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BeyondSpring

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The market data and certain other statistical information used throughout this presentation are based on independent industry publications, governmental publications, reports by market research firms or other independent sources. Some data are also based on our good faith estimates. Although we believe these third-party sources are reliable, we have not independently verified the information attributed to these third-party sources and cannot guarantee its accuracy and completeness. Similarly, our estimates have not been verified by any independent source.

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: 170 granted/allowed patent to 2038 in 48 jurisdictions
Regulatory Strategy	**Multiple Phase 1/2 studies reading out in 2024 that will inform potentially pivotal randomized clinical studies beginning 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)
Late stage	**CIN Prevention**	Plinabulin + Pegfilgrastim						Studies 105 & 106 (PROTECTIVE-1 & PROTECTIVE-2)
Investigator Initiated Trials	**SCLC (2nd/3rd line)**	Plinabulin + Nivolumab + Ipilimumab						Rutgers
Investigator Initiated Trials	**NSCLC (2nd/3rd line PD-1 failed)**	Plinabulin + Pembrolizumab + Docetaxel						Study 303
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						The University of Texas MD Anderson Cancer Center
Investigator Initiated Trials	**AHCT (hematopoietic stem cell transplantation) in Multiple myeloma**	Plinabulin + Pegfilgrastim						Memorial Sloan Kettering Cancer Center
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						SEED Therapeutics, Lilly, Eisai

BeyondSpring Subsidiaries: 1) Dalian Wanchunbulin Pharmaceuticals Ltd., which owns Greater China rights to Plinabulin, and 2) Seed Therapeutics, a target protein degradation company.

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

First-in-class Asset: Plinabulin

Advanced Clinical Stage Agent	• Positive Phase 3 study in 2L/3L NSCLC, successfully demonstrated significant OS benefit, doubling 2-year, 3-year OS rate – proving plinabulin's clinical utility
Enhances Cancer-Immunity Cycle	• Promising efficacy data in combination with PD-(L)1 and radiation, in IO-refractory patients across various cancers • Dual-acting IO MOA enhances the cancer immunity cycle, with potential to increase the efficacy and durability of checkpoint inhibitors and other immunotherapy agents
Favorable Safety Profile	• **> 700 cancer patients treated with good tolerability** • Clinically-proven to significantly reduce chemotherapy-induced neutropenia, enabling extended dosing of neutropenia-limited regimens such as chemotherapy and potentially ADCs
Ease of Use	• Intravenous (IV) Infusion: 1 or 2 doses per cycle
Strong Global Patent Protection	• 170 Granted/Allowed Patent to 2038 in 48 jurisdictions, including the US, EU, Japan and China

Plinabulin is a Differentiated First-in-Class Tubulin Binder with a Unique Clinical Activity and Favorable Safety Profile

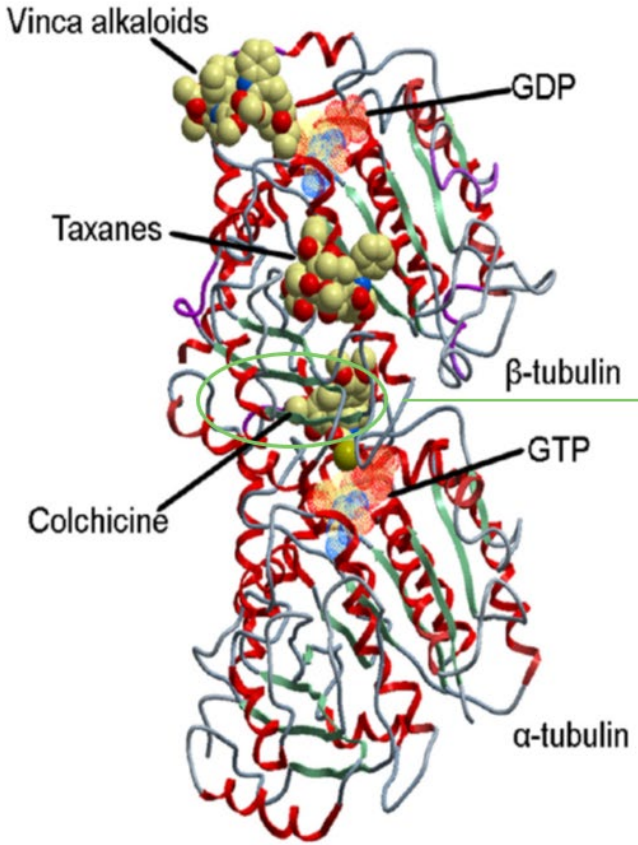
Plinabulin is a reversible tubulin binder and does not change tubulin dynamics

Conventional tubulin binding agents (such as taxanes, vinca alkaloids, and colchicine) alter tubulin dynamics upon binding, resulting in neutropenia and cardiac side effects.

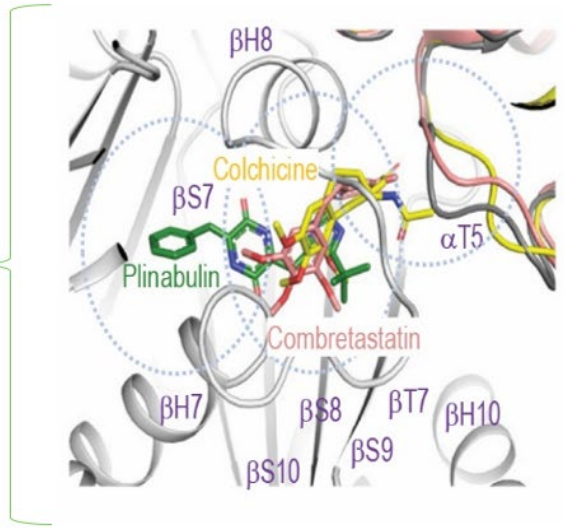
Plinabulin's tubulin binding site is distinct from that of these other agents (first in class). Because **binding is reversible**, plinabulin does not change tubulin dynamics.

Consequently, **plinabulin exhibits a favorable safety profile**, differentiating it clinically from other tubulin binding agents with concerning side effects that restrict their clinical utility.

Tubulin Binding Sites



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

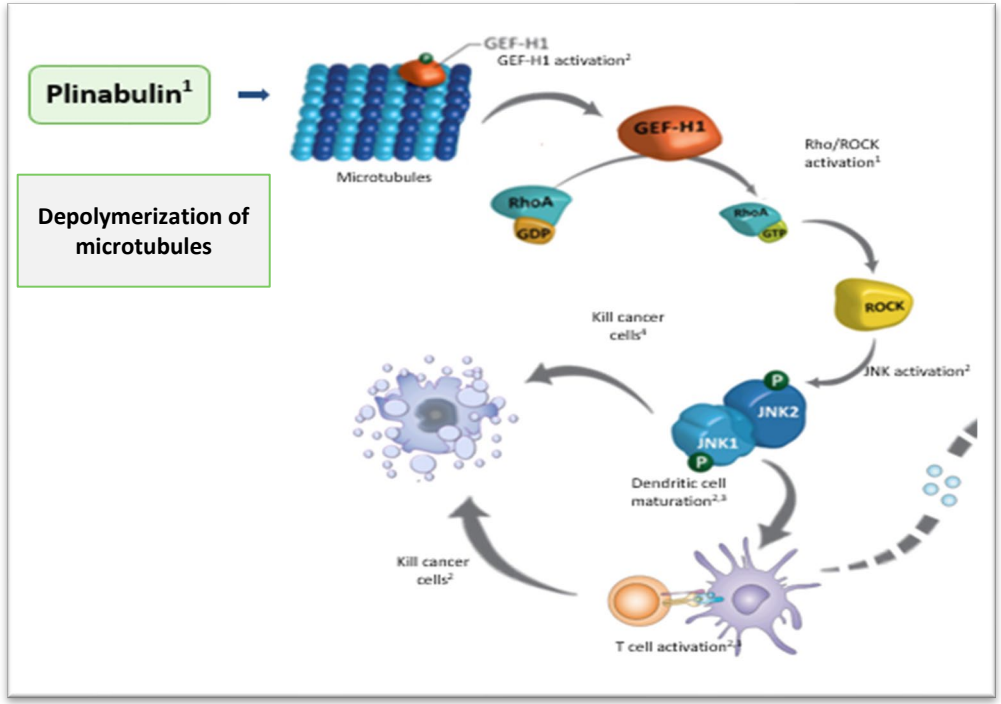


[1] La Sala et al., 2019 Chem

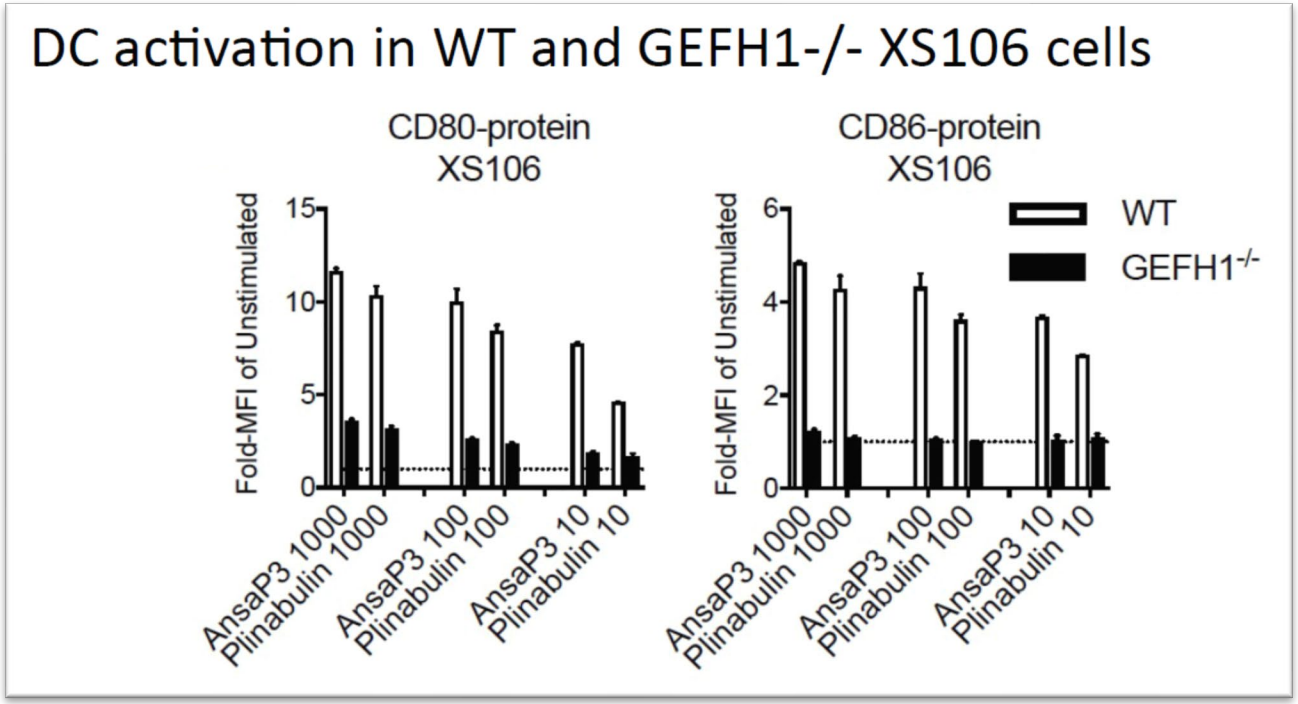
Plinabulin: Induces Innate and Adaptive Immunity

By depolymerizing microtubules, plinabulin releases, or activates, immune-defense protein GEF-H1. This leads to dendritic cell maturation (the most potent APC).

Plinabulin Novel Target: Immune Defense Protein GEF-H1[1]



In WT DC cells, plinabulin can induce DC maturation, but not in GEF-H1 deleted DC cells[2]
CD80 and CD86 up-regulation are biomarkers for DC maturation



AnsaP3, Maytansinoid cytotoxic (positive control compound), too toxic for human study

[1] La Sala et al., Chem 5(11): 2969-2986 (2019)

[2] Kashyap et al., Cell Reports 28(13): 3367-3380 (2019)

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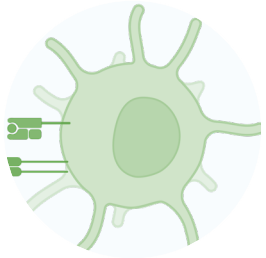
Plinabulin's Immunomodulation and Neutropenia-Mitigating Activities Position It as a Valuable Partner for Immuno-Chemotherapy Combination Regimens

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

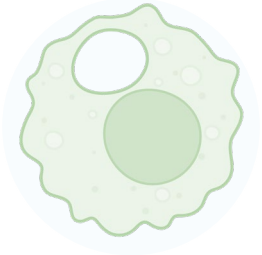


Dendritic Cells

Plinabulin induces

dendritic cell maturation

Enhanced antigen presentation and T cell priming



M1-like Macrophages

Plinabulin stimulates

M1-like macrophage polarization and proliferation

Increased tumor cell killing and cytotoxic T cell recruitment

Enhances PD1/PD-L1 targeting agents to boost T cell function and kill tumor cells

Improves Safety*

Plinabulin **reduces chemotherapy-induced neutropenia**

Improved therapeutic index of chemotherapy-based regimens

Extends therapeutic duration and improves anti-cancer benefit

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

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

Publication on The Lancet Respiratory Medicine
Han B., Feinstein T., Shi Y. et al. Plinabulin plus docetaxel versus docetaxel in patients with non-small-cell lung cancer after disease progression on platinum-based regimen (DUBLIN-3): a phase 3, international, multicentre, single-blind, parallel group, randomised controlled trial. The Lancet Respiratory Medicine, published online first on September 9, 2024.

World Conference on Lung Cancer 2024
Feinstein T, Han B, Shi Y, et al. Plinabulin/docetaxel vs. docetaxel in 2L/3L NSCLC after platinum regimens (DUBLIN-3): a phase 3 randomized controlled trial. Presented at: 2024 IASLC World Conference on Lung Cancer; September 7-10, 2024; San Diego, CA. Abstract OA08.04.

European Society for Medical Oncology (ESMO) Congress 2024
Feinstein, T.M. Han B, Shi Y-K. et al. 1358P Plinabulin/docetaxel versus docetaxel in survival benefits of 2L/3L EGFR wild-type NSCLC after platinum regimens (DUBLIN-3): A randomized phase III trial. Annals of Oncology, Volume 35, S856.

The EGFR-wild Type 2L/3L NSCLC Have Been a Historically Difficult Development Space

Treatment options in 2L/3L NSCLC are limited

Docetaxel-based therapies are the mainstay therapy in 2L/3L NSCLC (EGFR wt).

However, **docetaxel-based therapies (SOC) demonstrate limited efficacy and are associated with >40% severe (grade 3/4) neutropenia.**

Other approved agents:

- Ramuciramab + Docetaxel vs. Docetaxel: OS HR=0.86, severe neutropenia 49% vs. 40%;
- Pemtrexed vs. Docetaxel: OS HR=0.99, severe neutropenia 5% vs. 40%.

Additionally, with immunotherapies moving to first line NSCLC, **there is a growing population of 2L/3L patients that are refractory to immunotherapy.**

Attempts to address treatment needs have been challenging

Since Nivolumab's approval 8 years ago, no new agent with a novel mechanism has been approved in this indication.

Multiple Phase 3 studies (PD-1/PD-L1 failed patients, 2L/3L NSCLC), did not meet OS endpoint vs. docetaxel:

1. SAPPHIRE: BMS' Nivolumab (PD-1 antibody) + Mirati's Sitravatinib (TKI)
2. CONTACT-01: Roche's Atezolizumab (PD-L1 antibody) + Exelixis's Cabozantinib (TKI)
3. LEAP-008: Merck's Pembrolizumab (PD-L1 antibody) + Eisai's Lenvima (TKI)
4. CANOPY-2: Novartis' Canakinumab (IL-1b antibody) + docetaxel
5. EVOKE-01: Gilead's sacituzumab govitecan-hziy (ADC - antibody drug conjugate)
6. CARMEN-LC03: Sanofi's tusamitamab ravtansine (ADC)

Recent successful phase 3 studies with mixed results:

- Lunar (TTfields vs. docetaxel): OS benefit (HR=0.74), but no PFS and ORR benefit;
- TROPION-Lung01 (Datopotamab deruxtecan - ADC vs. docetaxel): OS benefit (HR=0.90) in ITT population, with better OS (HR=0.75) in non-squamous NSCLC.

Plinabulin Has Been Successfully Evaluated with Docetaxel in a Phase 3 Study with Advanced, Pre-treated NSCLC 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

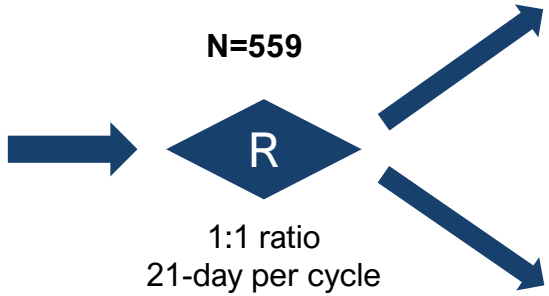
Overall survival (OS)

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**

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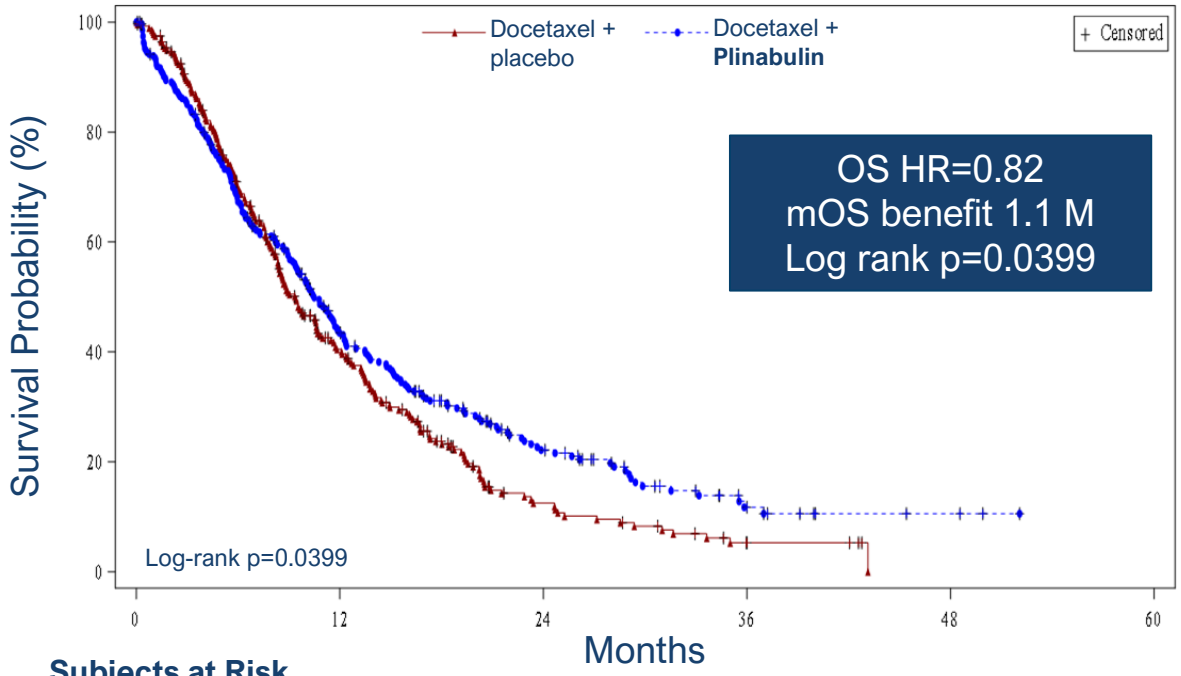
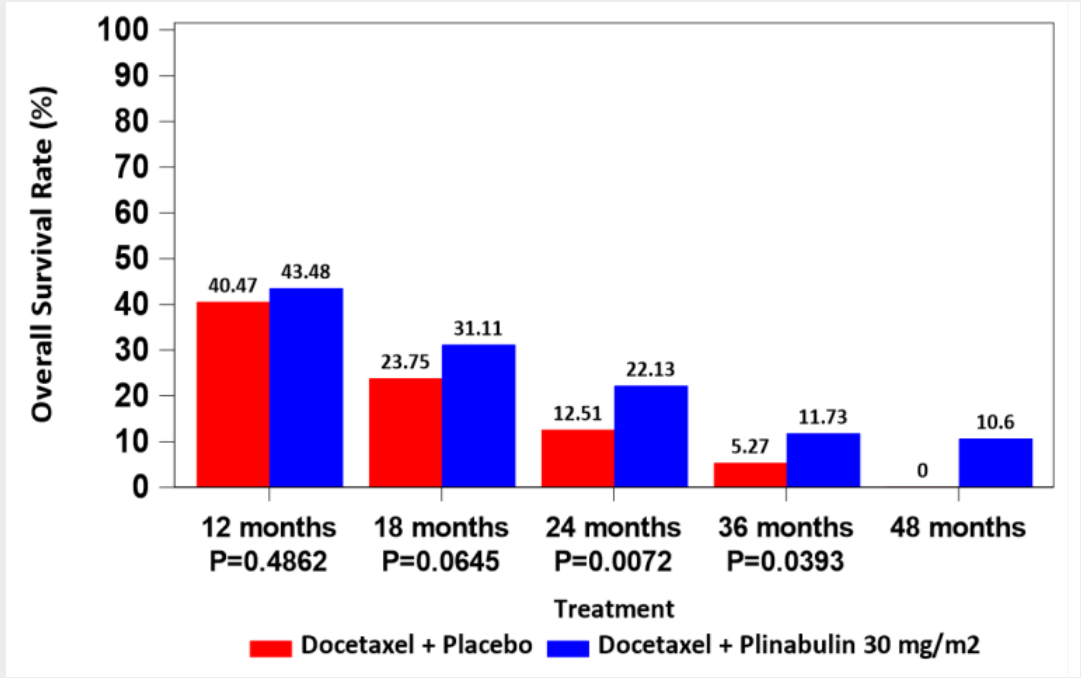
Plinabulin + Docetaxel Met its Primary Endpoint (OS) and Showed Significant Improvement in Long-term OS Rate



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)

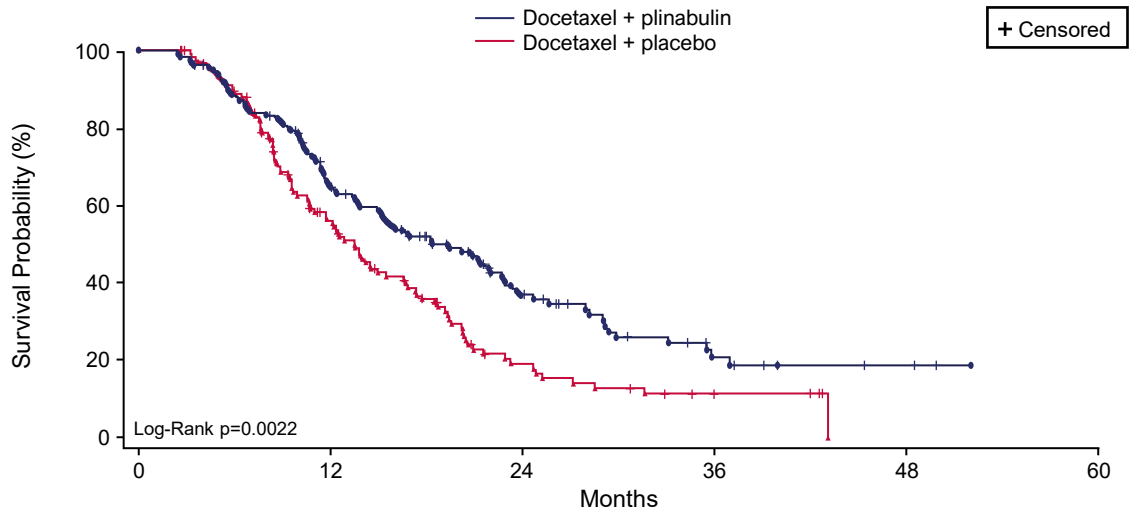


OS Rate Increase Results

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

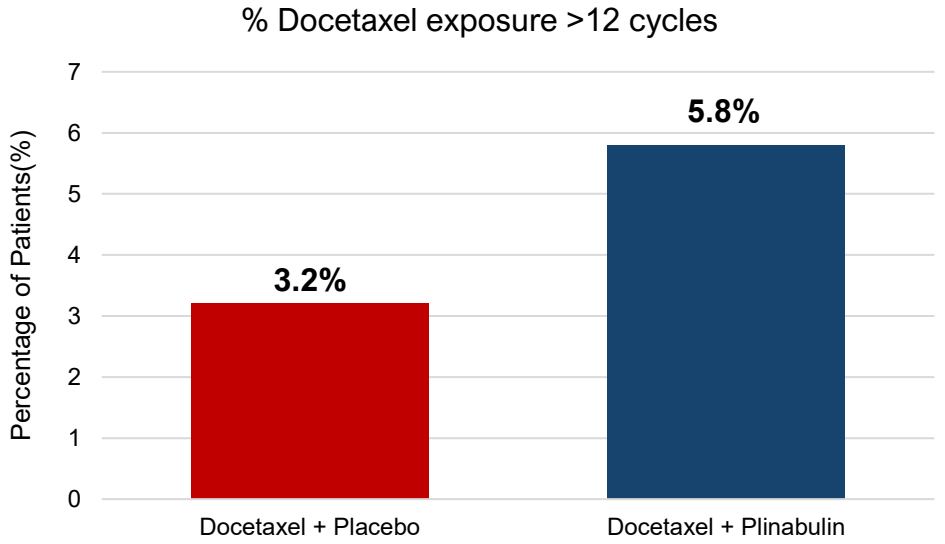
Plinabulin Increases Cycles of Treatment and Improved OS Benefit with More Cycles of Treatment

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**

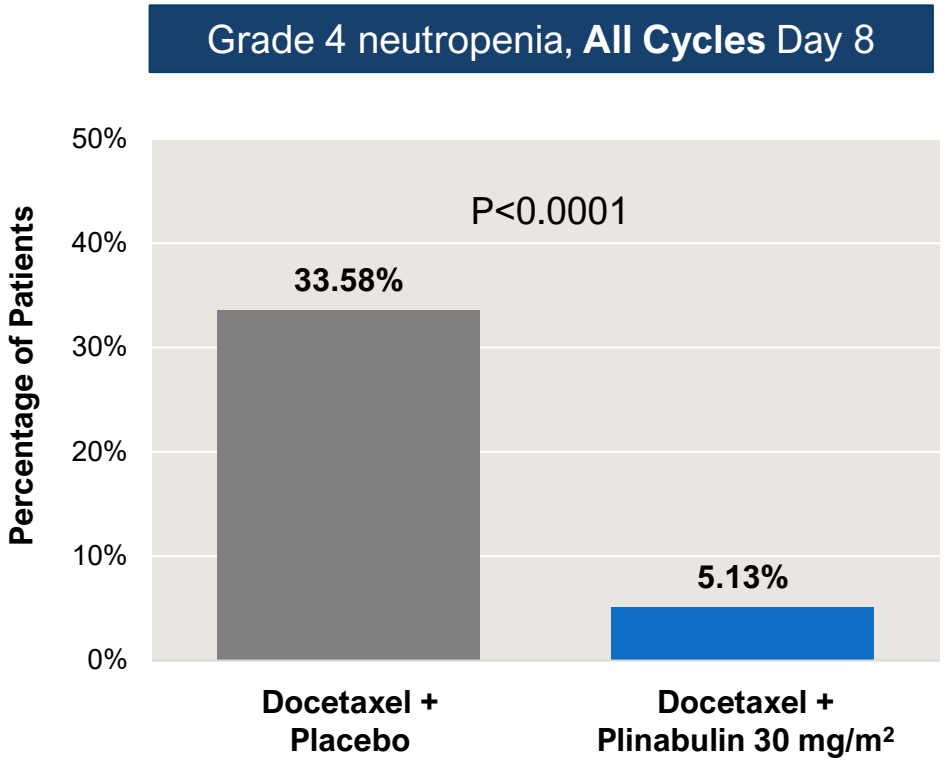
…allowing more patients to remain on docetaxel for a longer duration



Addition of plinabulin to docetaxel also increased docetaxel exposure by mean dose (mg)

Plinabulin Reduces >80% of Grade 4 Neutropenia of Docetaxel

Use of plinabulin significantly reduced Grade 4 neutropenia



Similar results were observed for Grade 4 neutropenia on Cycle 1 Day 8

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 standard-of-care led to improved overall survival and enhanced safety

Efficacy

- Significant survival benefit in ITT (OS HR=0.82)
- Even more pronounced survival benefit in 2L (HR=0.78), or non-squamous NSCLC (HR=0.76)

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 neutropenia was reduced, allowing increased treatment exposure

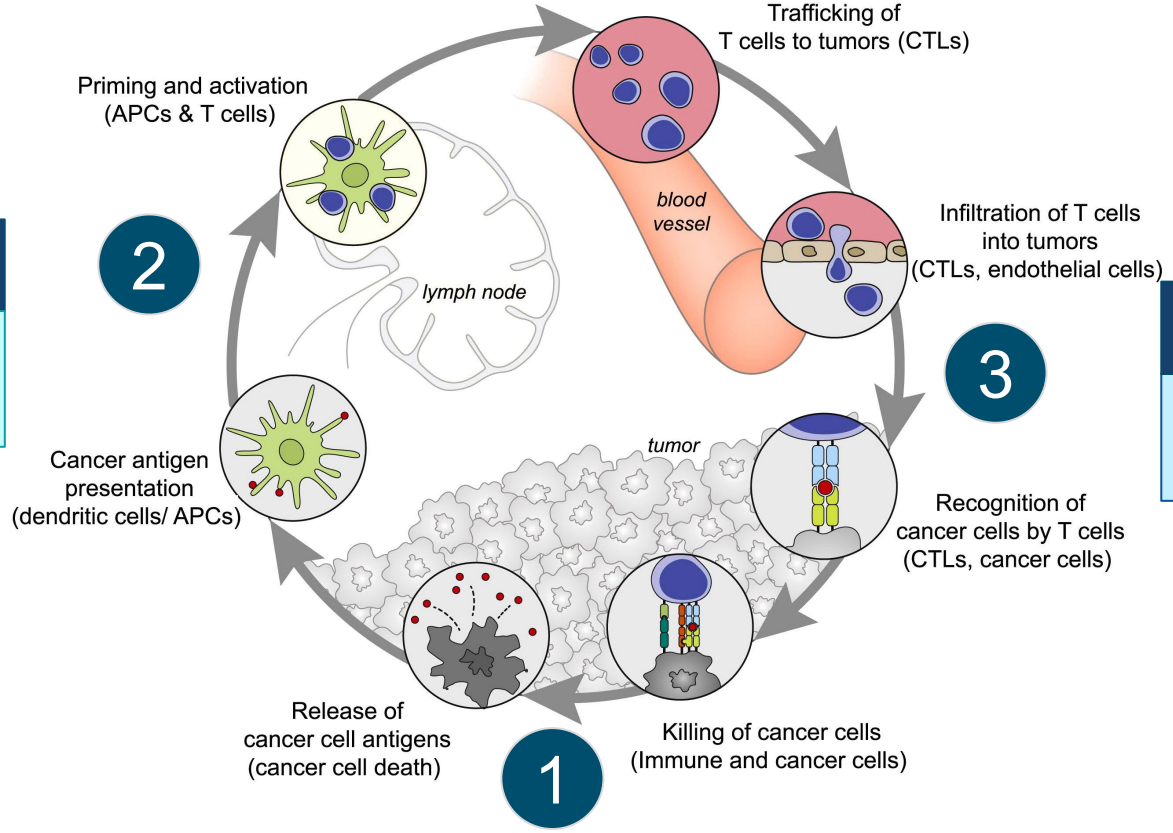
Encouraging RT+PD-1+Plinabulin Clinical Data Demonstrates Plinabulin's Partnering Potential with IO Agents

RT: Radiation therapy

Plinabulin Enhances the Cancer Immunity Cycle When Used with Radiation and Anti-PD1

② Plinabulin

Improved antigen presentation
Stimulate maturation of dendritic cells to increase antigen presentation.



③ Checkpoint Inhibitors

Anti-tumor T cell activation
Optimize T cell response

① Chemotherapy
Radiation Therapy
Oncolytic Viruses
Antibody Drug Conjugates
Targeted Therapy

① Radiation/Chemotherapy

Release tumor antigens
For more potent anti-cancer effect

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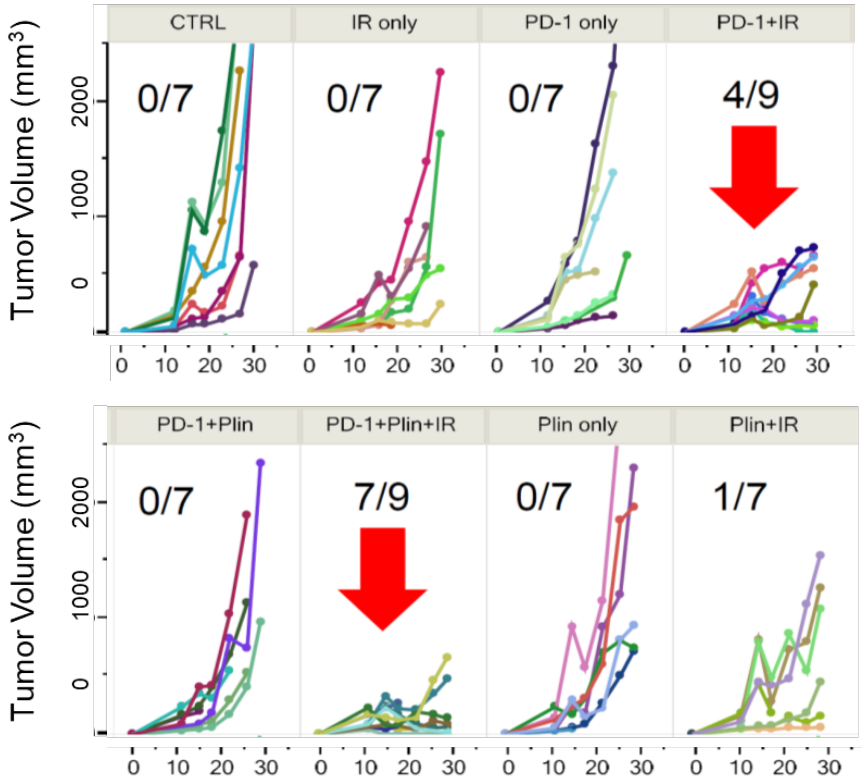
Plinabulin is Being Evaluated in Multiple Immunotherapy Combination Trials in Collaboration with Major Pharmaceutical Companies

	Indication/Target	Program	Preclinical	Phase 1	Phase 2	Phase 3	Trial Name / Collaborator
Investigator Initiated Trials	**ES-SCLC (1st line)**	Plinabulin + Pembrolizumab + Etoposide / Platinum					Study 302
	NSCLC (2nd/3rd line PD-1/PD-L1 progressed)	Plinabulin + Pembrolizumab + Docetaxel					Study 303
	Multiple cancers (PD-1/PD-L1 progressed)	Plinabulin + PD-1/PD-L1 + Radiation					THE UNIVERSITY OF TEXAS MD Anderson Cancer Center

- MD Anderson Phase 1 study clinical data and biomarker studies was presented at SITC conference in November 2023.
- Plinabulin's MOA is not restricted to Lung Cancer; all solid tumors may benefit in combination with I/O

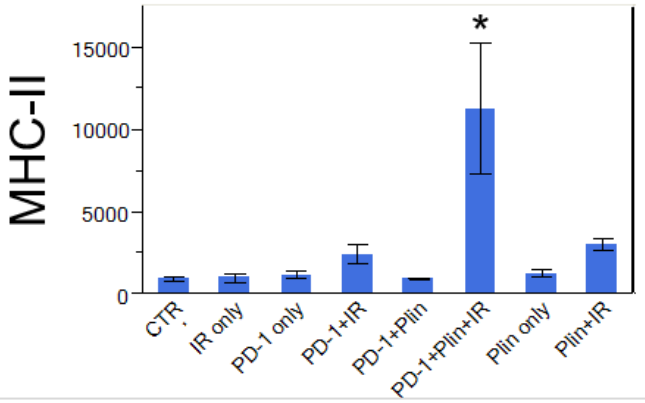
RT+anti-PD1+Plinabulin Triple Combination POC in Animals Provides Evidence of Plinabulin's Immunomodulatory activity

Tumor reduction is most robust in triple I/O combination

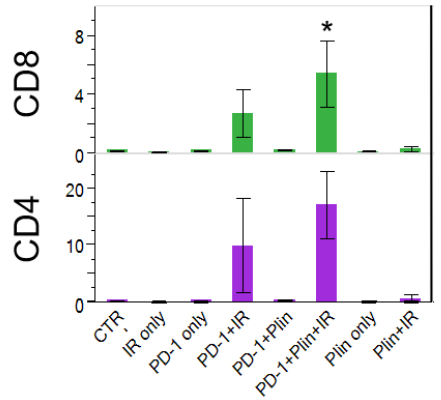


Plinabulin+RT+PD-1 induced ~80% tumor volume reduction in a preclinical cancer model

DC activation is most dramatic in triple I/O combination



T cell doubles in triple I/O combination vs. PD1 + IR



Plinabulin+ RT+PD-1

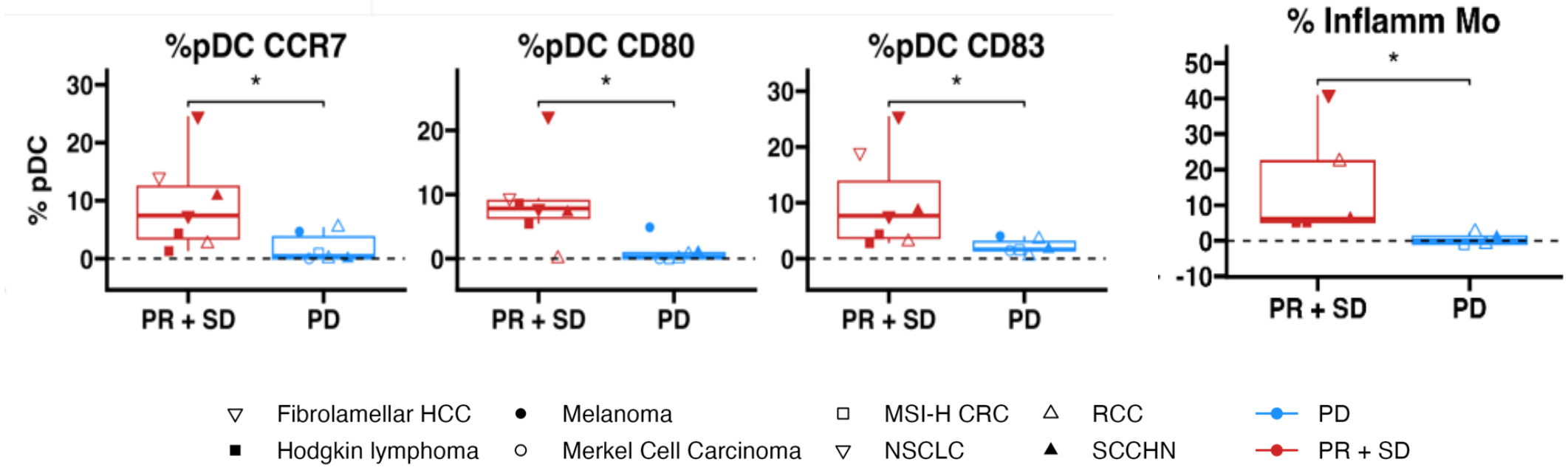
increased DC maturation and doubled CD4+ and CD8+ T cells in tumor samples 30 days after treatment

Clinical PoC in MOA: Plinabulin-Responding Patients Show Early Immune Activation Evidenced by DC Maturation and Proinflammatory Monocytes in the Peripheral Blood

In different cancers, DC maturation and anti-tumor inflammatory macrophages were observed in plinabulin-responding patients

Dendritic Cell Maturation & Migration

Proinflammatory monocyte/macrophages



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Additional Data from Patients are Available in the Appendix

A Phase 2 Study of Pembrolizumab (Pemb) plus Plinabulin (Plin) and Docetaxel (Doc) in Metastatic NSCLC Patients (pts) Who Failed First-Line Immune Checkpoint Inhibitor: Initial Efficacy and Safety Results

European Society for Medical Oncology (ESMO) Congress 2024
Xu, Y. et al. 1330P Phase II study of pembrolizumab (pemb) plus plinabulin (plin) and docetaxel (doc) for patients (pts) with metastatic NSCLC after failure on first-line immune checkpoint inhibitor alone or combination therapy: Initial efficacy and safety results on Immune Re-sensitization. Annals of Oncology, Volume 35, S845.

Merck IIT Phase II 303 Study (KeyPelms-004): 2L/3L NSCLC, PD-1/L1 relapsed – Single Site, Single Arm

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

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

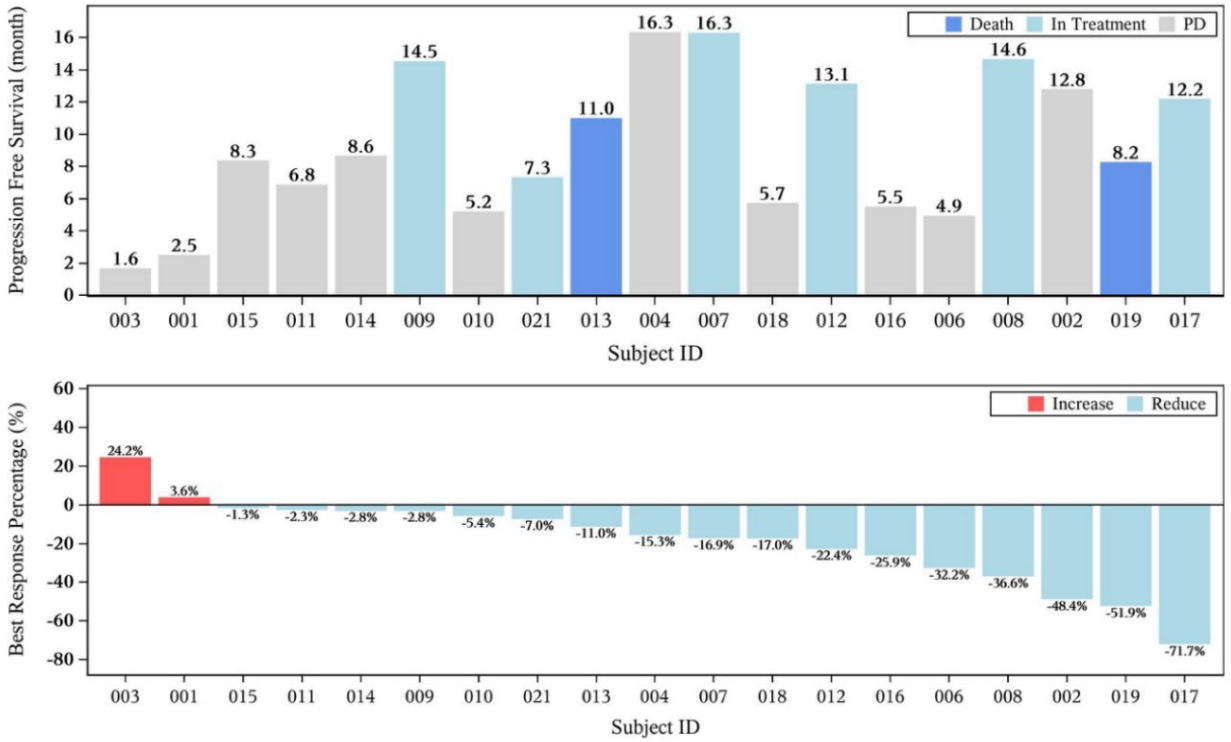
Efficacy data (cut-off date on 29-Apr-2024)

First stage Analysis: 19 patients
(Proportion of patients who had previously received Pembro: 73.7%)
median follow-up time: 12.4 month

Primary endpoint	
Confirmed ORR (RECIST 1.1)	21.1%
Secondary endpoints	
Median PFS (RECIST 1.1)	8.63 months
Median OS	Not reached
Median DoR (RECIST 1.1)	11.40 months
Disease Control Rate (DCR) (PR + SD > 4 months)	89.5%
6 months PFS	67.1%
12 months PFS	49.2%

DoR, duration of response; ORR, overall response rate; OS, overall survival; PFS, progression-free survival; PR, partial response; RECIST, Response Evaluation Criteria in Solid Tumours; SD, stable disease.

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



Plinabulin as Potential Add-on Therapy to Current I/O Regimens to Address Severe Unmet Medical Needs

PD-1/PD-L1 Inhibitors
- >$40B global annual sales

→ Potential to greatly expand the addressable market

Current Severe Unmet Medical Needs

2L/3L: PD-1/PD-L1 relapsed/refractory patients

1L: PD-1/PD-L1 + chemo doubles anti-cancer efficacy of PD-1, but with CIN risk

"Cold" Tumor: PD-1/PD-L1 non-responsive tumor

Plinabulin:
APC Inducer with easy administration*

Plinabulin Clinical Development

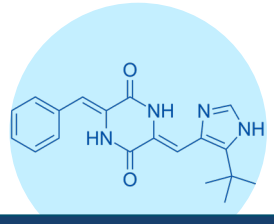
Re-sensitize: Plinabulin + PD-1/PD-L1 + chemo/radiation/ADC

Increase Combo Anti-cancer Efficacy: Plinabulin + PD-1/PD-L1 + chemo/ADC

Turn "cold" into "hot" Responding Tumor: Plinabulin+ PD-1/PD-L1 + chemo/ADC; Plinabulin + chemo/ADC

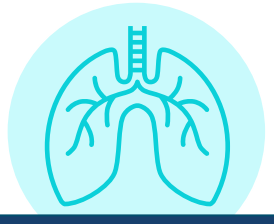
*Plinabulin IV Infusion: 1 or 2 dose per cycle (DUBLIN-3 Trial)

Plinabulin's DC Maturation MoA, Proven Clinical Activity, and Strong Global Patent Protection are Highly Favorable for Partnerships with Immunotherapy Agents…and Beyond



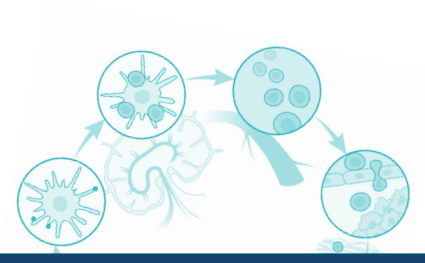
Lead Asset Plinabulin displays dual IO MOAs

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



Proven clinical efficacy and safety

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



Enhances the Cancer-Immunity cycle

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

Strong global patent protection

BeyondSpring (est. 2010) is a global company that has **170 Granted/Allowed Patents to 2038 in 48 jurisdictions**

Plinabulin enhances the cancer immunity cycle to increase patient survival and reduce adverse events in combination use settings with a minimal patient administration schedule.

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

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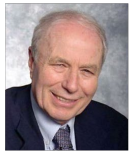
SEED Therapeutics: Target Protein Degradation (TPD 2.0) Company

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

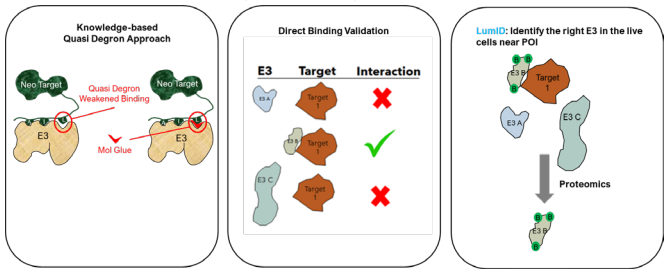
Significant and Speedy Value Creation at SEED Therapeutics

Seed Investment by Lilly
- $10 M Investment;
- $10 M upfront from R&D collaboration with Lilly, up to $780 M milestone, tiered royalties
- BeyondSpring: $6 M Investment and TPD platform patents

Founding (2020)

Avram Hershko MD, PhD	Ning Zheng, PhD	Michele Pagano, MD	Lan Huang, PhD
			
Pioneer in the ubiquitin proteasome system **Nobel Laureate**	Pioneer in Molecular Glue discovery and scientific structural rationale	World leader in the discovery and application of ubiquitin ligase biology and cancer biology	Solved the first E2-E3 ligase structure and pioneered the understanding of Ras structure
SEED Co-Founder and SAB Member	SEED Co-Founder and SAB Member	SEED Co-Founder and SAB Member	SEED CEO, Co-Founder and SAB Member

Proprietary Platform & Confidential Know-How (2021)



- Supported by multiple classes of patents
- Started R&D collaboration and invested by Lilly

R&D Infrastructure, Organization and Pipeline (2022)

- 10,000 Sq. ft headquarters
- State of the art laboratories
- Expert in-house R&D team

High Value Drug Candidates, Partnership Milestones and Cash Flow

- Achieved multiple Lilly collaboration milestones
- Lead program in oncology for first human dosing in 1H2025
- Oral Tau degrader reaching IND candidate by YE2025 for neurodegeneration

Raised $24 M Series A (first close) led by Eisai
- Concurrent R&D collaboration with Eisai in neurodegeneration and oncology indications with upfront and milestone payments up to $1.5B and tiered royalties

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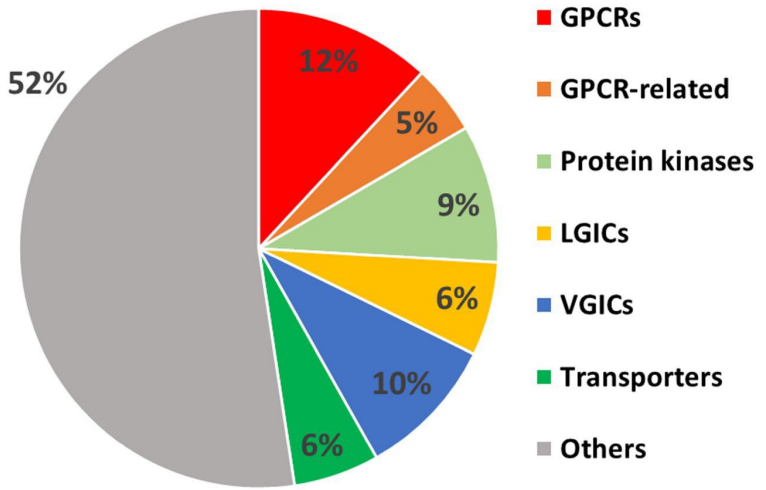
SEED Differentiation

Scalable Business Model	TPD has potential to target 80% of undruggable disease-causing proteins. > 600 E3 ligases to be used for multiple disease areas.
Target-Centric Differentiation	Identify the right E3 for POI to increase the success rate in drug discovery: Platforms using **Quasi-degron, LumID, and Basal Affinity**
Pioneering Effort	World-leading scientific founding team and experienced development team in successful translation of TPD platforms to 9 disclosed Assets
Two Prong Approach	De-risked revenue model: 1) R&D partnership for non-diluting financing (Lilly + Eisai); and 2) internal program development for value generation

Targeted Protein Degradation (TPD) Addresses 80% of Disease-Causing Proteins That Are Undruggable

TPD for Undruggable Proteins

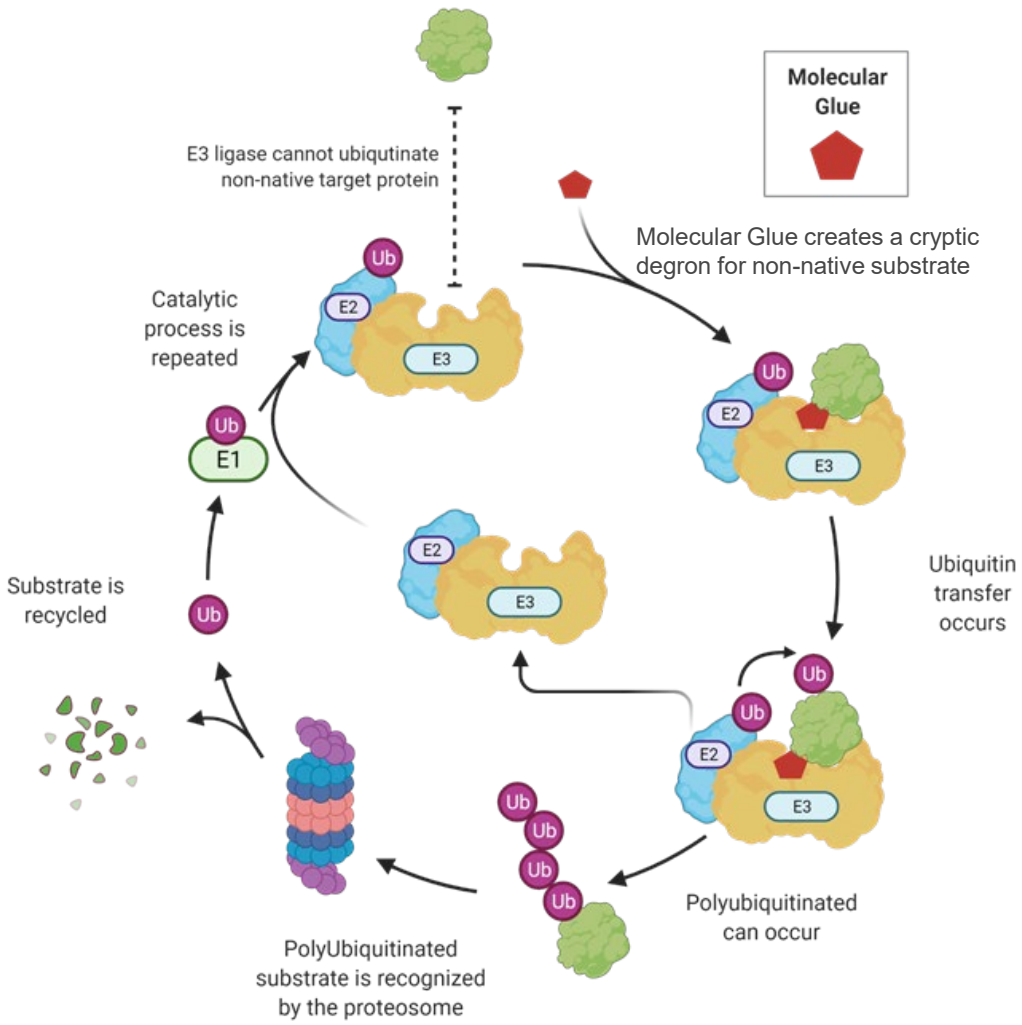
Druggable Proteins



Sriram et al., Molecular Pharmacology, 2018

TPD Development History and Recent Renaissance

TPD Process

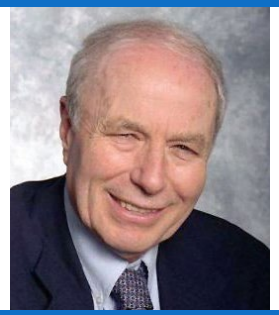


SEED Co-founders played pivotal roles in the advancement of TPD field

- 1996: **Dr. Michele Pagano (SEED co-founder)** discovered cell cycle regulation by TPD, including E3 ligases; published in *Science*
- 1999: **Dr. Lan Huang (SEED co-founder and CEO)** solved the 1st of the two E3 structures (HECT domain E3); published in *Science*
- 2002: **Dr. Ning Zheng (SEED co-founder)** solved the 2nd of the two E3 structure (Ring-finger E3); published in *Nature*
- 2003: US FDA approved **Velcade**, the first proteasome inhibitor for multiple myeloma. **Dr. Avram Hershko (SEED co-founder)** advised on Velcade development. Other companies started to develop new E3 inhibitors with no success
- 2004: **Dr. Avram Hershko won Nobel Prize** for his pioneering work in discovering all essential enzymes for TPD, including E1, E2, E3, and proteasome
- 2007: **Dr. Ning Zheng coined the term "Molecular Glue (MG)"** after solving TIR1 E3 structure and discovering the true function of Auxin, a plant hormone and the **first natural MG to be identified**; published in *Nature*
- 2010-2014: Revolutionary discovery of the mechanism of action of **Revlimid** (for treating multiple myeloma, had peak global annual sale of $12.8b), a derivative of thalidomide, is in fact a MG, that binds to Cereblon (a E3) to degrade Ikaros (a mutated POI). This discovery, published in *Nature,* ushered in the **renaissance of TPD drug discovery**.

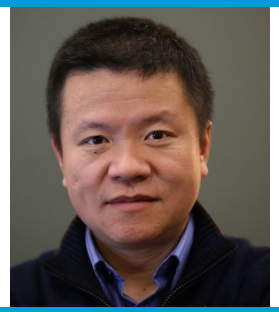
World Class Leadership Team and Exceptional Insights in TPD Drug Development

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**

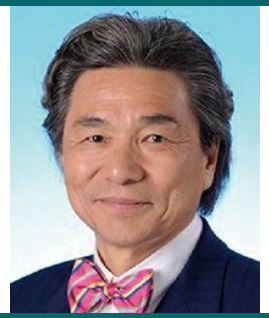
Lan Huang, PhD + * (Chairman & CEO)

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

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

Ko-Yung Tung, JD*

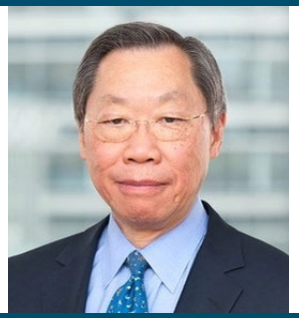


Former Eisai director, World Bank general counsel, and lecturer at Harvard and Yale Law School; Expert in law and international business

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

Jackson Tai*



Wuxi Biologics Audit Committee Chair; retired board member for Lilly, HSBC, Mastercard; former DBS Bank CEO, former J.P. Morgan & Co, investment banker

Yoshiharu Mizui, PhD*

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

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+SEED Co-founder and Scientific Advisory Board Member
*Board Member

Experienced in-House R&D Team with 40 IND and 12 NDA Track Record

SEED's headquarter, King of Prussia, PA

- 10,000 ft^2 including 7000 ft^2 lab space
- All crucial discovery work are conducted by internal research team

Highly Experienced Internal R&D Team

- >100 years combined small molecule hit-to-lead and lead optimization work
- >60 years Medicinal Chemistry and SBDD work
- >60 years DMPK work
- >60 years nonclinical development/safety work
- **>40 IND filings**
- **>12 drug approvals**, including multiple biologics and the small molecules Paritaprevir, Glecaprevir, XERMELO, REZUROCK, GV-971 and Modafinil

Productive Development History

SEED Internal Program Milestones

Development of SEED's unique TPD platforms and filed patents

- Multi-dimensional platforms to select the right E3 for any target;
- HTS screening and medicinal chemistry platforms which incorporate AI-predicted blood brain barrier penetration properties for CNS drug development,
- Proprietary statistical learning algorithms and neural networks (AI)

Infrastructure and Organization Building

- Renovated and occupied 10,000 sq ft SEED Headquarter, with 7,000 sq ft lab space;
- Hired full time drug R&D personnel, with significant focus on expertise in early-stage drug discovery and development

Translation of SEED Platforms into Drug Pipeline of 9 disclosed programs in various disease areas

RBM39 Degrader: POC in cell and animal models; lead candidate in oncology advancing to FHD around Mid-2025

2020 | 2021 | 2022 | 2023 and beyond

Nov. 2020: SEED received $10 M investment and entered into a research collaboration and license agreement with Lilly on multiple targets in TPD (upfront $10 M, up to $780 M milestone payments and tiered sales royalties)

Jun. 2022: Received additional investment upon achieving 1st milestone by Lilly

Feb. 2023: Received 2nd milestone payment by Lilly

Mar. 2024: Received 3rd milestone payment by Lilly

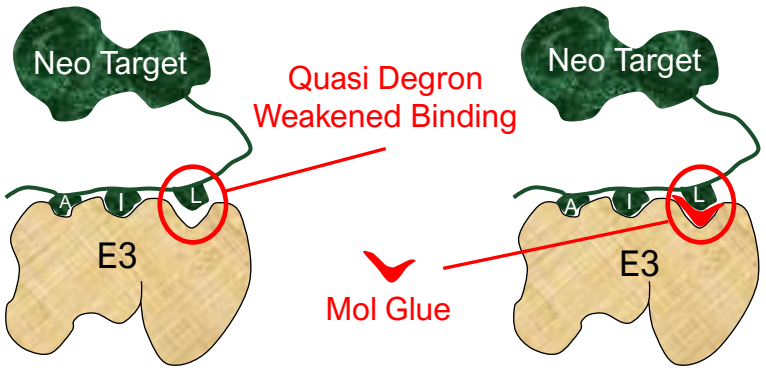
Aug. 2024: Received $24M Series A (first close) led by Eisai

2024-2025: Target meaningful milestone payments from Lilly

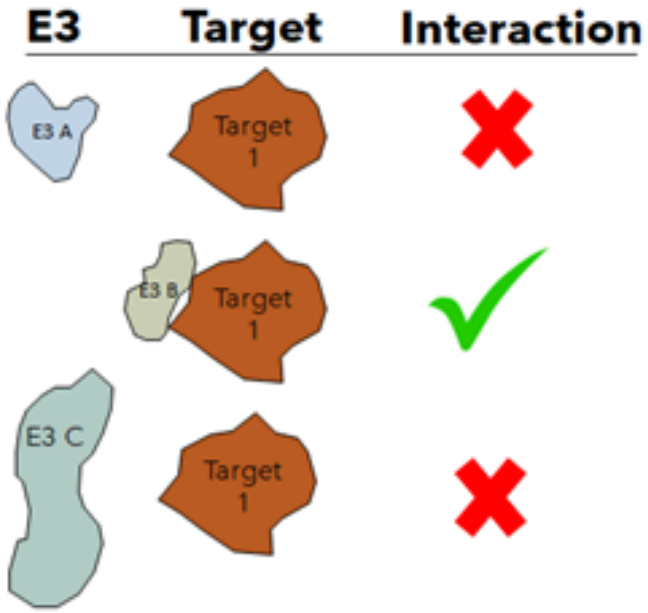
Global Partner Program Milestones

SEED's Differentiation: Multi-dimensional Platforms for E3 Selection

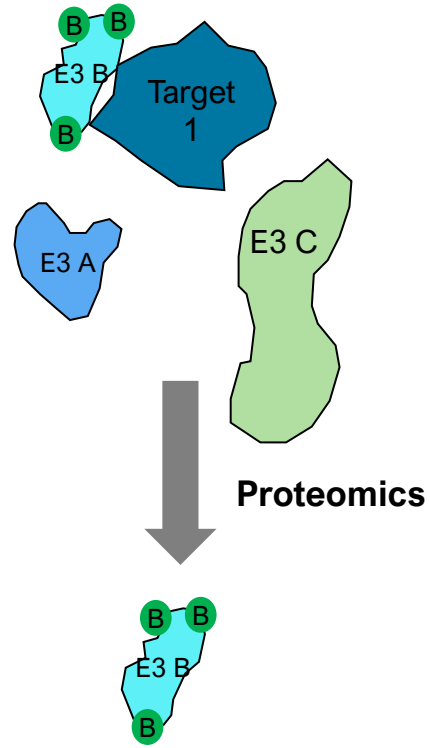
Knowledge-based Quasi Degron Approach



Direct Binding Validation



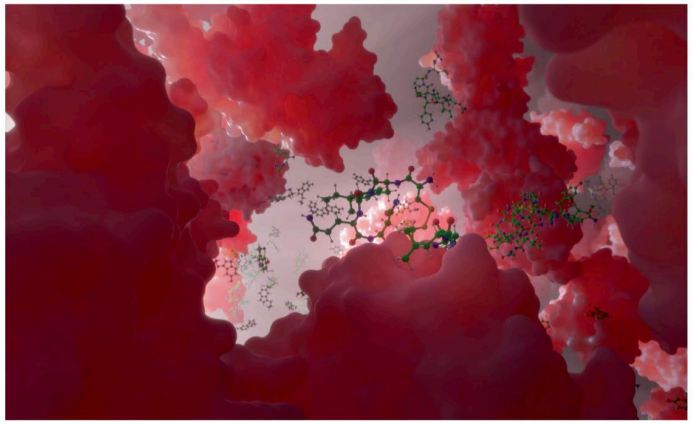
LumID: Identify the right E3 in the "living cell" near protein of interest



“Nature Biotechnology” Review on “The Glue Degraders” (Mar. 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.

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, GSP degrader, phas (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.

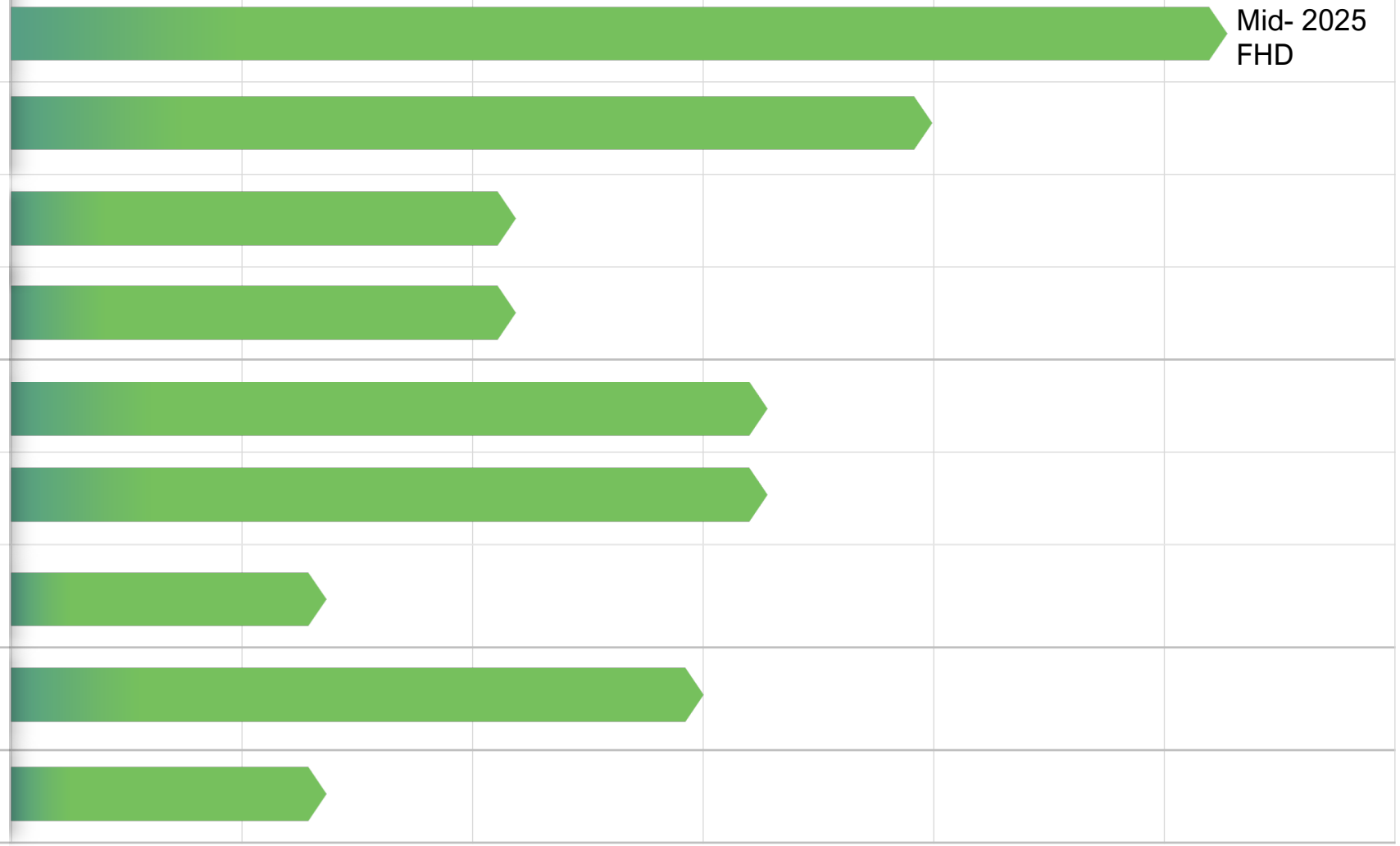
Sticking without glue

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

Diversified and Fast Progressing Proprietary SEED Pipeline

Indication	Target Protein	Target Selection	E3 Ligase ID	Molecular Glue HTS	Lead ID	IND Candidate	IND Filing
Oncology	RBM39						Mid- 2025 FHD
	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 two joint programs with Eli Lilly and Company

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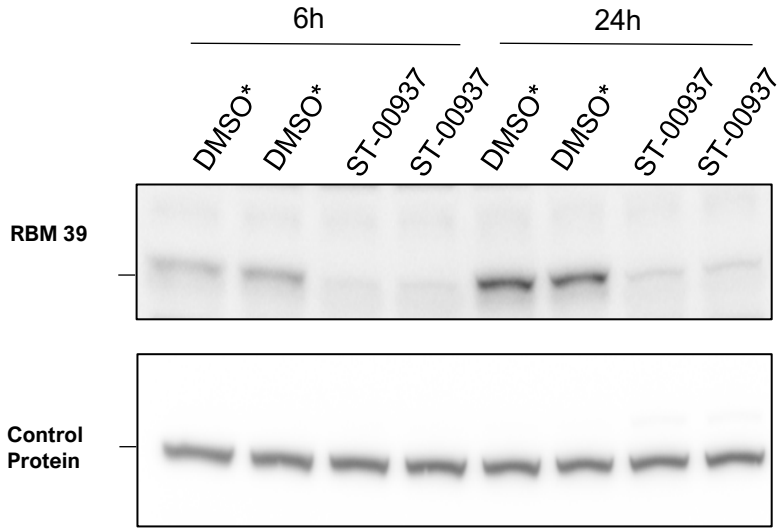
Our RBM39 Degrader Class: Potentially Best-in-Class and First-to-Market

Program Summary

- **POI**: RNA splicing factor RMB39; **E3**: DCAF15; **MOA**: RMB39 degrader MG
- **Target indications**: Biomarker selected colon cancer, prostate cancer, neuroblastoma, and others
- **Development stage**: IND candidate; Mid-2025 FHD
- **Differentiation**: Our novel degrader demonstrates superior anticancer potency in cell line, improved pharmacokinetics and brain permeability, improved metabolic stability and absent hERG activity vs. comparators
- **Preclinical POC**: Animal data demonstrates its potential to have powerful anticancer effects with excellent safety profile
- SEED owns **global rights**

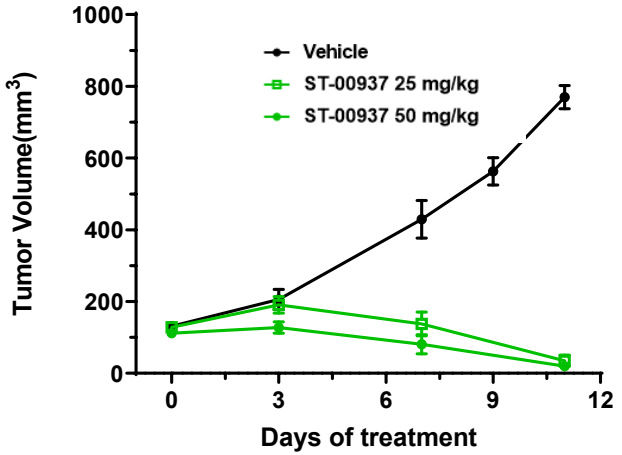
POC: RBM39 Degradation in Cell Line



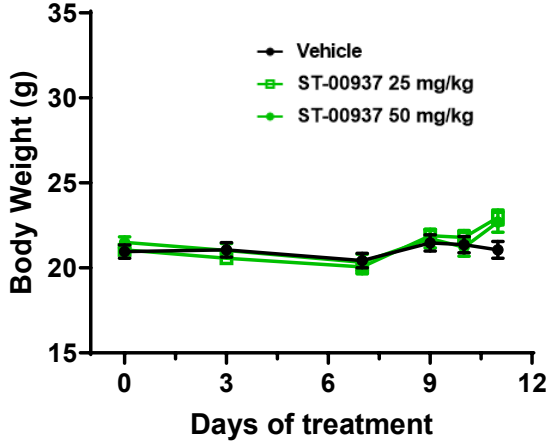
*Vehicle

Human colorectal cancer cell line

Superb In Vivo Efficacy: Complete Tumor Regression



Good In Vivo Safety: No Weight Loss



Colorectal xenograft in immunodeficient mice (Oral dose, twice daily)

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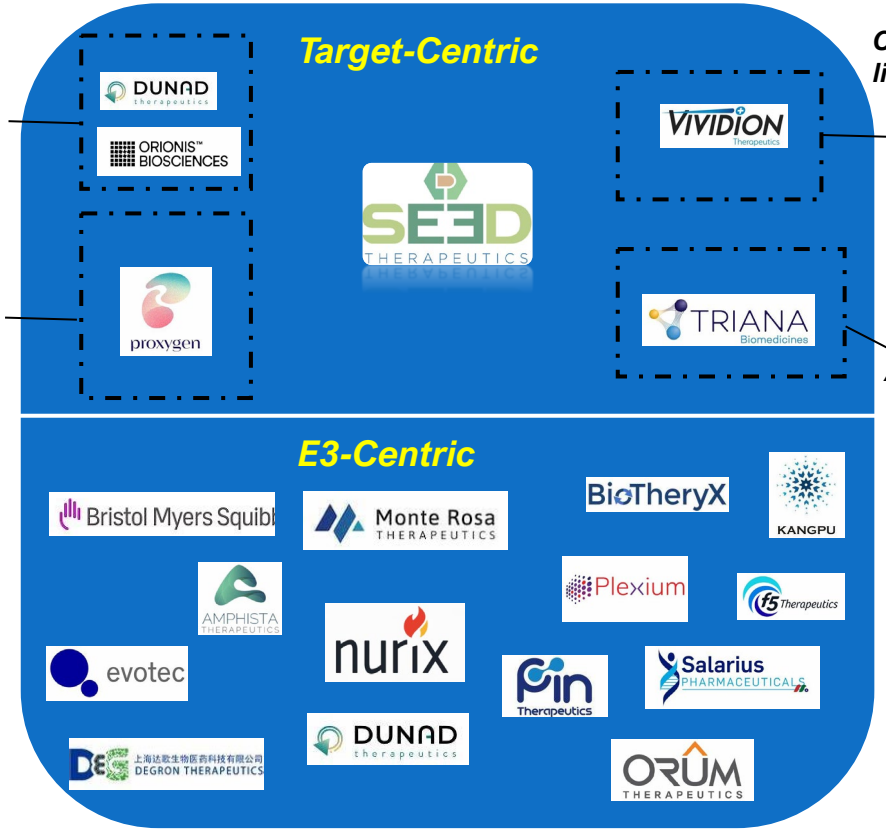
TPD: a High Value and Novel Therapeutic Modality

Allosteric effect based
- Not MG selective
- Lack of evidence for TPD through small molecule-induced allosteric changes in protein structure

Cell-based HTS assays
- May not be MG selective
- Difficult to screen at higher compound concentrations that may be required



Covalent binder libraries
- Lack of evidence of target specificity
- No consideration for importance of Basal Interaction

AI-based approach
- Lack of evidence for applicability to Molecular Glue discovery from scratch and E3 selection

All top 20 global pharma have TPD programs internally and / or through collaboration

- **Discovery stage TPD assets** has been commanding **$35 - $60 million** upfront and **$500 million - $5 billion** milestone payment. Notable transactions include licensing and R&D collaboration deals between
  - ✓Genentech and Orionis; Genentech and Monte Rosa
  - ✓Astellas and Cullgen
  - ✓BMS and Evotec
  - ✓Genentech and Jemincare
  - ✓Bayer's acquisition of Vividion for **$1.5 billion** in 2021
  - ✓Merck's acquisition of Peloton for **$1.05 billion** in 2019

- **Pre-IND/ IND stage TPD assets** has been commanding **$100 - $300 million** upfront and **up to $2 billion** milestone payment. Notable transactions include licensing deals of
  - ✓Lilly from Foghorn
  - ✓Sanofi from Kymera
  - ✓GSK from IDEAYA
  - ✓BMS and Orum

- **Clinical stage TPD asset** (early Phase II) has commanded **$650 million** upfront and **$350 million** equity investment in
  - ✓ Pfizer / Arvinas' collaboration

Investment Highlights

Plinabulin: Safety & Efficacy	Lead Asset Plinabulin: >700 cancer patients treated with good tolerability; Positive Phase 3 data in 2 indications
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 2024
Premier Partnerships	SEED: Investments and R&D Collaborations from Eli Lilly and Company and Eisai
Intellectual Property	Strong IP and technology protection

thank you!

www.beyondspringpharma.com