycle 2	70/220 (31·8)	125/242 (51·7)
Cycle 3	47/160 (29·4)	71/155 (45·8)
Cycle 4	39/134 (29·1)	55/127 (43·3)

Consistent OS Benefit in 24-month follow up after Database Lock; Non-squamous OS HR=0.72

ITT



Non-squamous



ITT	N	Median OS (95% CI)	HR	Log rank P value
Docetaxel	281	9.3 (8.35, 10.65)		
Plinabulin + Docetaxel	278	10.8 (9.37, 11.97)	**0.81 (0.68, 0.98)**	**p = 0.0270**

Non-squamous	N	Median OS (95% CI)	HR	Log rank P value
Docetaxel	178	8.81 (7.73, 10.65)		
Plinabulin + Docetaxel	154	11.37 (9.37, 12.95)	**0.72 (0.57, 0.92)**	**P = 0.0078**

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DUBLIN-3: Treatment Related Adverse Events

	Docetaxel + Placebo N=278 n (%)			Docetaxel + Plinabulin N=274 n (%)		
TEAE	All grades	Grade 3	Grade 4	All grades	Grade 3	Grade 4
Any	276 (99.3)	85 (30.6)	119 (42.8)	273 (99.6)	141 (51.5)	52 (19.0)
Hematological						
Anemia	121 (43.5)	13 (4.7)	0	137 (50.0)	15 (5.5)	0
WBC decreased	189 (68.0)	102 (36.7)	33 (11.9)	160 (58.4)	47 (17.2)	32 (11.7)
Neutrophil count decreased	196 (70.5)	46 (16.5)	107 (38.5)	142 (51.8)	48 (17.5)	39 (14.2)
Platelet count decreased	48 (17.3)	2 (0.7)	1 (0.4)	77 (28.1)	12 (4.4)	6 (2.2)
Other TEAEs						
Diarrhea	62 (22.3)	3 (1.1)	0	118 (43.1)	23 (8.4)	1 (0.4)
Constipation	80 (28.8)	1 (0.4)	0	95 (34.7)	1 (0.4)	0
Nausea	67 (24.1)	0	0	100 (36.5)	3 (1.1)	0
Vomiting	39 (14.0)	1 (0.4)	0	82 (29.9)	6 (2.2)	0
Abdominal pain	23 (8.3)	1 (0.4)	0	42 (15.3)	0	0
Abdominal distension	13 (4.7)	0	0	29 (10.6)	2 (0.7)	0
Lung infection	42 (15.1)	23 (8.3)	1 (0.4)	31 (11.3)	15 (5.5)	2 (0.7)
Blood pressure increased	16 (5.8)	8 (2.9)	0	93 (33.9)	50 (18.2)	0
Hepatic enzyme increased	45 (16.2)	1 (0.4)	0	47 (17.2)	2 (0.7)	0
Weight decreased	24 (8.6)	0	0	32 (11.7)	1 (0.4)	0
Cough	77 (27.7)	2 (0.7)	0	64 (23.4)	1 (0.4)	0
Dyspnea	47 (16.9)	6 (2.2)	6 (2.2)	38 (13.9)	5 (1.8)	1 (0.4)
Hemoptysis	27 (9.7)	1 (0.4)	0	31 (11.3)	4 (1.5)	1 (0.4)

Plinabulin Successfully Improved Overall Survival Relative to SOC in 2L/3L NSCLC, an Achievement that has Eluded Other Novel Approaches

The addition of plinabulin as a single agent added to 2L/3L NSCLC (EGFR wt) standard-of-care docetaxel led to improved overall survival and enhanced safety

Efficacy

- Significant survival benefit in ITT (OS HR=0.82) and significant improvement in ORR and PFS
- Almost double 2-year and 3-year OS rate

Safety and tolerability

- The regimen is well tolerated. Side effects include transient hypertension which resolves in 4-6 hours, nausea, vomiting and GI side effects.
- Significant QoL benefit
- Docetaxel-induced grade 4 neutropenia was reduced (>80%), allowing increased treatment exposure

Phase 1b IIT Study: Plinabulin Triple IO Regimen in Resensitizing Patients who Failed PD-1/L1 in Multiple Cancers

MD Anderson Cancer Center

Presentation at SITC Conference (Nov 2023); Manuscript Under Review

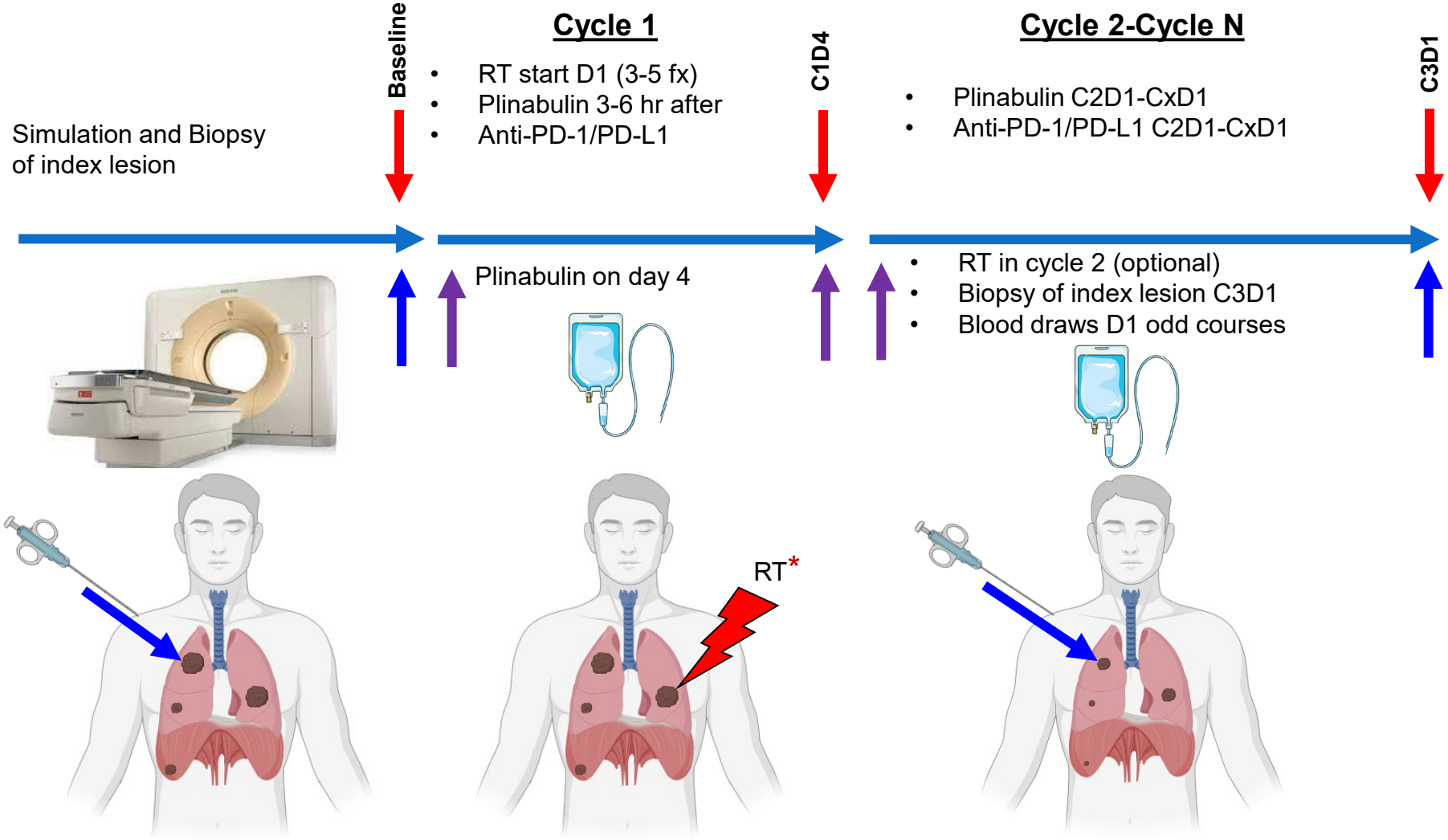
Phase 1b Study to Evaluate Safety of Adding Plinabulin + RT + PD-1 in IO Relapsed/Refractory Solid Tumors (Plinabulin use after RT)

Eligibility:
- Any cancer w/ progression on prior SOC anti-PD-1/PD-L1 agents
- Must have at least one site to be treated with RT and biopsy, with another metastatic site to assess response outside of index lesion

Study Design:
- Open label
- 3+3 design, DLT w/in 30 days

Primary endpoint:
- Safety and ORR/DCR at non-radiated tumor

7 IO-relapsed/refractory cancers:
NSCLC; Merkel cell; RCC; FL-HCC; CRC; HNSCC; Hodgkin



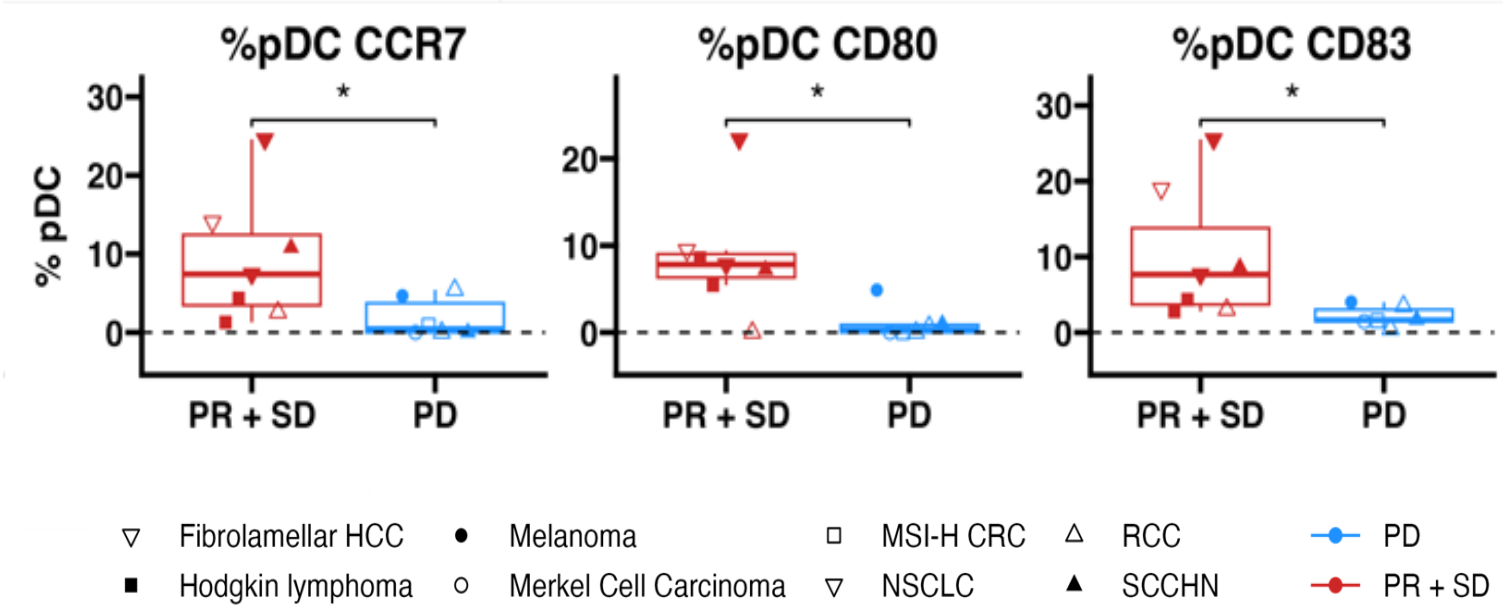
***RT = 24 Gy/3 fx; 50 Gy/4 fx; 20 Gy/5 fx**

BeyondSpring

Plinabulin-Responding Patients Show Early Immune Activation Evidenced by Rapid DC Maturation in the Peripheral Blood

Phase 1b study in a number of IO Relapsed/Refractory solid tumors, rapid DC maturation at cycle 1 Day 4 (in blood samples) were observed in plinabulin-responding (PR + SD) patients

Dendritic Cell Maturation & Migration



Clinical Center: MD Anderson

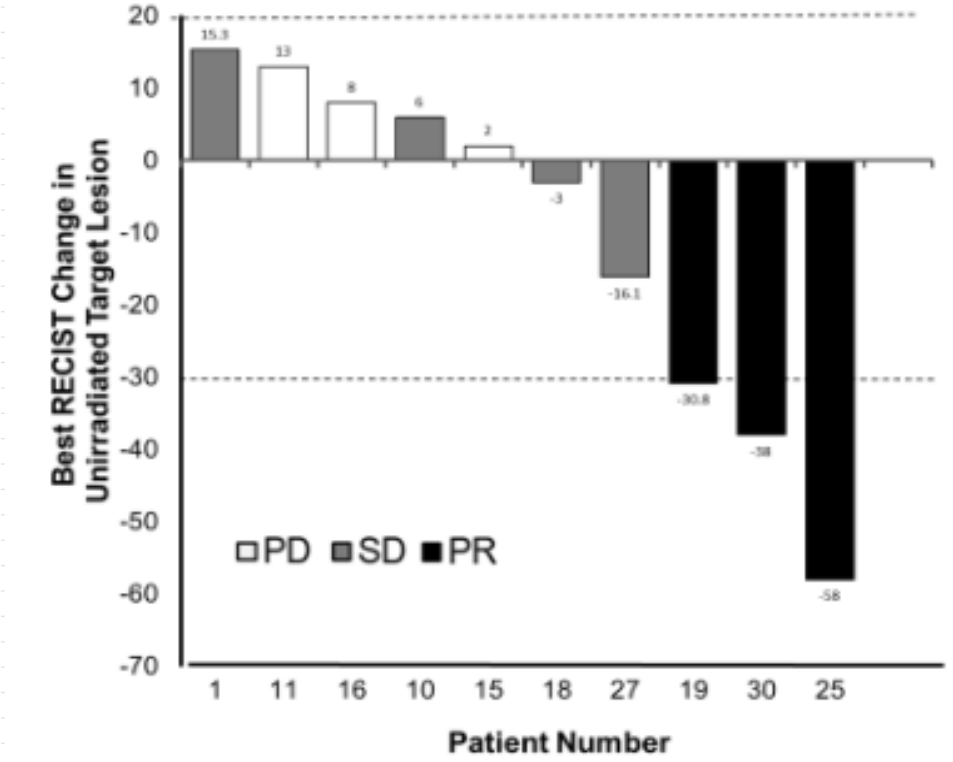
CCR7, CD80 and CD83 up-regulation, biomarkers for DC maturation and migration, are upregulated in the responding patients (PR+SD).

- Responding patients includes Patients with PR (partial response, tumor reduction over 30%) and SD (stable disease).
- Non-responding patient include PD (progressive disease).

BeyondSpring

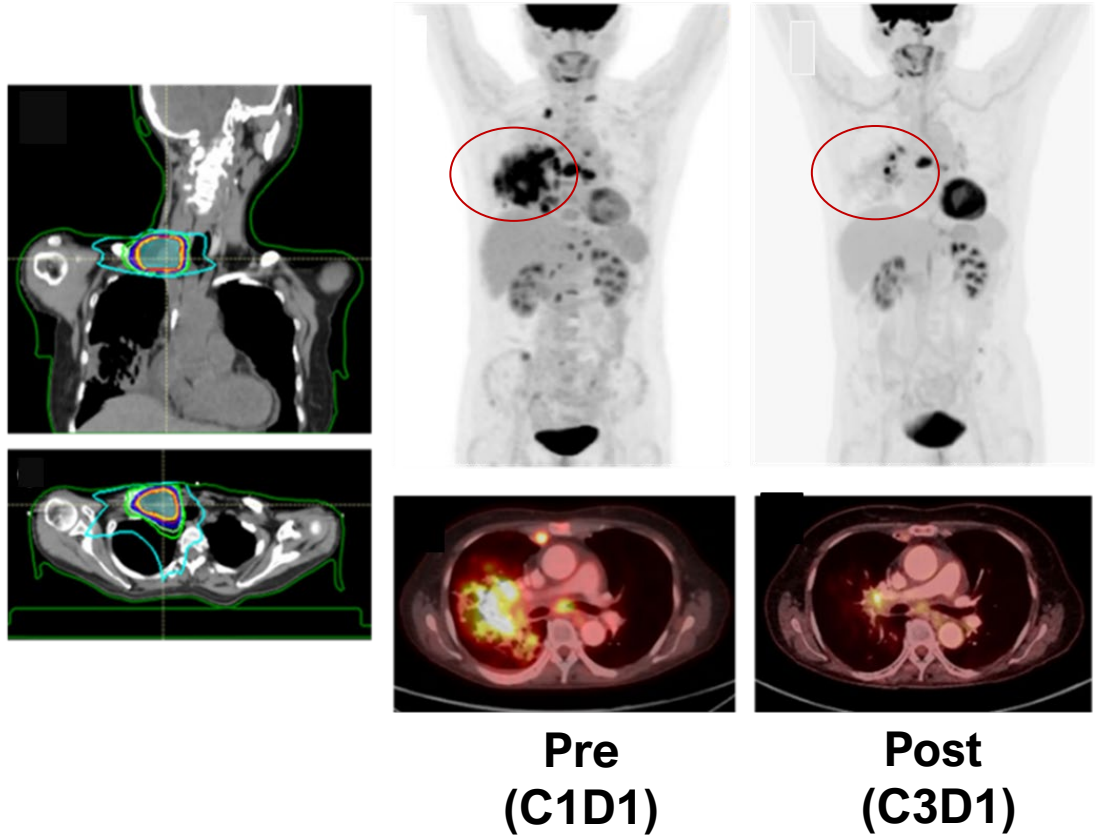
Clinical PoC in Efficacy: Plinabulin Triple Combo Produces Clinically Meaningful Responses in the Non-Irradiated Tumor Across Multiple Cancers in CINR

Topline Preliminary Data: presented at SITC 2023: Plinabulin triple combination led to >50% DCR (3 PR, 4 SD) in 10 IO-failed patients with Tumor assessment



Durable response has been observed in 2 Hodgkin lymphoma patients who progressed after 12 or 16 prior lines of therapy.

Systemic abscopal effect seen comparing baseline and C3D1 for one Hodgkin lymphoma patient (after 12 prior line failure)

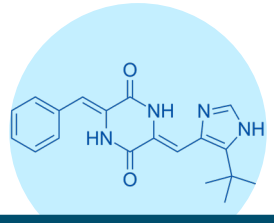


Pre (C1D1) **Post (C3D1)**

Seven IO-relapsed/refractory cancers: NSCLC (Patient #1, #19); Merkel cell (#11); RCC (#16, #18); FL-HCC (#10); CRC (#15); HNSCC (#27); Hodgkin (#25, #30)

BeyondSpring

Plinabulin, Combined with Radiation and Immune Checkpoint Inhibitors, Induces DC Maturation and Potentially Re-sensitizes IO-failure Tumors



Plinabulin is a Unique Tubulin Binder

Plinabulin's tubulin binding site is distinct from that of other tubulin binding agents such as taxanes, vinca alkaloids, and colchicine.

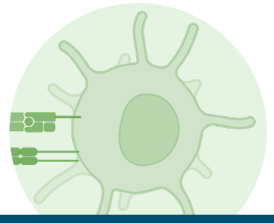
Strong Preclinical Proof of Concept

Plinabulin in combination with radiation and anti-PD-1 **activates DCs, stimulates T-cell proliferation**, and achieves **abscopal effects**.

Clinical Evidence of Efficacy

In IO-relapsed patients in multiple cancers, >50% disease control rate and durable responses in heavily pre-treated patients.

Exploratory biomarker analysis correlates **GEF-H1 signature with Plinabulin responders.**



Clinical Evidence of Immune Activation

Responding patients exhibit early immune activation **with DC maturation.**

These IO effects are observed across multiple different cancer types, NSCLC, HNSCC and Hodgkin's Lymphoma, indicating **broad applicability**.

Phase 2 IIT (303 Study): Pembrolizumab (Pemb) plus Plinabulin (Plin) and Docetaxel (Doc) in Metastatic NSCLC Patients (pts) Who Progressed on First-Line Immune Checkpoint Inhibitor

Peking Union Medical Hospital, Beijing, China

Presentation at ESMO (Sept 2024) and SITC Conference (Nov 2024)

Limited Options for 2L/3L NSCLC Patients Who Failed Prior PD-1/L1 Inhibitor

Historical Comparison Data

- **Docetaxel remains the standard of care** for patients with 2L/3L NSCLC without targetable alterations who progress on immune checkpoint inhibitors (ICI) with and without standard chemotherapy.

✓ Seven phase 3 studies, including ADC, PD-1 or PD-L1 combo with TKI had failed to show OS benefit vs. docetaxel.

- In the recent TROPION Lung-01 phase 3 study[1], a similar patient population had an overall response rate **(ORR) of 12.8%** and median progression free survival (**mPFS) of 3.7 months with docetaxel**. Overall survival is around 12 months.
- In NSCLC patients who progressed after clinical benefit from anti-PD-1/PD-L1 (PFS>=3 months), **Keytruda + docetaxel combination** had **mPFS of 5.5 months** and **ORR of 23.5%[2]**.

Mechanism of Acquired Resistance to Prior IO Therapies

- Acquired resistance in NSCLC or other solid tumors could be due to “T cell exhaustion” or “antigen presenting cell pathway mutation”[3].

1. Ahn et al., TROPION Lung-01 Study, Journal of Clinical Oncology, https://doi.org/10.1200/JCO-24-0154 (2024)
2. Salous T. et al., Cancer 129: 264-7 (2023); 3. Memon et al. Cancer Cell 42, 209–224 (2024)).

IIT Phase 2 303 Study: 2L/3L NSCLC, All Progressed on PD-1/L1

N=47

- Metastatic NSCLC
- Progressed from PD-1/L1 monotherapy or in comb with platinum doublet
- 1L PFS > 6 months
- ECOG PS 0-1
- No prior use of docetaxel or plinabulin
- No need to use steroid to treat ILD, or pneumonia. EGFR, ALK, ROS1 target therapy not as primary therapy
- No brain metastasis, or no leptomeningeal metastasis

Regimen

- Pembrolizumab 200mg D1 Q3W (up to 35 cycles)
- Plinabulin 30mg/m^2 D1 Q3W (Until PD, intolerable SAE, or withdraw from patient)
- Docetaxel 75mg/m^2 D1 Q3W Until PD, intolerable SAE, or withdraw from patient)

Endpoints

- Primary:
  - -ORR (RECIST 1.1)
- Secondary:
  - -PFS (RECIST 1.1)
  - -OS
  - -DOR (RECIST 1.1)
  - -OS rate
  - -Safety

Stage 1: Enroll 19 patients. Futility analysis: if not more than 2 patients with PR, stop the study. If > 2 patients with PR, process to stage 2.

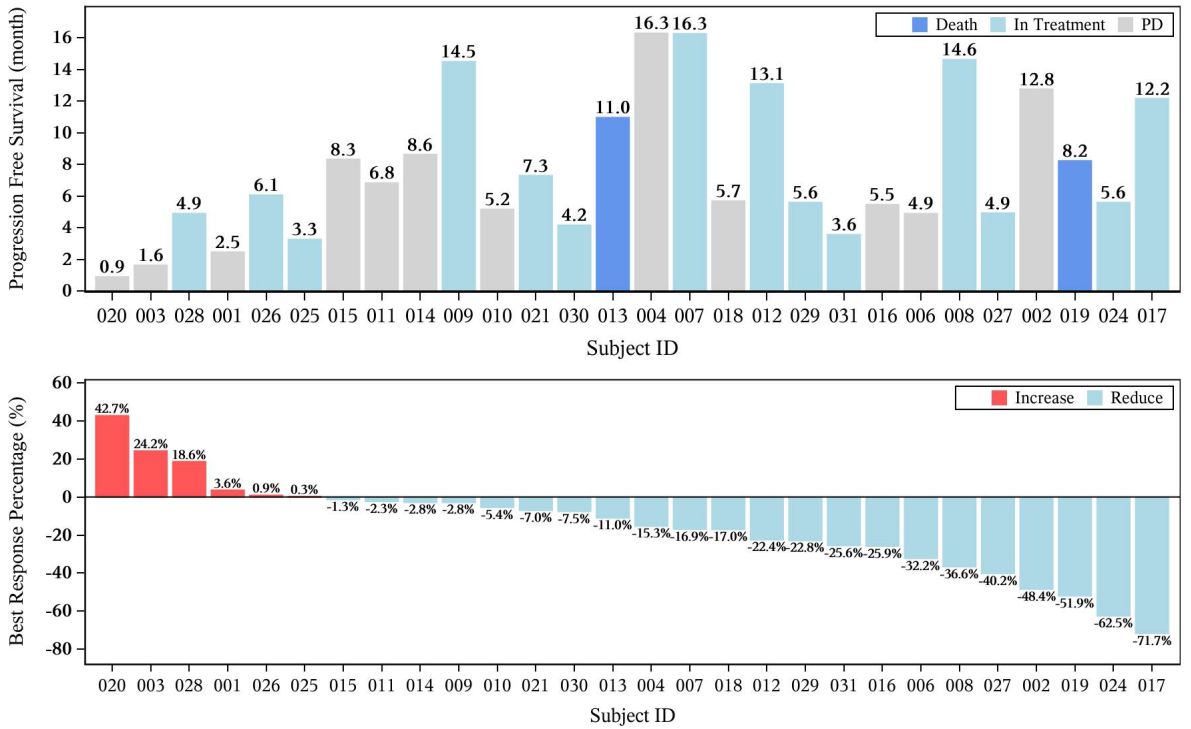
Stage 2: Total enrollment of 47 patients. If > 8 patients with PR, the study meets its objective.

Efficacy data (cut-off date on 29-Aug-2024) – 2024 SITC Presentation

Updated Analysis: 30 patients (ITT)
median follow-up time: 11.5 month (m)

Histology	
Squamous	43%
Non-squamous	57%
Primary endpoint	
Confirmed ORR (RECIST 1.1)	21.1%
Secondary endpoint	
mPFS (RECIST 1.1)	8.6 m
mDoR (RECIST 1.1)	11.4 m
DCR (PR+SD > 4 m)	89.3%*
mOS	NE

Best Change (%) in Target Lesions Sum of Diameters (SOD) and PFS



*25/28 – 2 withdrawn after first dose

Safety Summary

Treatment-related adverse events (CTCAE 5.0 ≥ Grade 3)

System organ class, Preferred term	Pemb + Plin + Doc (N=30), n (%)
All TRAE, CTCAE ≥ Grade 3	14 (46.7)
Blood and lymphatic system disorders	5 (16.7)
Myelosuppression	4 (13.3)
Febrile neutropenia	1 (3.3)
Gastrointestinal disorders	4 (13.3)
Ileus	2 (6.7)
Diarrhea	1 (3.3)
Abdominal distension	1 (3.3)
Investigations	2 (6.7)
Neutrophil count decreased	2 (6.7)
Metabolism and nutrition disorders	1 (3.3)
Hyperglycaemia	1 (3.3)
Acidosis	1 (3.3)
Infections and infestations	2 (6.7)
Lung infection	1 (3.3)
Sepsis	1 (3.3)
Respiratory, thoracic and mediastinal disorders	1 (3.3)
Respiratory failure	1 (3.3)
Vascular disorders	2 (6.7)
Hypertension	2 (6.7)
Renal and urinary disorders	1 (3.3)
Acute kidney injury	1 (3.3)
Cardiac disorders	1 (3.3)
Atrial fibrillation	1 (3.3)

Phase 2 IIT - 303 Study Summary

Efficacy

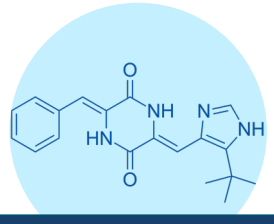
- **Easy to use regimen** (Pemb + Plin + Doc on day 1 of each cycle) in patients with metastatic NSCLC who had disease progression after clinical benefit with PD-1/PD-L1 (with 80% as pemb) showed encouraging clinical benefit for 30 patients of **mPFS (8.6 months) and DCR (89.3%),** higher than historical control of SOC docetaxel (mPFS 3.7 months).
- **Prolonged PFS and OS is supported by Plinabulin's DC maturation MOA**; DC can activate and prolong T cell effect.

Safety

- The combination is well tolerated.
- Grade 3+ AE includes transient hypertension (6.7%), Diarrhea (6.7%), and Ileus (3.3%) which is manageable.

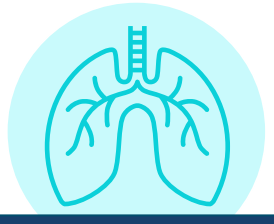
Funding Source: MSD China and BeyondSpring.

First-in-class agent Plinabulin: Transforming Oncology with Novel Mechanisms and Clinically Meaningful Patient Benefits



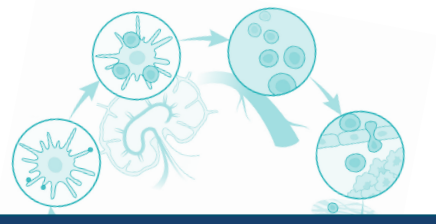
Unique MOA

A unique tubulin modulator that activates **dendritic cell** maturation and **M1-like macrophage** proliferation which **enables the cancer immunity cycle**



Clinical Success

Successfully demonstrated significant **OS benefit** in 2L/3L NSCLC, as well as **reduction in severe neutropenia,** allowing **extended regimen duration**



Unmet Medical needs and Market Potential

Clinically enhanced the anti-tumor response to checkpoint inhibitors in combination with radiation or chemotherapy, in **IO-resistant or progressed patient population**

Strong global patent protection

Plinabulin has **Granted/Allowed Patents to 2039 in over 40 jurisdictions,** including US, EU, Japan, and China

1. Easy to use (Day 1 IV); 2. Clinical Benefit in overall survival and durable response; 3. Reduce AE including CIN

Plinabulin's multiple mechanisms of action provide strong rationale for its combination with both immunotherapy agents as well as neutropenia-limited agents such as chemotherapy and ADCs

BeyondSpring

SEED Therapeutics: Target Protein Degradation (TPD 2.0) Company

TPD Targets 80% of Disease-Causing Proteins That are Currently Undruggable

Investment Highlights

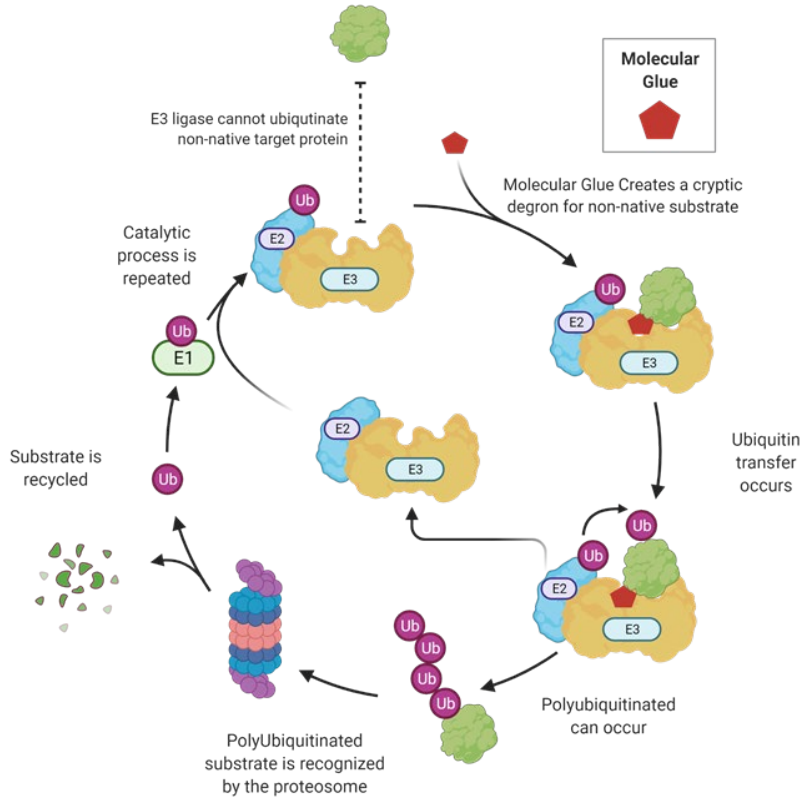
SEED is a leading Targeted Protein Degradation (TPD) 2.0 company focusing on developing novel “Molecular Glues” (MG) for breakthrough therapeutics

TPD Commercial Potential	Focusing on Molecular Glues (MG) to **address 80% of disease-causing proteins considered "undruggable"** by traditional methods.
World-class Founding Team	SEED Co-Founders **are preeminent global scientific leaders on TPD** with unrivaled insights of E3 structure and biology, including the Nobel Prize Winner Dr. Hershko.
Validated Technology Platform	• RITE3 platform deploys proprietary Quasi-degron, LumID and Basal Affinity tests; • Featured as one of leading companies in TPD in two Nature review papers in 2024; • **RITE3 platform is validated** with the investment and R&D collaboration with global pharma: **Lilly and Eisai**. Potential deal values exceeding **$2.3 billion**.
Rapidly Advancing Pipeline	• Developed **9 programs (6 internal and 3 are partnering assets)** across oncology, neurodegeneration, immunology, and antiviral indications, including 6 internal programs and involving **6 novel E3s**. • Lead internal oncology asset (**RBM39 degrader**) on track for **IND submission in mid-2025** and clinical data release in 2H 2026. • Neurodegeneration program (**Tau degrader**) targeting in vivo efficacy by 2H 2025.

Targeted Protein Degradation (TPD)

TPD for 80%Undruggable Proteins

- **E3 ligase** is the key protein which **recognizes** the disease protein (**POI**) for degradation



TPD Research is an Important and **High-value Area**

- Large Pharma In-license and Collaboration Activities

- **Discovery-Stage TPD Assets**: Command $35–60M upfront and $500M–5B milestones; notable deals include Bayer's $1.5B acquisition of Vividion and Merck's $1.1B acquisition of Peloton.
- **Pre-IND/IND-Stage TPD Assets**: Fetch $100–300M upfront and up to $2B milestones; key partnerships include Novartis–Monte Rosa and Lilly–Foghorn.
- **Clinical-Stage TPD Assets (Phases I & II):** Secure $150–650M upfront, $350M equity, and $2.1B milestones; highlighted in Pfizer–Arvinas and Novartis–Monte Rosa collaborations.

Sriram et al., Molecular Pharmacology, 2018

Experienced Team with Success Track Record

Founders

Nobel Prize winner,

Pioneers in TPD Space

Management Team

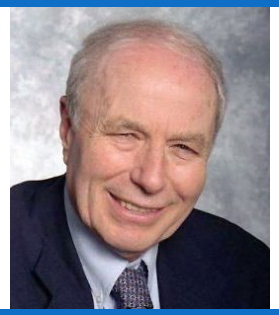
40 IND and 12 NDA experience

Board Members

Experienced business and legal expert and independent board member from Eli Lilly and Eisai

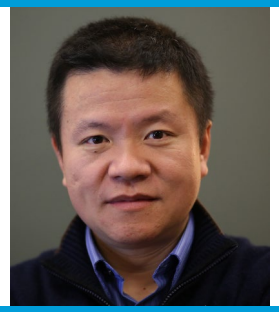
World Class Founding and Leadership Team

Avram Hershko MD, PhD[+]



"Godfather" of TPD; 2004 Nobel Laureate; Advisor to Millennium on developing **Velcade**

Ning Zheng, PhD[+]



Howard Hughes Professor, University of Washington; World's foremost **thought leader on E3 and MG**

Michele Pagano, MD [+]

Howard Hughes Professor, NYU Medical School; Global **thought leader on TPD biology and application**

Lan Huang, PhD [+] * (Chairman & CEO)

E3 structural expert; Serial biotech entrepreneur with **20+ years** of drug development experience, including NDA-ready assets

James Tonra, PhD* (President & CSO)

20+ years of drug discovery experience that led to **5 NDAs**; Ex leadership role in Regeneron, Millennium, ImClone, Kadmon, and BYSI

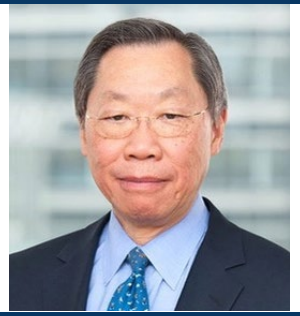
Linus Lin, PhD*

Global head of Lilly Chorus; Ex GM of Lilly China R&D Center, Head of Chemistry at WuXi AppTec, and **led multiple drug discovery teams at Merck**

Yoshiharu Mizui, PhD*

Founder and President of Eisai Innovations, Inc.; former Global Business Development and Strategy Head in Eisai's Oncology Business Group

Jackson Tai*



Retired board member for Lilly, HSBC Holdings, Mastercard; **Former DBS Bank CEO**, former J.P. Morgan & Co. investment banker; **Expert in finance and risk**

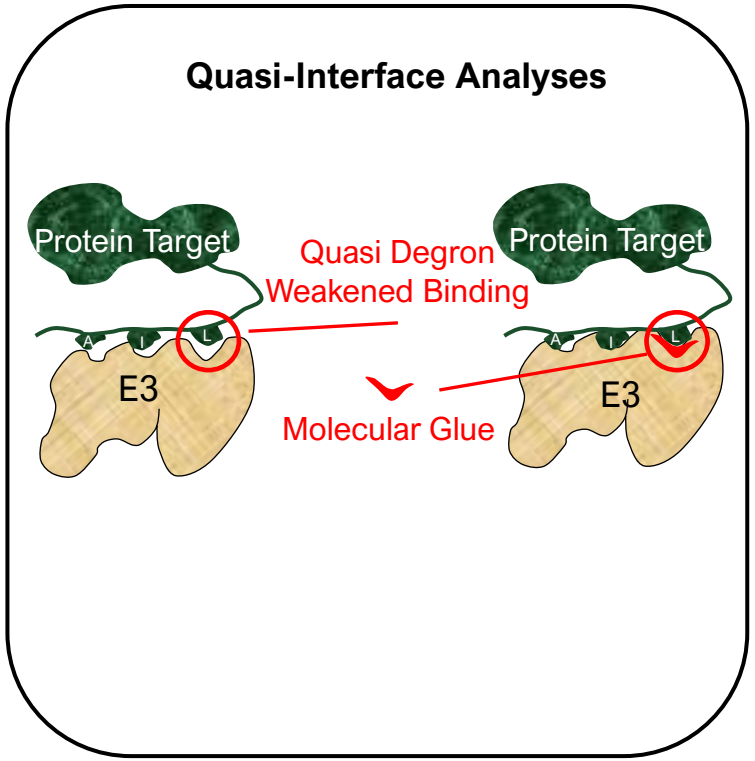
Ko-Yung Tung, JD*

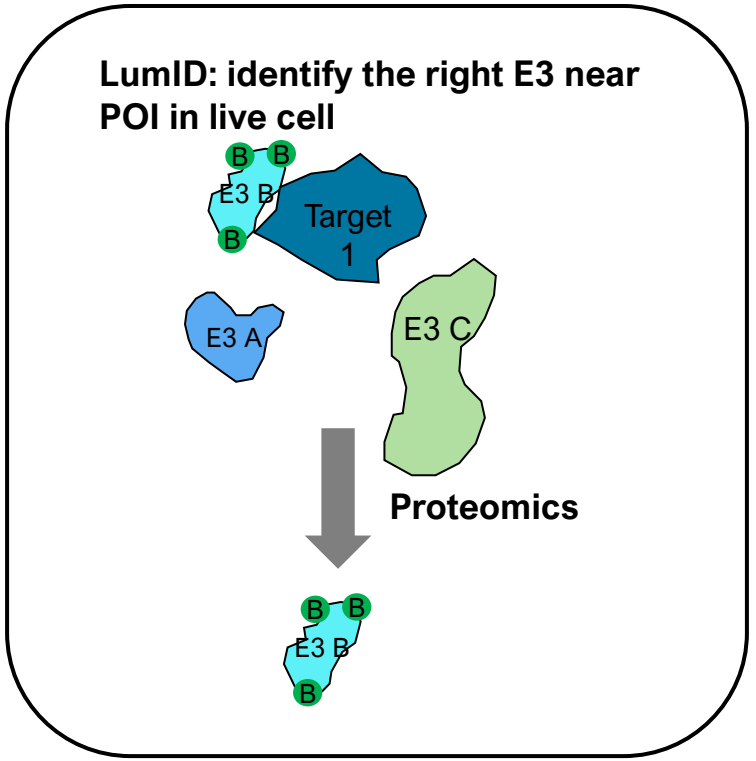
Former Eisai director, World Bank general counsel, and lecturer at Harvard and Yale Law School; **Expert in law and international business**

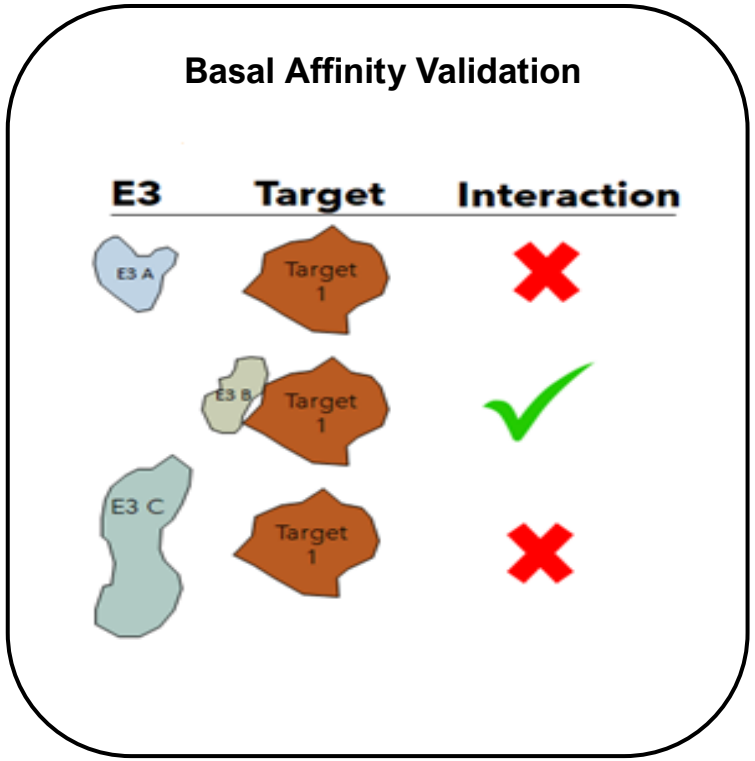
BeyondSpring

[+]SEED Co-Founder and Scientific Advisory Board Member
*Board Member

Technology Platform: RITE3™ – Target-Centric TPD 2.0





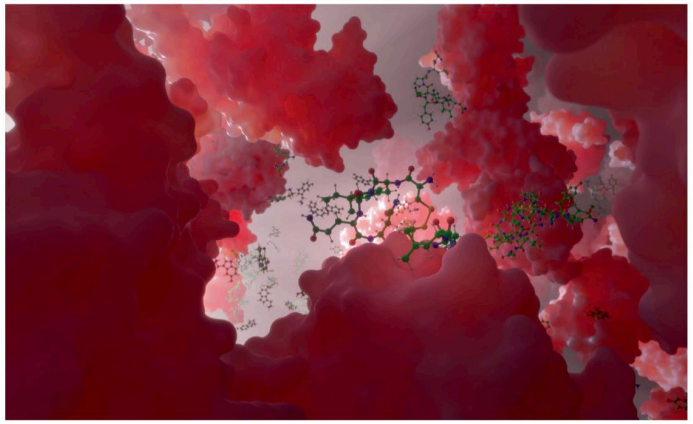


- **Target-driven approach** - Efficiently identifies the "right" E3 ligase for each Protein of Interest (POI), with 9 POIs and 6 novel E3s successfully matched.
- **Multi-dimensional platform**:
  - **Quasi-degron** (computational and structural biology)
  - **LumID™** (cell biology, real-time monitoring of target-E3 interactions)
  - **Basal Affinity** (biophysics, distinguishing productive vs. non-specific interactions)
- **Molecular Glue properties** - Small molecules (<500 Da), no need for high-affinity binding, potential for blood-brain barrier penetration.

“Nature Biotechnology” Review on “The Glue Degraders” (3/6/2024)

News feature

https://doi.org/10.1038/s41587-024-02164-9



THE GLUE DEGRADERS

Companies are hoping to discover small molecules that remove undruggable proteins. It won't be easy. **By Ken Garber**

In December 2023, two days after the US Food and Drug Administration approved separate gene editing and gene therapy treatments for sickle cell disease, Novartis biochemist Pamela Ting made a plenary presentation at the American Society of Hematology annual meeting[1]. She described a phenotypic screen that yielded hits causing a surge of fetal hemoglobin, the same protein that the recently approved gene editing therapy is engineered to produce. But unlike that treatment, which is priced at $2.2 million, Novartis's compounds are small-molecule protein degraders, molecular 'glues' that would be much cheaper to produce and administer. Animal studies were positive. "We are currently conducting the experiments necessary to translate these findings to a human clinical trial," Ting said at the meeting. The Novartis work is the latest sign that molecular glue degraders, which hijack the cell's disposal machinery to remove disease-related proteins, have arrived.

Much of pharma is invested, directly or through partnerships. In 2019 Bristol Myers Squibb spent $74 billion to acquire Celgene and its portfolio of molecular glue degraders. More than two dozen biotech companies are now seeking these drugs (Table 1). "We're very active in this space and see tremendous potential in molecular glues," says Ryan Potts, head of the induced proximity platform at Amgen.

Yet the field faces some serious obstacles. Prospective screening for molecular glue degraders is a major undertaking (Fig. 1). It's often done in cells, unlike standard biochemical assays with recombinant proteins, adding time and expense, and involves extensive follow-up work to validate hits and understand mechanism of action. And those hits are rare because it is hard to drug protein–protein interactions. With hit rates low, small-molecule libraries must be sizable. And the field does not yet know what chemical features molecular glues have in common, making it difficult to select these libraries. Biological information on the more than 600 E3 ligases – the enzymes that molecular glues recruit to degrade a drug's target – is scant, except for a handful of these proteins. For all these reasons, molecular glue discovery remains a high-risk enterprise. "The field needs a success story," says Simon Bailey, head of drug discovery at Plexium.

CREDIT: SCIENCE LAB / ALAMY STOCK PHOTO

nature biotechnology

Garber, *Nature Biotechnology* (2024)

SEED was prominently featured in “Nature Biotechnology” Review.

Table 1 | Selected molecular glue degrader companies discussed

Company	Pharma partners	Discovery approach	Deployed E3 ligases	Lead program
Monte Rosa Therapeutics	Roche	Remodel cereblon to recruit neosubstrates; proximity assays, proteomics	Cereblon	MRT-2359, GSPT1 degrader, phase 1 (cancer)
Plexium	Amgen, AbbVie	Miniaturized, cell-based DNA-encoded library screening; target-centric	Cereblon, DCAF11, others undisclosed	IKZF2 degrader, phase 1 (cancer) December 2023
Seed Therapeutics	Eli Lilly	Target centric; detect basal E3–target interactions; proximity assays	Working with 25–30 E3s, including DCAF15	ST-00937, RBM39 degrader (cancer), IND filing, 2H24
Novartis	Dunad Therapeutics	Phenotypic screens, cereblon binders, others undisclosed	Cereblon, others undisclosed	Wiz degrader (sickle cell anemia), IND-enabling studies
Proxygen	Boehringer Ingelheim, Merck KGaA, Merck & Co.	Broad range, from unbiased phenotypic screens to target-centric	Many; undisclosed	Undisclosed
A-Alpha Bio	Amgen, Bristol Myers Squibb, Kymera Therapeutics	Detect basal E3–target interactions using yeast cell surface display, mutagenesis to interrogate interface	Many; undisclosed	Undisclosed

Others in this space include Ambagon Therapeutics, Astellas Pharma, AstraZeneca, Bayer, Biotheryx, Celgene (Bristol Myers Squibb), ChemPartner, Coho Therapeutics, Degron Therapeutics, Gandeeva Therapeutics, GSK, GluBio Therapeutics, Magnet Biomedicine, Neomorph, Orionis Biosciences, PhoreMost, Pin Therapeutics, Progenra, Proximity Therapeutics, Ranok Therapeutics, Revolution Medicines, Salarius Pharmaceuticals, SK Biopharmaceuticals, SyntheX and Triana Biomedicines. IND, Investigational New Drug.

Sticking without glue

Molecular glue company Seed Therapeutics, like Proxygen, is looking beyond cereblon. It's a majority-owned subsidiary of Beyond-Spring Pharmaceuticals, a drug company co-founded by Lan Huang, who published the first E3–E2 crystal structure[15], and Ning Zheng, who solved the structure of auxin bound to its transport inhibitor response 1 (TIR1) receptor[4].

Seed emphasizes proper E3 selection. The discovery process is lengthy: pick a candidate E3 on the basis of complementarity with the target protein (as predicted by AlphaFold and other computational methods) and cell location of the E3; detect a basal E3–target interaction in a cell system; confirm ability of the E3 to ubiquitinate the target; and perform high-throughput screening for degraders, followed by validation assays and then medicinal

“Nature Reviews Drug Discovery” Review on “Protein Degraders Push into Novel Target Space” (10/14/2024)

News & analysis

News https://doi.org/10.1038/d41573-024-00170-9

Protein degraders push into novel target space

By Asher Mullard

Clinic-ready molecular glues and heterobifunctional PROTAC drugs are taking targeted protein degradation into uncharted territory.

With the rise of targeted protein degraders over the past decade, early adopters promised that these small molecules would be able to unlock previously intractable targets. A first wave of molecular glue and heterobifunctional degraders mostly focused on well-validated targets. A second surge is now pushing into more novel target space.

"We're on the cusp of a revolution," says Neil Bence, head of oncology discovery at Bristol Myers Squibb (BMS), which is using both molecular glues and ligand-directed degraders to breakdown novel targets in cancer and other indications.

Traditionally hard-to-drug targets — including transcription factors, GTPases and guanine nucleoside exchange factor (GEFs) — are increasingly within reach, shows the growing degrader pipeline (Table 1).

> "We're on the cusp of a revolution"

This is enabling molecular glue degraders — small molecules that reshape an E3 ligase to make it tag targets with ubiquitin, shunting problem proteins to the cell's proteasomal recycling system — to expand beyond their oncology origins. BMS is testing a transcription-factor-degrading glue for sickle cell disease, while Monte Rosa has advanced its VAV1-targeted GEF degrader into the clinic for autoimmune diseases.

Heterobifunctional degraders — larger dumbbell-like molecules that bind a target of interest with one end and an E3 ligase with the other — are making headway in novel target space too. Kymera is advancing a first-in-class degrader against the immune-mediating transcription factor STAT6, for example, while both BMS and Arvinas are taking on the oncogenic transcription factor BCL6.

Zoran Rankovic, director of the Centre for Protein Degradation at the Institute of Cancer Research, is buoyed by this progress. Degraders against previously drugged targets could be a boon to patients, he explains, if they can outperform approved inhibitors. But most of the human proteome is still undrugged, and the bigger opportunity for degraders is to push these boundaries.

The field has a way to go, he adds. Glue degrader discovery remains limited as yet mostly to serendipitously identified targets, and heterobifunctional degraders remain constrained by ligandability issues and rational-design limitations. But researchers are making progress across the entirety of the degrader modality.

"This is a hype that actually lives up to its promise," says Rankovic.

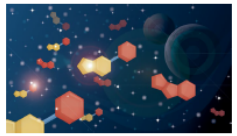
> "This is a hype that actually lives up to its promise"

Old glues, new clues

Interest in targeted protein degraders has exploded in the past 10 years, and dozens of companies are now operating in this space. While heterobifunctional drug discovery companies were faster out of the gate, the ranks of the glue degrader biotechs are growing too — fuelled especially by the field's understanding of how the FDA-approved myeloma drug lenalidomide and related immunomodulatory drugs (IMiDs) bind and reshape the E3 ligase cereblon to ubiquitinate the transcription factors IKZF1 and IKZF3. Other small-molecule glues might be able to reshape cereblon to take on other targets too, researchers quickly realized.

The first programmes to advance into the clinic, however, took on targets that were also degraded by lenalidomide. Celgene, now part of BMS, for example, worked quickly with its lenalidomide analogues to discover and optimize CC-92480, now mezigdomide, to breakdown IKZF1 and IKZF3. That drug is now in phase III development for myeloma. The kinase CK1α was another low-hanging fruit that is degraded by lenalidomide.

A further stepping stone was GSPT1, a GTPase that researchers pulled down during an immunoprecipitation assay of cereblon and a lenalidomide analogue. GSPT1 helps the protein-making machinery to disengage from completed proteins, and its blockade kills cells — especially fast-growing cancerous ones — creating oncology applications for the previously undrugged GTPase target. BMS first advanced its GSPT1 degrader CC-90009 into the clinic in 2016, but has since terminated that glue for undisclosed reasons.



"GSPT1 degradation shuts down global protein translation, and there are a number of adverse events that are likely to be associated with that," cautions Ian Churcher, a consultant with Janus Drug Discovery and a former degrader developer at both Amphista and GSK. "It's all about therapeutic index."

At BMS, that now means using an antibody–glue conjugate to better deliver the degrader to cancer cells. Its BMS-986497, acquired from Orum Therapeutics, consists of a GSPT1-degrading glue tacked on to a CD33-targeted antibody, to home in on malignant B cells.

"To improve both the efficacy and tolerability of GSPT1 degradation, an antibody–conjugate approach would be ideal," says Bence. "We're excited to see how this type of approach performs. It's a really exciting time right now for degrader–antibody conjugates."

BMS has also moved a glue degrader forward against another transcription factor for sickle cell disease, but as yet has not disclosed its target. "Stay tuned," says Bence.

A cereblon-based glue degrader that targets the transcription factor WIZ can boost fetal haemoglobin levels in mice and primates, Novartis reported this year, showcasing one way a glue could be useful in sickle cell disease.

Target hopping

Monte Rosa was another early mover against GSPT1, developing MRT-2359. Clinical data as yet shows that this glue has a viable therapeutic index and a tolerable safety profile in patients with MYC-driven solid tumours.

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SEED was prominently featured in “Nature Reviews Drug Discovery”.

Table 1 | Degraders move into novel target space

Target	Target properties	Molecule (degrader type)	Company	Indication	Status
Newly prosecuted targets					
GSPT1	GTPase, translation termination factor	BMS-986497 (antibody–glue conjugate); MRT-2359 (glue); CC-90009 (glue)	BMS/Orum; Monte Rosa; BMS	Haematological malignancies; MYC-driven cancer	Phase I; Phase I/II; Discontinued
VAV1	GEF, scaffold protein	MRT-6160 (glue)	Monte Rosa	Autoimmunity	Phase I
Not disclosed	Transcription factor	HbF-activating CELMoD (glue)	BMS	Sickle cell disease	Phase I
WIZ	Transcription factor	NA (glue)	Novartis	Sickle cell disease	Preclinical
BCL6	Transcription factor	ARV-393 (heterobifunctional); BMS-986458 (heterobifunctional)	Arvinas; BMS	B-cell malignancies	Phase I; Phase I
STAT6	Transcription factor	KT-621 (heterobifunctional)	Kymera	Allergic diseases	Phase I in 2024
IKZF2	Transcription factor	Helios CELMoD (glue); PLX-4545; DKY709 (glue)	BMS; Plexium; Novartis	Cancer	Phase I; Phase I; Discontinued
HuR (ELAVL1)	mRNA stability regulator, RBP	NA (glue)	Degron	Cancer	Preclinical
Previously prosecuted targets, without approvals					
IRAK4	Kinase, scaffold protein	KT-474 (heterobifunctional)	Kymera/Sanofi	AD and HS	Phase II
LRRK2	Kinase, scaffold protein	ARV-102 (heterobifunctional)	Arvinas	Parkinson's disease	Phase I
STAT3	Transcription factor	KT-333 (heterobifunctional)	Kymera	Cancer	Phase I
MDM2	E3 ligase	KT-253 (heterobifunctional)	Kymera	Cancer	Phase I
RBM39	Splicing factor, RBP	NA (glue)	Seed	Cancer	Phase I in 2025
NEK7	Kinase	MRT-8102 (glue); NA (glue)	Monte Rosa; Novartis	Inflammation	Preclinical; Preclinical

Pipeline data from Cortellis database and company websites. AD, atopic dermatitis; CELMoD, cereblon E3 ligase modulatory drug; GEF, guanine nucleotide exchange factors; HS, hidradenitis suppurativa; RBP, RNA-binding protein.

SEED Therapeutics is amongst those who are nevertheless working to let other E3 ligases shine. Its lead programme harnesses the DCAF15 ligase to degrade the splicing factor RBM39. This programme builds on over 25 years of research on aryl sulfonamide small molecules, adds SEED president and CSO James Tonra. In 1999, Eisai reported that its indisulam stalls cell cycle progression in cancer cells — prompting a failed attempt to develop the drug as a chemotherapy candidate. In 2017, researchers reported that this class of drug in fact acts by remodelling DCAF15 to ubiquitinate RBM39, a protein that regulates the splicing of mRNA precursors.

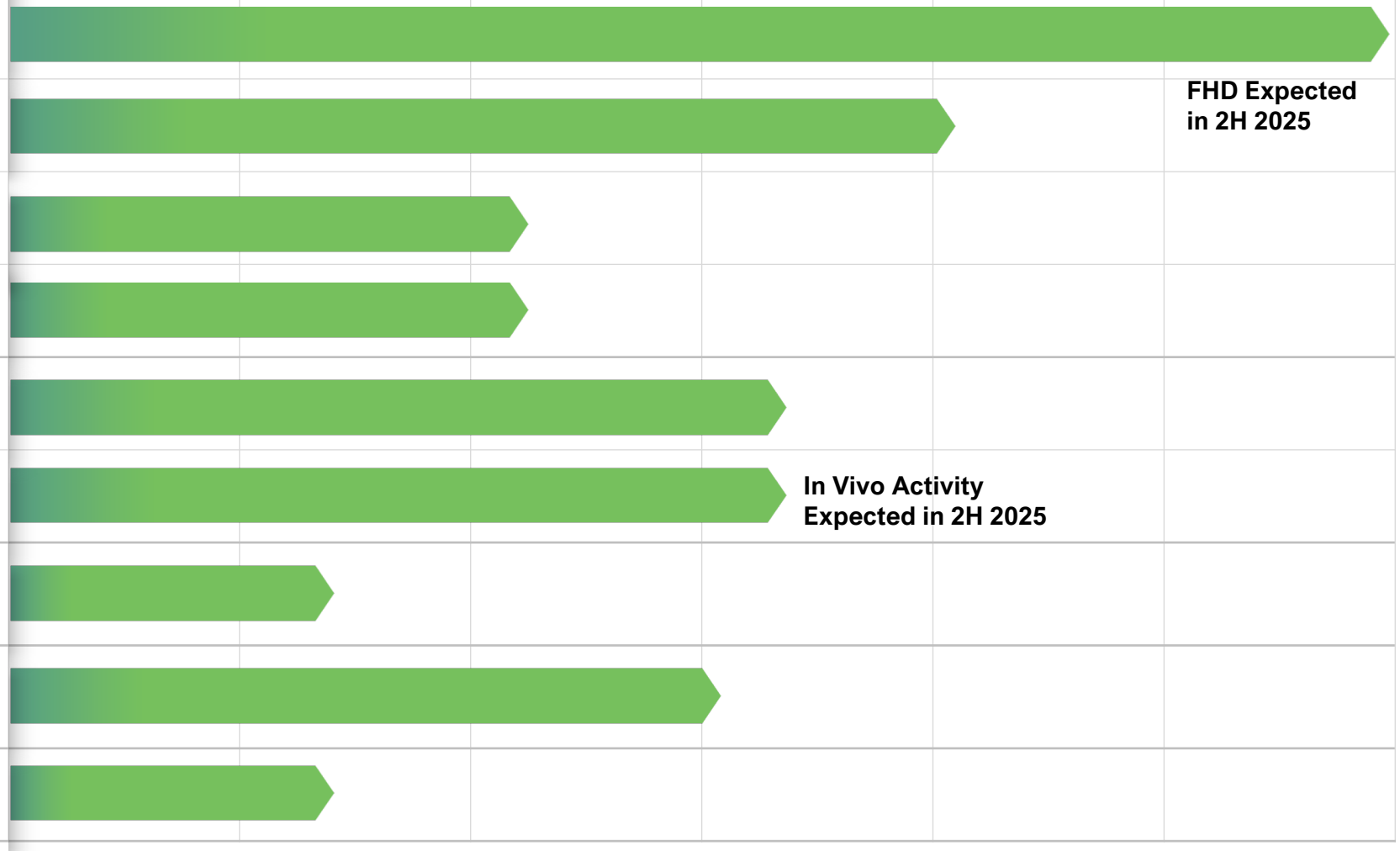
Armed with a better understanding of RBM39 biology, SEED is set to advance an optimized RBM39 degrader into the clinic next year.

"There's a big opportunity for RBM39 degraders in the clinic for new indications, in everything from neuroblastoma to liver cancer," says Tonra.

Mullard, *Nature Reviews Drug Discovery* (2024)

Pipeline: Diversified and Fast Progressing

Indication	Target Protein	Target Selection	E3 Ligase ID	Molecular Glue HTS	Lead ID	IND Candidate	IND Filing
Oncology	RBM39						
	KRAS-G12D						
	Target Beta						
	FEN1						
Neurodegeneration	Target Alpha*						
	Tau						
	Target Delta*						
Immunology	Target Gamma*						
Antiviral	HBx						



SEED owns global IP on all programs except for three joint programs with Eli Lilly and Company (labeled with *)

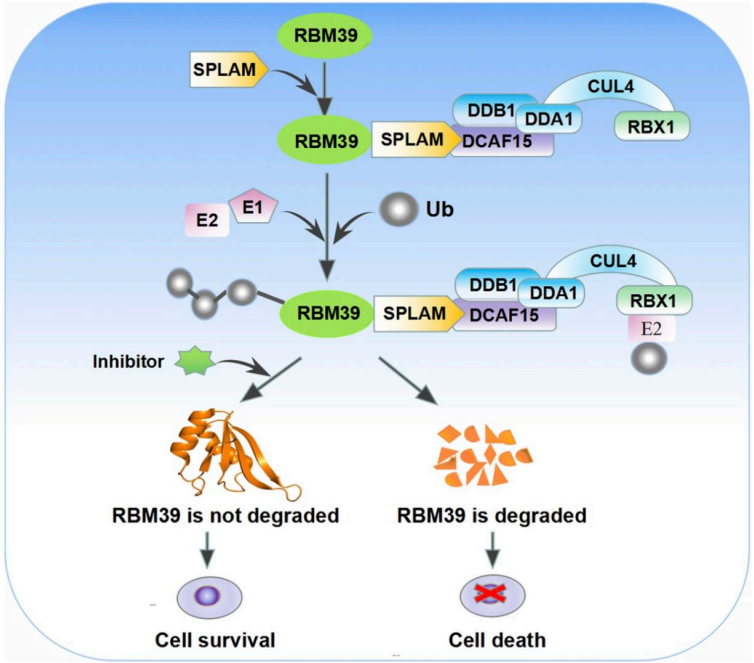
Pipeline: Rapid Progress and High-Value Potential

Program	Indication	Milestones	Market Potential
RBM39 Degrader (ST-01156)	Liver cancer, KRAS-mutant cancers, neuroblastoma	Expected: IND submission mid-2025, first human dose H2 2025; clinical data for around 50 patients H2 2026	Peak sales >$7B
Tau Degrader	Alzheimer's disease (AD)	Expected: In vivo efficacy by H2 2025, IND candidate by 2026	Global AD market >$30B
Other Programs	Immunology, antiviral, anti-aging	Rapid advancement of 4 more internal programs + 3 joint R&D programs with Eli Lilly and Eisai	

RBM39 Degrader Advantages:

- **Preclinical data**: Complete tumor regression (colon cancer, neuroblastoma models), excellent safety profile (no weight loss).
- **Differentiation**: Brain permeability, metabolic stability, no hERG toxicity, outperforming competitors (Triana, Peloton and Recursion).

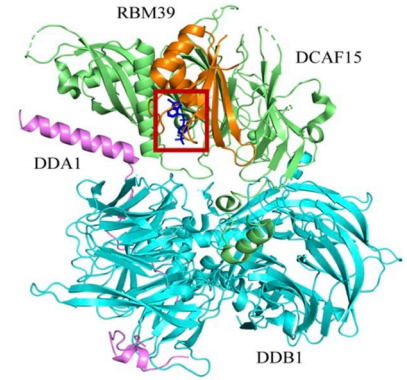
RBM39 Degrader: RNA Splicing for Various Cancers

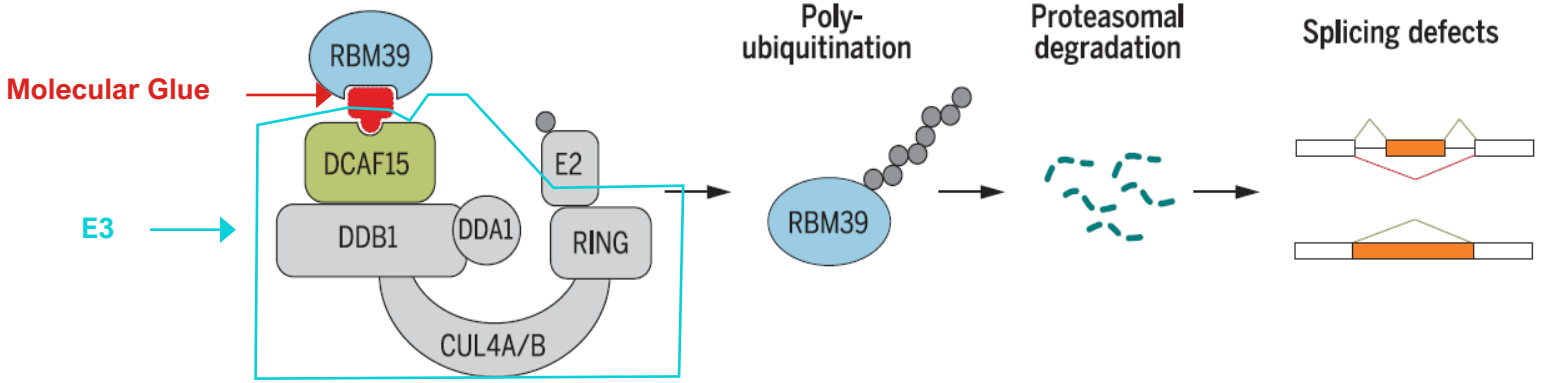


RBM39: RNA splicing protein

RNA splicing selects Exons and removes Introns to form normal mRNA and proteins

RBM39 degradation kills cancer cells through RNA splicing defects of key target genes

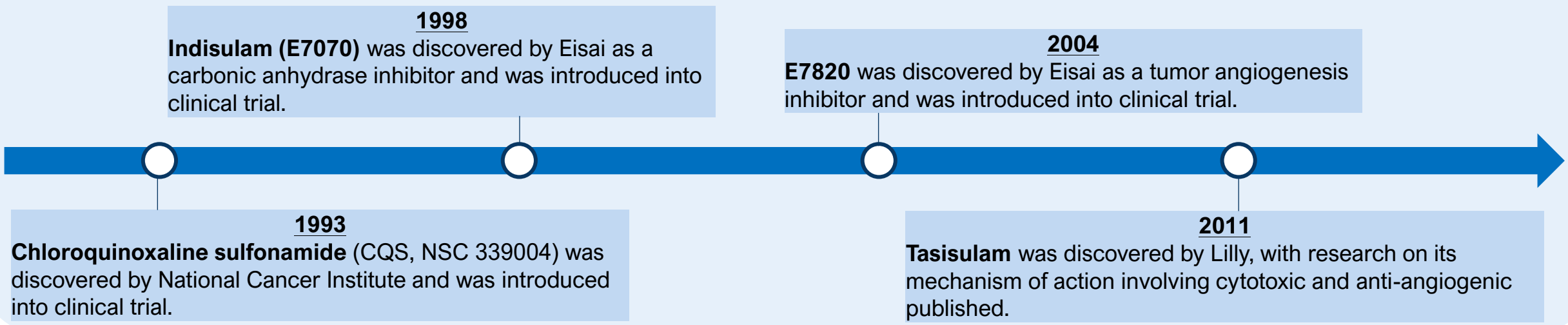




Han et al., *Science*, 2017

RBM39 Degradation: Recognized as a Validated Target

Discovery Timeline of Aryl Sulfonamides

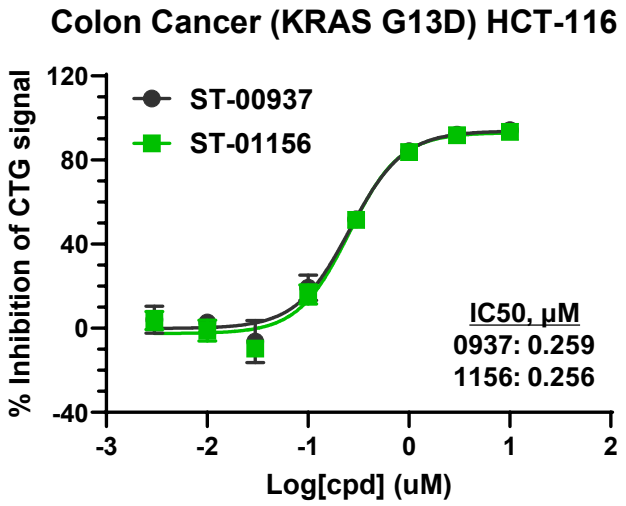


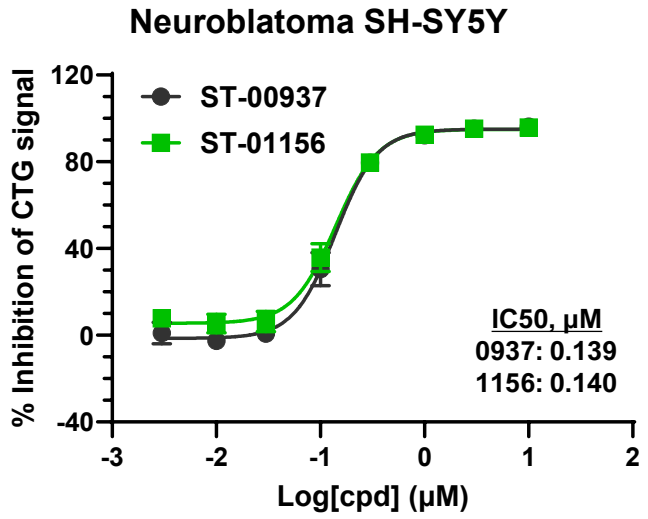
- Aryl sulfonamide class first reported as **RBM39 degraders** in 2017
- Burst of publications in 2021 to 2023 preclinically validating new cancer indications for RBM39 degraders, most not yet tested in the clinic;
- Companies advance novel RBM39 degraders into the clinic to test new indications: Recursion Pharmaceuticals, Trianna Biomedicines, and Peloton Therapeutics.

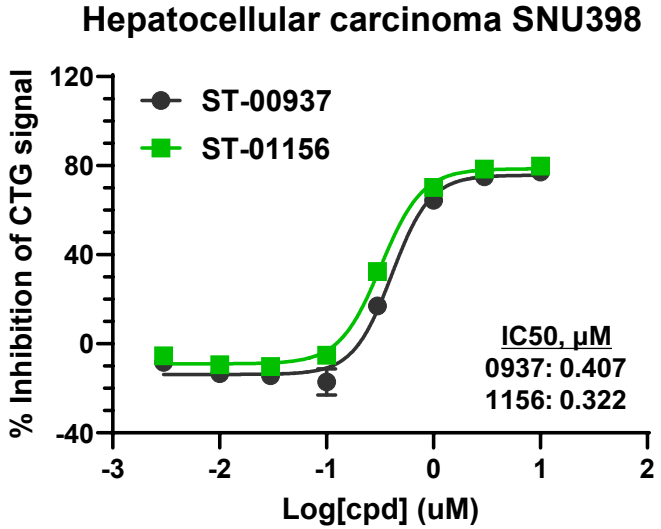
SEED's Novel RBM39 degrader ST-01156

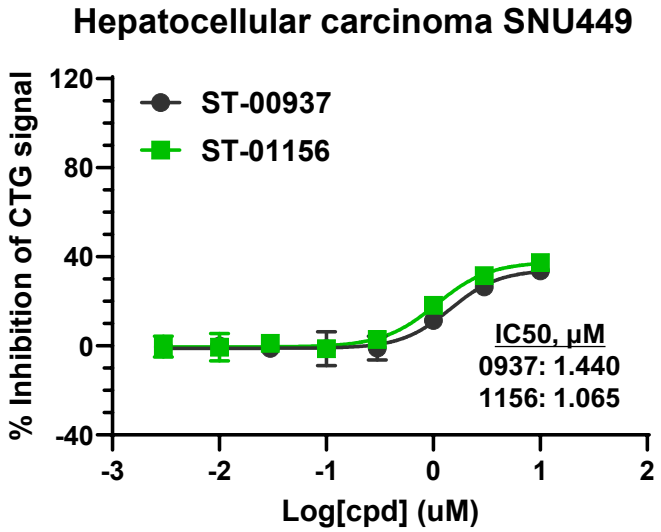
✓ Optimized for drug-like properties and dramatic "total tumor regressions" in cancer models;
✓ Patient-derived cancer model testing establishes ST-01156 potential in rationally selected cancer indications.

ST-01156 (IND Candidate) – Total Tumor Regression in Animal Model

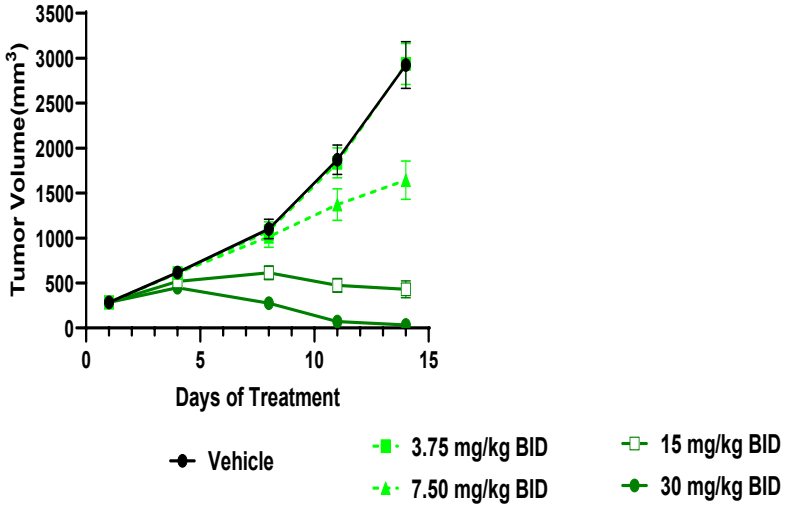








IND candidate ST-01156 **Demonstrates total tumor regression** in an Orphan Cancer Indication Model, with limited weight loss

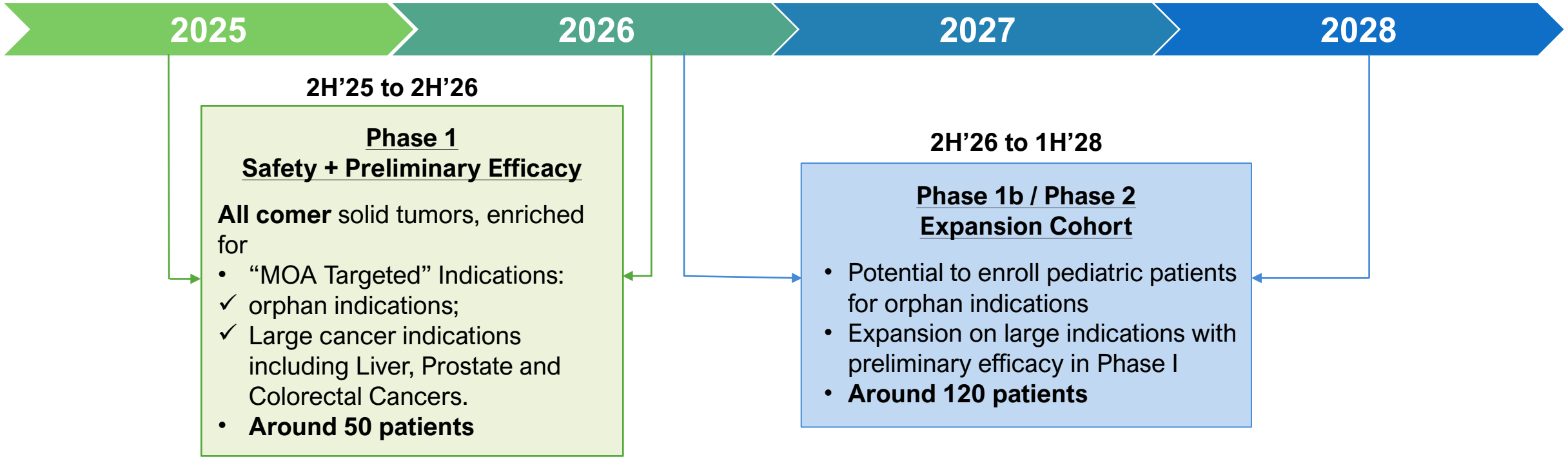


ST-01156: Oral RBM39 Degrader Advancing to Clinical Trials in 2025

SEED Focus on Successful Clinical Testing in MOA-based Indications with Speed to NDA

- MOA understanding and preclinical screening on patient-derive models provide the opportunity for **rationale clinical indication selection**, with increased probability of significant anticancer effects;
- **Orphan and large cancer indications to be enriched** in the first clinical trials to accelerate progress to NDA for responsive cancer types;
- **Nonclinical PK/PD and Tox/TK established** and set to inform dose escalation to speed progress to dosing regimens with a therapeutic window.
- **Experienced innovative oncology drug development team** with extensive clinical and regulatory experience. Initiate clinical studies with investigators from leading institutions.

RBM39 Degrader: Clinical Development Plan - “Precision Medicine” Approach



- **Three US leading cancer centers** have been recruited for **phase I dose escalation and expansion studies**.
- **Study Design:**
  - Oral dosing;
  - Phase 1 dose escalation to demonstrate safety and target engagement in blood; tumor responses to guide expansion;
  - Phase 1b / Phase 2 dose expansion in Phase 1a and/or preclinically validated cancer types (2-stage with futility);
- **Value Inflection points** are expected to be in **2H 2025** for First Human Dose and **2H 2026** for preliminary efficacy and safety data in a number of cancer indications.

Global Pharma Partnerships: Validating SEED's Leadership in TPD Space

- SEED entered a research collaboration with **Eli Lilly** on TPD with multiple targets since SEED's inception in November 2020.
- Under the terms of the collaboration agreement with Lilly, SEED received a **$10 million upfront** cash payment to fund research, and a **$10 million** equity investment in series A-2.
- SEED is also eligible to receive up to **$780 million** in potential pre-clinical and clinical development, regulatory and commercial milestones, and **tiered royalties** on net sales of products.

- SEED launched Series A-3 financing with a first close of **$24 million** from investors led by **Eisai** in August 2024.
- The Series A-3 financing will advance clinical development of SEED's internal lead program in cancer, expand its TPD platform and pipeline, and supplement prior investments in SEED from Eli Lilly and BeyondSpring.
- The SEED-Eisai Research Collaboration leverages Eisai's leading expertise in neurodegeneration and cancer. SEED is entitled to receive upfront and milestone payments of up to **$1.5 billion** plus **tiered royalties** upon Eisai's exercise of their exclusive rights under the strategic research collaboration.

Upcoming Catalysts

Strengthening RITE3 Platform
Advancing Internal and R&D Pipelines with Lilly and Eisai

2H 2025 Catalysts:

- SEED's lead oncology asset RBM39 degrader expected to enter IND in mid-2025 with FIH in 2H 2025;
- SEED's Tau degrader current with cell activity, is expected for in vivo efficacy in 2H 2025.

2H 2026 Catalysts:

- Safety, target engagement and clinical response data available for SEED's RBM39 degrader for 50 patients; orphan indications (rare pediatric disease designation by the FDA) and large oncology indications.
- SEED's IND candidate identification expected for Tau degrader.

Investment Highlights

Plinabulin: Safety & Efficacy	Lead Asset Plinabulin: >700 cancer patients treated with good tolerability; Positive Phase 3 data in 2/3L NSCLC, EGFR wild type
Plinabulin Potential	Plinabulin: Dual Benefit in anti-cancer and prevention of CIN; Potential in re-sensitizing in PD-1/PD-L1 progressed patients in multiple cancers
SEED: Novel TPD Platform & Pipeline	SEED: 9 Disclosed Pipeline Assets with 1 expected to enter IND in 2025
Premier Partnerships	SEED: Investments and R&D Collaborations from Eli Lilly and Company and Eisai
Intellectual Property	Strong IP and technology protection

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