



April 2023 | NASDAQ: BYSI



BeyondSpring

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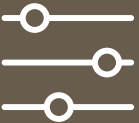



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By attending this presentation, you acknowledge that you will be solely responsible for your own assessment of the market and our market position and that you will conduct your own analysis and be solely responsible for forming your own view of the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

Highlights

	SEED: Novel TPD Platform& Pipeline	Subsidiary SEED: Target Protein Degradation (TPD) Company with Eli Lilly R&D Collaboration
	Plinabulin: Phase 3 Clinical Asset	Positive Phase 3 data in 2 indications with Lead Asset - Plinabulin
	Global Regulatory Strategy	Plinabulin: Target US, China, and EU Regulatory Agencies
	Intellectual Property	Strong IP and technology protection
	Premier Partnerships	Key commercial partnership in China for Plinabulin

Pipeline

	Indication/Target	Program	Preclinical	Phase 1	Phase 2	Phase 3	Registration	Trial Name / Collaborator
Late stage	NSCLC (2 nd /3 rd line)	Plinabulin + Docetaxel						DUBLIN-3
	CIN Prevention	Plinabulin; Plinabulin + Pegfilgrastim						PROTECTIVE-1 & PROTECTIVE-2
Investigator Initiated Trials	SCLC (2 nd /3 rd line)	Plinabulin + PD-1 + CTLA-4						 Bristol Myers Squibb™ 
	7 cancers (PD-1/PD-L1 failed)	Plinabulin + PD-1/PD-L1 + Radiation						THE UNIVERSITY OF TEXAS 
	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 Therapeutics	KRAS and additional targets	Targeted Protein Degradation (TPD) Molecule Glue Platform						
	Multiple Targets	TPD (Molecular Glue)						

SEED Overview



SEED is a Molecular Glue company overcoming the critical hurdle for E3 selection to target any Disease-Causing Protein



Since Lilly partnership in Nov. 2020, SEED has developed and applied its breakthrough target-centric MG discovery platform to internal and partnered projects

Develop a novel MG E3 ligase platform with significant potential to exceed the success of VHL and cereblon in TPD

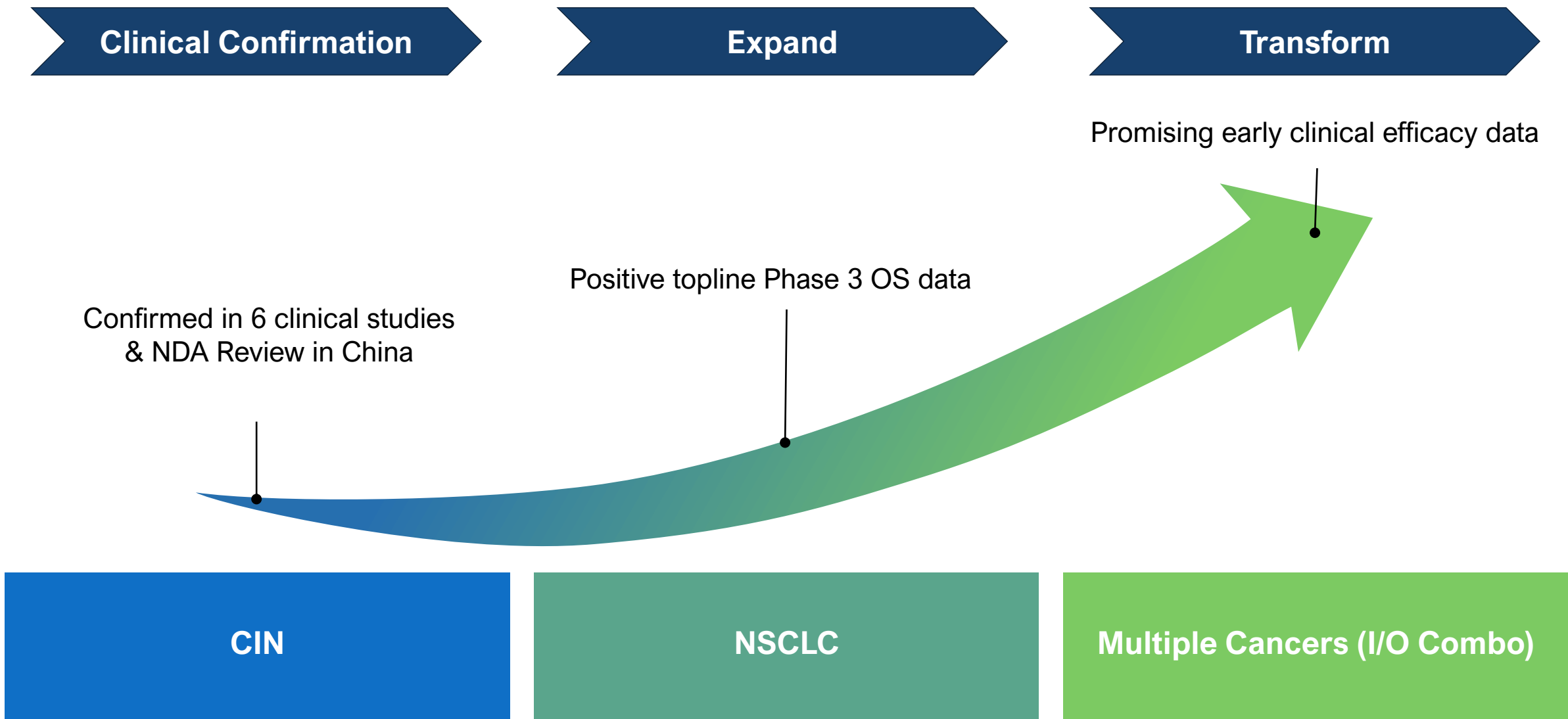
Utilize basal E3:target interaction and cell-based proximity platforms to increase the likelihood of drug development success



Future Plan: advancing a lead asset to IND in 2024, with 1 IND per year goal thereafter

Utilize unique capabilities in CNS disease target for de novo discovered MGs

Plinabulin Franchise





SEED Therapeutics: TPD Company



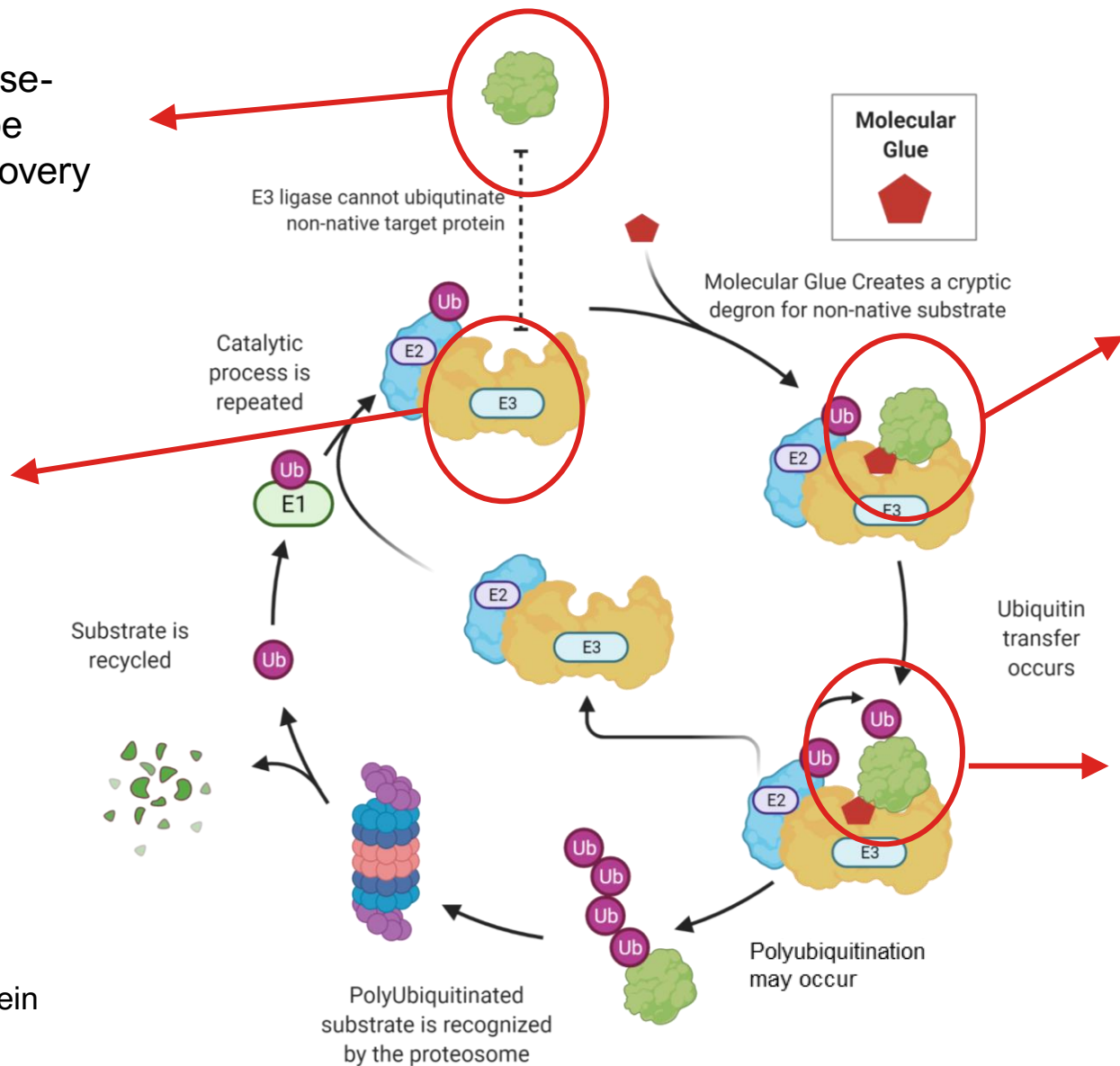
Impossible Task of Identifying the Right E3 Ligase by HTS

Which of the thousands of disease-causing protein targets should be selected for molecular glue discovery and development?

Critical Challenge:
Which of the >600 E3 ligases should be selected to target the disease-causing protein?

Must only one E3 ligase be selected for HTS for molecular glue Hit ID?

**Basic science underlying targeted protein degradation covered in Appendix



Which protein-protein interaction (PPI) assay platform should be developed for HTS?

Which chemical library should be utilized for screening?

What strategies will limit the dropout of PPI-inducing Hits for lack of induction of target protein (K48) polyubiquitination?

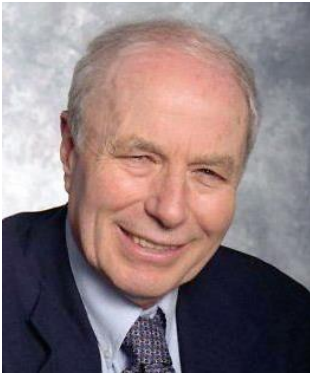
SEED's Unique Platform to Identify Novel E3 for Protein of Interest (POI)

- **Selection of E3 based on structure complementarity with POI**
- **Selection of E3 in cell-based LumID platform**
- **Biochemical assays to confirm baseline interaction of selected E3 and POI**

Ideas and Support from World-Leading Experts

Translate at SEED to Future Medicine

Avram Hershko
MD, PhD



Pioneer in the
ubiquitin
proteasome
system
**Nobel Prize
Recipient**

SEED co-Founder
and SAB Member

Ning Zheng,
PhD



Pioneer in
Molecular Glue
discovery and
scientific
structural
rationale

SEED co-Founder
and SAB Member

**Michele
Pagano, MD**



World leader in
the discovery and
application of
ubiquitin ligase
biology and
cancer biology

SEED co-Founder
and SAB Member

James Tonra,
PhD



Expert in bench-
to-bedside
translation in
multiple disease
areas

President and
CSO

Lan Huang,
PhD



Ubiquitin ligase
expert and
proven biotech
entrepreneur at
BYSI and SEED

CEO, SAB
Member and co-
Founder

R&D Expertise and Infrastructure



Discovery Labs, City of Science, King of Prussia, PA

- Occupied 10,000 ft² in June 2022
- 7000 ft² lab space

SEED: Combined R&D Team Experience

- >100 years combined in 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

Partnership with Eli Lilly Provides Early Validation and Funding



- **On November 13, 2020, SEED Therapeutics announced it has entered into a research collaboration and license agreement with Eli Lilly on targeted protein degradation.**
- Under the terms of the agreement, SEED Therapeutics will
 - Receive a \$10 million upfront cash payment to fund research
 - Eligible to receive up to \$780 million in potential pre-clinical and clinical development, regulatory and commercial milestones
 - Eligible to receive tiered royalties on net sales of products that result from the collaboration
- In addition, Lilly has made a \$10 million equity investment into SEED Therapeutics

The collaboration leverages SEED Therapeutics' strong expertise in TPD and Lilly's capabilities and resources in drug development and commercialization

Success with Eli Lilly Project 1: High Value Disease-Causing Target

1. Lilly
Target rationale

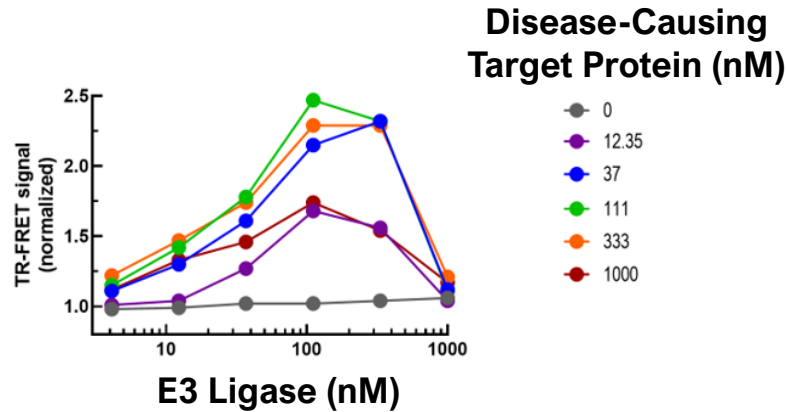
2. SEED
Potential E3 Ligase
Identification

3. SEED / Lilly
Workflow Development
Joint Steering Committee Approval

4. SEED
Protein Synthesis

5. SEED
HTS TR-FRET Assay
Development

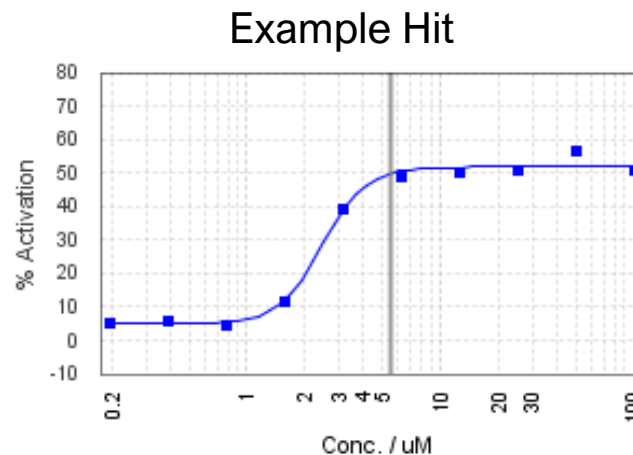
6. SEED / Lilly
HTS



E3 Ligase

MALDI

Multiple chemotypes with tractable SAR identified for strengthening E3:Target PPI



Ongoing

- Medicinal chemistry to optimize small molecule glues
- Cellular activity evaluation
- Biophysics of ternary complex

* **Project 2 underway

Molecular Glue Nonclinical R&D Flow to Success

Molecular Glue
Disease-Causing
Protein Target(s)

Structure-based drug design
(SBDD) from known chemical
matter, combined with key
screening assays
(e.g. SEED's Project X)

For Partners, SEED delivers Molecular
Glue Leads against Nominated Targets,
with activity in cells and disease models.

Partner typically takes over these Lead
molecules for more traditional
advancement to IND and through clinical
testing

In Partnership, Partner
Nominates a single target
based on SEED analysis and
recommended
prioritization*

1 month

E3 Candidate Selection

1. UPS expertise
2. Basal Interaction
 - In Silico prediction/
Structural biology
 - E3: target baseline
interaction
 - LumID™

~4-6 months

HTS Active*

1. Assay
development
2. Library screening
3. Confirmation
testing

~4-6 months

Hit ID*

1. MedChem
2. SBDD
3. Cell activity

~6 months

Lead ID*

1. MedChem
2. SBDD
3. Disease model
activity

~6-8 months

IND Filing*

Lead Optimization
IND-enabling efforts

One SEED IND/year,
beginning in 2024

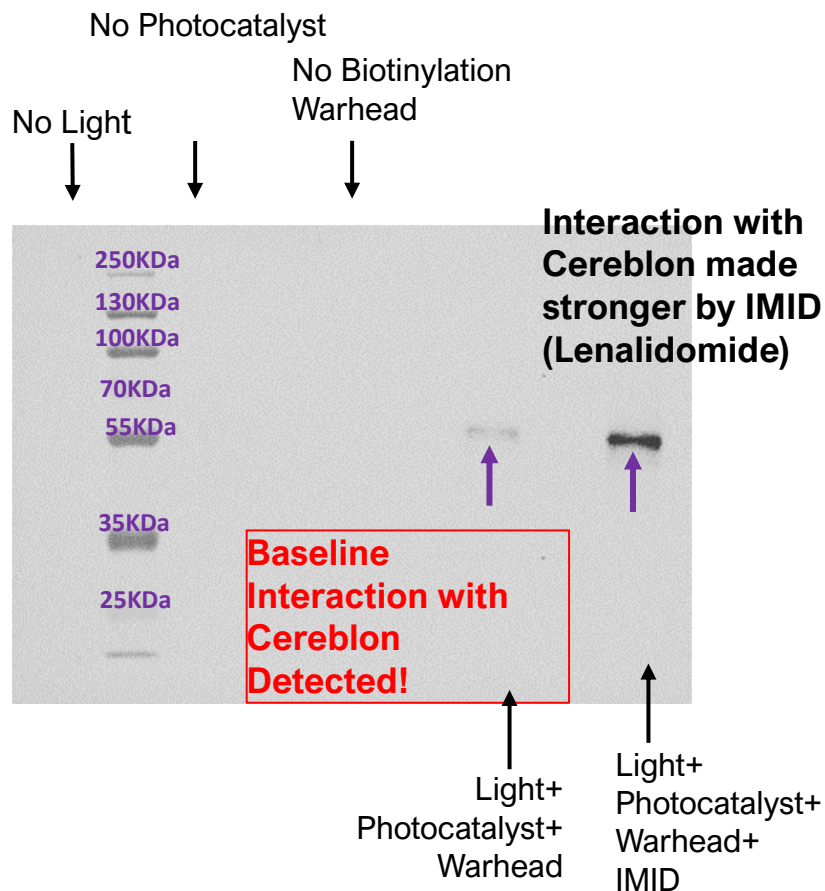
~12-18 months

Timeline

*typical R&D and Partnership milestones

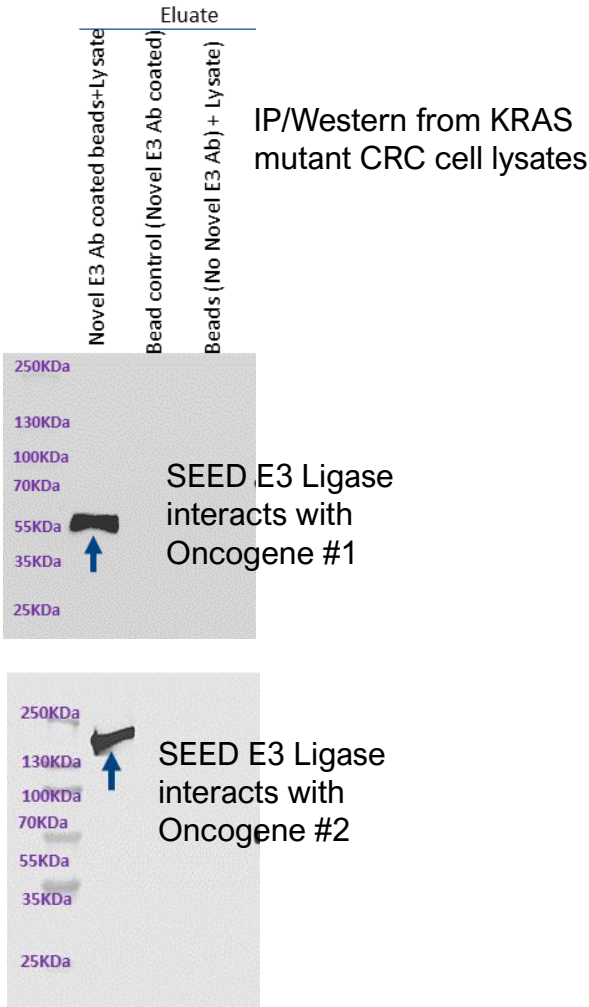
SEED's Breakthrough and Exclusive Molecular Glue Discovery Advantage: Discovery and Use of Basal Interaction

LumID: identify nearby E3 in a cell



Novel E3 Discovery

E3 ligase/ subunit	Number of records
CRBN	309
VHL	207
MDM2	189
SCF	86
RNF	63
SKP	55
cIAP	50
DDB1	47
KEAP1	31
FBXO	23
UBR2	19
βTRCP	9
DCAF	8
SIAH1	4
STUB1	4
ASB6	2
CDC34A	1
UBE4A	1

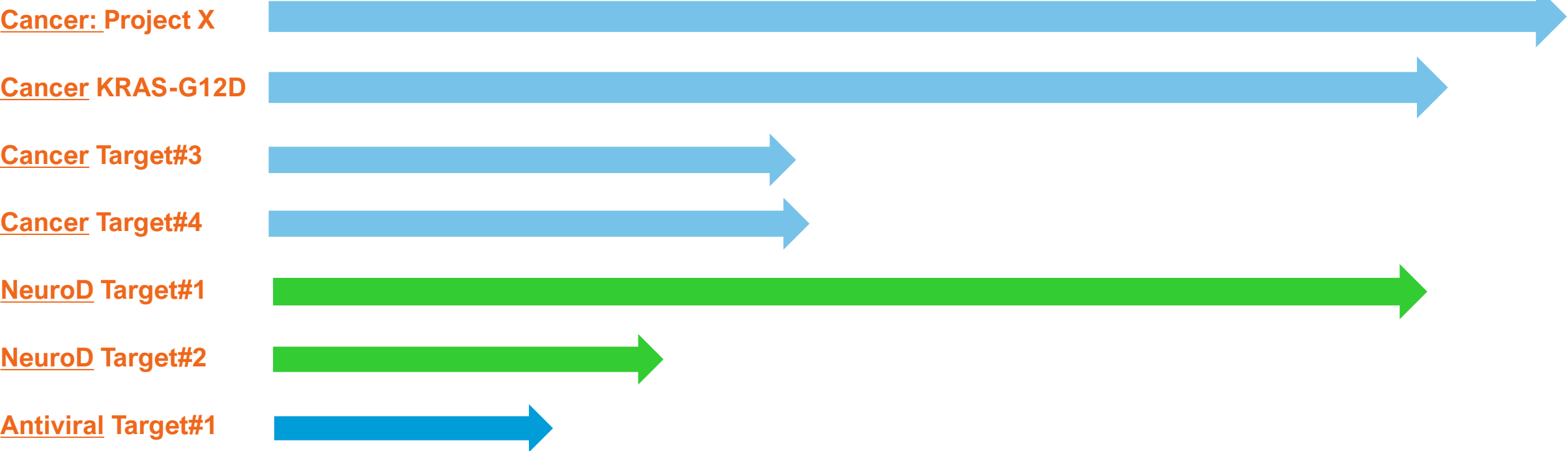


Source: CAS Content Collection; Sasso et al., *Biochemistry* 2022

SEED Drug R&D Pipeline in Various Important Disease Areas



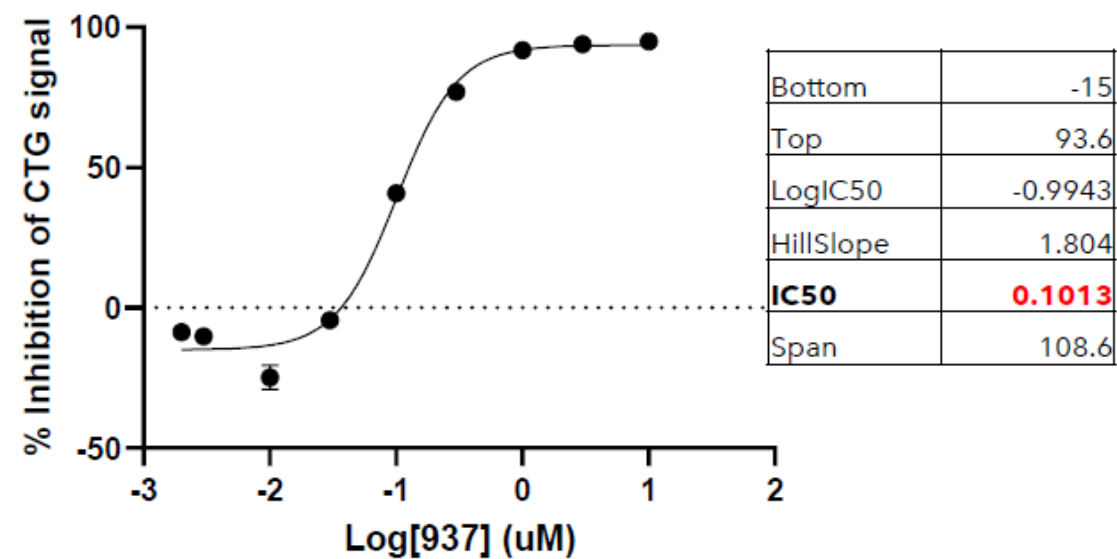
Target Protein Initiative



6 of 7 Targets Unpartnered

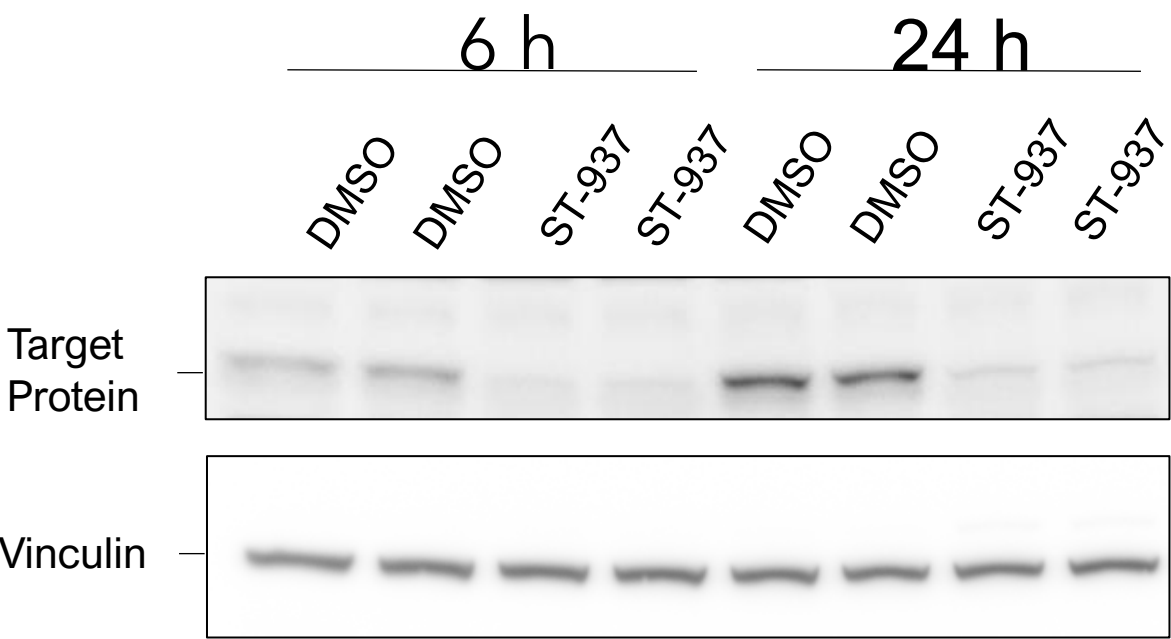
Project X: Lead ST-00937 is Active To Degrade Target Protein in Cell

Potent Cancer Cell Killing



CTG: CellTiter-Glo®

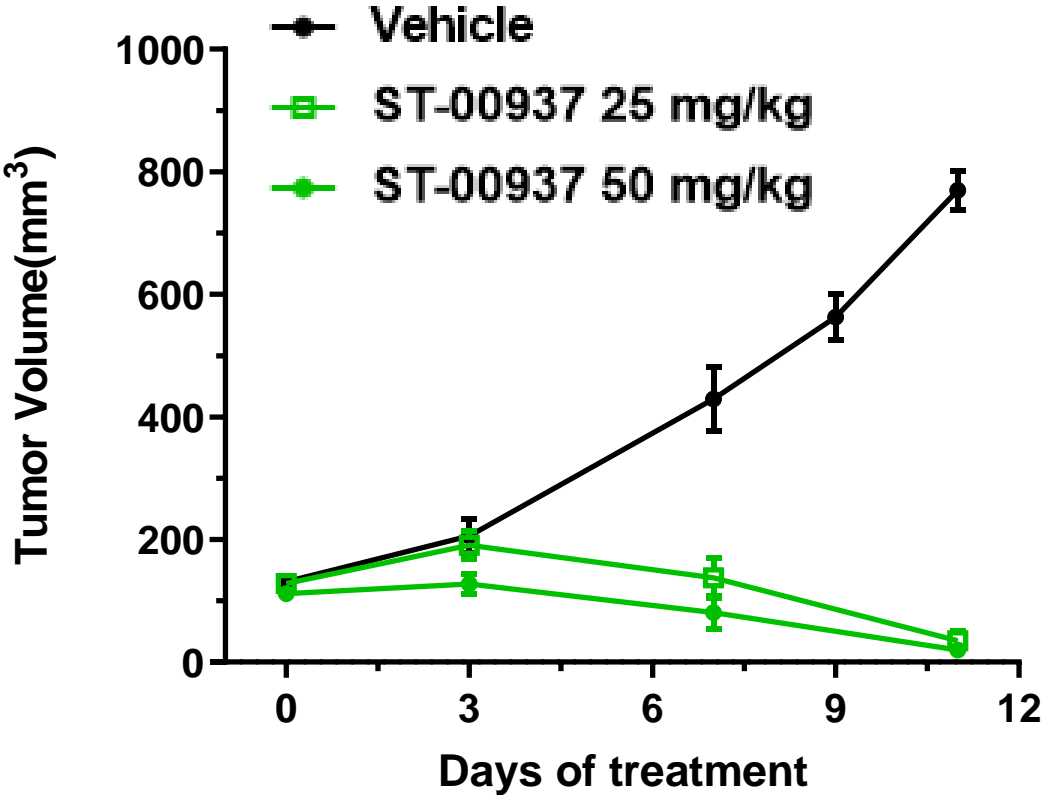
Disease-Causing Protein Degradation



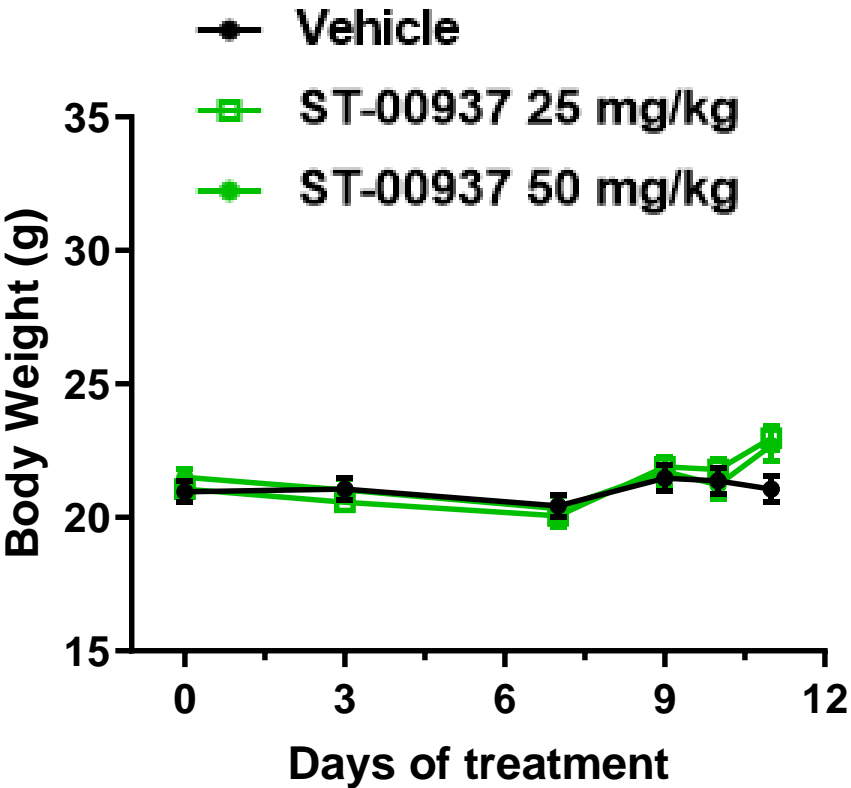
Project X: Lead ST-00937 Regresses Tumors Growing in Mice

Human colorectal cancer xenograft in immunodeficient mice; Oral dose, twice daily

Superb In Vivo Efficacy:
Complete Tumor Regression



Good Safety:
No Weight Loss



TPD Growth Opportunities in TPD Biotechs

PROTAC
/Heterobifunctional

Companies in the PROTAC/Heterobifunctional category:

- Hinova 海创药业
- DIALECTIC THERAPEUTICS
- ARVINAS
- Accutar Biotech
- nurix
- FOGHORN THERAPEUTICS
- RANOK Therapeutics
- FIMECS
- Ubix Therapeutics
- cullgen
- POLYPROX THERAPEUTICS
- Progenra
- PHOREMOST
- ORIGAMI Therapeutics
- VENQUIS Therapeutics

Non-UPS Degrador
or Technology
Focused

Companies in the Non-UPS Degrador or Technology Focused category:

- AVILAR THERAPEUTICS
- LYCIA THERAPEUTICS
- Ambagon THERAPEUTICS
- PAQ Therapeutics
- stablrix
- TRILO THERAPEUTICS
- FRONTIER MEDICINES

Molecular Glue

Companies in the Molecular Glue category:

- KANGPU
- Bristol Myers Squibb
- Salaris PHARMACEUTICALS
- Monte Rosa THERAPEUTICS
- DEG 上海达歌生物医药科技有限公司 DEGRON THERAPEUTICS
- SEED THERAPEUTICS
- ORUM THERAPEUTICS
- VIVIDION Therapeutics
- TRIANA Biomedicine
- Cedilla
- evotec
- DUNAD therapeutics
- Plexium
- proxigen
- IF5 Therapeutics
- MEGABION

Molecular Glue
& PROTAC

Companies in the Molecular Glue & PROTAC category:

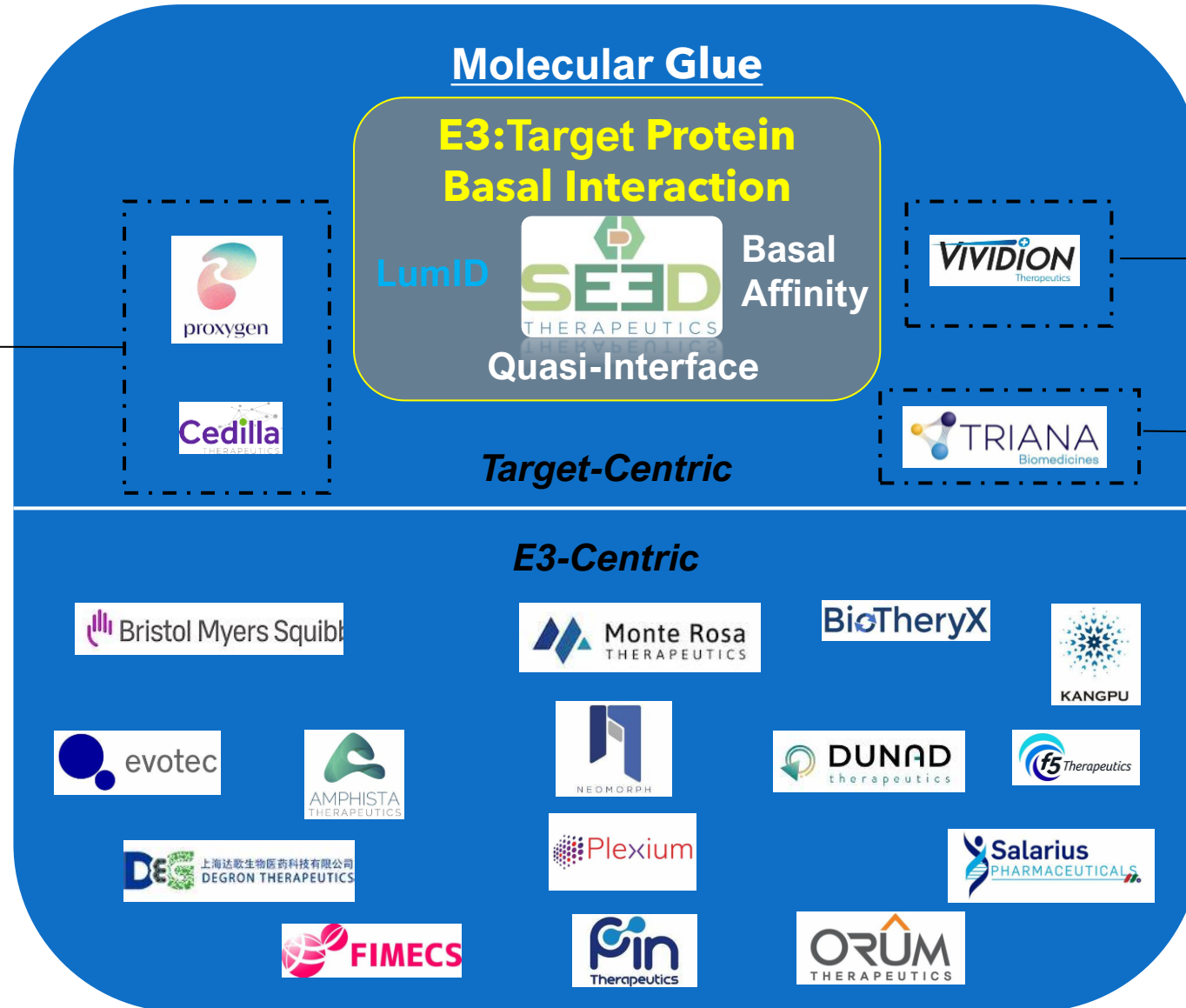
- CelerisTx
- AMPHISTA THERAPEUTICS
- proteovant THERAPEUTICS
- Fin Therapeutics
- Captor Therapeutics®
- ORIONIS™ BIOSCIENCES
- C4 Therapeutics
- BioTheryX
- KYMERA

Clinical Stage Preclinical Stage Discovery

Differentiation by TPD Strategies

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



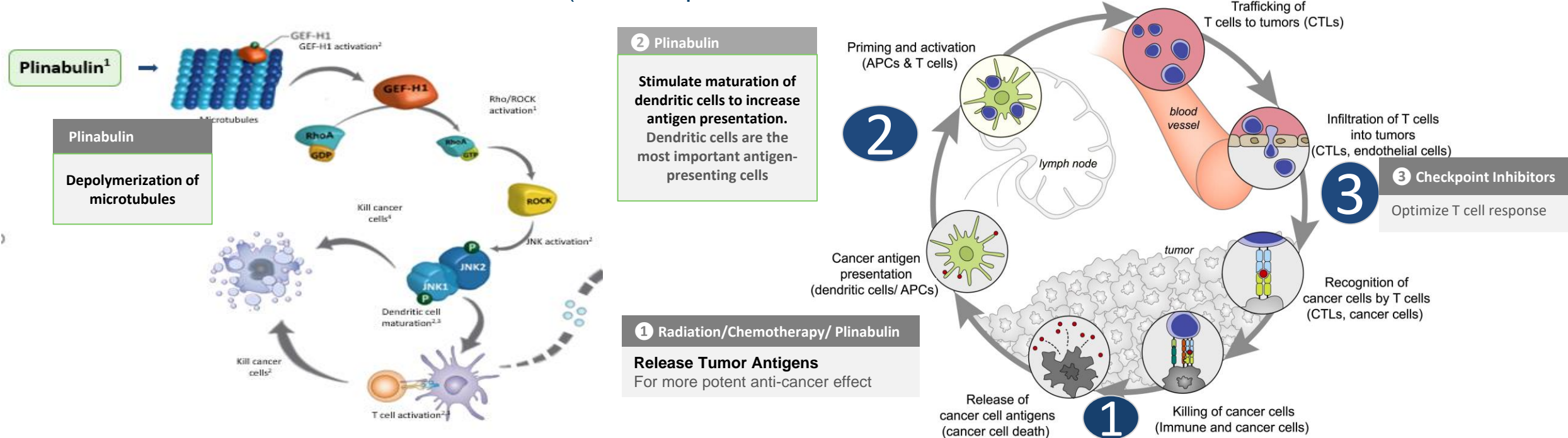
Plinabulin: First-in-class Agent for Multiple Cancer Indications



Plinabulin: First-in-class MOA and Novel Chemical Entity

Plinabulin: First-in-Class, Selective Immunomodulating Microtubule-Binding Agent (SIMBA)

- Plinabulin Induces Dendritic Cell Maturation (the most potent APC). a Key Step in Initiating Anti-Cancer Durable Response



Plinabulin Novel Target: Immune Defense Protein GEF-H1

1 + 2 + 3 → Optimal Immuno-Oncology Response

Plinabulin Overview

1 Favorable Safety Profile

1. >700 patients have been treated with plinabulin
2. Ease of Use: 1 or 2 doses per cycle given by 30~60 minutes IV infusion

2 CIN Prevention Benefit

1. Single Agent Plinabulin
2. Combination Plinabulin + Pegfilgrastim

3 Dual Anti-Cancer Mechanism of Action

1. Immune-enhancing effect
2. Direct anti-cancer effect

4 Trials Demonstrating Anti-Cancer Effects

1. 101: Phase 2 study in NSCLC
2. 103 (DUBLIN-3): Phase 3 in NSCLC
3. Big Ten Trial: Phase 1/2 in SCLC



Chemotherapy-Induced Neutropenia (CIN) Prevention Indication

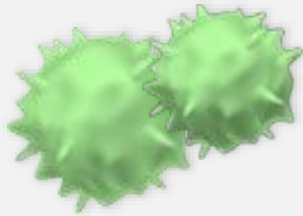


CIN Is an Unmet Medical Need in Week 1 After Chemotherapy

Despite widespread G-CSF use, CIN is #1 reason for FN, ER visits, hospitalization, sepsis, mortality, and chemotherapy dose reduction and disruption¹

Short-term

G-CSF is more effective in week 2 after chemo in raising neutrophil, which leaves a significant clinical gap in week 1



**Patients less Protected
in week 1
after Chemotherapy
with G-CSF**

Long-term

Chemotherapy's anti-cancer effectiveness is linear to its dose

**Reduction in
Relative Dose
Intensity (RDI)
of Chemotherapy**



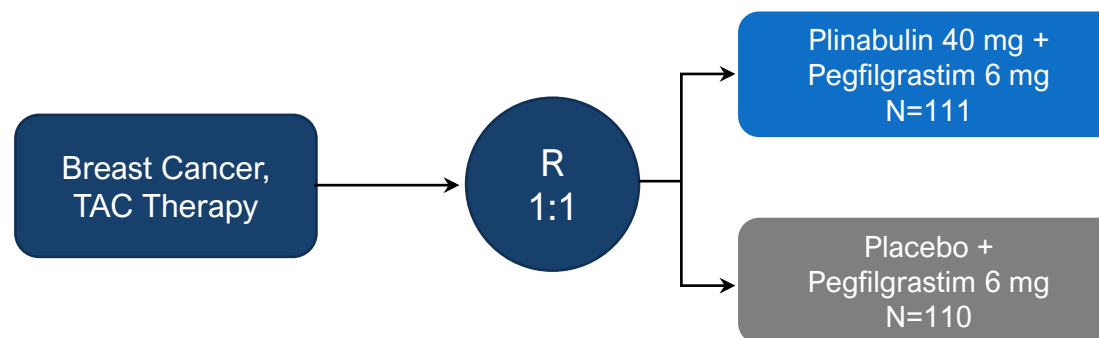
**Reduction in
Overall Survival²**

The Unmet Medical Need: Week 1 “Neutropenia Vulnerability Gap” (NVP)

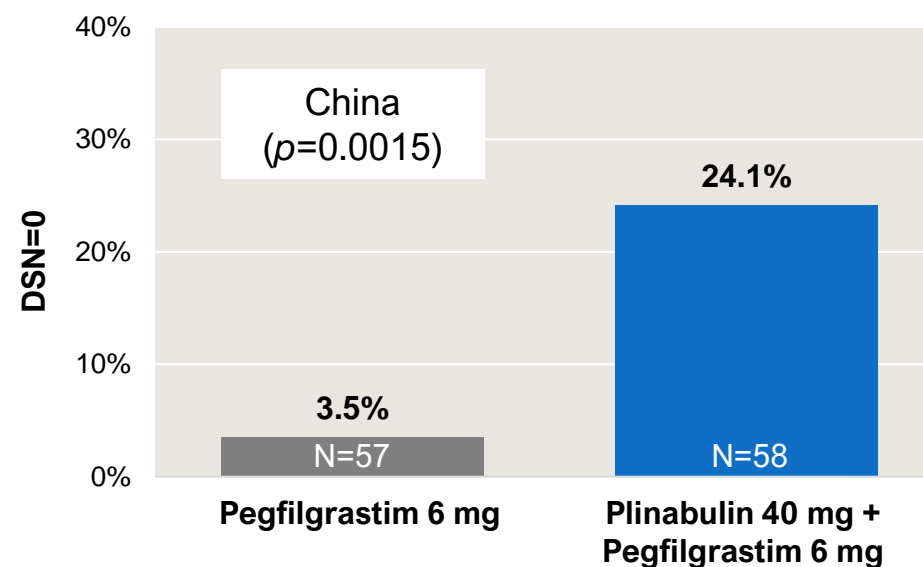
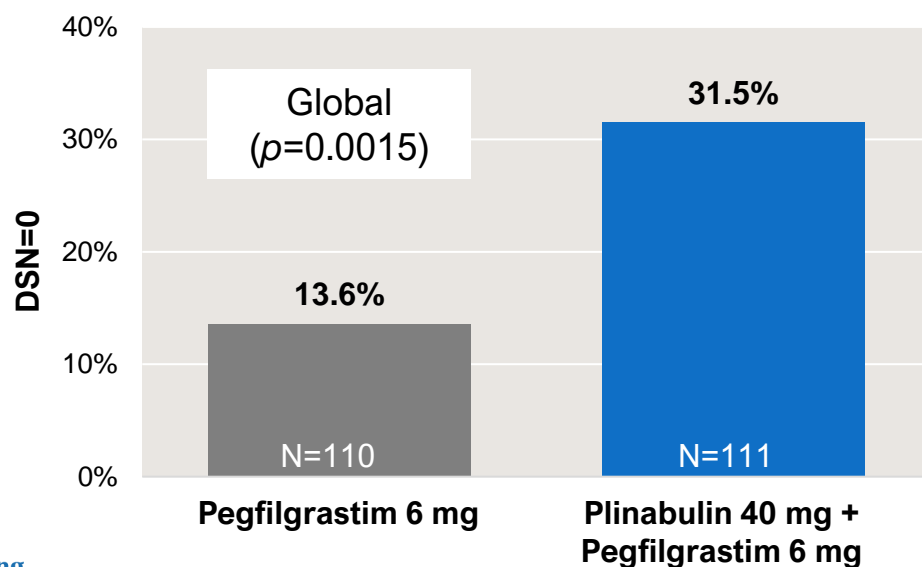
- >75% clinical complications occur in week 1 after chemo, which G-CSF cannot protect

Met Primary Endpoint in PROTECTIVE-2 Phase 3 Study

Design: Double blind, global study (19 centers); 4 cycles

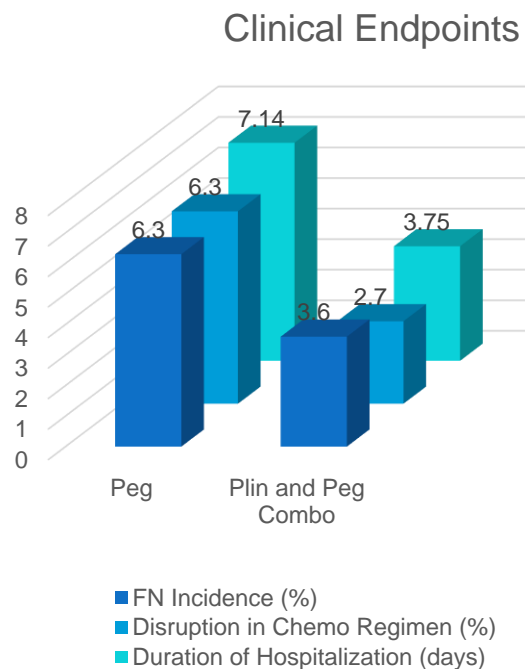


Results: Proportion of Patients with NO Grade 4 Neutropenia (or DSN= 0 Days) in Cycle 1

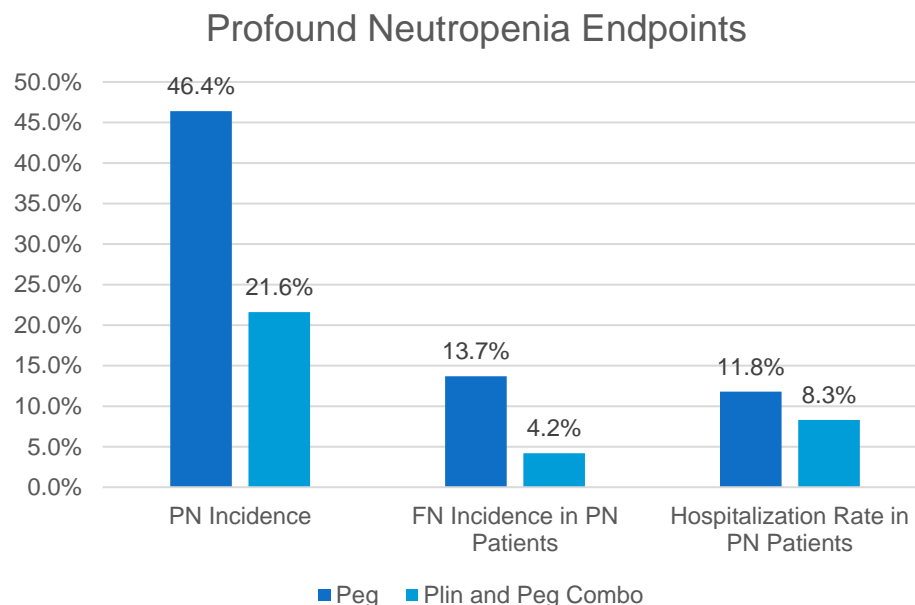


The Combination with Superior Improvement in Clinically Meaningful Endpoints Compared to Pegfilgrastim Alone

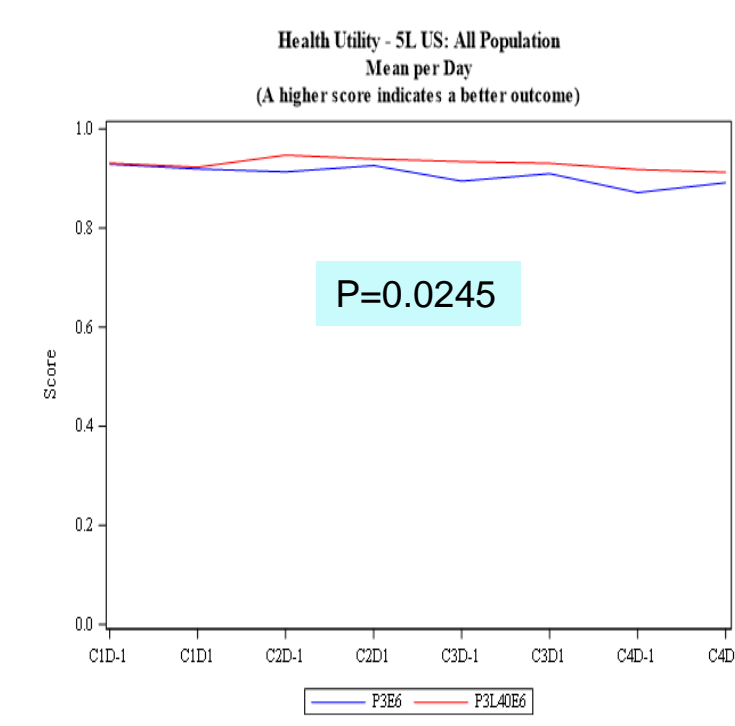
Reduction of Incidence and Severity of FN and Hospitalization



Reduction of Profound Neutropenia (PN) Related Benefits



Improvement of Quality of Life



June 2021 ASCO Presentations



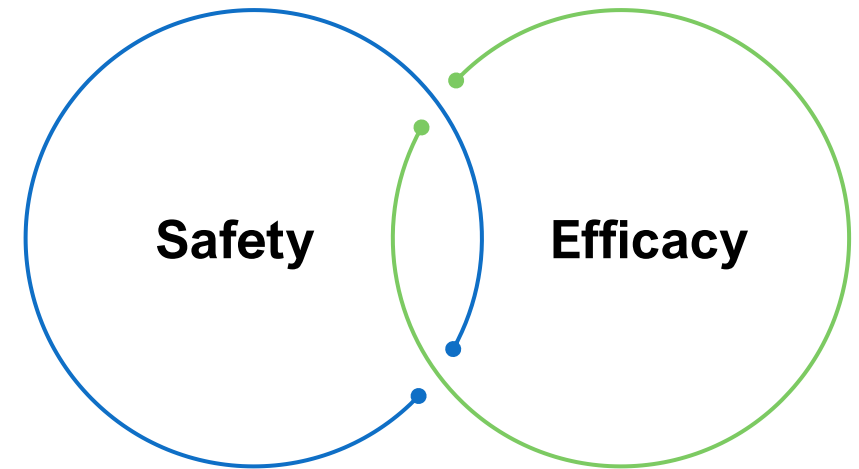
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2nd/3rd Line NSCLC Indication



Severe Unmet Medical Needs – 2nd/3rd Line NSCLC, EGFR Wild Type

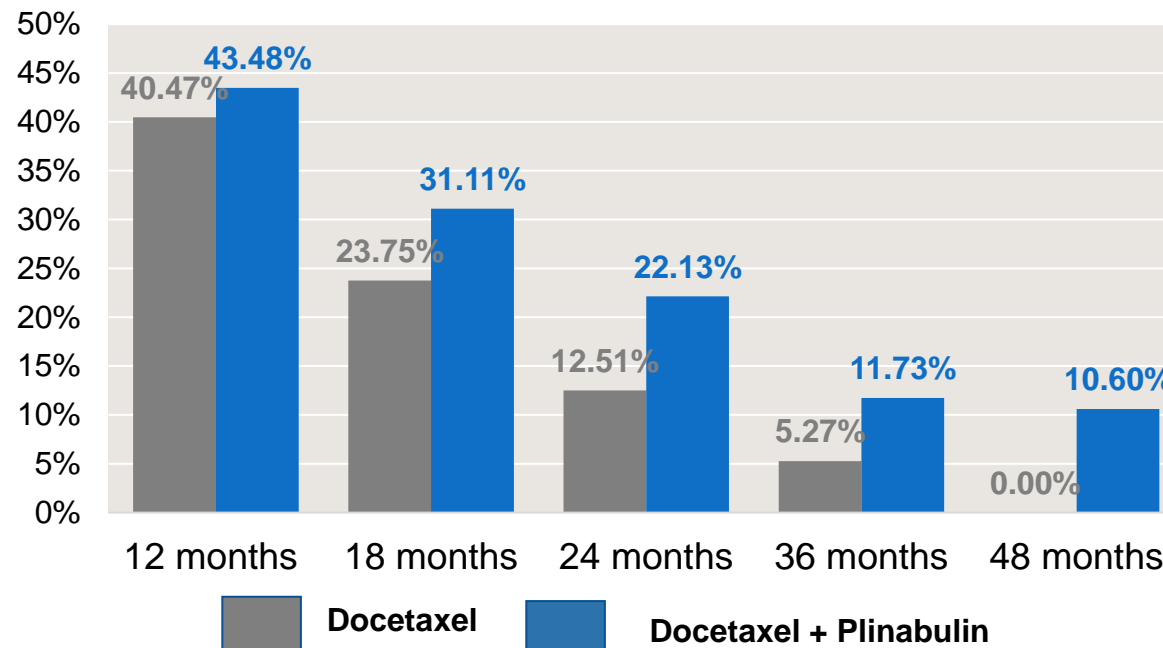
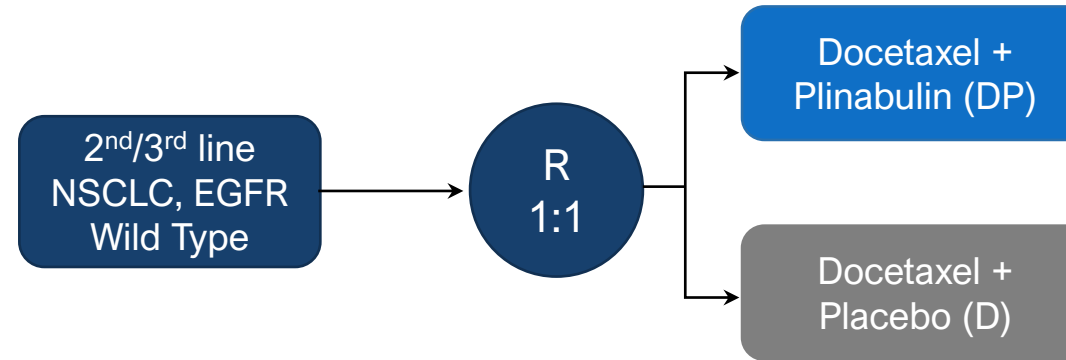
- Large patient population with limited treatment options
 - EGFR wild type: ~85% western NSCLC and ~70% of Asian NSCLC patients
 - With immunotherapies moved to first line, Docetaxel-based therapies are the mainstay therapy
 - TKIs are worse than docetaxel¹
- Docetaxel-based Therapies (SOC)
 - Limited efficacy
 - >40% severe neutropenia



Since Nivolumab's approval 6 years ago, no new agent with a novel mechanism has been approved in this indication.

Met Primary Endpoint of OS in DUBLIN-3 Phase 3 Trial

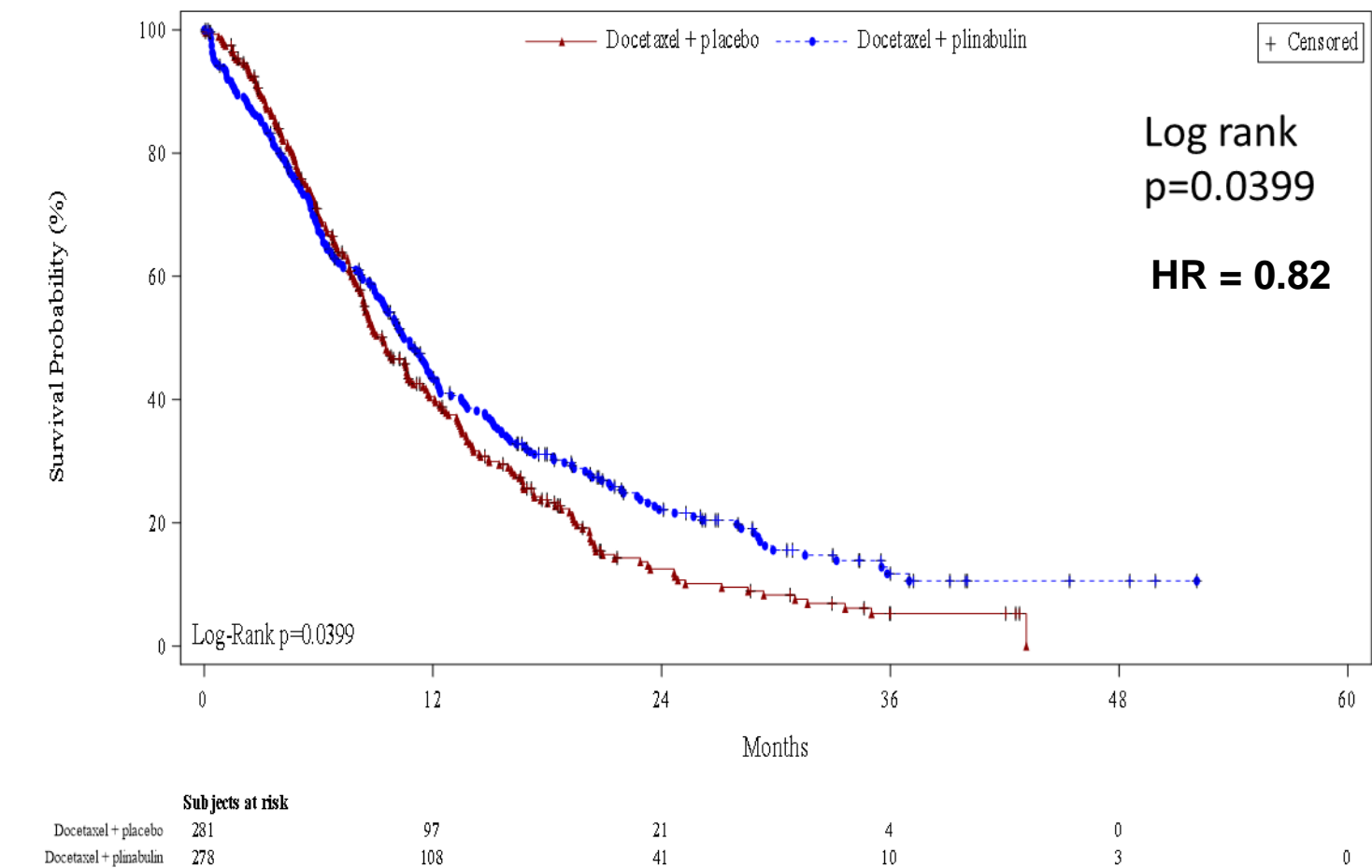
Design: Single-Blinded (blinding for patients only), global study, around 60 sites



Results:

- Significantly increased OS rate;
- Doubling of OS rate in 24M, 36M, and 48M OS rate in DP (10.6%) vs D (0%).

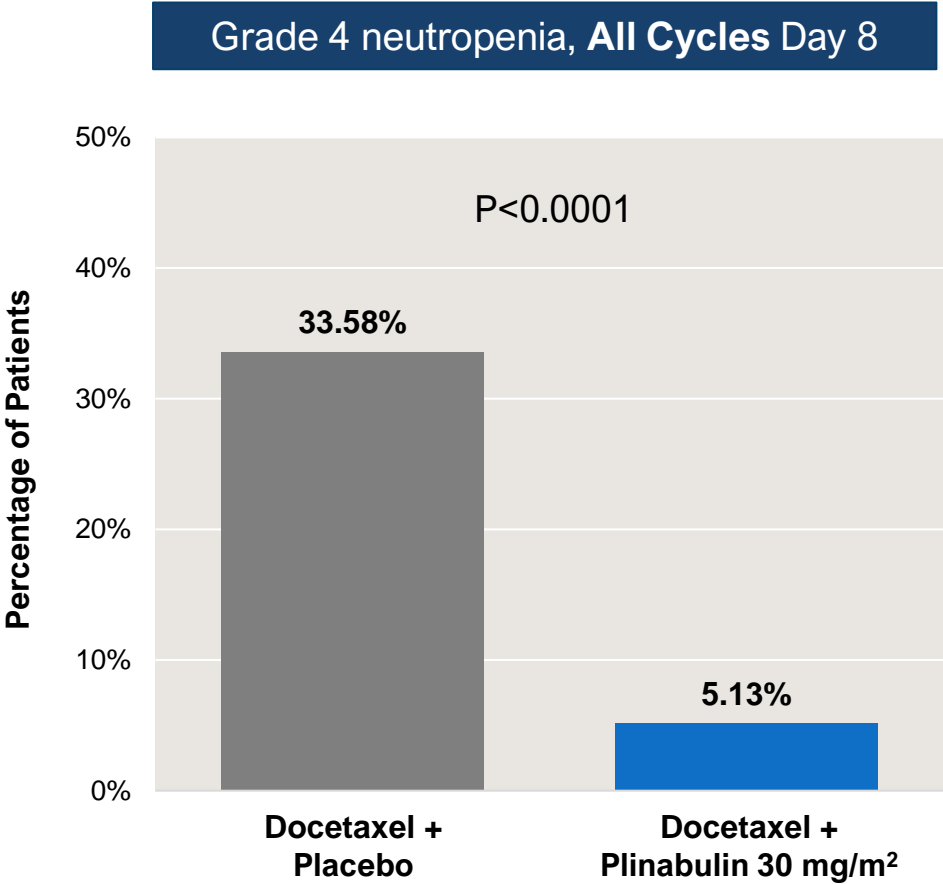
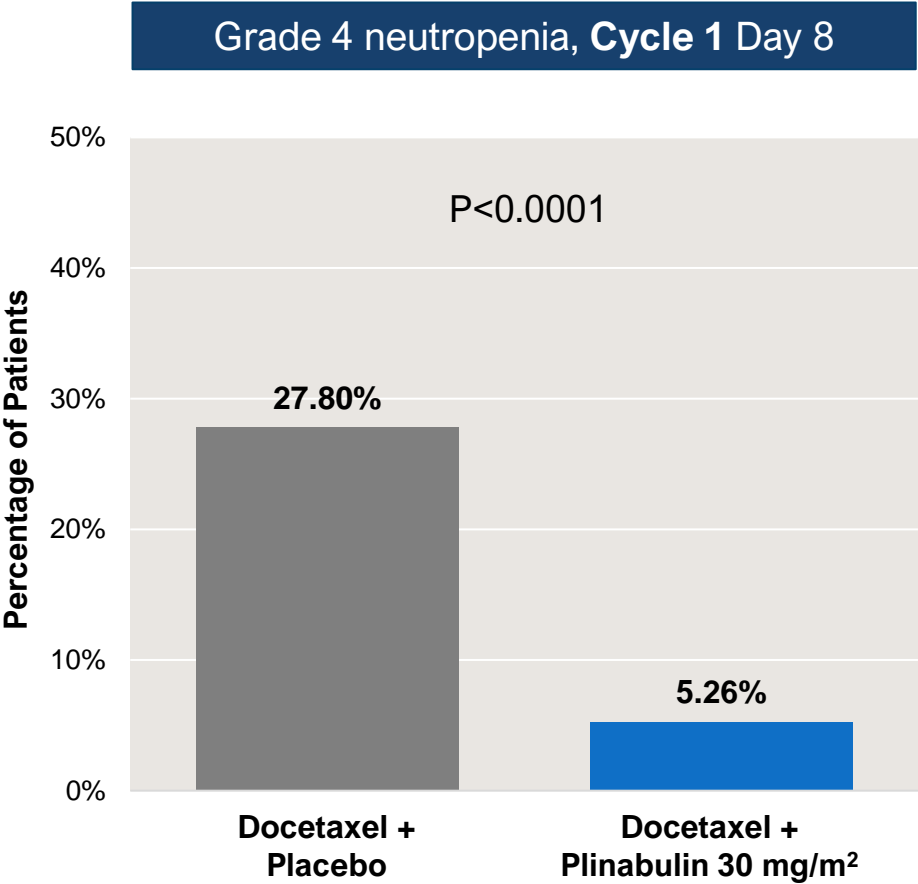
Met Primary Objective in Overall Survival (OS)



ITT population	Docetaxel (75 mg/m2) N=281	Plinabulin (30 mg/m2) + Docetaxel (75 mg/m2) N=278
OS (Months)	Mean OS (SE): 12.77 (0.676) Median OS (95% CI): 9.4 (8.4, 10.7)	Mean OS (SE): 15.08 (0.848), p=0.0332 Median OS (95% CI): 10.5 (9.3, 11.9) Log-rank p=0.0399; HR = 0.82 (0.68,0.99)

Significant Reduction in Grade 4 Neutropenia

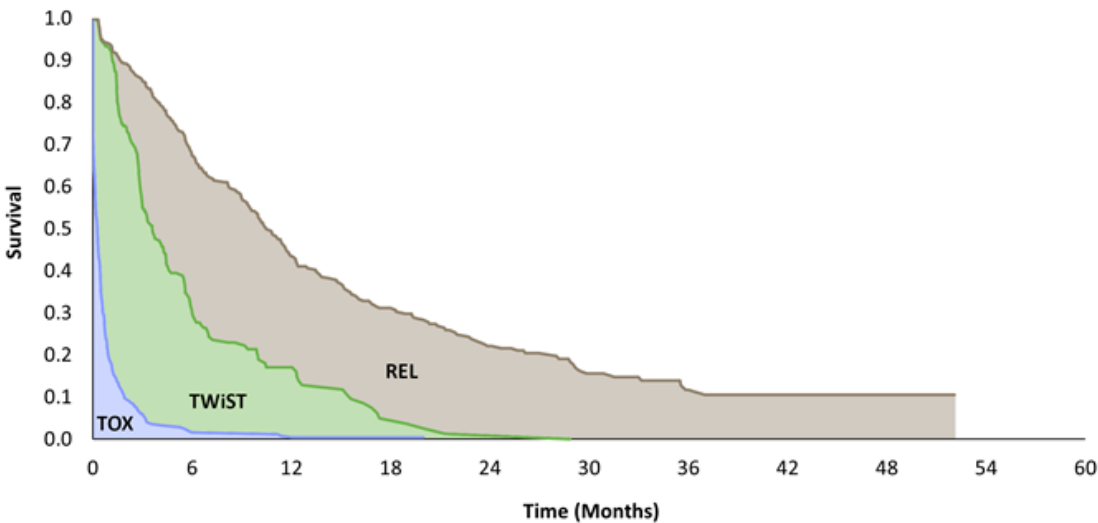
Cycle 1 Day 8 and All Cycles Day 8



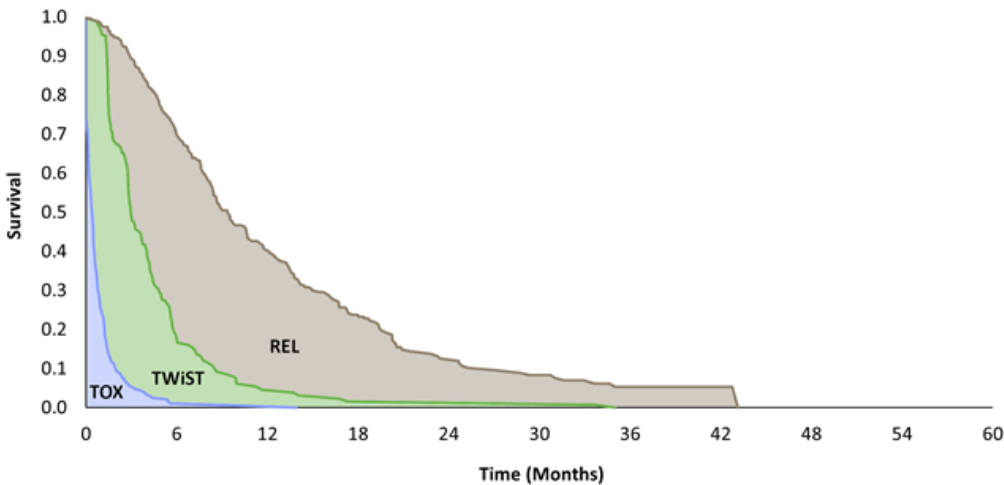
Significant Improvement in Quality of Life

- Q-TWiST (Quality-Adjusted Time Without Symptoms of Disease and Toxicity)

Plinabulin + Docetaxel



Docetaxel alone



Q-TWiST Gain	Relative Gain to OS Restricted Mean	Relative Gain to Q-TWiST
1.93	15.11%	18.43%
	(1.72% to 30.63%)	(2.07% to 37.20%)
	p-value=0.0396	p-value=0.0393



Clinically Meaningful Improvement of >18% in Q-TWiST.

Potential Benefit of Plinabulin + Docetaxel in NSCLC (2nd/3rd line)

With PD-1/PD-L1 moving to 1st line NSCLC, plinabulin + docetaxel could be the potential choice, with benefits vs. Docetaxel.

- **Significant survival benefit, with more pronounced survival benefit in non-squamous NSCLC population;**
- **Significant neutropenia reduction;**
- **Significant QoL benefit.**



Immuno-Oncology Combinations



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

PD-1/PD-L1 Inhibitors
- \$30B global annual sales



Potential to greatly expand the
addressable market

Current Severe Unmet Medical Needs

2/3rd Line: PD-1/PD-L1 resistant patients

1st Line: PD-1 + chemo double efficacy of PD-1, but with CIN risk

High immune-related SAE: PD-1 or PD-1+CTLA-4

“Cold” Tumor: PD-1/PD-L1 non-responsive tumor

Plinabulin:
APC Inducer
with easy
administration



Plinabulin Clinical Development

Plinabulin + I/O + chemo/radiation

Plinabulin is developed as a CIN prevention agent (pan cancer, pan chemo)

Plinabulin+PD-1+CTLA-4 in SCLC

- Plinabulin+ I/O + chemo/radiation
- Plinabulin + chemo

Promising Efficacy (Phase I) Plinabulin + PD-1 + CTLA-4 Inhibitors in 2nd/3rd line SCLC

Efficacy Analysis (ASCO 2021 Presentation)

Efficacy Analysis	PD-1/PD-L1 therapy naïve (n= 6)	PD-1/PD-L1 resistant (n=7)
Number of patients with PR* (ORR)	3 (50%)	3 (43%)

*PR –Partial Response - RESIST 1.1 : At least a 30% decrease in the sum of diameters of target lesions, taking as reference the baseline sum diameters.

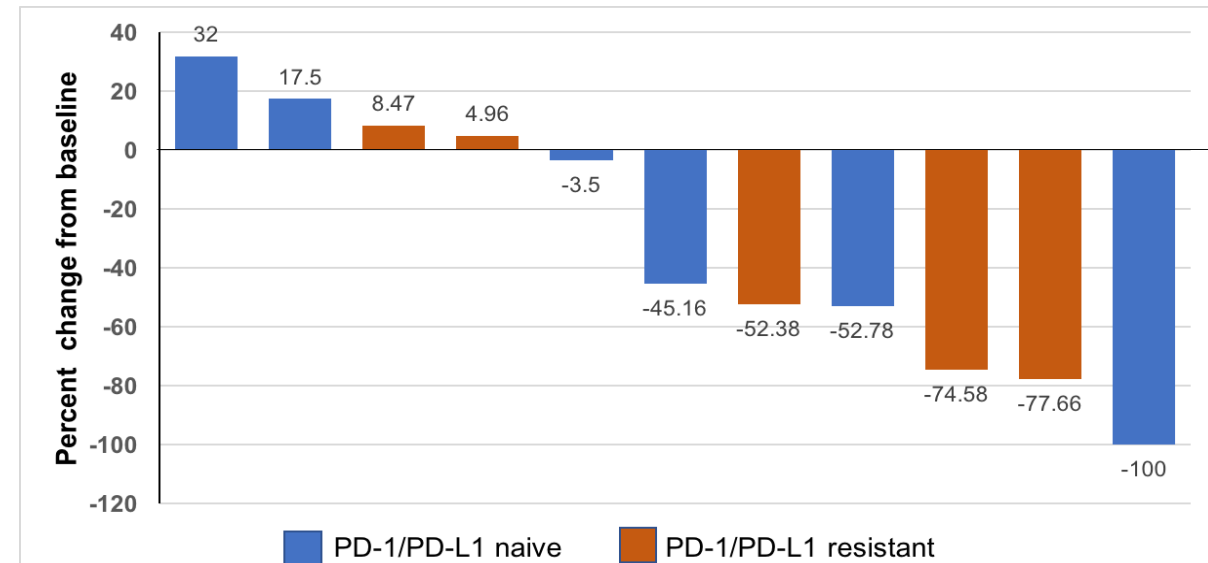
Treatment Regimen:

- First 4 cycles with Plinabulin + PD-1 + CTLA-4 inhibitors;
- Cycle 5 and later cycles: Plinabulin + PD-1 inhibitor.

13 patients were evaluable for efficacy, with 6 patients had PR (ORR 46%).

- There were 3 PRs in PD-1/PD-L1 therapy naïve patients (3/6; 50%).
- There were 3 PRs in PD-1/PD-L1 resistant patients (3/7; 43%).
- These 3 patients continued treatment for 3 months, 10 months and 42 months (still ongoing).

Waterfall plot of best overall response in target lesions compared to baseline





Regulatory Pathway & Commercial Plan



Regulatory Pathway

Near-Term

CIN: Resubmit NDA to NMPA in China;

NSCLC: Submit for NDA approval in China.

Long-Term

Seek regulatory clarity and additional approvals in the US and EU, and countries around the world.

Hengrui is the Ideal Partner for Plinabulin in Greater China

Exceptional synergy between plinabulin and Hengrui pipeline

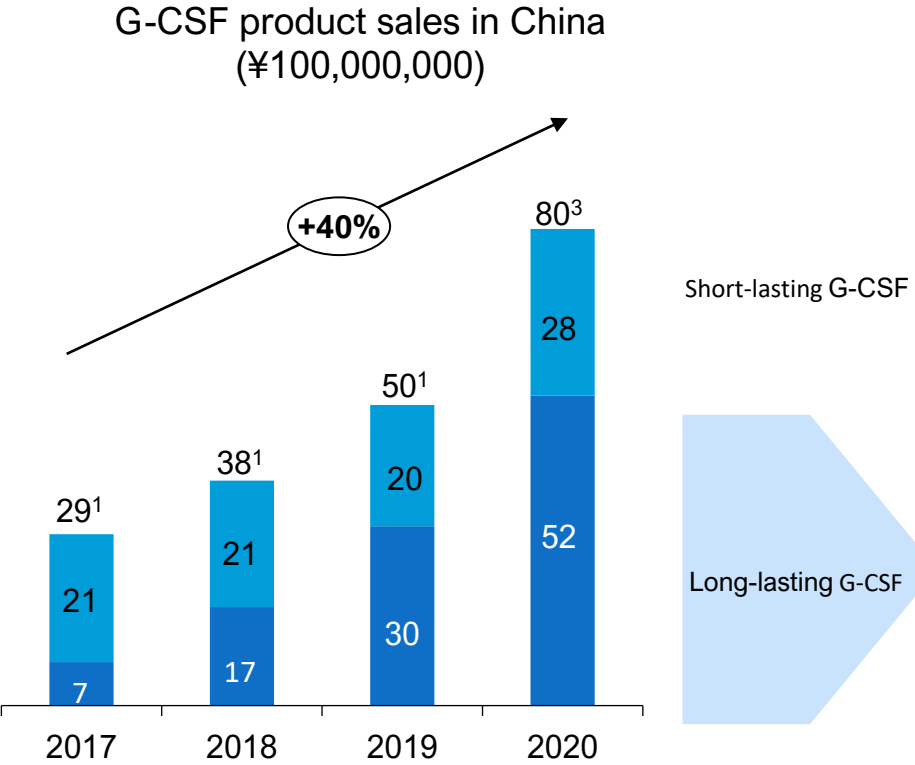
➤ Hengrui is the leader in oncology product R&D and commercialization in China

- Established in 1970; Listed on Shanghai Stock Exchange in 2000 (Shanghai stock exchange ticker: 600276)
- 24,000 employees globally, primarily in Greater China; with >10,000 people in sales and marketing in China





➤ Superior pipeline synergy with plinabulin in Greater China, allowing for faster market penetration and product combinations in new cancer indications

- Hengrui's top selling oncology products in China (sales in 2020) include:
 - ✓ **Ranks in top 3 sales in long-lasting G-CSF's¹** – (CIN indication: plinabulin + G-CSF – NDA priority review in China)
 - ✓ **#1 sales in Docetaxel¹** – (NSCLC indication: plinabulin + docetaxel – phase 3 completed meeting OS endpoint, plan for NDA filing in 1H 2022)
 - ✓ **#1 sales in PD-1 inhibitor²** – (Multiple tumor indications: plinabulin + PD-1 + chemo/radiation; plinabulin + PD-1 + CTLA-4 – phase 1/2 development)

Commercial Potential in CIN Prevention Market in China


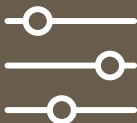





Overview of marketed long-acting G-CSF products in China²

Product	Company	Availability	Cost per cycle (Original)	Cost per cycle (Latest winning bid)	Medical Insurance
津优力	 CSPC 石药集团	2012	¥ 7,810	¥ 1,620	2017
新瑞白	 齐鲁制药	2015	¥ 3,450	¥ 1,620	2017
艾多	 恒瑞	2018	¥ 6,800	¥ 3,080	2019
申力达		2021	-	¥ 1,537	-

- Three long-lasting G-CSF were approved in China, with the current cost per cycle is 3,300-3,700 RMB; assuming an average of four cycles of chemotherapy per patient, the annual treatment cost is 13,000-15,000 RMB (or approximately \$2000-2400 USD).
- G-CSF sales in 2019 is at 5 billion RMB (\$790 M USD) with annual growth of >30%.**

Summary

	SEED: Novel TPD Platform& Pipeline	Subsidiary SEED: Target Protein Degradation (TPD) Company with Eli Lilly R&D Collaboration
	Plinabulin: Phase 3 Clinical Asset	Positive Phase 3 data in 2 indications with Lead Asset - Plinabulin
	Global Regulatory Strategy	Plinabulin: Target US, China, and EU Regulatory Agencies
	Intellectual Property	Strong IP and technology protection
	Premier Partnerships	Key commercial partnership in China for Plinabulin

thank you!

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