



# Corporate Presentation



January 2022 | NASDAQ: BYSI

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Such statements are subject to known and unknown risks, uncertainties, and other factors that may cause our or our industry’s actual results, levels of activity, performance, or achievements to be materially different from those anticipated by such statements. In some cases, you can identify forward-looking statements by terminology such as “may,” “will,” “should,” “expects,” “plans,” “anticipates,” “believes,” “estimates,” “predicts,” “potential,” “intends,” or “continue,” or the negative of these terms or other comparable terminology. Forward-looking statements contained in this presentation include, but are not limited to, (i) statements regarding the timing of anticipated clinical trials for our product candidates and our research and development programs; (ii) the timing of receipt of clinical data for our product candidates; (iii) our expectations regarding the potential safety, efficacy, or clinical utility of our product candidates; (iv) the size of patient populations targeted by our product candidates and market adoption of our product candidates by physicians and patients; and (v) the timing or likelihood of regulatory filings and approvals.

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# BeyondSpring Investment Highlights (Nasdaq: BYSI)



**Committed to raising the standard of care for cancer patients with first-in-class treatments that improve lives and clinical outcomes for millions of patients in need**

## Headquarters

New York, NY

## Lead Asset

Plinabulin for CIN: NDA under review in China, CRL received in US

Plinabulin for NSCLC: NDA filing est. 2H 2022

## Partnerships

Plinabulin in Greater China – Co-development & Commercial Partnership with Hengrui

## Affiliates

Subsidiary SEED Therapeutics (proprietary TPD Platform)  
\$800M partnership with Eli Lilly

## Cash position

\$91.6M as of September 30, 2021

## Plinabulin: “A Pipeline in a Drug”

### NSCLC

- DUBLN-3: Plinabulin + docetaxel for 2<sup>nd</sup>/3<sup>rd</sup> line NSCLC, EGFR wild type
- Positive topline Ph 3 results reported Aug. '21
- Late-breaking ESMO oral presentation Sept. '21
- NDA filing planned for 2H 2022

### CIN

- Plinabulin + G-CSF for CIN Prevention Indication
- Breakthrough Designation (BTD)
- NDA accepted with Priority Review (US and China)
- CRL from US FDA received Nov. 2021, ongoing regulatory pathway discussions
- China NMPA review ongoing

### I/O

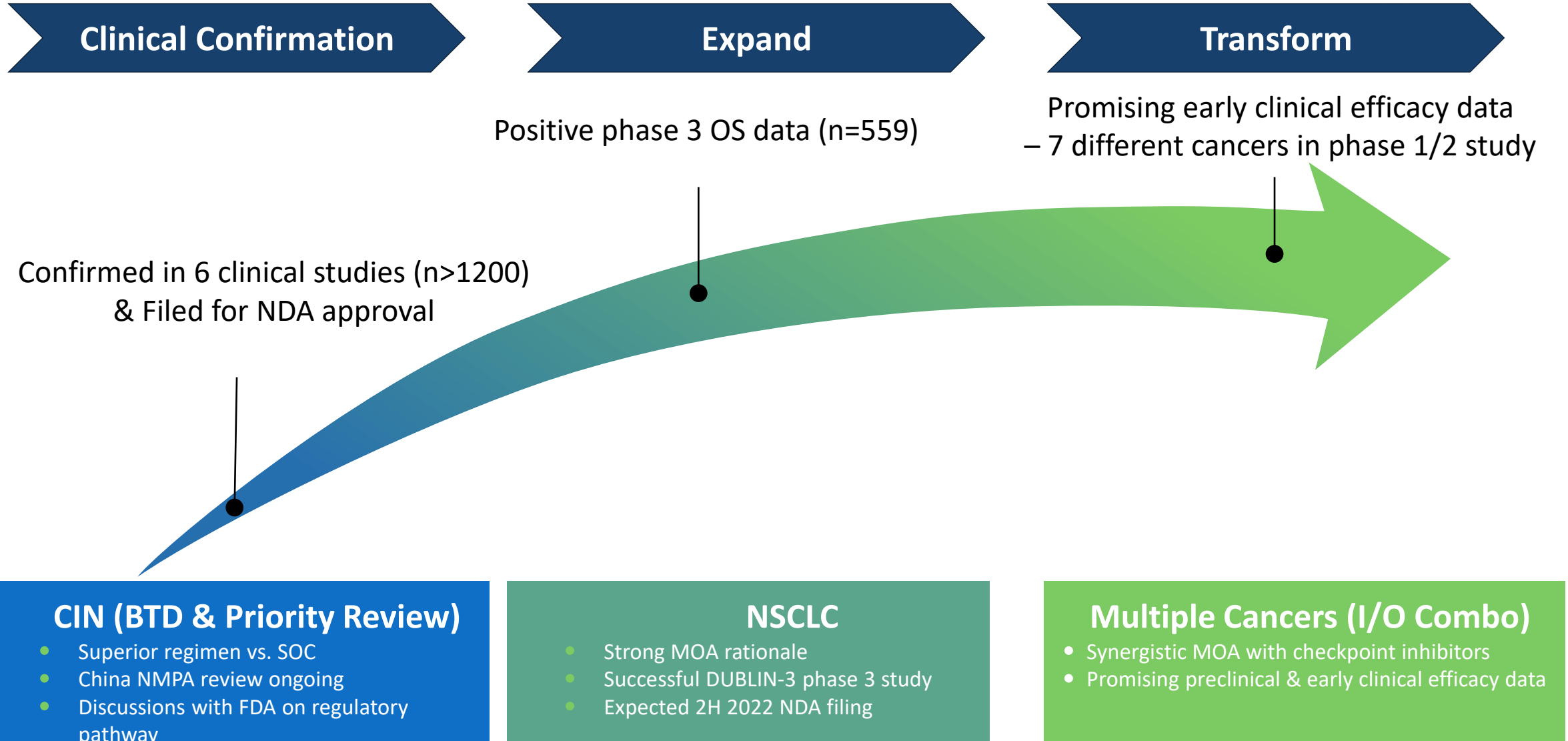
- Triple I/O combo in multiple cancer indications in early development, including 7 cancers at MD Anderson
- Efficacy data for Ph 1 SCLC at ASCO '21
- Phase 2 SCLC in I/O failed patients expected in 2H 2022

# Robust Plinabulin Pipeline: 2 Near-Term NDAs & I/O Clinical Trials

	Indication / Target	Program	Trial Name / Collaborator	Preclinical	Phase 1	Phase 2	Phase 3	Commercial Rights <sup>1</sup>	Status/Next Milestone
Late stage	NSCLC (2 <sup>nd</sup> /3 <sup>rd</sup> line)	Plinabulin + docetaxel	DUBLIN-3	Ph. 3 primary and secondary endpoints presented at ESMO '21				Global	<ul style="list-style-type: none"> <li>Positive topline Ph 3 data August '21</li> <li>Late-breaking presentation at ESMO '21</li> <li>Hengrui partnership in Greater China</li> </ul>
	CIN (All cancer, all chemo)	Plinabulin + pegfilgrastim	PROTECTIVE-1 & PROTECTIVE-2	Ph. 3 primary endpoint met Nov. '20				Global	<ul style="list-style-type: none"> <li>Priority review for NDA in US and China</li> <li>NDA under review in China; ongoing discussions with FDA on Nov '21 CRL</li> <li>Hengrui partnership in Greater China</li> </ul>
Triple Combo IO (IT)	SCLC	Plinabulin + nivolumab + ipilimumab	US sites, including Rutgers University as lead site					Global	Phase 2
	7 cancers (PD-1/PD-L1 failed)	Plinabulin + PD-1/PD-L1 + radiation/chemo	THE UNIVERSITY OF TEXAS MD Anderson Cancer Center					Global	Phase 1 in 7 cancers in June '21
Investigator-initiated IO	Oral T cell co-stimulator	BPI-002						Global	
	IKK inhibitor	BPI-003						Global	
	Oral neo-antigen generator	BPI-004						Global	
SEED Therapeutics	KRAS and additional targets	Targeted Protein Degradation (TPD, molecule glue platform)	SEED THERAPEUTICS					Global	Potential additional partnerships
	Multiple		Lilly					Global	\$800M collaboration

<sup>1</sup>Global rights to Plinabulin ex-China. 58% ownership of Chinese subsidiary, Dalian Wanchunbulin Pharmaceuticals Ltd., which owns Chinese rights to Plinabulin. BeyondSpring owns 100% of global rights to Plinabulin. SEED Therapeutics is a ~60%-owned BeyondSpring subsidiary.

# Plinabulin Franchise: “Pipeline in a Drug”





## Plinabulin: “Pipeline in a Drug”

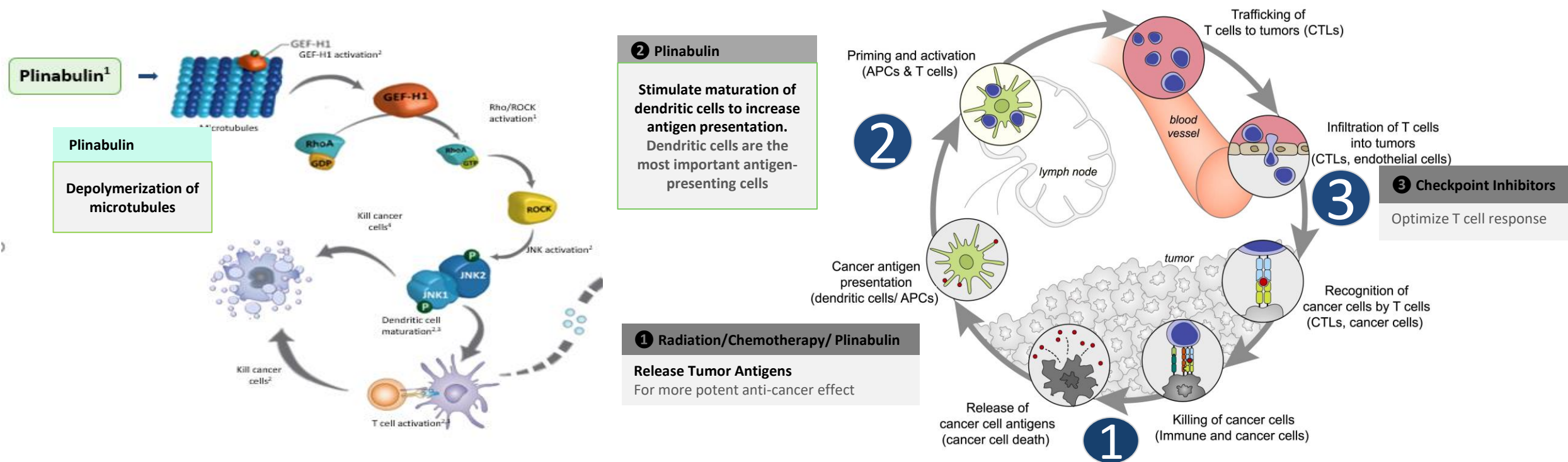
- First-in-Class, *Selective Immunomodulating Microtubule-Binding Agent (SIMBA)*



# Novel Mechanism of Action

## 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



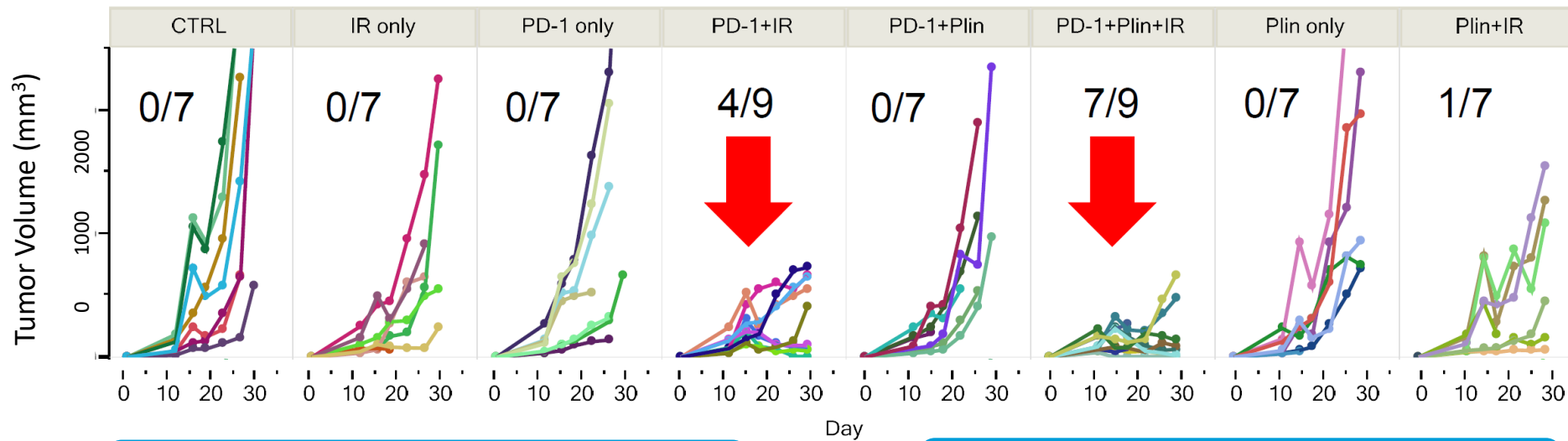
**Plinabulin Novel Target: Immune Defense Protein GEF-H1**

**1 + 2 + 3 → Optimal Immuno-Oncology Response**

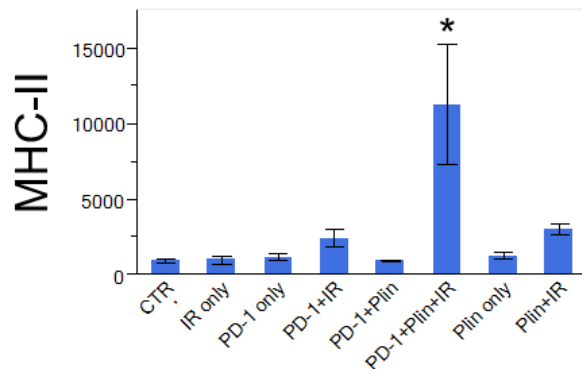
Note: <sup>1</sup> La Sala et al., 2019 Chem. <sup>2</sup> Kashyap et al., 2019 Cell Reports. <sup>3</sup> Zhang et al., 2005 Mol Cell Biol. <sup>4</sup> Singh et al., 2011 Blood. <sup>5</sup> Suwa et al., 2000 Am J Physiol Heart Circ Physiol; Ghosh et al., 2018 ACR Annual Conference; Blayney et al., Society of Leukocyte Biology. <sup>6</sup> Asensi et al., 2004 Infection and Immunity.

# Triple I/O Combo: Plinabulin + PD-1 + Radiation (IR)

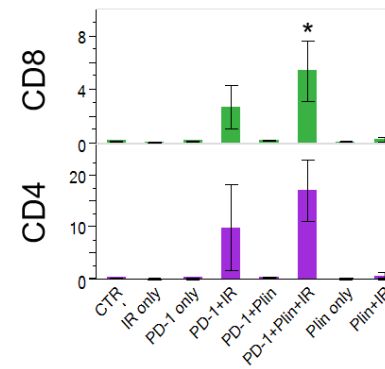
## Best Tumor Response in PD-1 Non-Responsive Tumor Model (MD Anderson)



DC activation is most dramatic in triple I/O combination



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

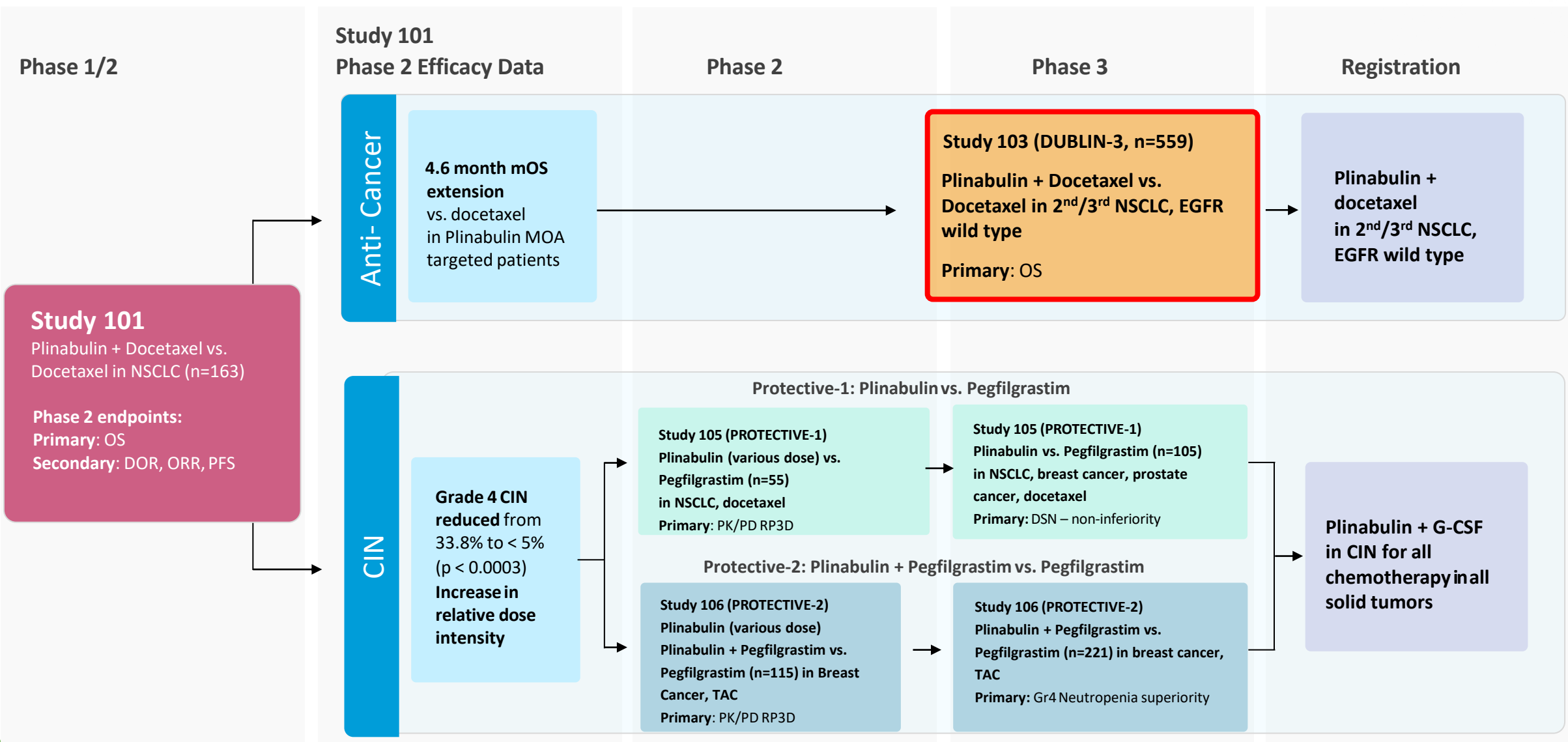


Biomarker data in tumor 30 days after drug intake

Doubled the Anti-Cancer Benefit in Tumor Reduction in Triple I/O Combo vs. PD-1+IR



# Plinabulin Clinical Development Program



# Plinabulin Opportunity



1

**Plinabulin is a novel mechanism, first-in-class immunomodulating microtubule-binding agent, complementary to existing standard of care**

2

**DUBLIN-3 provides compelling clinical data in 2L/3L NSCLC; potential to move into earlier lines of therapy and into broad range of tumor types**

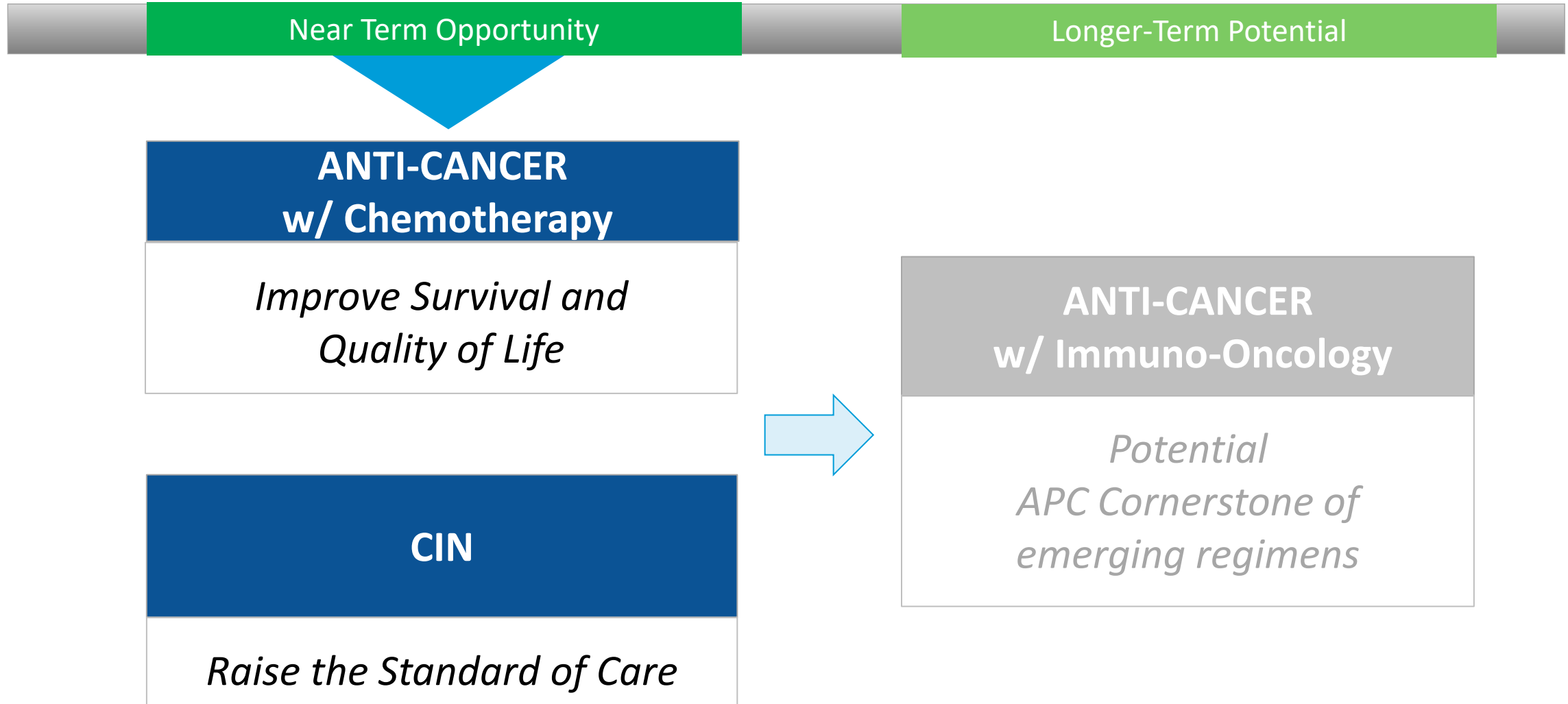
3

**Near-term revenue opportunity in China for Chemotherapy Induced Neutropenia (CIN)**

4

**Transformative potential as a cornerstone in immuno-oncology combinations**

# Delivering the Plinabulin Value Proposition



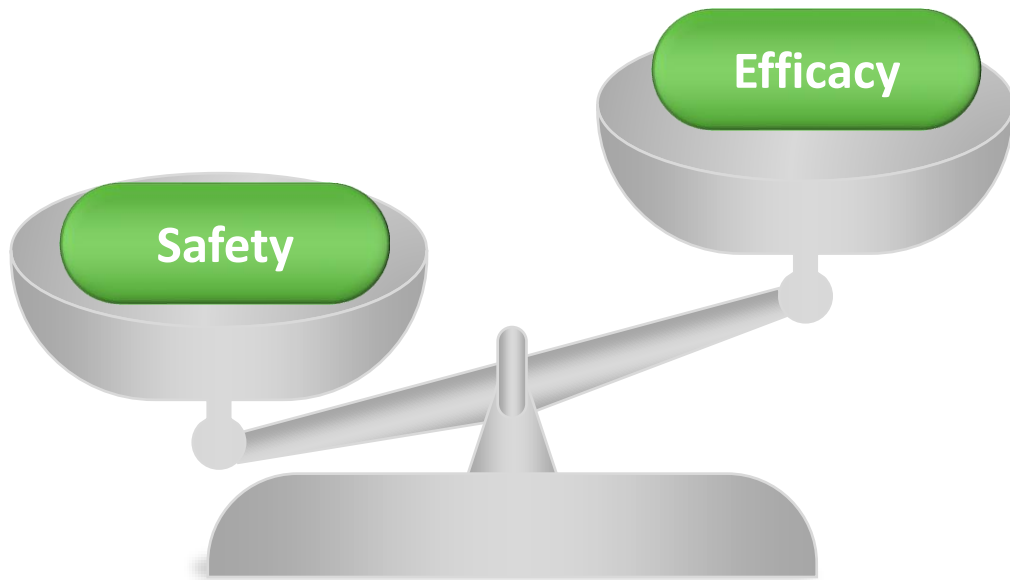


**BeyondSpring**

## Anti-Cancer with Chemotherapy



# NSCLC: Severe Unmet Medical Needs – 2<sup>nd</sup>/3<sup>rd</sup> Line, 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 docetaxel<sup>1</sup>
- Docetaxel-based Therapies (SOC)
  - Limited efficacy
  - >40% severe neutropenia

**Since nivolumab was approved 6 years ago, no new agent with novel mechanism has been approved in this indication.**

# Underserved Market: 2<sup>nd</sup>/3<sup>rd</sup> Line NSCLC Treatment

With PD-1/PD-L1 Moved To First Line, Patients are Left with Efficacy and Safety Tradeoffs and Suboptimal Regimens

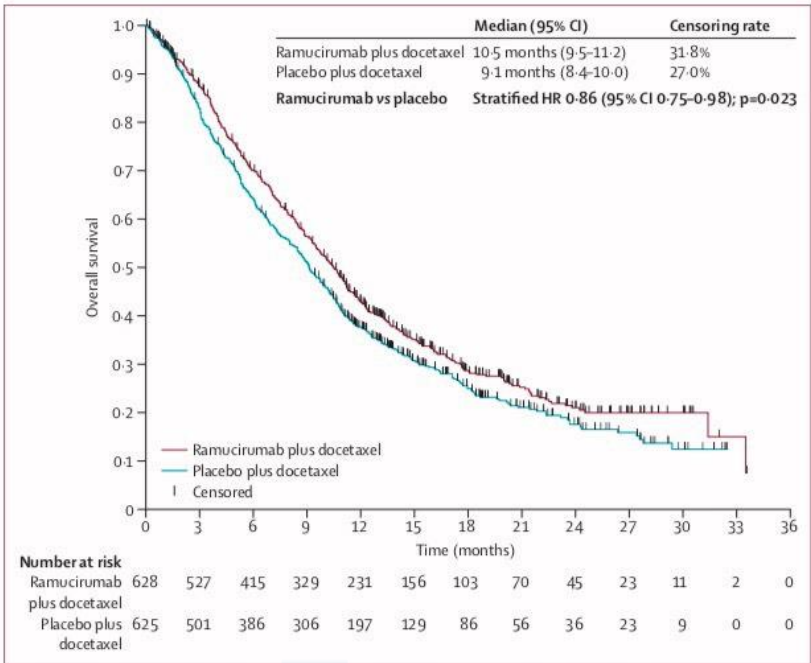
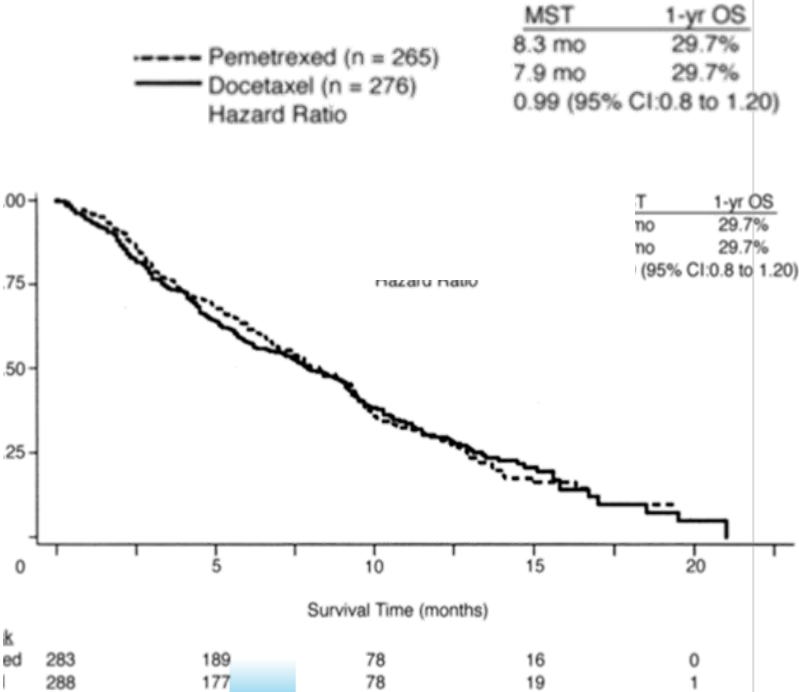


Figure 2: Kaplan-Meier estimates of overall survival in the intention-to-treat population  
HR=hazard ratio.



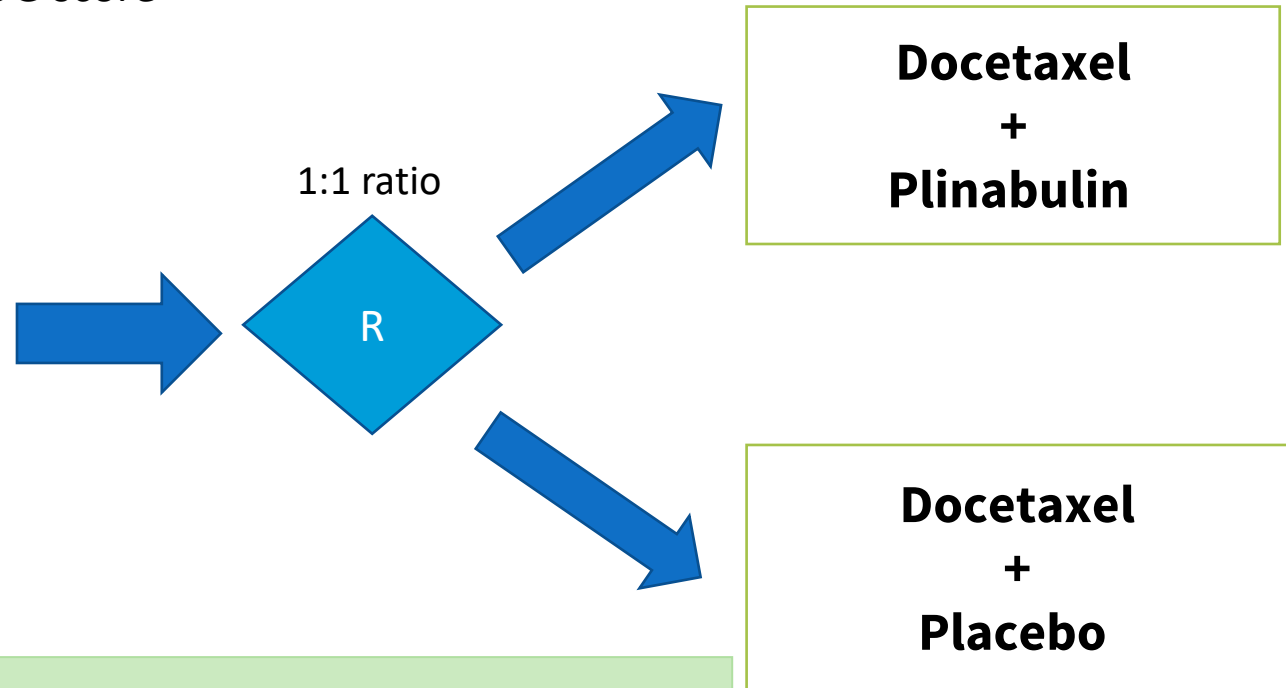
Treatment	Ramucirumab + Docetaxel vs. Docetaxel <sup>1</sup>	Pemetrexed vs Docetaxel <sup>2</sup>
Pros	Limited efficacy; OS HR: 0.86	Low CIN risk (severe neutropenia: 5.3% pemetrexed vs. 40.2% docetaxel)
Cons	High CIN risk (severe neutropenia: 49% combo vs. 39% docetaxel) Bleeding or hemorrhage: 29% combo vs. 15% in docetaxel	Low Efficacy, OS HR: 0.99 (no survival benefit vs. docetaxel)

<sup>1</sup> Lancet 384 (9944): 665-673 (2014). <sup>2</sup> JCO 22(9): 1589-1597 (2004).

# DUBLIN-3: Docetaxel + Plinabulin (DP) vs. Docetaxel + Placebo (D) in Patients With 2<sup>nd</sup>/3<sup>rd</sup> line NSCLC, EGFR wild type

Global, Randomized, Single-Blinded (blinding for patients only)  
Stratified for: Region (Asia/non-Asia), Prior Line, ECOG score  
Around 60 sites: U.S., China, and Australia  
CRO: ICON; Central Lab for PK and ANC: Covance.

- Non-squamous or squamous **NSCLC**
- Stage IIIb/IV
- ECOG performance status  $\leq 2$
- Progression during or after treatment with one or two treatment regimen containing platinum
- Must have at least one measurable lung lesion
- Prior checkpoint inhibitor therapy allowed

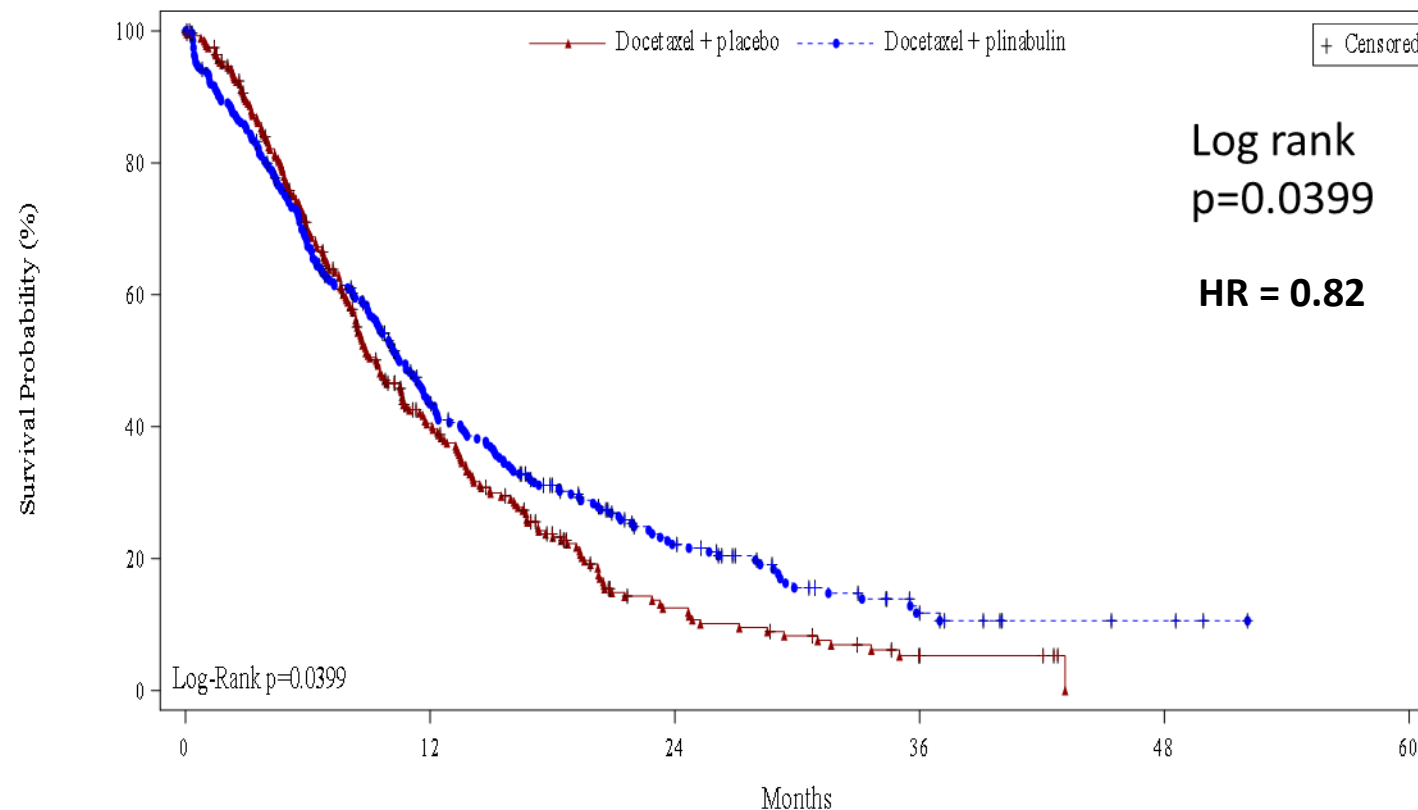


**Primary Endpoint:** Overall Survival

**Secondary Endpoints:**

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

# Met Primary Objective in Overall Survival (OS)



Subjects at risk	
Docetaxel + placebo	281
Docetaxel + plinabulin	278

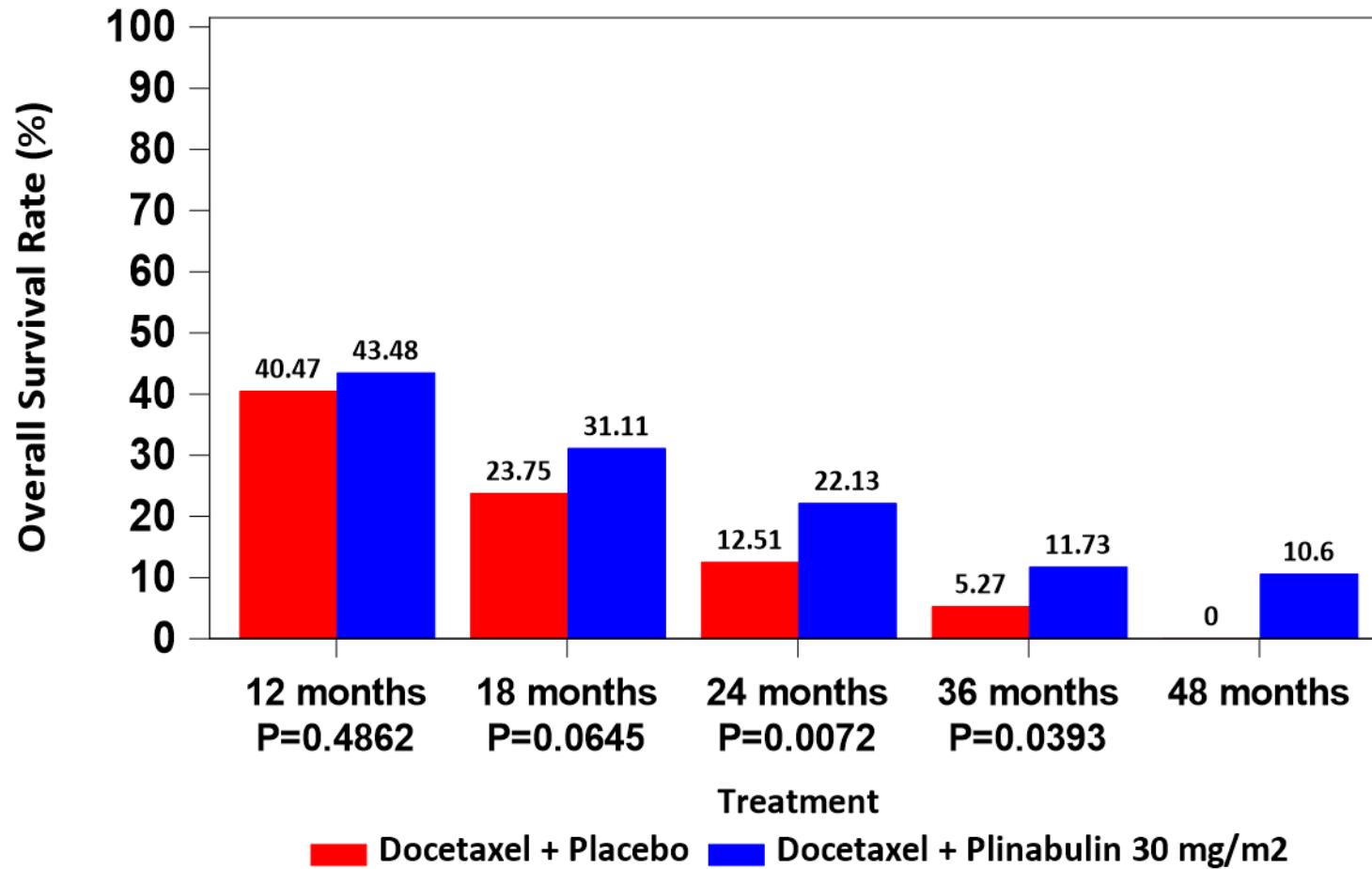
97	21	4	0
108	41	10	3
			0

ITT population	Docetaxel (75 mg/m <sup>2</sup> ) N=281	Plinabulin (30 mg/m <sup>2</sup> ) + Docetaxel (75 mg/m <sup>2</sup> ) 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)

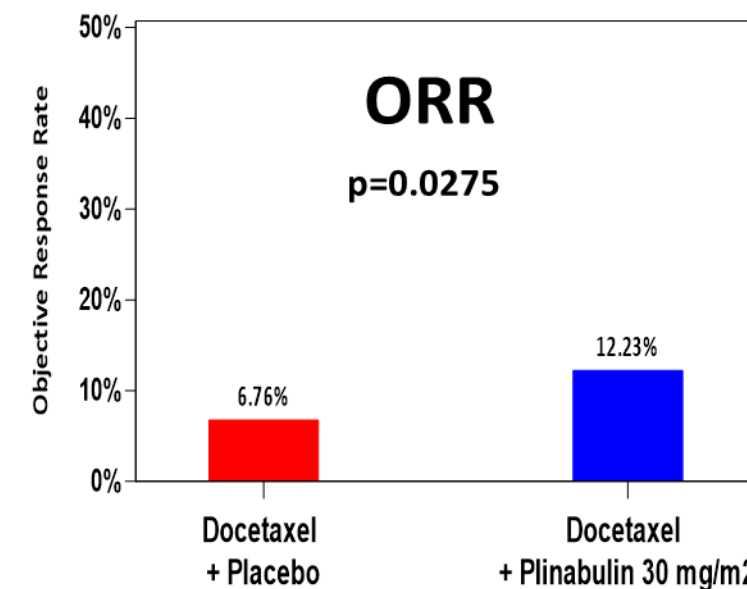
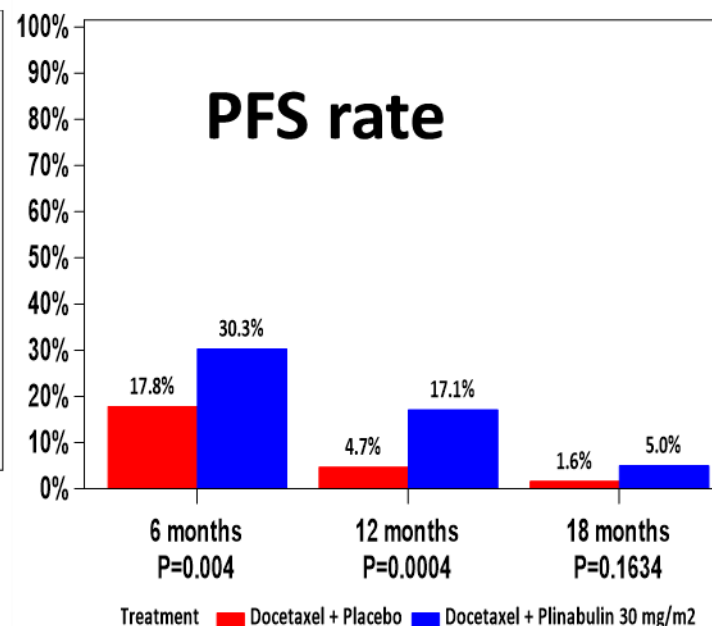
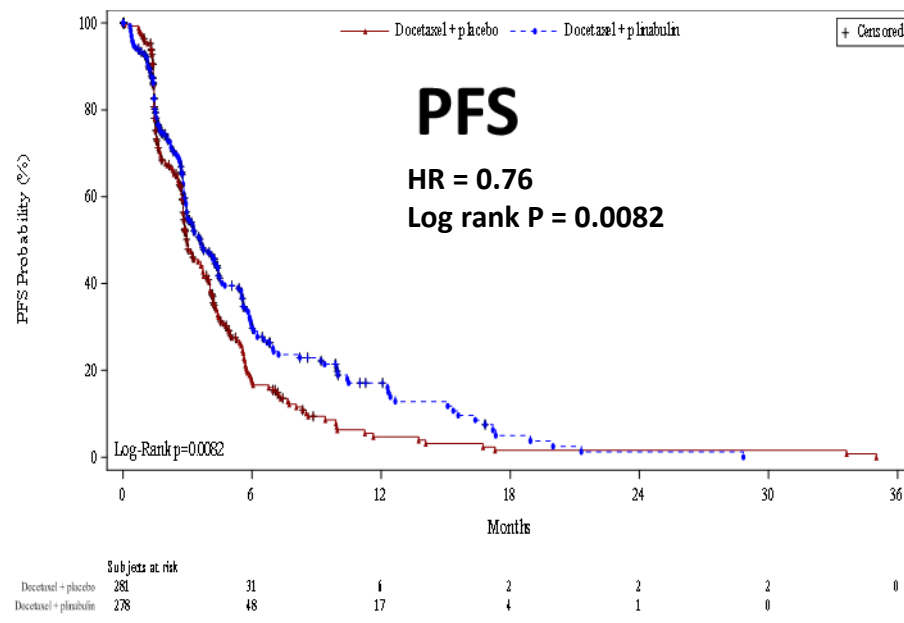


# Significantly Increase Long-term OS Rate at 24 M and 36 M

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



# Significant Improvement in PFS, Double ORR



**Secondary Endpoint  
(ITT population)**

**Docetaxel(75 mg/m2)  
N=281**

**Plinabulin (30 mg/m2)  
+ Docetaxel (75 mg/m2) N=278**

**Mean PFS (SE): 4.4 (0.3)**

**Mean PFS (SE): 6.0 (0.4); p=0.0062**

**PFS\* (months or M)**

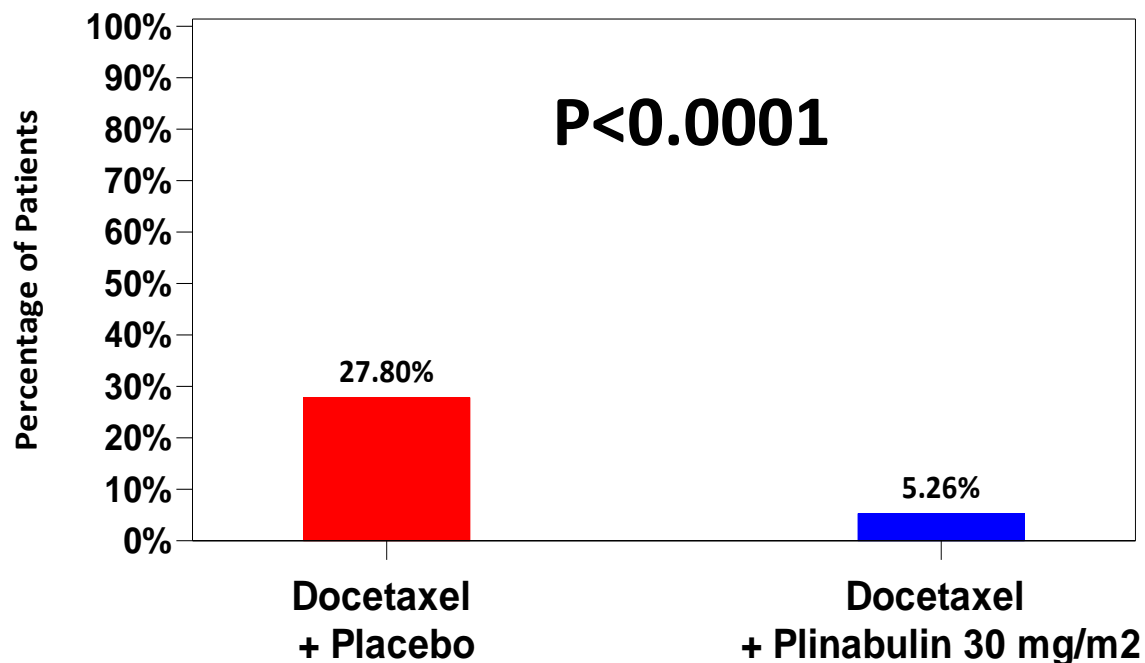
**Median PFS (95% CI): 3.0 (2.8, 3.7)**

**Median PFS (95% CI): 3.6 (3.0, 4.4),  
Log-rank p=0.0082; HR=0.76 (0.63, 0.93)**

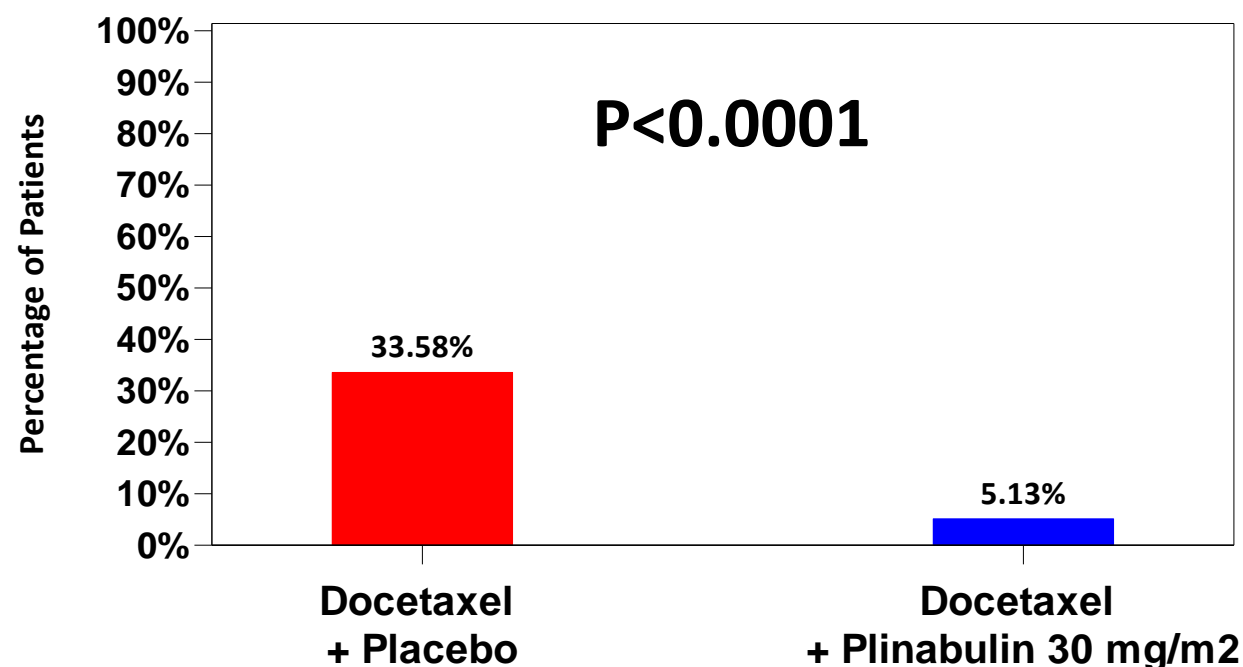
\*Investigator-Assessed

# Significant Reduction in Grade 4 Neutropenia Cycle 1 Day 8 and All Cycles Day 8

Grade 4 neutropenia, Cycle 1 Day 8



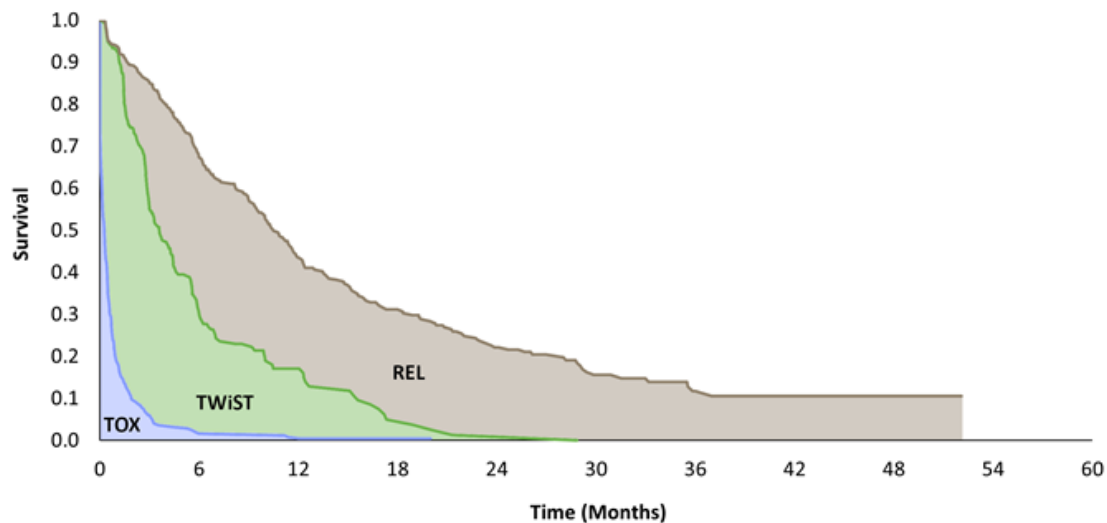
Grade 4 neutropenia, All Cycles Day 8



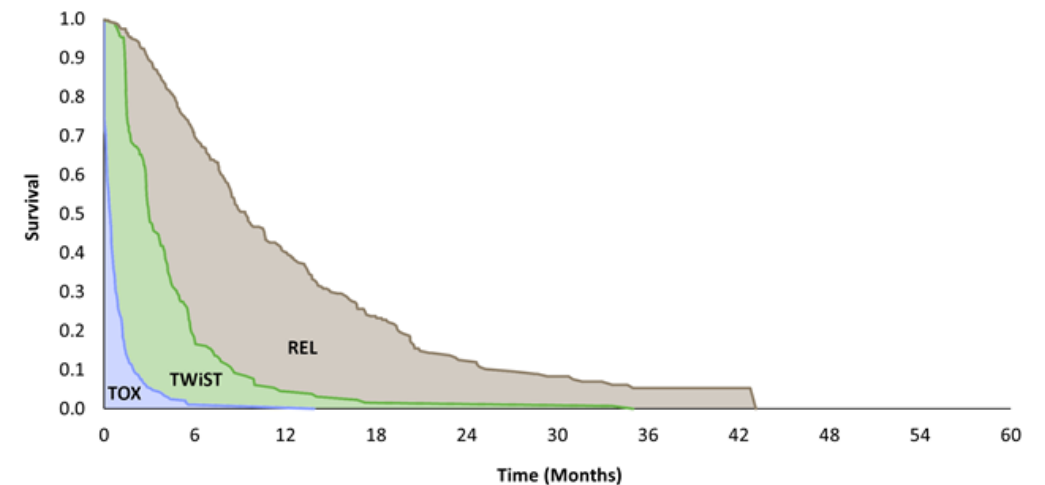
# Significant Improve Quality of Life Benefit

## - 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



**Improvement >18% in Q-TWiST, which is clinically meaningful.**

# Dublin-3: Superior Efficacy (OS, PFS, ORR) and Significant Reduction in Grade 4 CIN (DP vs. D)

Primary Endpoint	Docetaxel (75 mg/m2) N=281	Plinabulin (30 mg/m2) + Docetaxel (75 mg/m2) N=278
OS (months or M)	Mean 12.77 M (0.676)  Median 9.4 M (8.4, 10.7)	Mean 15.08 M (0.848); p=0.03 Median 10.5 M (9.3, 11.9), Log-rank p=0.0399 HR = 0.82 (0.68 – 0.99)

**Doubling OS rate in 24 M, 36 M, and 10.6% >48 M OS rate – Plinabulin Immune Durable Anti-cancer Benefit**

Secondary Endpoint - Hierarchy Order		
ORR (%)	6.76%	12.23%; p=0.0275
PFS (months or M)	Mean 4.4 M (0.3) Median 3.0 M (2.8, 3.7)	6.0 M (0.4); p=0.006 3.6 M (3.0, 4.4), Log-rank p=0.008 HR = 0.76 (0.63, 0.93)
Grade 4 neutropenia, cycle 1 Day 8 (%)	27.8%	5.3%; p<0.0001
24 Month OS Rate (%)	12.5%	22.1%; p = 0.0072
36 Month OS Rate (%)	5.3%	11.7%; p = 0.0393
48 Month OS Rate (%) - exploratory	0%	10.6%; p value cannot be calculated
Q-TWiST		12.40 M (10.99, 13.83)
• Relative Gain to Q-TWiST	10.47 M (9.34, 11.63)	18.43% (2.07%, 37.20%); p=0.0393

# NSCLC: Favorable Benefit/Risk Profile vs. Standard of Care (SOC)

(Plinabulin + Docetaxel for 2<sup>nd</sup>/3<sup>rd</sup> line NSCLC, EGFR wild type)

## Next steps:

- Discuss filing plan with FDA & NMPA with potential filing 2H 2022
- Consistent long survival trend in PD-1/PD-L1 exposed patients and in Western patients

### Docetaxel (Current SOC)

- Modest survival benefit
- Severe safety concerns, e.g., CIN
- Poor Quality of Life

### Plinabulin - Docetaxel Combination

- **Survival benefit**, doubling 2-year & 3-year OS rate; 4-year OS rate 10.6%
- **Favorable safety profile**, including significant CIN reduction
- **Improved quality of life** (Clinically meaningful Q-TWiST benefit)

- **Lower Grade 4 AE frequency and a shift to lower grade AE**
- **No unexpected AE concerns were identified**



## Chemotherapy Induced Neutropenia (CIN)

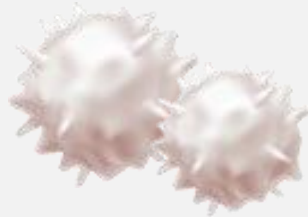




**Despite widespread G-CSF use, CIN #1 reason for FN, ER visits, hospitalization, sepsis, mortality, and chemotherapy disruption<sup>1</sup>**

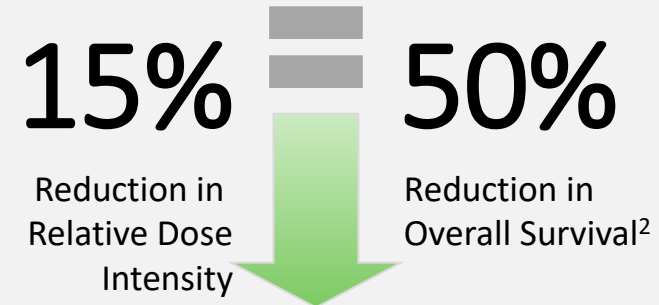
## Short-term Outcome Benefit

**G-CSF monotherapy is suboptimal and leaves a significant clinical gap**



## Long-term Outcome Benefit

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



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

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

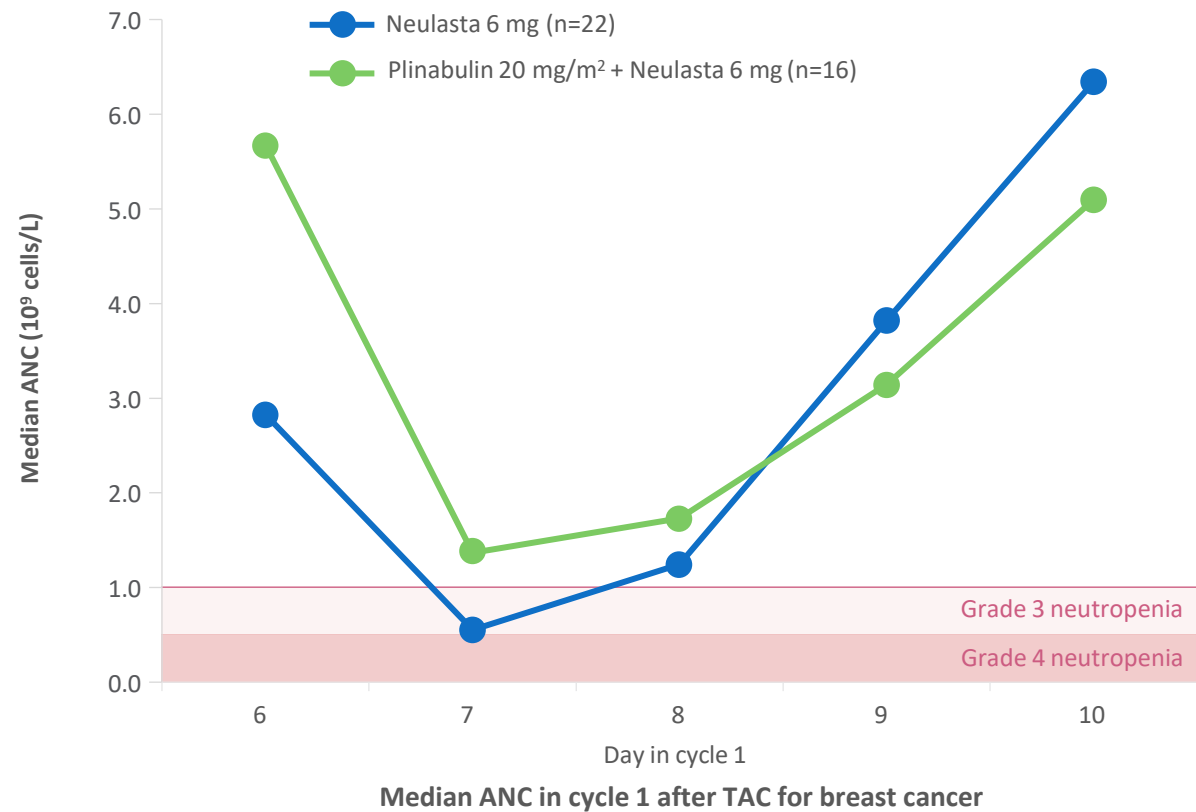


# Plinabulin + G-CSF Combination Addresses Unmet Medical Need

CIN

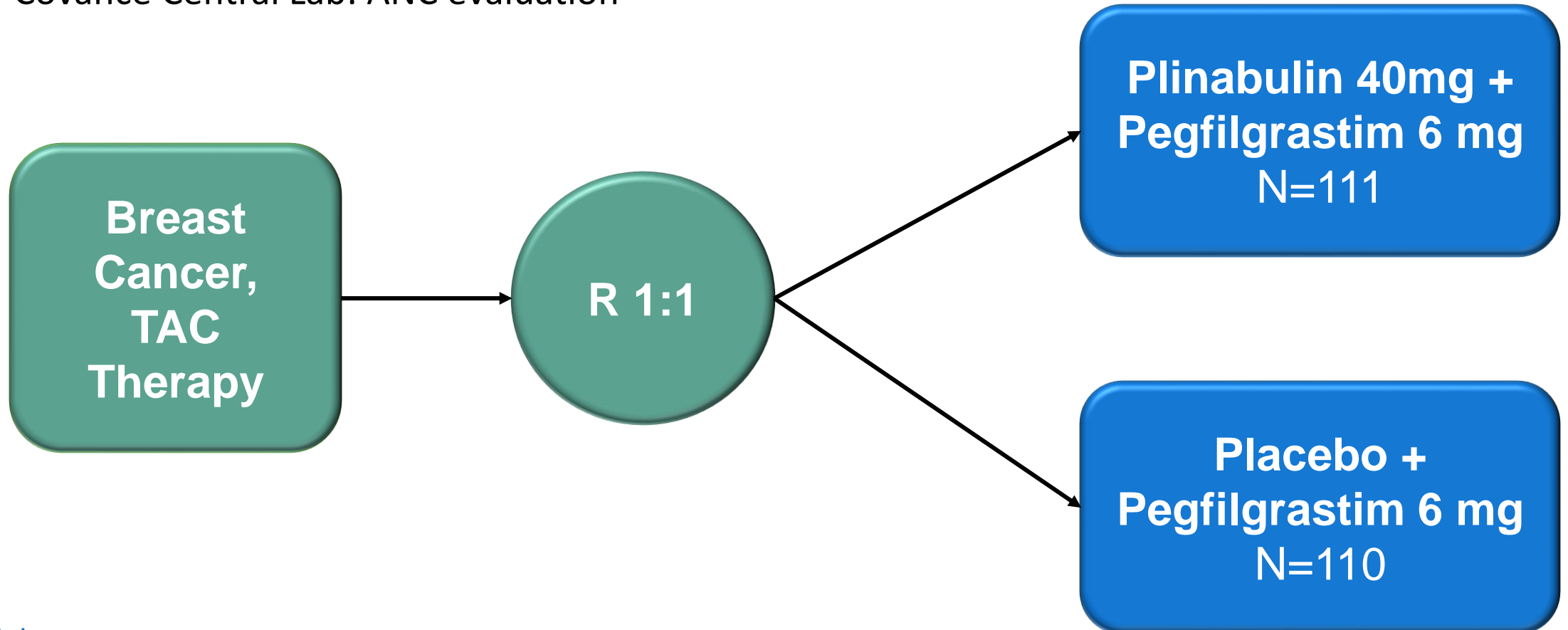
**Plinabulin is the only product – in development –  
that has demonstrated the potential to elevate the standard of care (SOC) to prevent CIN**

- Breakthrough Therapy Designation: Unmet need, and potential superior regimen vs. SOC recognized by FDA and NMPA
- Plinabulin prevents CIN in week 1; and G-CSF prevents CIN in week 2
- Combination maximizes the prevention of CIN for the full cycle

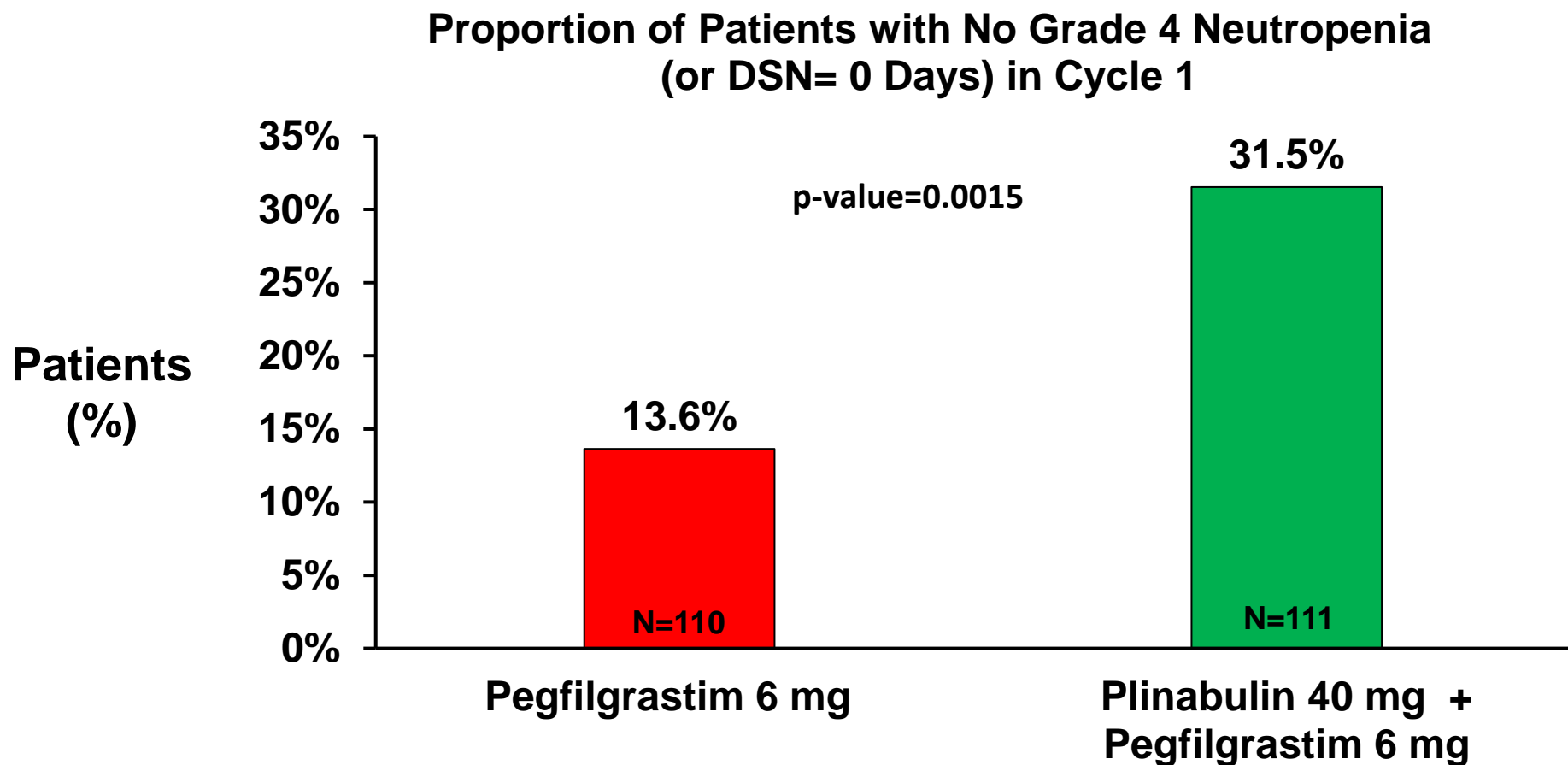


# Protective-2 (Study 106) Ph 3: Registration Study Design

- Double blind, global study (19 centers); 4 cycles
- Covance: CRO
- Covance Central Lab: ANC evaluation



# PROTECTIVE-2 Phase 3: Primary Endpoint Met



Grade 4 neutropenia ( $ANC < 0.5 \times 10^9$  cells/L) during Cycle 1 was prevented (DSN=0) for more than twice as many subjects in the plinabulin/pegfilgrastim arm than subjects in the pegfilgrastim arm

# Favorable Benefit/Risk Ratio (Plinabulin + G-CSF vs. G-CSF alone)

<u>Improved Efficacy (ANC based in Cycle 1) – 106 Phase 3</u>	<u>Improved Efficacy (FN) – 106 Phase 3</u>	<u>Favorable Safety – 106 Phase 2+3</u>
<p><b>No Grade 4 Neutropenia (primary endpoint)</b></p> <ul style="list-style-type: none"> <li>31.5% vs. 13.6% (incidence), p=0.0015</li> </ul> <p><b>No Grade 3/4 Neutropenia</b></p> <ul style="list-style-type: none"> <li>4.55% vs. 20.72% (incidence), p=0.0003</li> </ul> <p><b>Mean ANC Nadir</b></p> <ul style="list-style-type: none"> <li>0.54 vs. 0.31 (<math>\times 10^9</math> cells/L), p=0.0002</li> </ul> <p><b>DSN Cycle 1 day 1-8</b></p> <ul style="list-style-type: none"> <li>1.1 day vs. 1.4 day, p=0.0065</li> </ul> <p><b>DSN Cycle 1</b></p> <ul style="list-style-type: none"> <li>1.2 day vs. 1.5 day, p=0.0324</li> </ul> <p><b>Profound Neutropenia</b></p> <ul style="list-style-type: none"> <li>21.6% vs. 46.4% (incidence), p=0.0001</li> <li>0.3 day vs. 0.6 day (duration), p=0.0004</li> </ul>	<p><b>FN</b></p> <ul style="list-style-type: none"> <li>3.6% vs. 6.3% (incidence)</li> <li>0.9% vs. 3.6% (grade 4 incidence)</li> <li>1.25 day vs. 2.28 day (duration)</li> </ul> <p><b>Hospitalization for FN patients</b></p> <ul style="list-style-type: none"> <li>2.7% vs. 6.3%</li> <li>3.75 day vs. 7.14 day (duration)</li> </ul> <p><b>Change of Chemo dose/regimen in later cycles</b></p> <ul style="list-style-type: none"> <li>2.7% vs 6.3%</li> </ul>	<p><b>Grade 4 TEAE</b></p> <ul style="list-style-type: none"> <li>20% less Grade 4 TEAEs in the combination (55.9%) compared to pegfilgrastim alone (75.8%)</li> </ul> <p><b>SAEs</b></p> <ul style="list-style-type: none"> <li>Higher SAE frequency, however, less Grade 4 and more Grade 3 events</li> </ul> <p><b>AEs leading to discontinuation</b></p> <ul style="list-style-type: none"> <li>Similar frequency, mostly single events</li> </ul> <p><b>Bone pain (AE)</b></p> <ul style="list-style-type: none"> <li>6.3% bone pain in the combination vs. 28.0% in pegfilgrastim</li> </ul> <p><b>Low grade GI track side effects and transient hypertension</b></p>

## Seeking Approval for “Plinabulin + G-CSF Combination” in CIN Prevention

### Supporting Studies

#### Plinabulin vs. placebo (Dublin-3, phase 3)

- Grade 4 reduction highly statistically significant (Study 101 and DUBLIN-3,  $p < 0.0003$  and  $p < 0.0001$  respectively)

### Registration Study

#### Plinabulin + G-CSF combo vs. G-CSF mono (Protective-2, phase 3)

- Superior CIN prevention in primary and key secondary endpoints

**MOA support from 5 additional studies:**

**Plinabulin early onset in Week 1, G-CSF effect in Week 2 → combination provides maximum CIN prevention**

### Supporting Studies

#### Plinabulin vs. G-CSF (Protective-1, phase 2 & 3)

- Non-inferior CIN activity
- Superior adverse event profile: limited bone pain, limited platelet reduction, and limited immune suppression<sup>1</sup>

**Plinabulin shown to statistically reduce Grade 4 neutropenia in 6 clinical trials (1,200+ patients); 700+ cancer patients treated with Plinabulin (various doses)**



## Plinabulin + G-CSF Combination

- Commercial Plan in CIN Prevention



# Chemotherapy Without Compromise: Turning the 4 Ds into the 4 Ss



**DECREASED**  
recommended dose



**STABLE DOSE**  
maintaining  $\geq 85\%$



**DELAYED**  
cycles



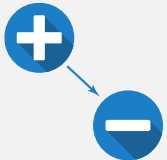
**SUSTAINED CYCLES**  
cycles on time



**DISCONTINUED**  
chemotherapy



**STAY THE COURSE**  
complete all cycles



**DOWNGRADE**  
chemotherapy regimen



**STRONGEST REGIMEN**  
of chemotherapy

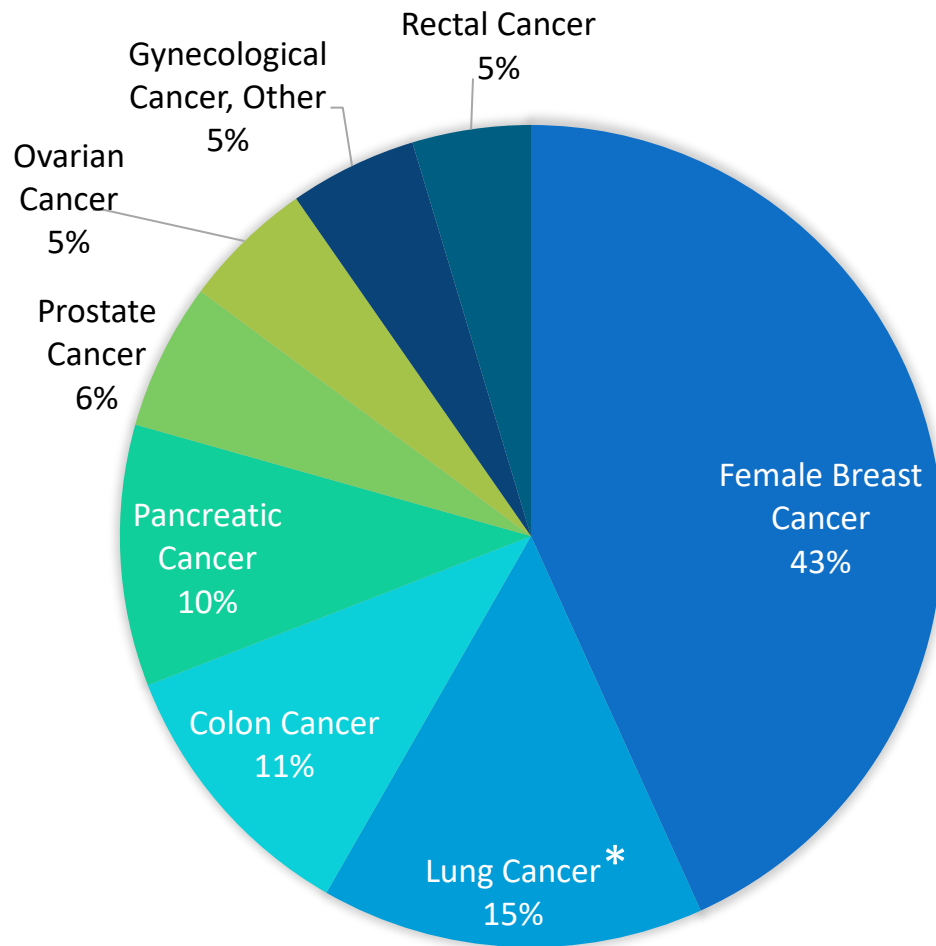
## Plinabulin + G-CSF

- Differentiated clinical profile, potential to improve SOC
- Greater clinical control
- Improved outcomes

# Plinabulin Has Potential Use Across the Spectrum of Solid Tumors

CIN

## G-CSF Administrations: Solid Tumor



## G-CSF Use by Cancer type:

- Improved control of CIN with Plinabulin can prove important in cancers with more aggressive therapeutic approaches
- Plinabulin's potential broad label has applicability in a broad array of cancer types and with a wide variety of chemotherapies

\* SCLC ~15% of all lung cancer diagnoses

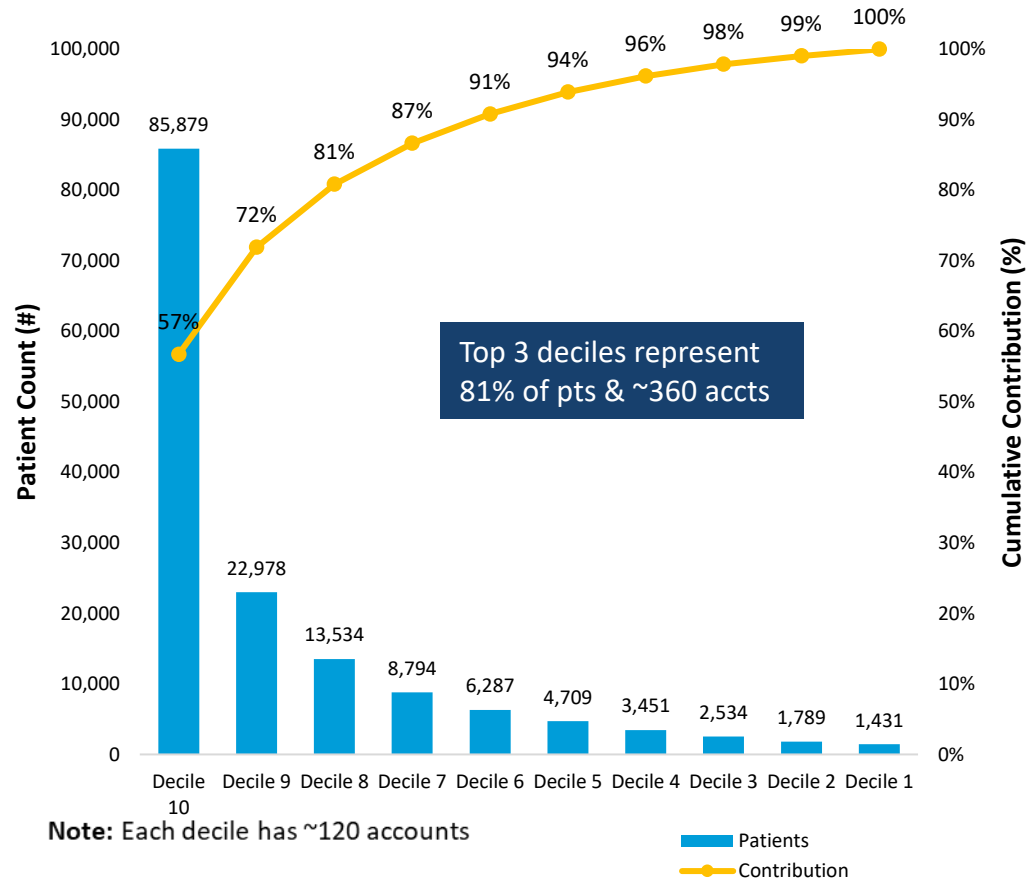
Source: IQVIA G-CSF Tumor Analysis; 7/19 – 6/20



# Efficient Commercialization Plan – Concentrated Accounts, Small Salesforce

CIN

Pegfilgrastim Patient Distribution<sup>1</sup> – Top 1200 Centers



## FOCUS: Elevating the SOC in Chemotherapy

Field Staff of approx. 83, including 60 sales reps



<sup>1</sup> Komodo Health, Inc. Komodo Health, Inc. makes no representation or warranty as to the accuracy or completeness of the data ("Komodo Materials") set forth herein and shall have, and accept, no liability of any kind, whether in contract, tort (including negligence) or otherwise, to any third party arising from or related to use of the Komodo Materials by BeyondSpring Inc. Any use which BeyondSpring Inc. or a third party makes of the Komodo Materials, or any reliance on it, or decisions to be made based on it, are the sole responsibilities of BeyondSpring Inc. and such third party. In no way shall any data appearing in the Komodo Materials amount to any form of prediction of future events or circumstances and no such reliance may be inferred or implied.

# Breakthrough Therapy Designation with Priority Review: Potential to Elevate Standard of Care for CIN Prevention

CIN

## Opportunity

- ✓ Market size
- ✓ Market growth
- ✓ NCCN guideline change
- ✓ Managed care coverage

## Unmet need

- ✓ Grade 4 neutropenia complications
- ✓ CIN: #1 reason for therapy change (4Ds)
- ✓ G-CSF – excellent drug; can't cover early cycle challenges
- ✓ 4Ds result in reduced OS

## Product differentiation

Plinabulin + G-CSF addresses 3 oncologist needs:

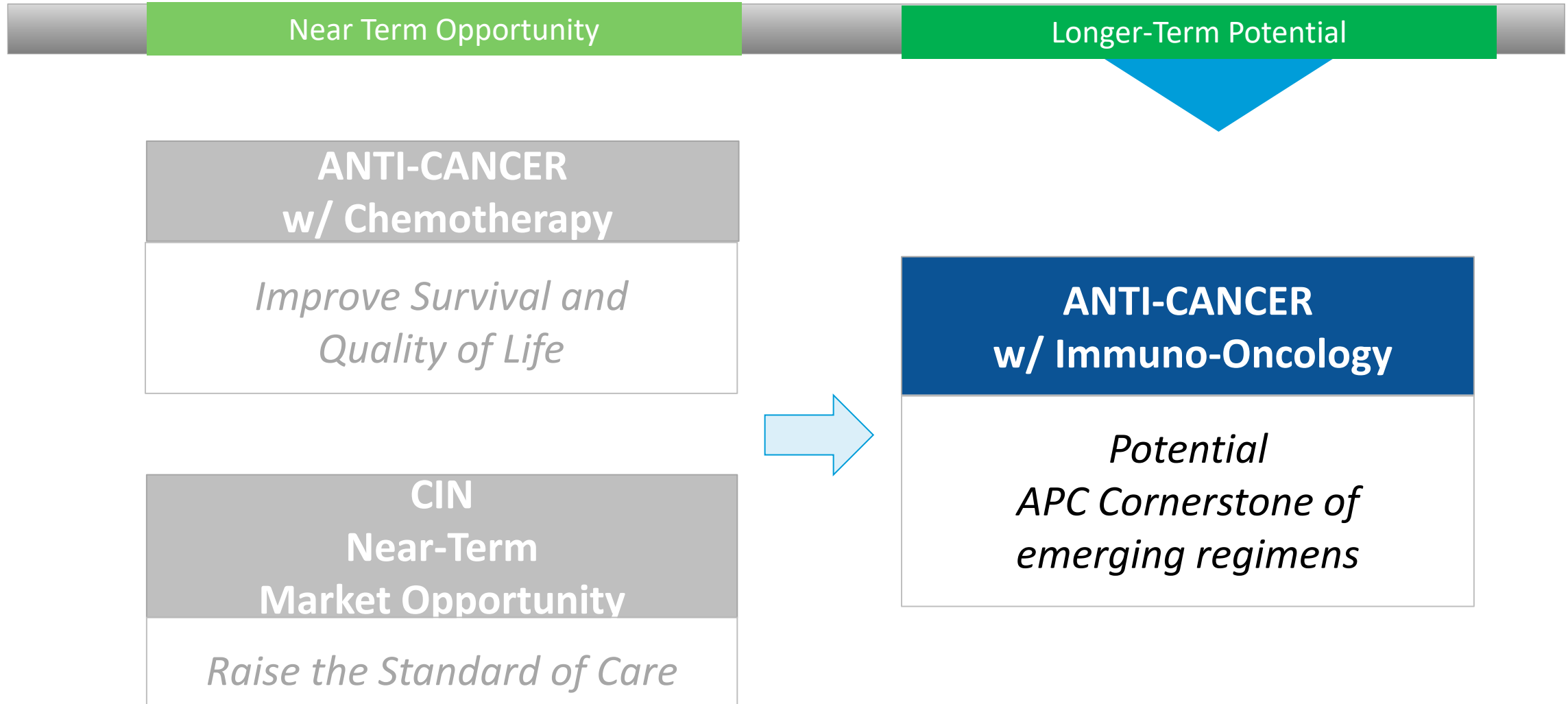
- ✓ Keeps ANC out of the danger zone and thus ***less*** severe CIN, FN, ER visits and hospitalization
- ✓ Significantly reduces bone pain
- ✓ Maintains chemo regimen

## Plinabulin+ G-CSF has the potential to:

- Address the oncologist's desire for increased control
- Reduce patient anxiety and fears associated with interrupted therapy and adverse events
- Deliver improved chemotherapy care with the potential for improved long-term outcomes
- Clear differentiation from G-CSF provides rationale for superior pricing vs G-CSF in CIN

**Anti-cancer potential – Opportunity for premium pricing and deeper market penetration**

# Delivering the Plinabulin Value Proposition



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

I/O

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

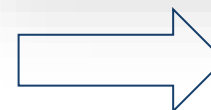


Potential to greatly expand  
the addressable market

## Current Severe Unmet Medical Needs

- PD-1/PD-L1 resistant patients need later line therapies
- PD-1 + chemo double efficacy of PD-1, but with CIN risk
- PD-1 or PD-1+CTLA-4 with high ir-SAE
- PD-1/PD-L1 non-responsive tumor;
- Patients who cannot use PD-1/PD-L1

+“Easy-to-use”  
APC Inducer



## 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

# Plinabulin in Triple Combo Development for Multiple Cancer Indications I/O in PD-1/PD-L1 Failed Patients

	Indication / Target	Program	Trial Name / Collaborator	Commercial Rights	Status
Triple Combo IO (IIT)	SCLC Checkpoint naïve and checkpoint refractory patients	Plinabulin + Nivolumab (PD-1) + Ipilimumab (CTLA-4)	7 US sites, including Rutgers University as lead center (Big Ten)	Global	Phase 1 completed, Presented at ASCO June 2021
	SCLC Checkpoint refractory patients	Plinabulin + Nivolumab (PD-1) + Ipilimumab (CTLA-4)	Big Ten Study	Global	Phase 2
	7 Cancers* PD-1/PDL1 failed pts	Plinabulin + PD- 1/PD-L1 + radiation/chemo	MD Anderson	Global	Initiated Phase 1 in 7 cancers in June 2021

# Efficacy Analysis (Phase I) Plinabulin + Nivolumab + Ipilimumab in SCLC

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

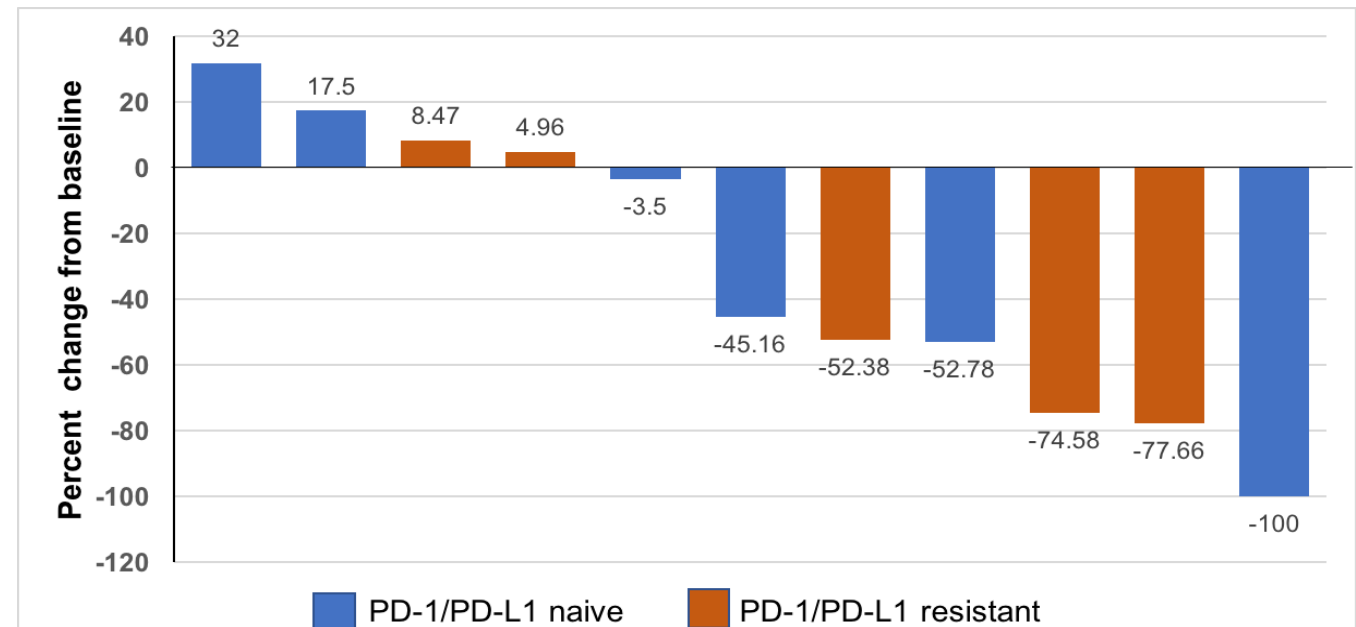
\*PR –Partial Response - RESIST 1.1 : At least a 30% decrease in the sum of diameters of target lesions, taking as reference the baseline sum diameters.

## ❖ 13 patients were evaluable for efficacy

- 1 withdrew consent.
- 1 death from unrelated cause.
- 1 replaced for DLT.

## ❖ 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, 5 months (still on treatment) and 18 months.



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

# Plinabulin as a Potential Synergistic “Cornerstone” Agent in I/O Therapy

I/O

## Data

- High response rate to previous CPI failures (43%)
- Improved Anti-cancer Response (46% ORR vs. 12-23% CPI)
- Durable response (1 pt on combo for 18 M vs. PFS 1.4-2.6 M for CPI)

## Conclusion

- **Immune system re-sensitized**
- **Increased antigen presentation** simulates T cell activation
- Immune response contributes to **long treatment duration**

Plinabulin reduces Immune related AE of checkpoint inhibitors.



**BeyondSpring**

## Corporate Highlights





# Plinabulin: Hengrui and Wanchunbulin Partnership in Greater China

(BeyondSpring Inc. owns 58% of Wanchunbulin)



**Hengrui is the oncology leader in China, with great synergies with Plinabulin**  
**- Manages commercialization risk and optimizes return on plinabulin franchise**

## Hengrui: Plinabulin Rights in Greater China

- Exclusive commercialization of all indications
- Receives fixed % of net sales
- Co-develops additional indications; Wanchunbulin leads clinical protocol design and development

## Terms (est. USD\*)

- Wanchunbulin receives \$30M upfront + up to \$170M in milestones
- Wanchunbulin books sales proceeds, retains significant fixed % of net sales
- Hengrui pays 100% commercial and 50% development costs for new indications
- Wanchunbulin retains manufacturing control & pays for 100% COGS
- Hengrui invests \$15M equity in Wanchunbulin at \$560M valuation

\* \$1 USD = 6.47 RMB

# SEED Therapeutics Subsidiary – Pipeline Potential



**SEED: Subsidiary pursuing "Molecular Glue" targeted protein degradation to degrade disease-causing proteins previously believed to be undruggable**

- \$800M collaboration with Eli Lilly on three targets
- Own targets (e.g., KRAS)
- Structure conducive to having additional collaborations

# BeyondSpring: Key Highlights



## Mission

Committed to raising the standard of care for cancer with first-in-class treatments that improve lives and clinical outcomes for millions of patients in need

### Near-term Global Market Opportunities

#### Plinabulin: Raising SOC in NSCLC & CIN

- ✓ First-in-Class Selective Immunomodulating Microtubule-Binding Agent (SIMBA)
- ✓ IP through 2036 in 36 jurisdictions

#### NSCLC: Combo with docetaxel – Global Market \$30+ B

- ✓ Positive Final Topline Ph 3 OS data 08/2021, ESMO late breaking oral presentation 09/2021
- ✓ Potential NDA submission in 2H 2022

#### CIN: Combo with G-CSF (superior efficacy vs. SOC) – Global Market: \$7B

- ✓ NDA accepted w/ Priority Review; China review ongoing; discussing regulatory pathway after CRL in US
- ✓ Breakthrough Designation (US, China)

### Broad Pipeline

#### Plinabulin: “A pipeline in a drug”

- ✓ Triple combo w/IO agents and radiation/chemo in 7 cancers
  - 2 Phase 1/2 trials underway
- ✓ Expansion to additional solid tumors and first line cancers

#### Three Pre-Clinical I/O Agents

#### Targeted Protein Degradation Platform

- ✓ SEED Therapeutics (Subsidiary)
- ✓ \$800 M Collaboration with Eli Lilly

### Global Capabilities Continuous Innovation

#### Strong clinical development

- ✓ Enrolled 1,000+ patients to final filing stage for CIN and NSCLC
- ✓ Dual U.S. and China development strategy
- ✓ Strong clinical investigator network

#### Deep Regulatory Expertise

**Attractive COGS** - Simple manufacturing process, work with leading global CMOs

**Commercialization Planning Underway, Hengrui partnership in Greater China**

**Strong cash position: \$91.6M at 9/30/21**



thank you!

[www.beyondspringpharma.com](http://www.beyondspringpharma.com)