



**BeyondSpring**

# Corporate Presentation



June 2021 | NASDAQ: BYSI

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# Investment Highlights



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

## Partnerships

Research subsidiary, SEED Therapeutics, with \$800 million partnership with Eli Lilly (Proprietary TPD Platform)

## Cash position

\$90.6 million as of March 31, 2021

## Headquarters

New York

## Nasdaq Ticker Symbol

BYSI

## Lead Asset Plinabulin: a Pipeline in a drug upcoming milestones

CIN

- Breakthrough Designation (BTD)
- US CIN NDA accepted with Priority Review
- China NDA submitted
- Preparing for commercialization

NSCLC

- Fully enrolled Phase 3 DUBLIN-3
- Topline OS data expected in mid-2021

IO

- Triple I/O combo in multiple cancer indications in early development, including 7 cancers at MD Anderson
- Efficacy data for SCLC at ASCO 2021

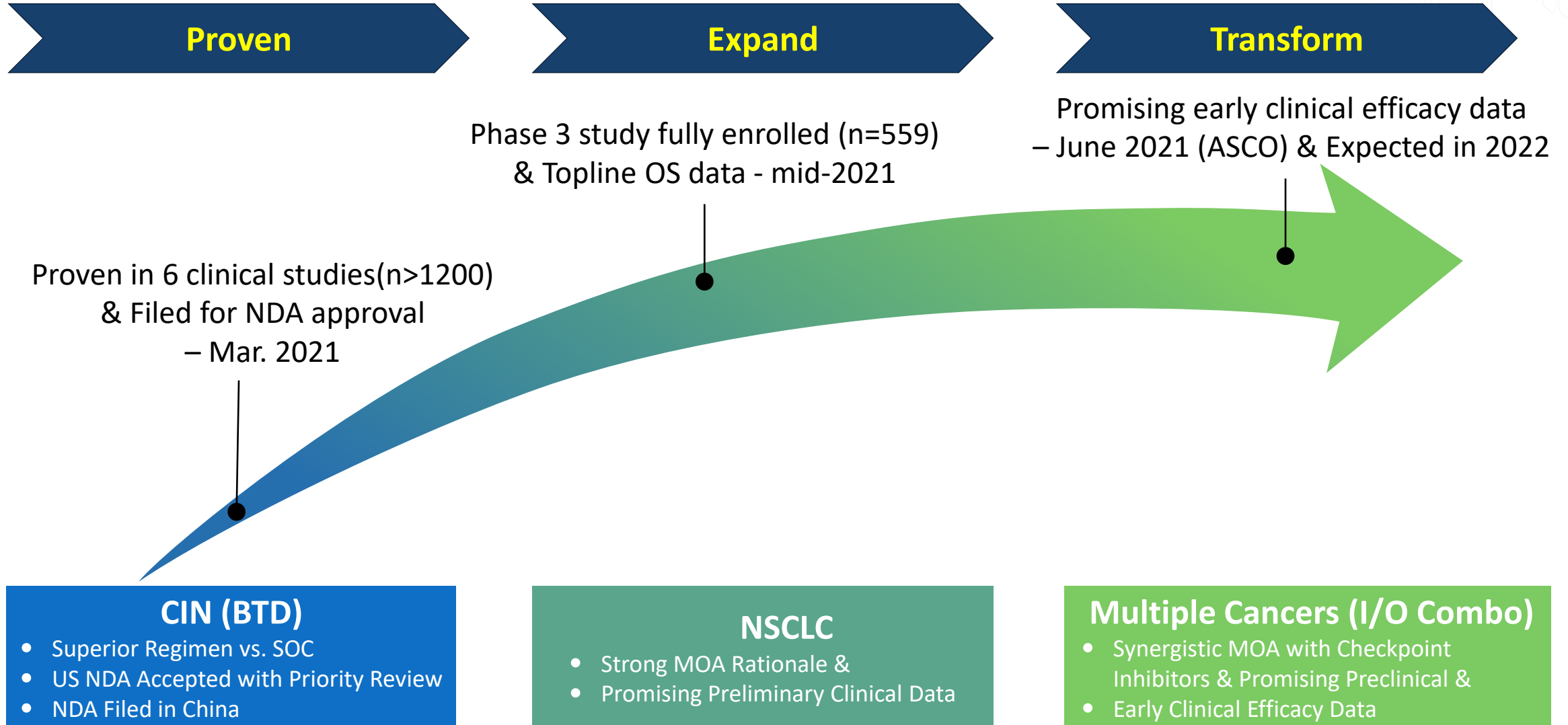
# Two Near-Term NDAs & Robust Drug Development Pipeline



	Indication / Target	Program	Trial Name / Collaborator	Preclinical	Phase 1	Phase 2	Phase 3	Commercial Rights <sup>1</sup>	Status/Next Milestone
Late stage	CIN (All cancer, all chemo)	Plinabulin + pegfilgrastim	PROTECTIVE-1 & PROTECTIVE-2	Phase 3 primary endpoint met in pivotal data announced November 2020				Global	<ul style="list-style-type: none"> <li>U.S. NDA accepted with Priority Review</li> <li>China NDA submitted March 2021</li> </ul>
	NSCLC (2 <sup>nd</sup> /3 <sup>rd</sup> line)	Plinabulin + docetaxel	DUBLIN-3	Phase 3 second interim analysis completed				Global	Global Final topline Phase 3 data Mid 2021
Triple Combo IO (IIT)	SCLC	Plinabulin + nivolumab + ipilimumab	10 US sites, including Rutgers University as lead site					Global	Phase 1 completed
	Multi-cancer (2 <sup>nd</sup> /3 <sup>rd</sup> line)	Plinabulin + PD-1/PD-L1 + radiation/chemo	THE UNIVERSITY OF TEXAS MD Anderson Cancer Center					Global	Initiate Phase 1 in 7 cancers Q2 2021
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						\$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 Value Generation Roadmap





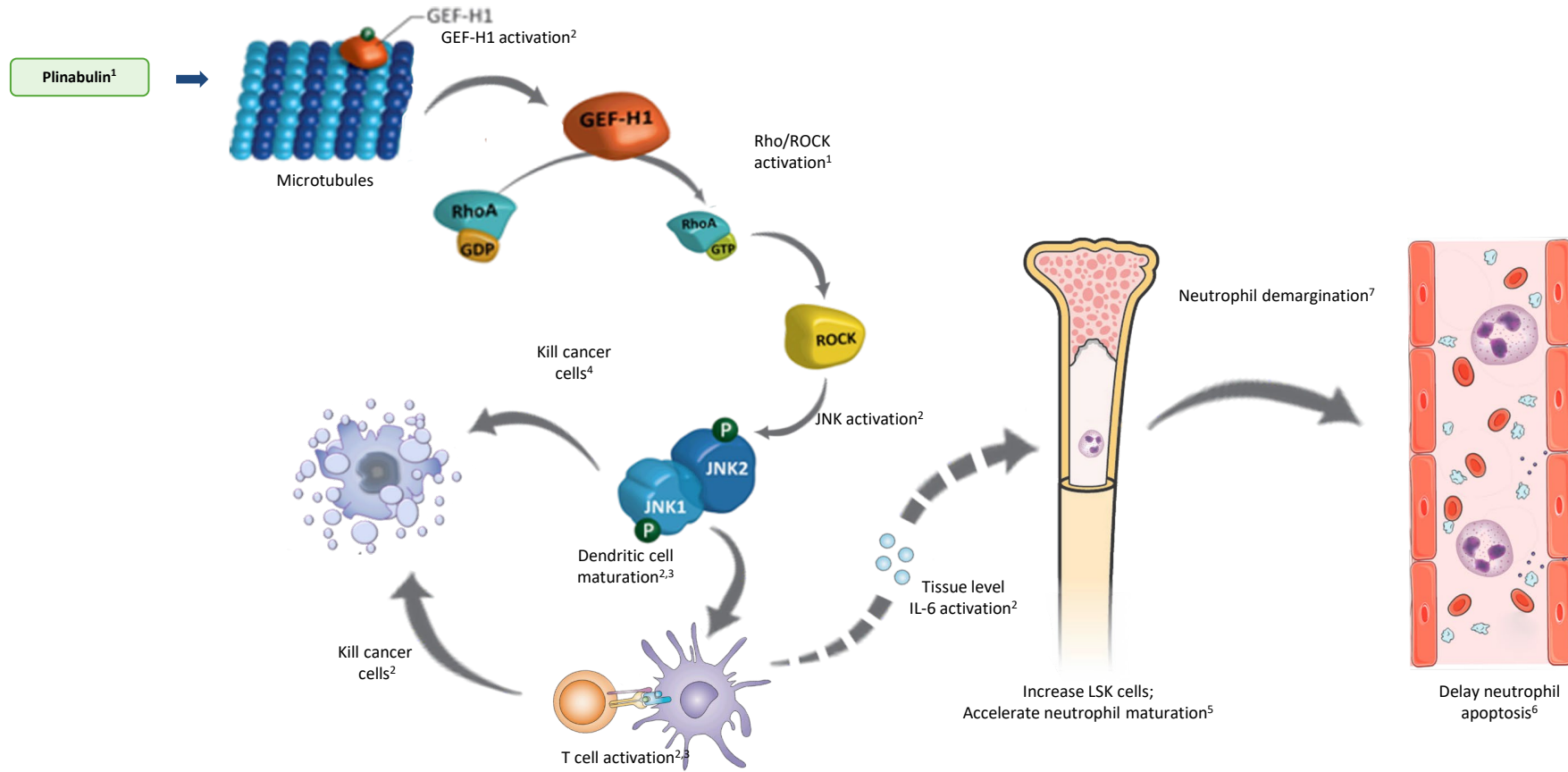
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## Plinabulin: “Pipeline in a Drug”

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



# Plinabulin: A SIMBA with Potential for Multiple Cancer Indications

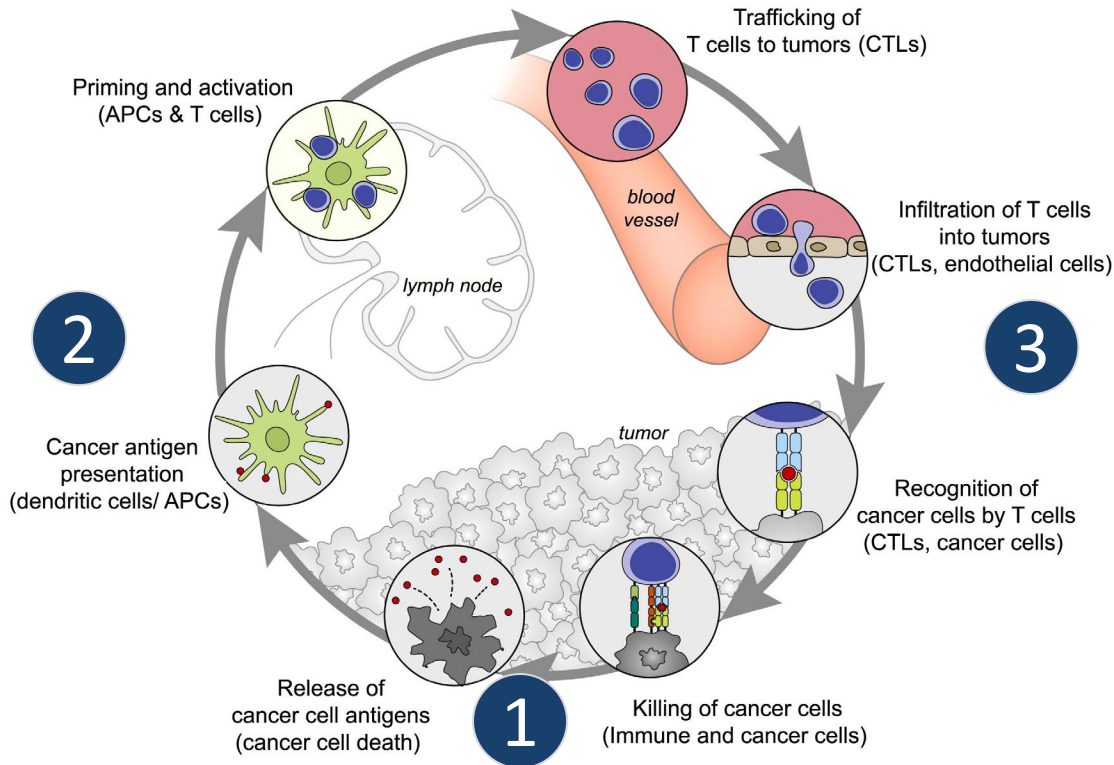


**First-in-class Agent Plinabulin's immune mechanism designed to enable its effects in multiple cancer indications:**

- **Chemotherapy Induced Neutropenia (CIN):** Designed to protect progenitor cells from chemo assault in bone marrow with week 1 benefit, which compliments G-CSF week 2 benefit for improved benefit potential
- **NSCLC:** Chemo (e.g. docetaxel) introduces real time tumor antigen, Plinabulin is designed to mature DC, leading to T cell activation, and durable anti-cancer benefit
- **Multiple Cancer Indications:** Triple combo combines “tumor antigen generation” from chemo/radiation, plinabulin “adding T cell gas”, and PD-1/PD-L1 “release the brake” for potential maximum durable anti-cancer benefit

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.

# Plinabulin Induces Dendritic Cell Maturation, a Key Step in Initiating Anti-cancer Durable Response in IO Combo



## 2 Plinabulin



### Hit the Gas

Stimulate maturation of dendritic cells to increase antigen presentation

Dendritic cells are the most important antigen-presenting cells

## 3 Checkpoint Inhibitors

### Release the Brakes

Optimize T cell response

## 1 Radiation/Chemotherapy

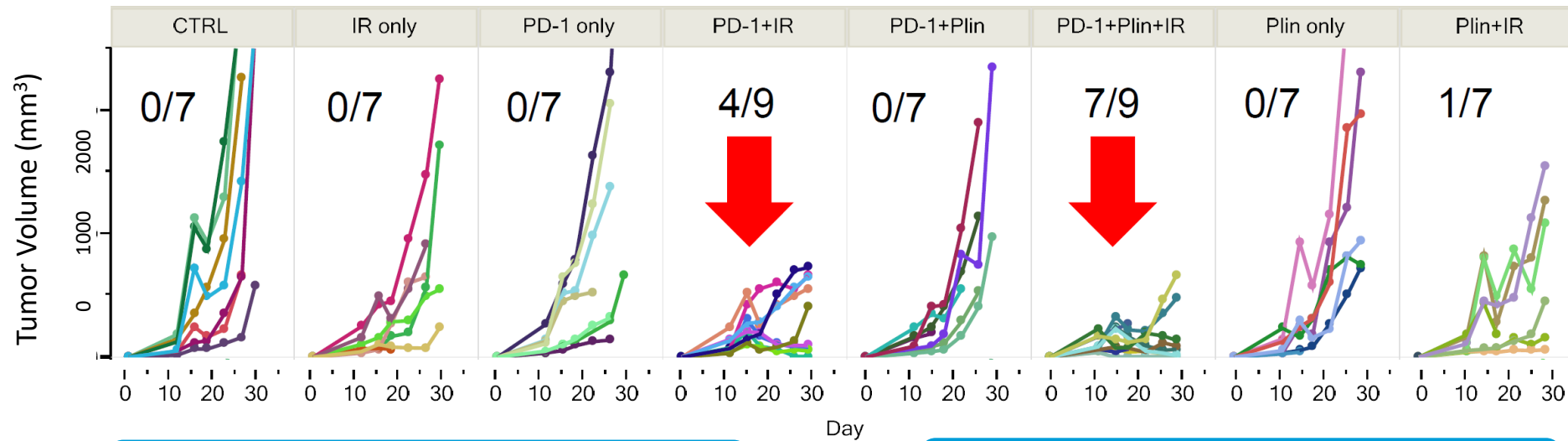
### Release Tumor Antigens

For more potent anti-cancer effect

1 + 2 + 3 → Optimal Immuno-Oncology Response

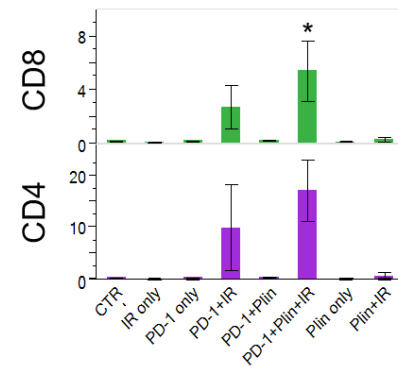
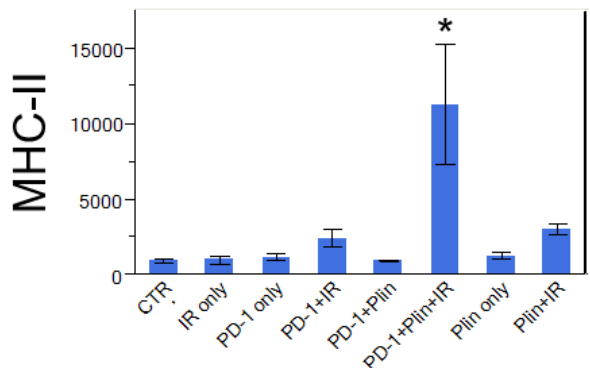


# Triple I/O Combo: Plinabulin + PD-1 + Radiation (IR), Best Tumor Response in PD-1 Non-Responsive Tumor Model (MD Anderson)



DC activation is most dramatic in triple I/O combination

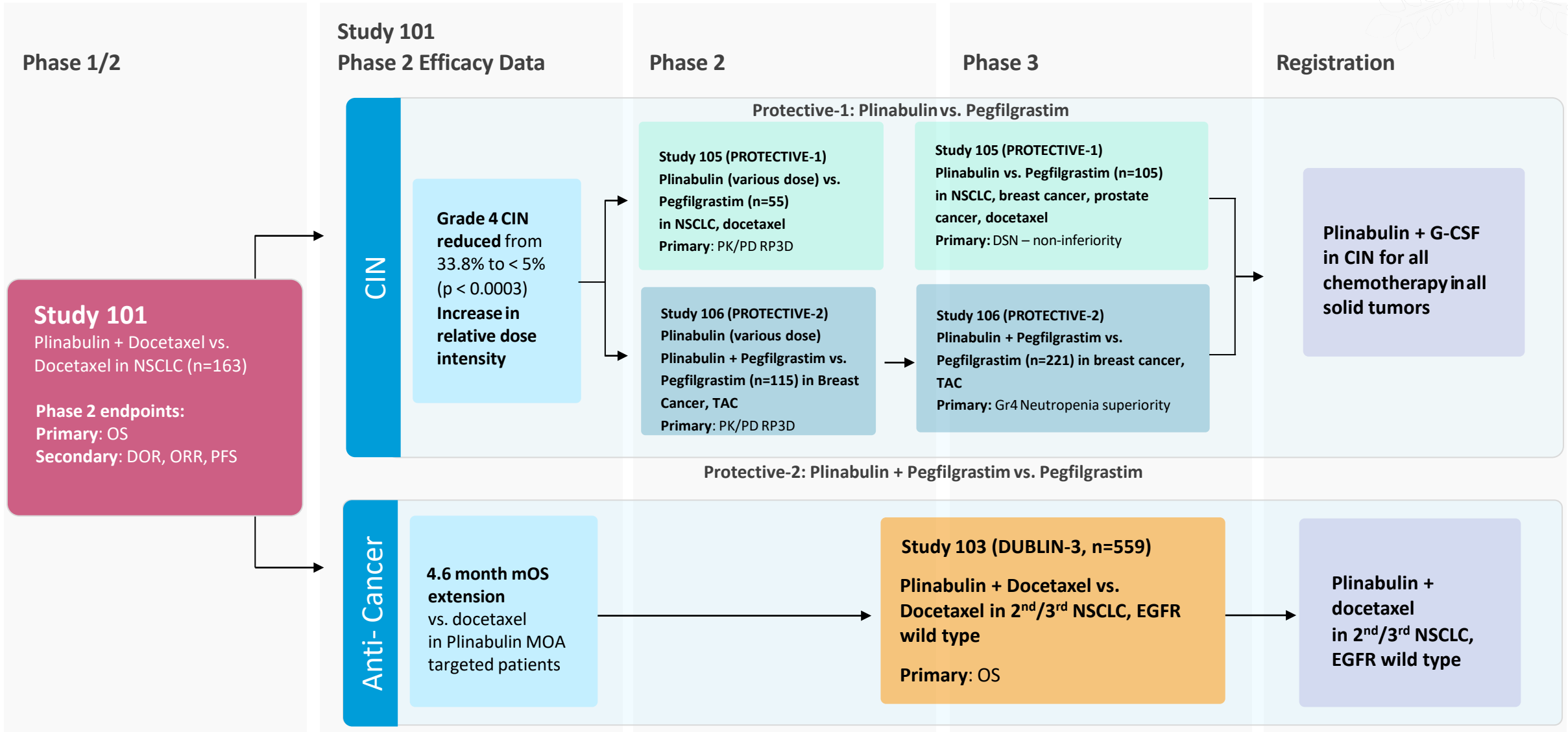
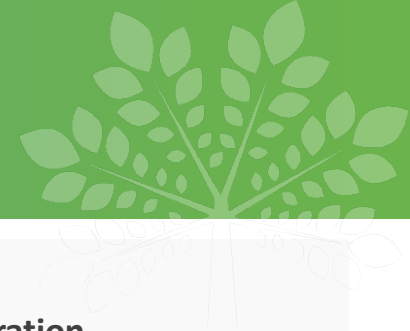
T cell doubles in triple I/O Combination vs. PD1 + IR



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



# Building the Plinabulin Franchise

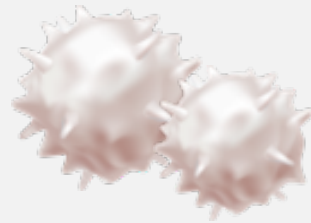


# Severe Unmet Medical Need is Basis for Breakthrough Designation and Priority Review for Plinabulin + G-CSF Regimen in CIN Prevention

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

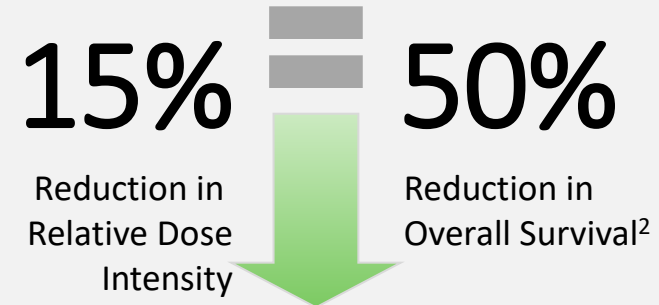
## Short-term Outcome Benefit

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



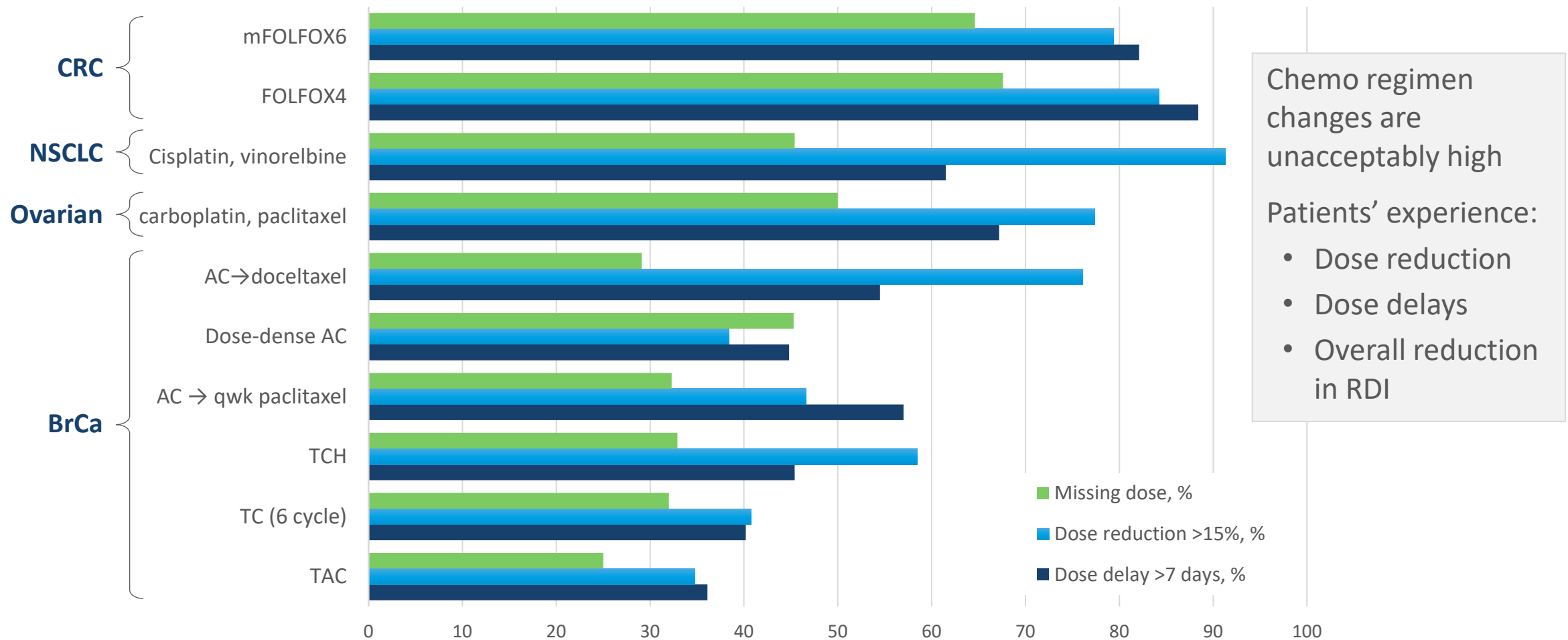
## The Unmet Medical Need: Week 1 “Neutropenia Vulnerability Gap (NVP)”

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

# Monotherapy G-CSF Fails to Prevent Chemo Regimen Changes



Percent of patients with **significant** regimen changes



Chemo regimen changes are unacceptably high

Patients' experience:

- Dose reduction
- Dose delays
- Overall reduction in RDI

<sup>1</sup>Published, 2015. Per EMR review of 16,233 patients with 6 different tumor types 2007-2011. JNCCN—Journal of the National Comprehensive Cancer Network Volume 13 Number 11 November 2015, <sup>2</sup>Denduluri et al.

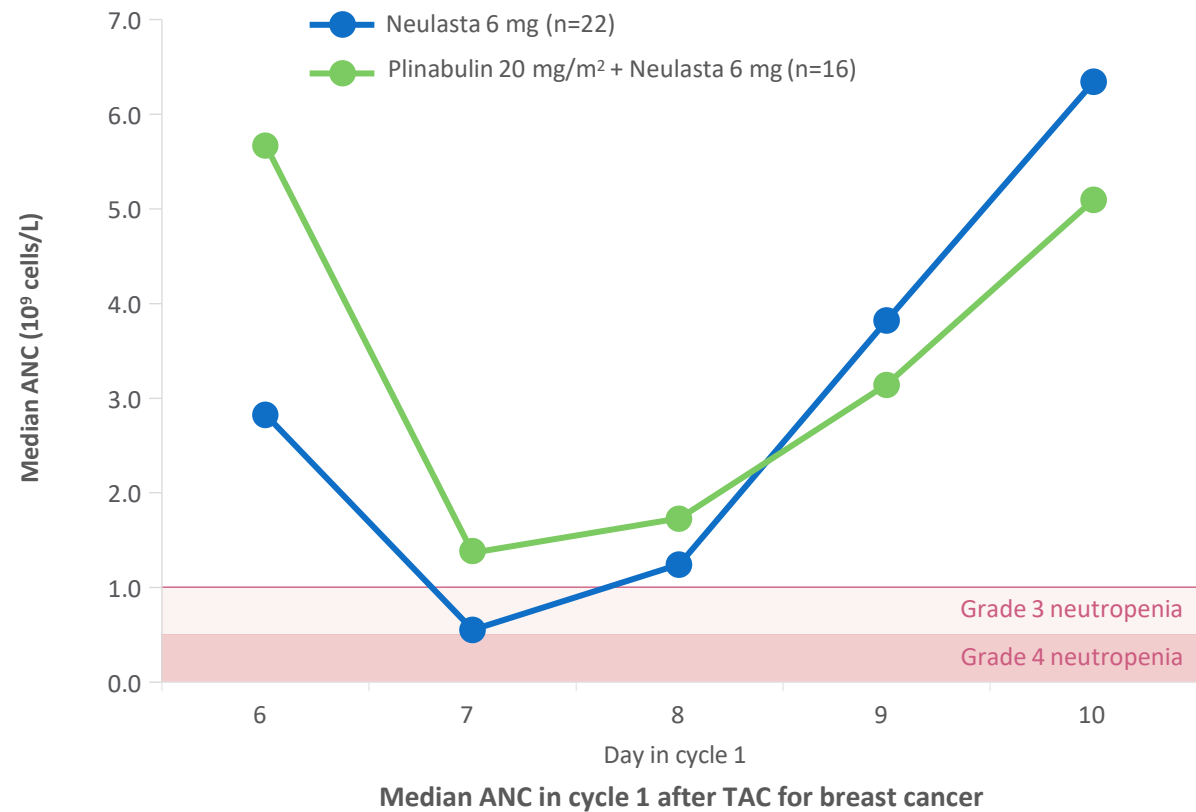
Abbreviations: 5-FU, 5-fluorouracil; ABVD, doxorubicin, bleomycin, vinblastine, dacarbazine; AC, doxorubicin, cyclophosphamide; CRC, colorectal cancer; FOLFOX4/mFOLFOX6, folinic acid, 5-fluorouracil, oxaliplatin; NHL, non-Hodgkin lymphoma; NSCLC, non-small cell lung cancer; R-CHOP/CHOP, cyclophosphamide, doxorubicin, vincristine, prednisone ± rituximab; RCVP/CVP, cyclophosphamide, vincristine, prednisone ± rituximab; RDI, relative dose intensity; TAC, docetaxel, doxorubicin, cyclophosphamide; TC, docetaxel, cyclophosphamide; TCH, docetaxel, carboplatin, trastuzumab.

# Plinabulin + G-CSF Combination Addresses Unmet Medical Need



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

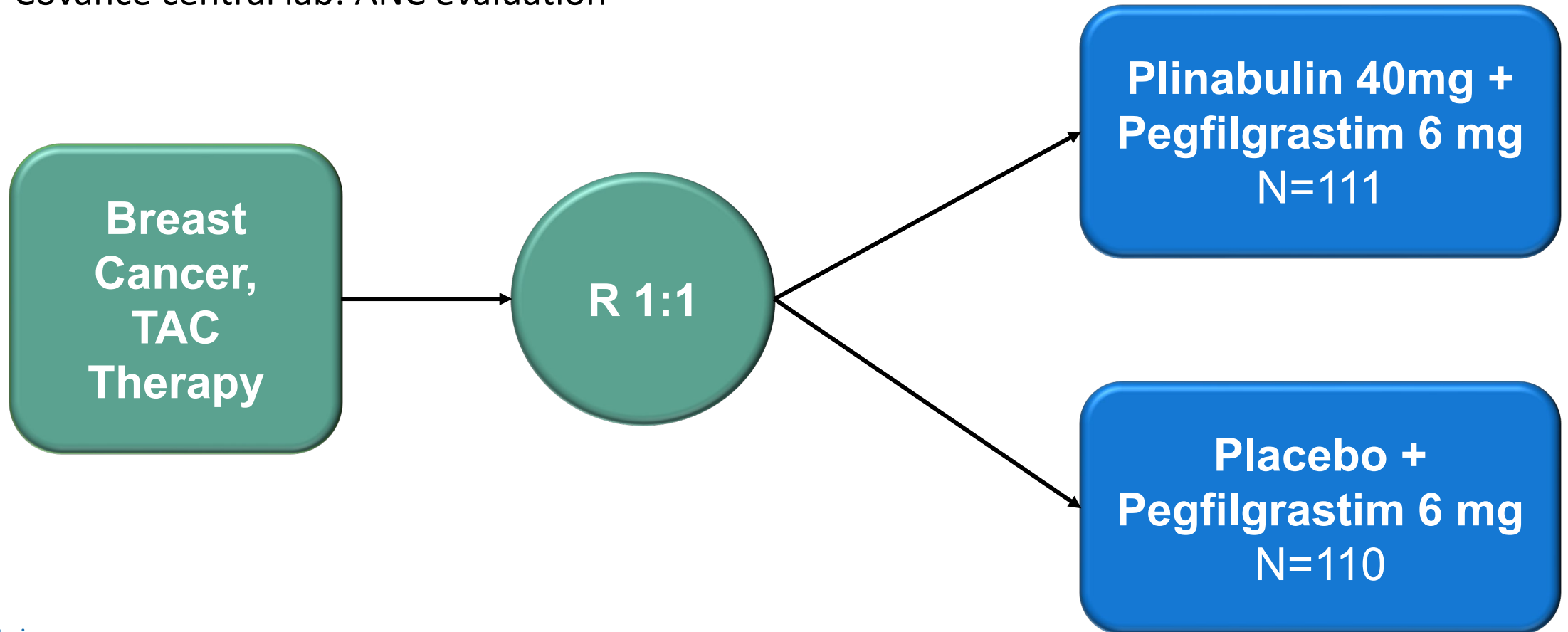
- Breakthrough Therapy Designation: Unmet need, and potential superior regimen vs. SOC recognized by FDA and NMPA
- Plinabulin prevents CIN in week 1; and G-CSF prevents CIN in week 2
- Combination maximizes the prevention of CIN for the full cycle



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

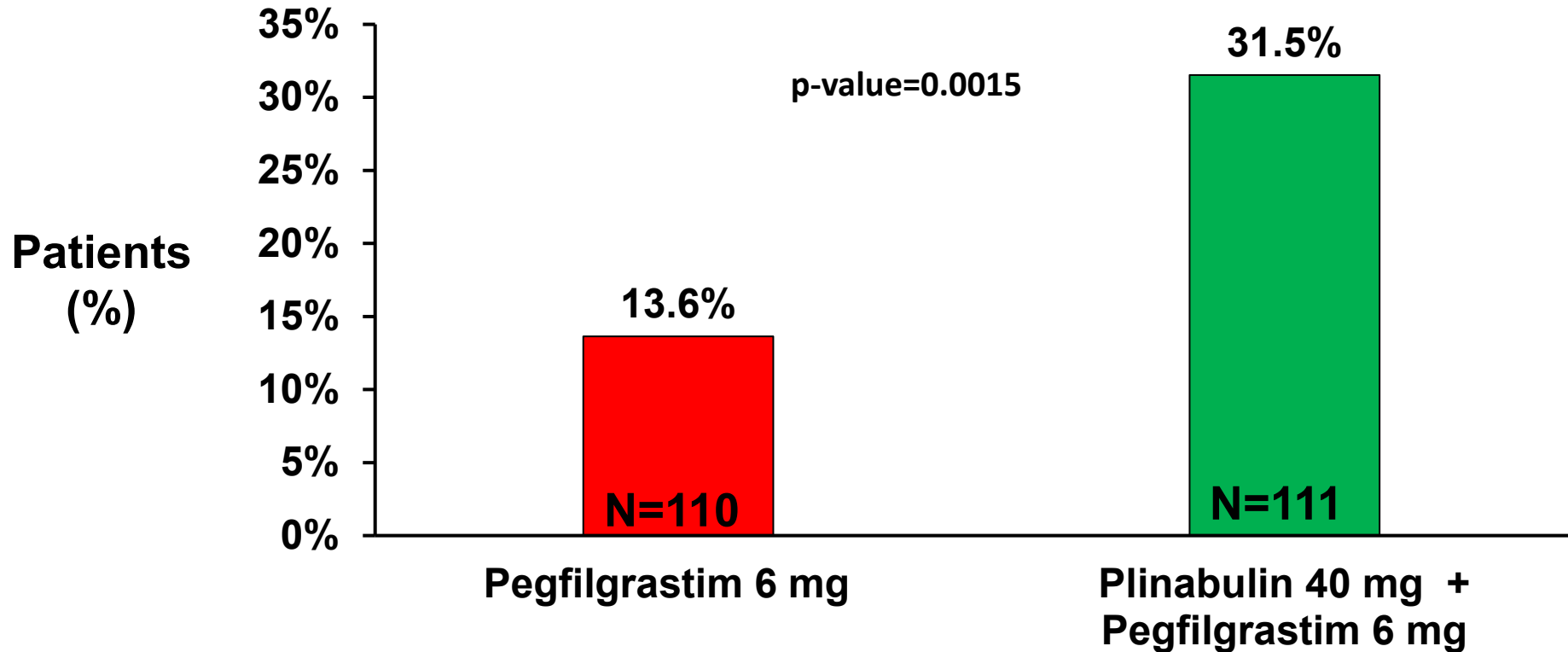


- Double blind, global study (19 centers); 4 cycles
- Covance: CRO
- Covance central lab: ANC evaluation





**Proportion of Patients with No Grade 4 Neutropenia  
(or DSN= 0 Days) in Cycle 1**



- 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



# PROTECTIVE-2 Ph 3: Clinical Consequences of CIN also Reduced by Combination



<b>ANC Nadir</b>	<b>Pegfilgrastim 6 mg N=110</b>	<b>Plinabulin 40 mg + Pegfilgrastim 6 mg N=111</b>
<b>Mean nadir for FN patients (x10<sup>9</sup> cells/L)</b>	<b>0.06</b>	<b>0.13</b>
<b>Mean nadir for all patients (x10<sup>9</sup> cells/L)</b>	<b>0.31</b>	<b>0.54</b>

**ANC benefit of the combination improves clinical benefit (~50% better)**

	<b>Pegfilgrastim 6 mg N=110</b>	<b>Plinabulin 40 mg + Pegfilgrastim 6 mg N=111</b>
<b>Incidence of FN by grade, (n) %</b>	<b>Total: 6.3% (n=7) Grade 3: 2.7% (n=3) Grade 4: 3.6% (n=4)</b>	<b>Total: 3.6% (n=4) Grade 3: 2.7% (n=3) Grade 4: 0.9% (n=1)</b>
<b>Duration of FN (days)</b>	<b>2.28 days</b>	<b>1.25 days</b>
<b>Hospitalization, %</b>	<b>6.3%</b>	<b>2.7%</b>
<b>Duration of hospitalization (days)</b>	<b>7.14 days</b>	<b>3.75 days</b>
<b>Change of chemotherapy dose and/or regimen in later cycles, %</b>	<b>6.3%</b>	<b>2.7%</b>

# Adverse Reactions Occurring in $\geq 5\%$ of Patients in the Plinabulin + Pegfilgrastim vs. Pegfilgrastim



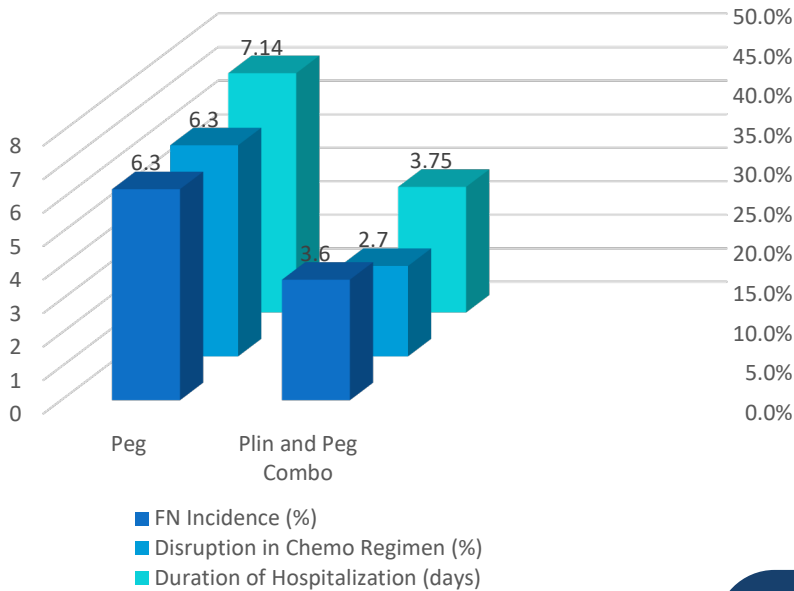
Body System/Preferred Term	Pegfilgrastim 6 mg N=132		Plinabulin 40 mg** + Pegfilgrastim 6 mg N=127	
	All Grade	Grade 3/4	All Grade	Grade 3/4
<b>Gastrointestinal disorders</b>	<b>22 (16.7%)</b>	<b>1 (0.8%)</b>	<b>49 (38.6%)</b>	<b>9 (7.1%)</b>
Diarrhea	6 (4.5%)	1 (0.8%)	33 (26.0%)	4 (3.1%)*
Nausea	11 (8.3%)	0	14 (11.0%)	1 (0.8%)*
Constipation	2 (1.5%)	0	10 (7.9%)	1 (0.8%)*
Vomiting	2 (1.5%)	0	10 (7.9%)	1 (0.8%)*
Abdominal pain	1 (0.8%)	0	9 (7.1%)	2 (1.6%)
Abdominal distension	1 (0.8%)	0	10 (7.9%)	2 (1.6%)
<b>General disorders and administration site conditions</b>	<b>17 (12.9%)</b>	<b>0</b>	<b>24 (18.9%)</b>	<b>1 (0.8%)</b>
Fatigue	2 (1.5%)	0	10 (7.9%)	0
Malaise	10 (7.6%)	0	11 (8.7%)	1 (0.8%)
<b>Musculoskeletal and connective tissue disorders</b>	<b>48 (36.4%)</b>	<b>0</b>	<b>20 (15.7%)</b>	<b>0</b>
Bone pain	37 (28.0%)	0	8 (6.3%)	0
Pain in extremity	7 (5.3%)	0	8 (6.3%)	0
Back pain	5 (3.8%)	0	4 (3.1%)	0
<b>Nervous system disorders</b>	<b>4 (3.0%)</b>	<b>0</b>	<b>12 (9.4%)</b>	<b>0</b>
Headache	1 (0.8%)	0	8 (6.3%)	0
<b>Vascular disorders</b>	<b>2 (1.5%)</b>	<b>0</b>	<b>10 (7.9%)</b>	<b>7 (5.5%)</b>
Hypertension	1 (0.8%)	0	8 (6.3%)	7 (5.5%)*

# The combination with Superior Improvement in Clinically Meaningful Endpoints compared to Pegfilgrastim alone



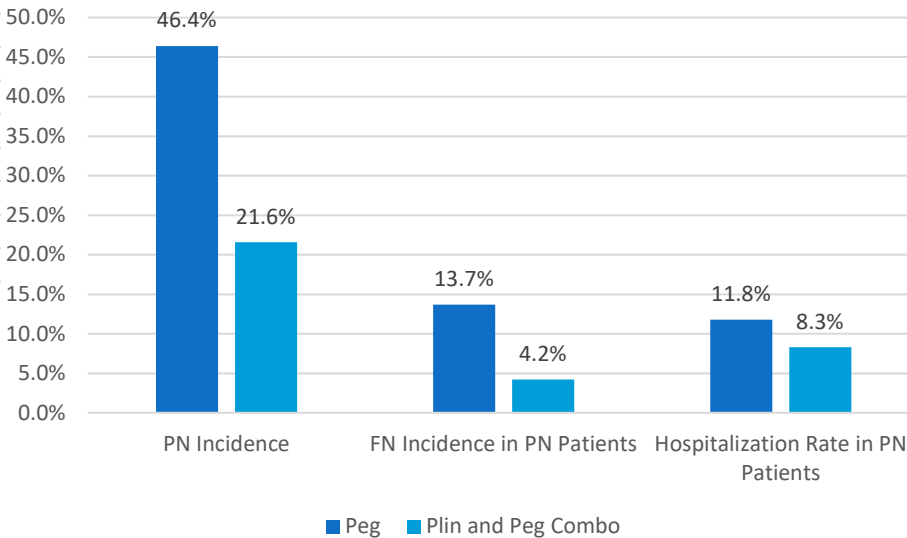
## Reduction of Incidence and Severity of FN and Hospitalization

Clinical Endpoints



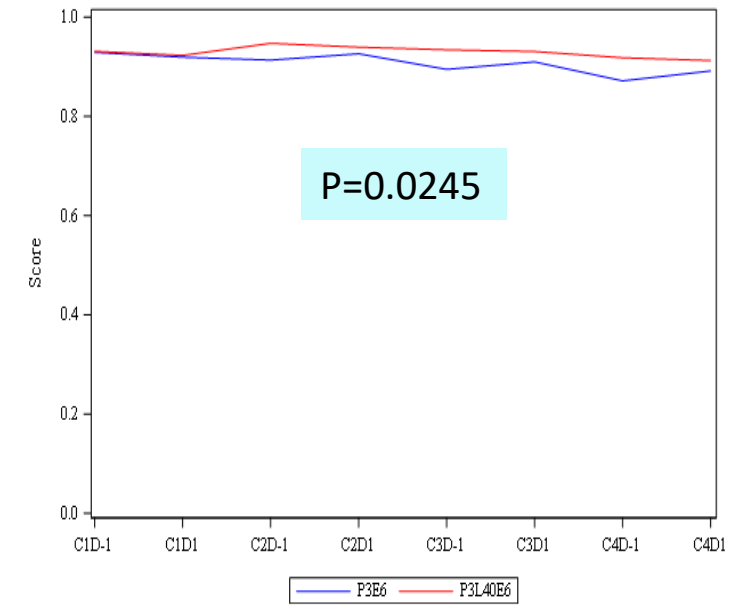
## Reduction of Profound Neutropenia (PN) Related Benefits

Profound Neutropenia Endpoints



## Improvement of Quality of Life

Health Utility - 5L US: All Population  
Mean per Day  
(A higher score indicates a better outcome)



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



<b>Improved Efficacy (ANC based in Cycle 1) – 106 Phase 3</b>	<b>Improved Efficacy (FN) – 106 Phase 3</b>	<b>Favorable Safety – 106 Phase 2+3</b>
<p><b>No Grade 4 Neutropenia</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 (x 10<sup>9</sup> 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>



## Plinabulin shown to statistically reduce Grade 4 neutropenia in 6 clinical trials (1,200+ patients)

### 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

### 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>

**700+ cancer patients treated with Plinabulin (various doses)**



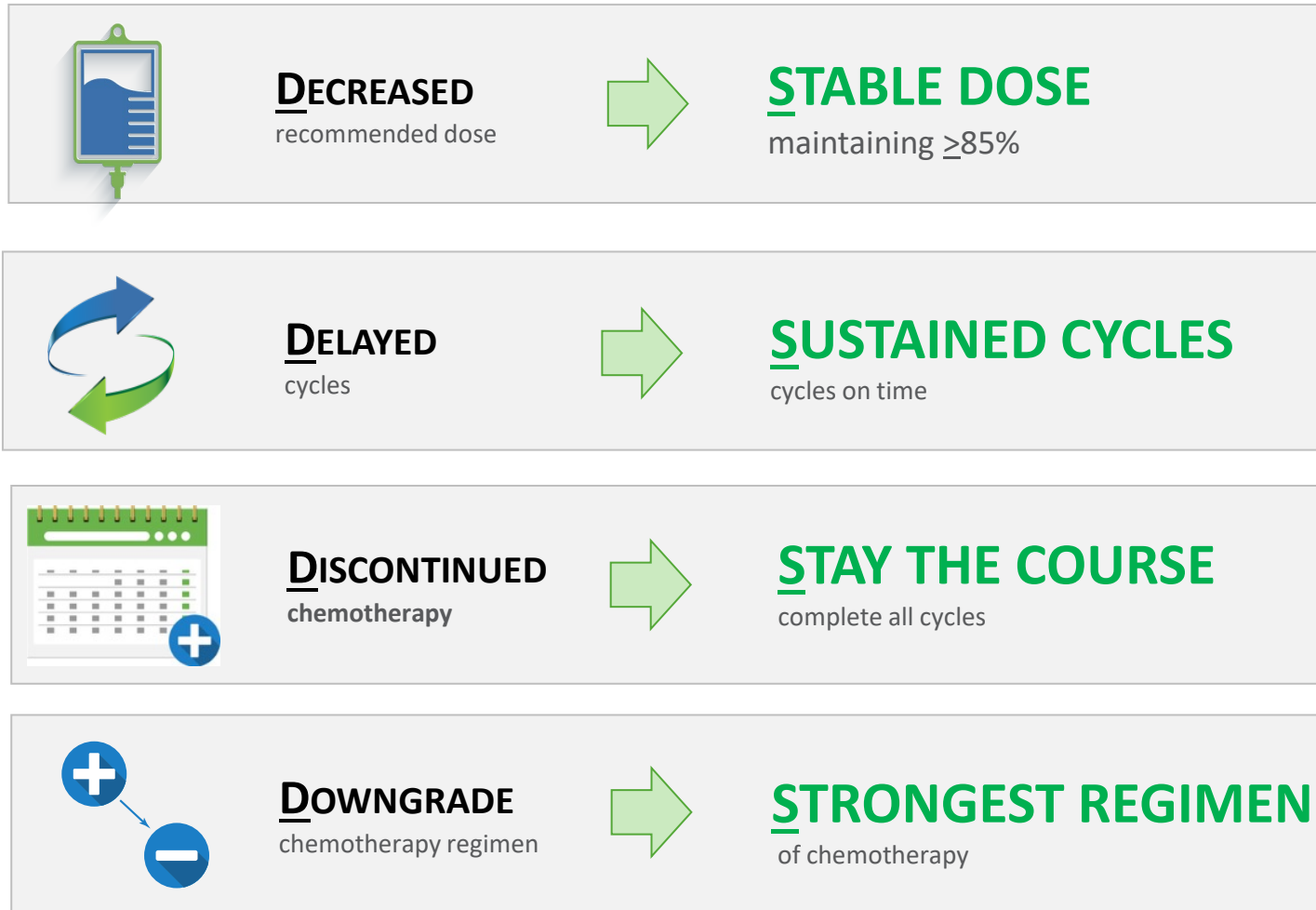
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# Plinabulin + G-CSF Combination

- Commercial Plan in CIN Prevention



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



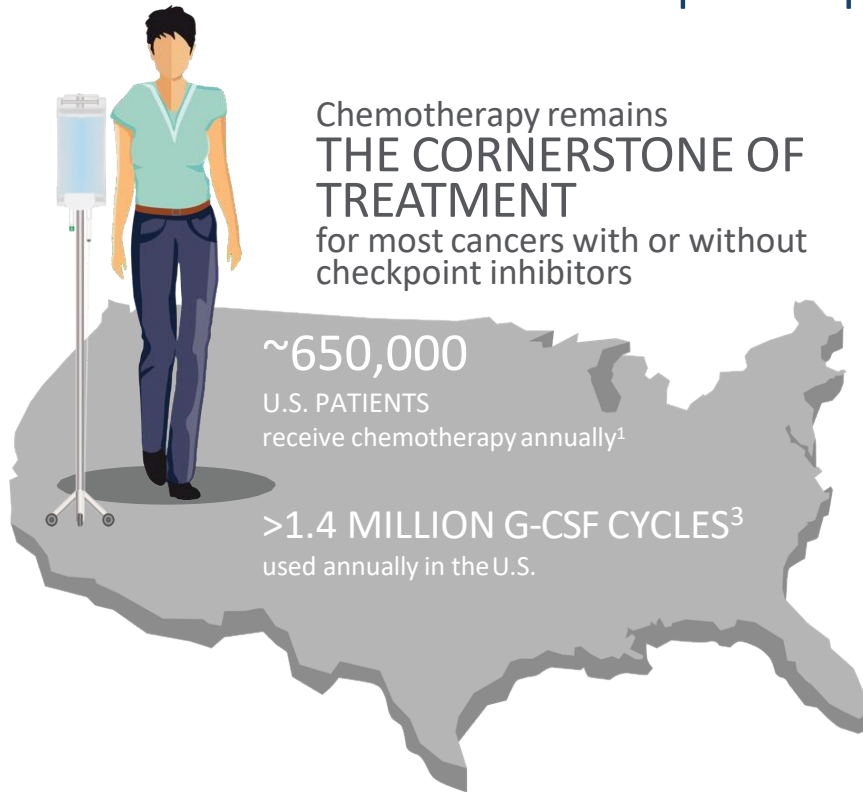
## Plinabulin + G-CSF

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

# CIN: Large and Expanding Market Potential



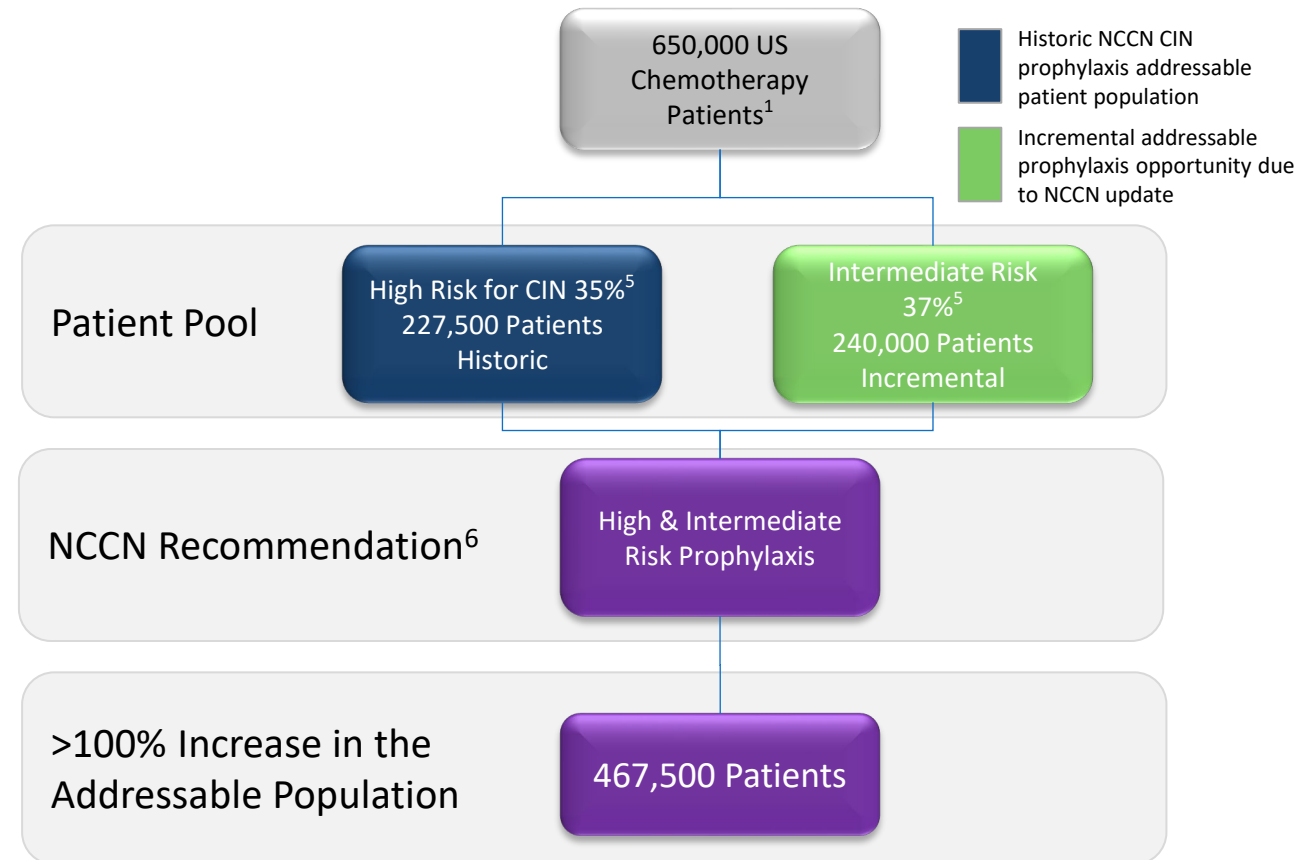
Plinabulin can be used with each cycle of G-CSF in non-myeloid cancers to provide improved protection from neutropenia



**Global:**<sup>3,4</sup>

- 4 million cycles of G-CSF per year
- \$7 billion in sales

## NCCN Guidelines Doubled the US Market for CIN

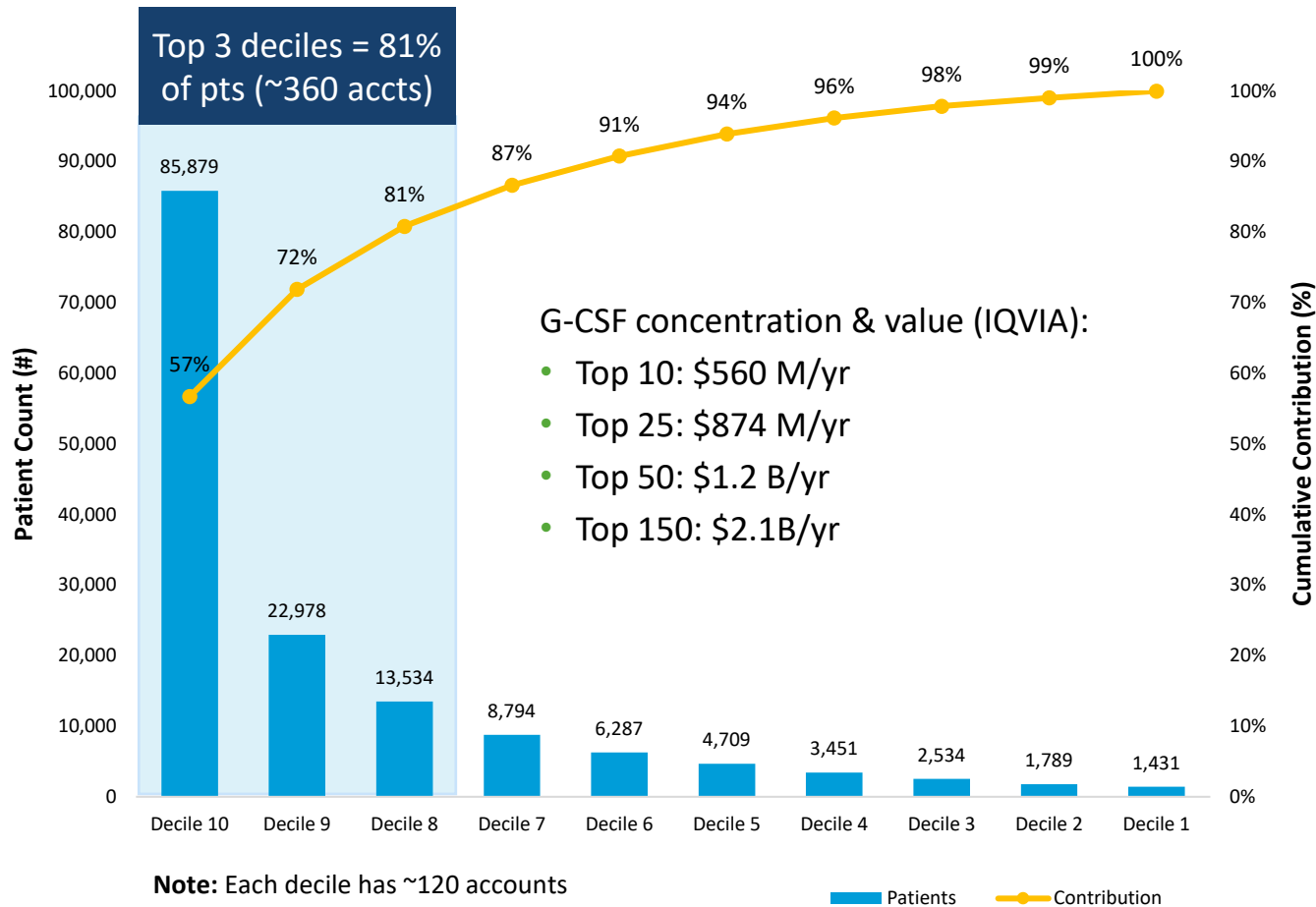




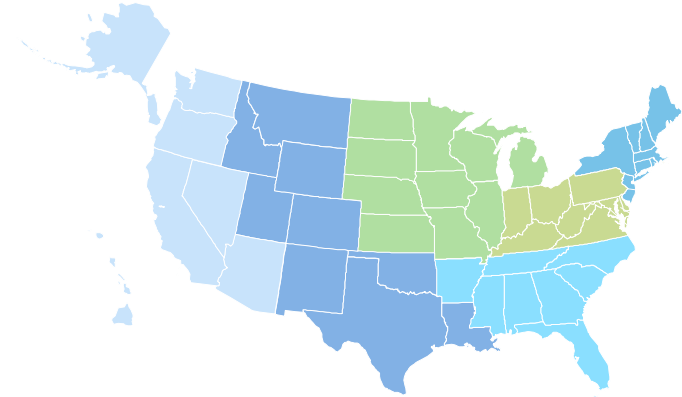
# Prioritize on Large and Rapid Adopters at Launch



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



## US Regional Coverage



Top 360 multi-location oncology accounts identified and prioritized

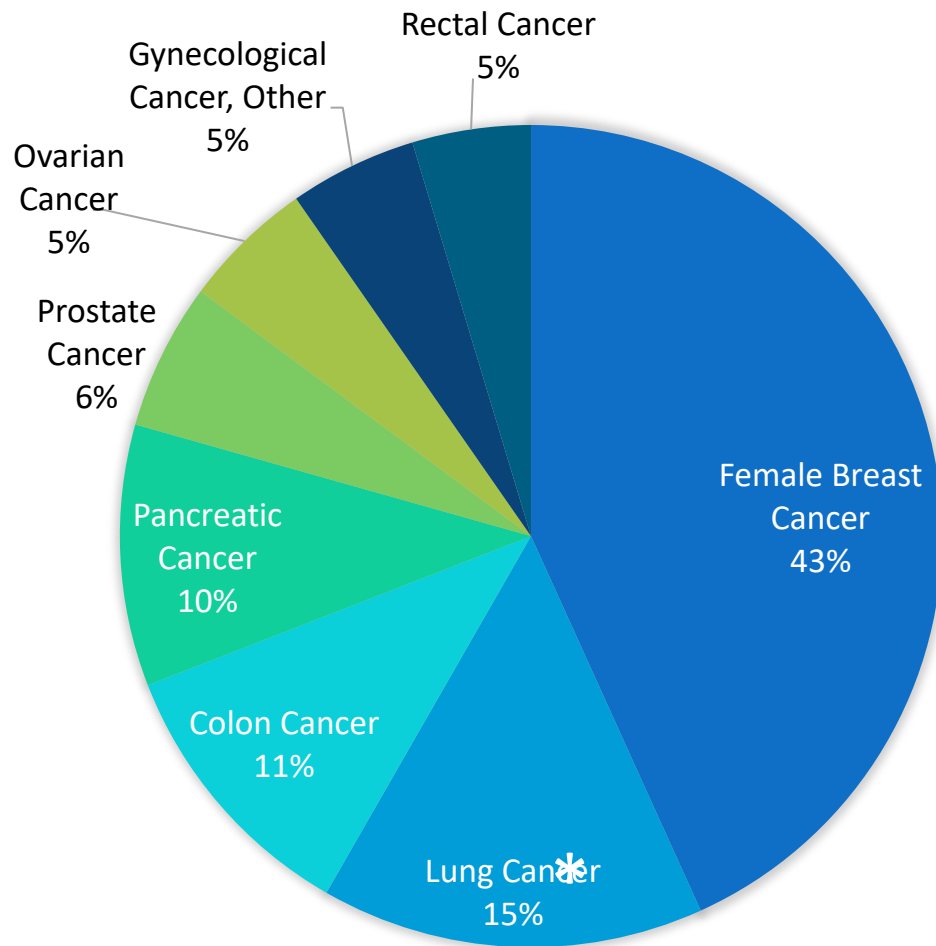
Field Team of 83, covering 6 regions:

- 6 Medical Science Liaisons
- 6 Regional Business Directors
- 60 Oncology Account Specialists
- 4 National/Regional Account Directors
- 1 Group Purchasing Director
- 6 Regional Reimbursement Specialists

# Plinabulin: Potential for Use Across the Spectrum of Solid Tumors



## 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 broad label has potential 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

# Targeted Commercialization Plan



01

Drive awareness of the "Neutropenia Vulnerability Gap" and unmet need

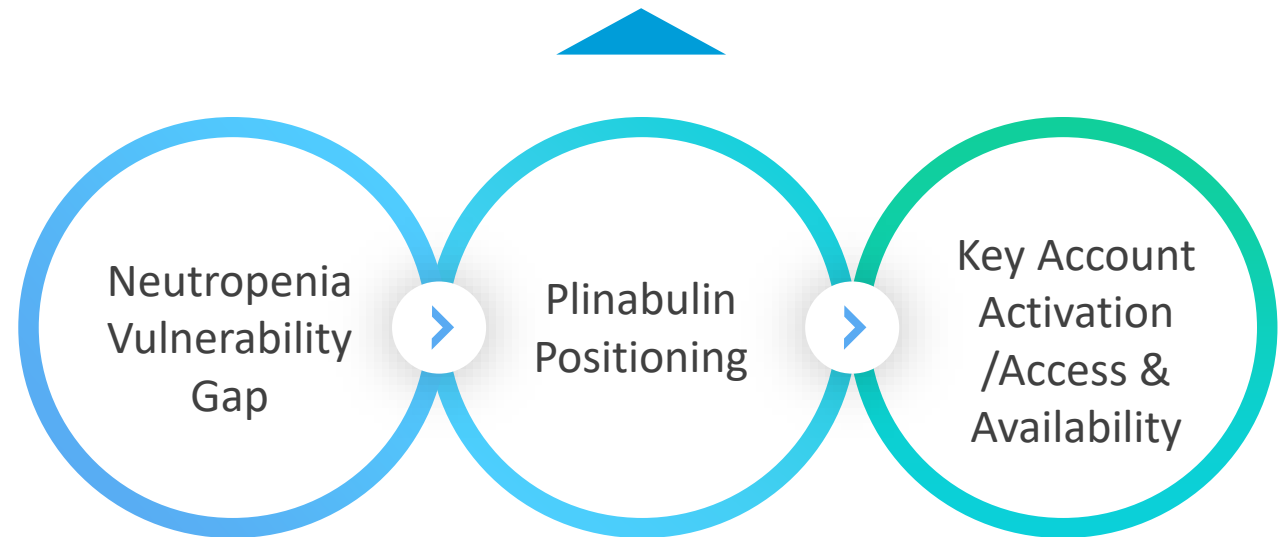
02

Position Plinabulin with key decision makers

03

Activate key accounts and ensure broad access and availability

## FOCUS: Elevating the SOC in chemotherapy



# Detailed Commercialization Plan

1

## Neutropenia Vulnerability Gap and Unmet Need Awareness

### KOLs:

- Major health care congresses:
  - ASCO, SABCC, Chemo Foundation
  - Publications/abstracts, booth
  - KOLs to lead all education efforts
  - MSL outreach

### Market Dynamics:

- Disease awareness:
  - CME sponsorship
  - CINRisk.com: >1M hits to date
- Advisory boards with HCPs, payers, practice managers
- > 700 market research interactions with U.S. oncologists, RNs and practice managers
- Payer interactions:
  - >40 with National, regional payers
  - Representing >130M unique lives
- Targeting the top 360 accounts (80%+ of the market) at launch

2

## Positioning Plinabulin with Key Decision Makers

- Advocacy and Expert network partnerships:
  - Guidelines:
    - Targeting NCCN, ASCO, Key IDNs
    - Apply immediately upon approval
  - Clinical Pathway adoption for broad use across large accounts
  - Targeted contracting with GPOs and high control payers to drive share

### Provider and Payer Focus:

- Dedicated field teams
  - National/Regional Account Managers
  - Group Purchasing/Government
  - MSL team clinical support
- J Code to secure reimbursement

### Education Programs:

- CME programs
- Top 400 oncology KOLs and key community-based HCPs
- Peer-to-peer; virtual/in-person

3

## Activating Key accounts and Ensuring Broad Patient Access

### State of the Art Promotion Programs:

- Dedicated team of Oncology Account Specialists
- Virtual Teach-ins and sales calls
- In person sales calls and programs
- Commercial focus:
  - High-volume/rapid adopting G-CSF oncologists
  - Top clinics/hospitals

### Plinabulin Plus – Patient Assistance:

- Dedicated Field Reimbursement Specialists
- Benefits investigation and adjudication
- Prior authorization support
- Co-pay assistance & Patient assistance programs\*
- Educational support for patients

# Breakthrough Therapy with FDA NDA Priority Review: Potential to Elevate SOC for CIN Prevention



## 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:

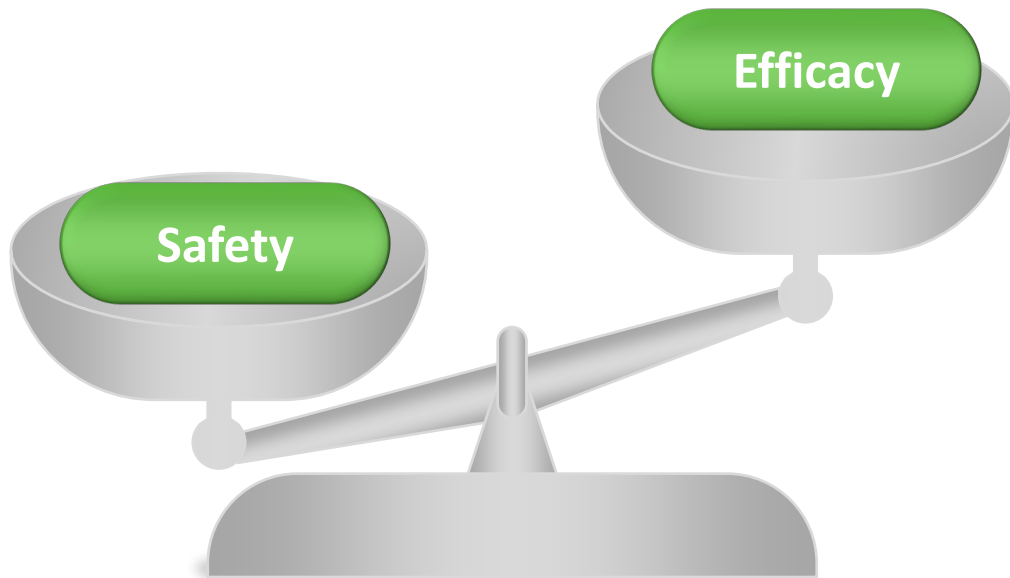
- Address the oncologist's desire for increased control
- Reduce patient anxiety and fears associated with interrupted therapy and adverse events
- Deliver improved chemotherapy care with the potential for improved long-term outcomes
- Clear differentiation from G-CSF provides rationale for superior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

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

# Building the Plinabulin Franchise



# Unmet Medical Need – 2<sup>nd</sup>/3<sup>rd</sup> Line NSCLC, EGFR Wild Type



- Large patient population with limited treatment options
  - EGFR wild type: ~85% western NSCLC and ~70% of Asian NSCLC patients
  - only four therapies approved
  - TKI is worse than docetaxel<sup>1</sup>
- Limited efficacy
- Severe side effects, including severe neutropenia

Factors such as the Efficacy and Safety tradeoff cause significant % of patients to forego their next round of chemotherapy for NSCLC

# Limited Options

- Four therapies approved in NSCLC (2<sup>nd</sup>/3<sup>rd</sup> line, EGFR wild type)
- SOC Docetaxel: Limited overall survival with CIN severe neutropenia ~40%

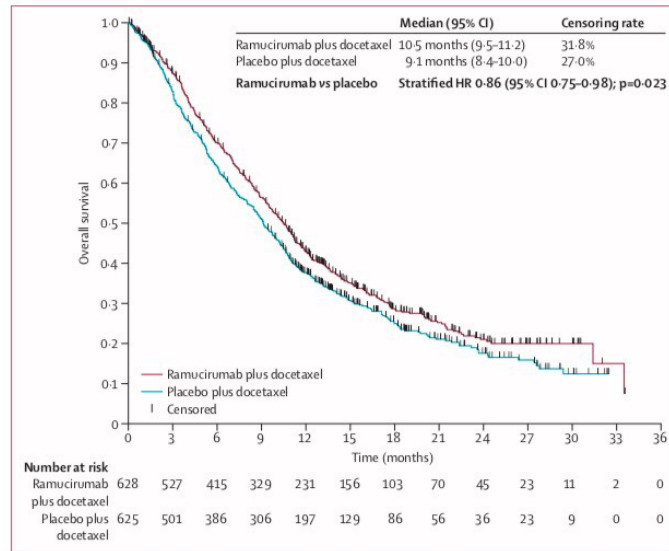
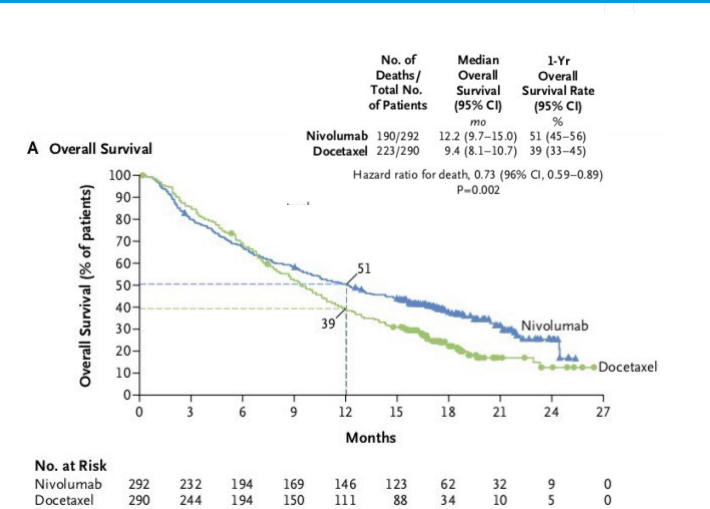
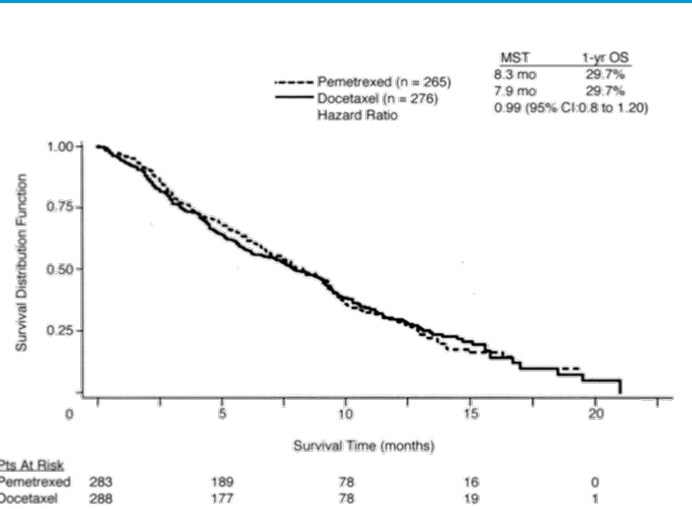


Figure 2: Kaplan-Meier estimates of overall survival in the intention-to-treat population  
HR=hazard ratio.



## Pemetrexed and PD-1/PD-L1 Moved To First Line



Treatment	Ramucirumab + Docetaxel vs. Docetaxel <sup>1</sup>	Pemetrexed vs Docetaxel <sup>2</sup>	Nivolumab (PD-1 Ab) vs. Docetaxel <sup>3</sup>
Pros	Limited efficacy; HR for mOS: 0.86 (1.4 M mOS benefit vs. Docetaxel)	Low CIN risk	Improved efficacy; HR for OS: 0.73 (2.8 M mOS benefit vs. Docetaxel)
Cons	High CIN risk (49% severe neutropenia)	Low Efficacy, HR for mOS: 0.99 (no survival benefit vs. Docetaxel)	potential cytokine storm, Moved to 1st line, thus PD-1 failed 1 <sup>st</sup> line pts cannot use this in 2 <sup>nd</sup> line.

Ideal regimen would improve efficacy (survival) without compromising on CIN

<sup>1</sup> Lancet 384 (9944): 665-673 (2014). <sup>2</sup> JCO 22(9): 1589-1597 (2004). <sup>3</sup> NEJM 373: 1627-1639 (2015).



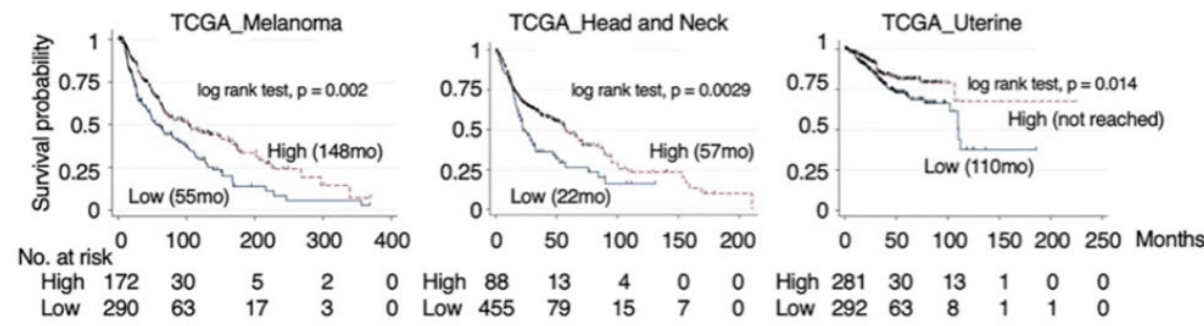
# Rationale for Advancing Plinabulin in NSCLC Study



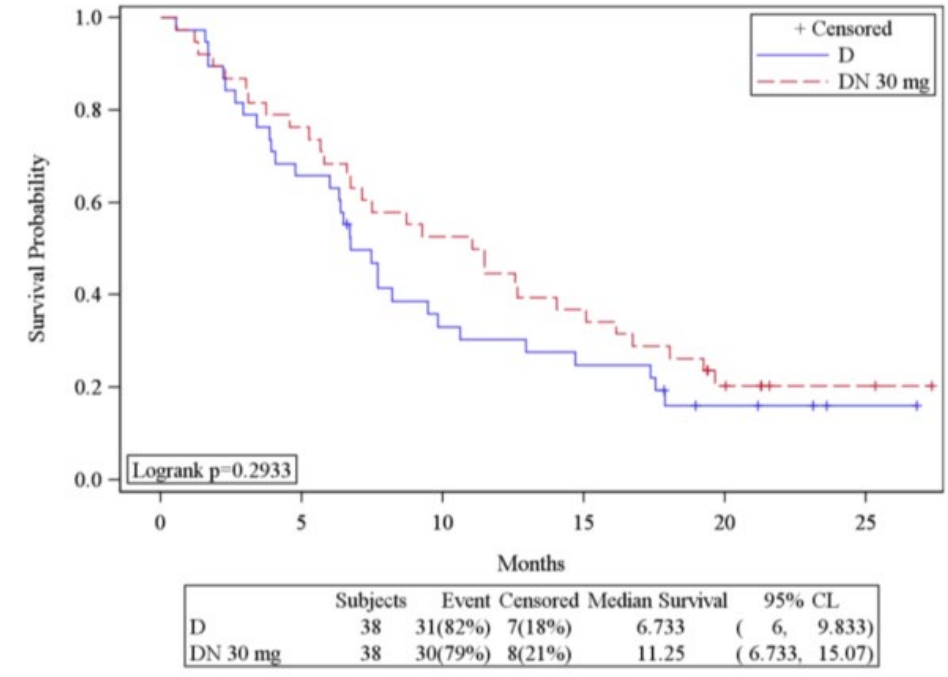
## Mode of Action Rationale

**Higher GEF-H1 immune signatures associated with longer OS in cancer <sup>1</sup>**

**Upper OS curve:** GEF-H1 immune signature high    **Lower OS curve:** GEF-H1 immune signature low



## Preliminary Clinical Evidence (Phase 2)



- Post-Hoc Ph2 data from Plinabulin in NSCLC in mechanism targeted patients (measurable lung lesion) shows overall survival benefit<sup>2</sup>
- **Represents Ph3 patient selection and study design**

<sup>1</sup> Kashyap et al., Cell Reports 28(13): 3367-80 (2019) <sup>2</sup> ASCO-SITC 2017 meeting oral presentation.

# DUBLIN-3 (Study 103): Phase 3 in 2<sup>nd</sup>/3<sup>rd</sup> NSCLC, EGFR Wild Type



## Design

### EGFR wild-type NSCLC (Pre-specified MOA target patients: Measurable lung lesion)

- Plinabulin + docetaxel vs docetaxel, 1:1 randomization, n=559 (fully enrolled)
- Approval possible with a single, qualified study
- Final analysis: at least 439 patient death events; study succeeds if  $p < 0.046$  for Overall Survival, Expected Mid-Year 2021

## Endpoints

### 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

- Secondary Endpoints go beyond OS
- Provide opportunity to demonstrate important benefits and address a range of unmet medical needs

## Preliminary Data

- 2 successful interim analyses: DSMB recommended trial to continue without modification



## Current Standard of Care

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

## Plinabulin - Docetaxel Combination

- Potential survival benefit, with more long survivals due to GEF-H1 IO MOA
- Potential superior safety profile, including CIN reduction
- Potential superior quality of life

# Building the Plinabulin Franchise



# Triple I/O Combo Development for Multiple Cancer Indications in PD-1/PD-L1 Failed Patients – Severe Unmet Medical Needs

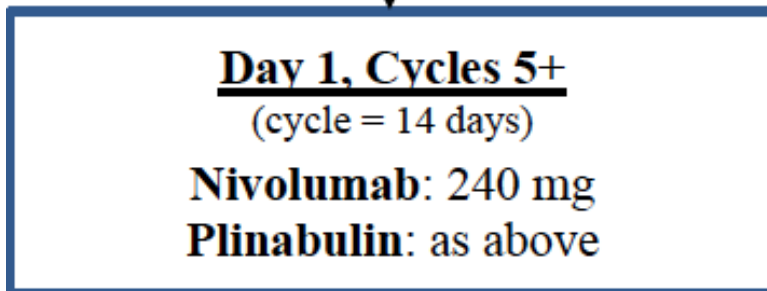
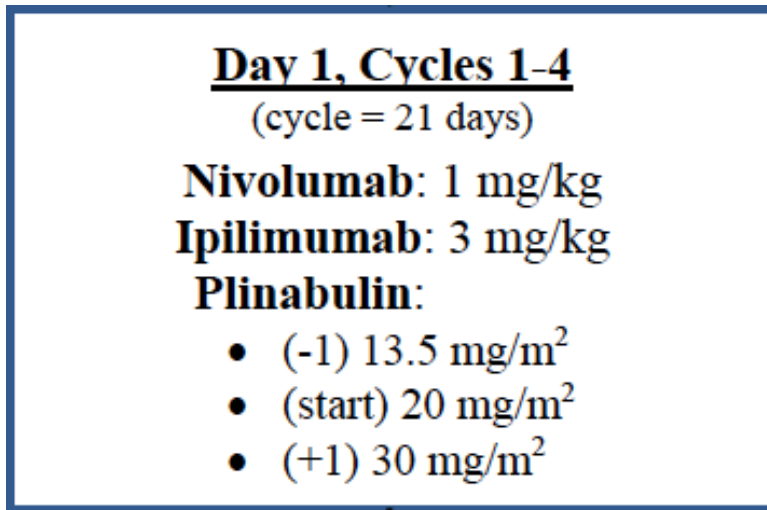


	Indication / Target	Program	Trial Name / Collaborator	Commercial Rights	Status
Triple Combo IO (IIT)	SCLC Checkpoint naïve and checkpoint refractory patients	Plinabulin + Nivolumab (PD-1) + Ipilimumab (CTLA-4)	7 US sites, including Rutgers University as lead center (Big Ten)	Global	Phase 1 completed, Presenting at ASCO June 2021
	SCLC Checkpoint refractory patients	Plinabulin + Nivolumab (PD-1) + Ipilimumab (CTLA-4)	Big Ten Study	Global	Initiating Phase 2
	7 Cancers* PD-1/PDL1 failed pts	Plinabulin + PD- 1/PD-L1 + radiation/chemo	MD Anderson	Global	Initiating Phase 1 in 7 cancers in Q2 2021



## Dose-escalation phase I study 3+3 Design

- In patients with extensive-stage SCLC who had progressed on or after prior platinum-based chemotherapy ( $\pm$ PD-1/PD-L1)



## Primary objective

- To determine dose-limiting toxicities (DLT's) and recommended Phase 2 dose (RP2D).
- Patients received treatment until progression or intolerable toxicity.
- Patients were evaluable for DLT if they received at least 2 cycles of therapy
- DLT period was defined as the first 6 weeks from C1D1.

## Secondary endpoints:

- ORR, PFS
- Frequency of Ir-AEs.

# Efficacy Analysis



## Data cutoff –December 30,2020

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%)

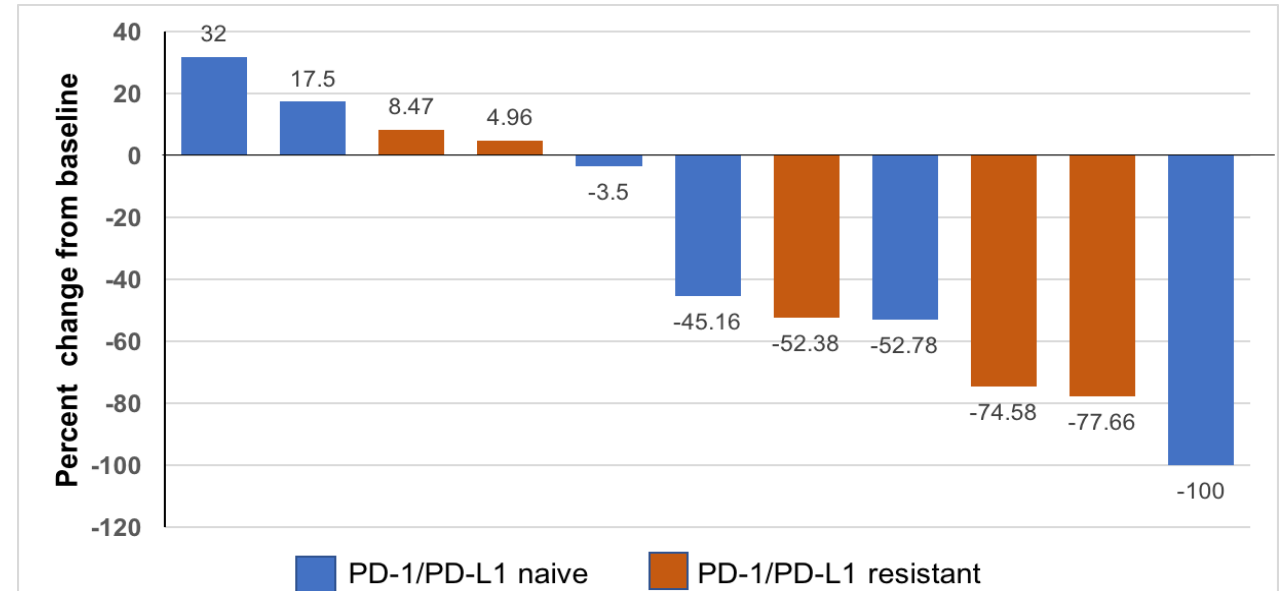
\*PR –Partial Response - RESIST 1.1 : At least a 30% decrease in the sum of diameters of target lesions, taking as reference the baseline sum diameters.

### ❖ 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

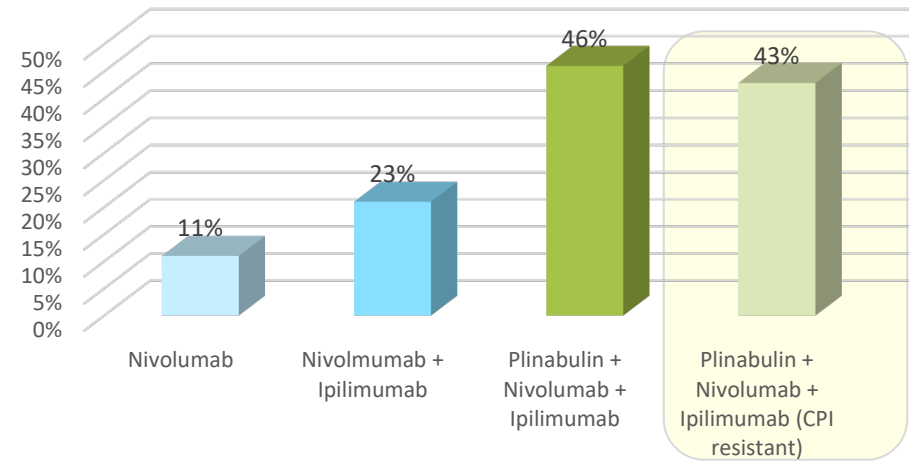


**Waterfall plot of best overall response in target lesions compared to baseline**

## Efficacy Summary

## Immune-Related AE Summary

Improvement of Overall Response Rate



## Reduction of Grade 3/4 Immune-Related AEs

- Plinabulin + Nivolumab + Ipilimumab: **12.5%**
- Nivolumab +Ipilimumab (historical): **37%**



# Plinabulin as a Potential Synergistic “Cornerstone” Agent in IO Therapy



## 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.

# Recent Goals Achieved, Near Term Milestones for Value Creation

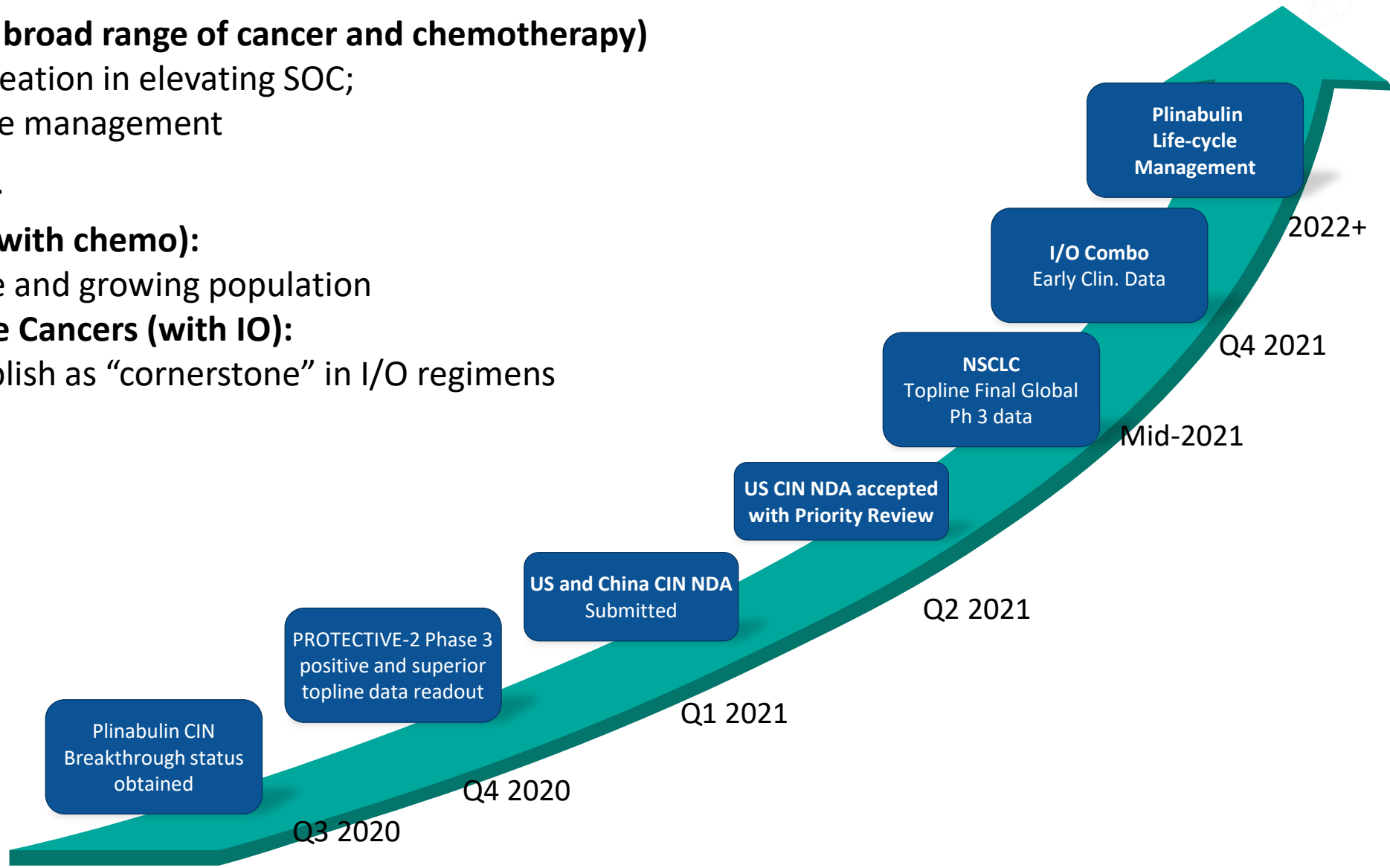


## CIN (Target broad range of cancer and chemotherapy)

- ✓ Value creation in elevating SOC;
- ✓ Life cycle management

## Anti-cancer

- ✓ **NSCLC (with chemo):**
  - Large and growing population
- ✓ **Multiple Cancers (with IO):**
  - Establish as “cornerstone” in I/O regimens





**BeyondSpring**

## Corporate Highlights



# 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 patients in the largest global markets 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 CIN & NSCLC

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

#### **CIN: Combo with G-CSF (superior efficacy vs. SOC)**

- ✓ US NDA accepted with Priority Review
- ✓ China NDA submitted March 2021
- ✓ Breakthrough Designation (US, China)
- ✓ Global Market: \$7B

#### **NSCLC: Combo with docetaxel**

- ✓ Final Topline Ph 3 data mid-year 2021
- ✓ Potential NDA submission in 2022
- ✓ \$30B+ global market

### Broad Pipeline

#### Plinabulin: A pipeline in a drug

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

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

#### Targeted Protein Degradation Platform

- ✓ SEED Therapeutics (Subsidiary)
- ✓ 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

**Cash position at \$90.6M at 3/31/2021 to enable execution on our vision**



thank you!

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