BeyondSpring

Corporate Presentation
39th Annual J.P. Morgan Healthcare Conference

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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.

Except as required by law, we assume no obligation to update these forward-looking statements publicly, or to update the reasons why actual results could differ materially from those anticipated in the forward-looking statements, even if new information becomes available in the future.

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.

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

2 near-NDA Assets Global Market Opportunities

PLINABULIN: Raising SOC in CIN & NSCLC

- ✓ First-in-Class immune agent
- ✓ New Chemical Entity
- ✓ IP through 2036 in 36 jurisdictions

CIN: Combo with G-CSF

- ✓ Final Ph 3 topline data Nov 2020
- ✓ NDA submission 1Q 2021
- ✓ Market: $4.5B (US)
- ✓ Breakthrough Designation (US, China)

NSCLC: Combo with docetaxel

- ✓ Final Ph 3 data 1H2021
- ✓ Early 2022 NDA submission
- ✓ $30B+ global market

Broad Pipeline

PLINABULIN: A pipeline in a drug

- ✓ Triple combo w/IO agents and radiation/chemo
- ✓ Expansion to additional solid tumors

Targeted Protein Degradation Platform

- ✓ Seed Therapeutics (Subsidiary)
- ✓ Collaboration with Eli Lilly

Three Pre-Clinical IO Agents

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

Commercialization Planning Underway

Experienced leadership team with 50+ product launches

LAN Huang, Ph.D.
CEO and Founder

Berkeley UNIVERSITY OF CALIFORNIA · Memorial Sloan Kettering Cancer Center · 无锡麦涛岚华

RAMON Mohanlal M.D., Ph.D.
Chief Medical Officer, EVP of R&D

gsk · VERTEX · NOVARTIS

RICHARD Daly
Chief Operating Officer

AstraZeneca · Takeda · Abbott

GORDON Schooley, Ph.D.
Chief Regulatory Officer

PACIRA BIOSCIENCES, INC. · Allergan · Newport an Evopharma Company

ELIZABETH Czerepak, MBA
Chief Financial Officer

J.P.Morgan · BASF · Roche · MERCK

JAMES Tonra, Ph.D.
Chief Scientific Officer

Lilly · REGENERON · MILLENNIUM

PAUL Friel
Chief Commercial Officer

Takeda · vyaire MEDICAL · kastle therapeutics

KENNETH Lloyd, Ph.D.
Chief Scientific Officer, Emeritus

Wyeth · nereus · Roche

50+ global pharma experiences	**40+** partnerships/ alliances	**20+** startups	**30+** billion financing experience	**50+** approvals and launches	**30+** initial public offerings (IPOs)

Two Near-term NDAs & robust drug development pipeline

	Indication	Program	Trial name / collaborator	Preclinical	Phase 1	Phase 2	Phase 3	Commercial rights	Status/Next Milestone	
Late stage	**CIN (All cancer, all chemo)**	Plinabulin + pegfilgrastim	PROTECTIVE-1 (Study 105)	Phase 3 primary endpoint met at interim analysis				Global[1]	China NDA Submission Q1 2021[1]	**U.S. NDA Submission Q1 2021**
			PROTECTIVE-2 (Study 106)	Phase 3 primary endpoint met at interim analysis						
	NSCLC (2nd/3rd line)	Plinabulin + docetaxel	DUBLIN-3 (Study 103)	Phase 3 second interim analysis completed				Global[1]		**Global Final Ph3 data H1 2021**
Investigator-initiated IO	NSCLC (2nd/3rd line)	Plinabulin + nivolumab	Fred Hutch/Univ. Washington/UCSD					Global[1]	Finished phase 1	
	SCLC	Plinabulin + nivolumab + ipilimumab	Rutgers University					Global[1]	Ongoing	
	Multi-cancer (2nd/3rd line)	Plinabulin + PD-1/PD-L1 + radiation/chemo	MD Anderson						Initiate phase 1 in 7 cancers Q1 2021	
Investigator-initiated IO	Oral T cell co-stimulator	BPI-002						Global		
	IKK inhibitor	BPI-003						Global		
	Oral neo-antigen generator	BPI-004						Global		
Subsidiary	1st target KRAS	Targeted Protein degradation (TPD, molecular glue)	Seed Therapeutics[3]					Global[1]		

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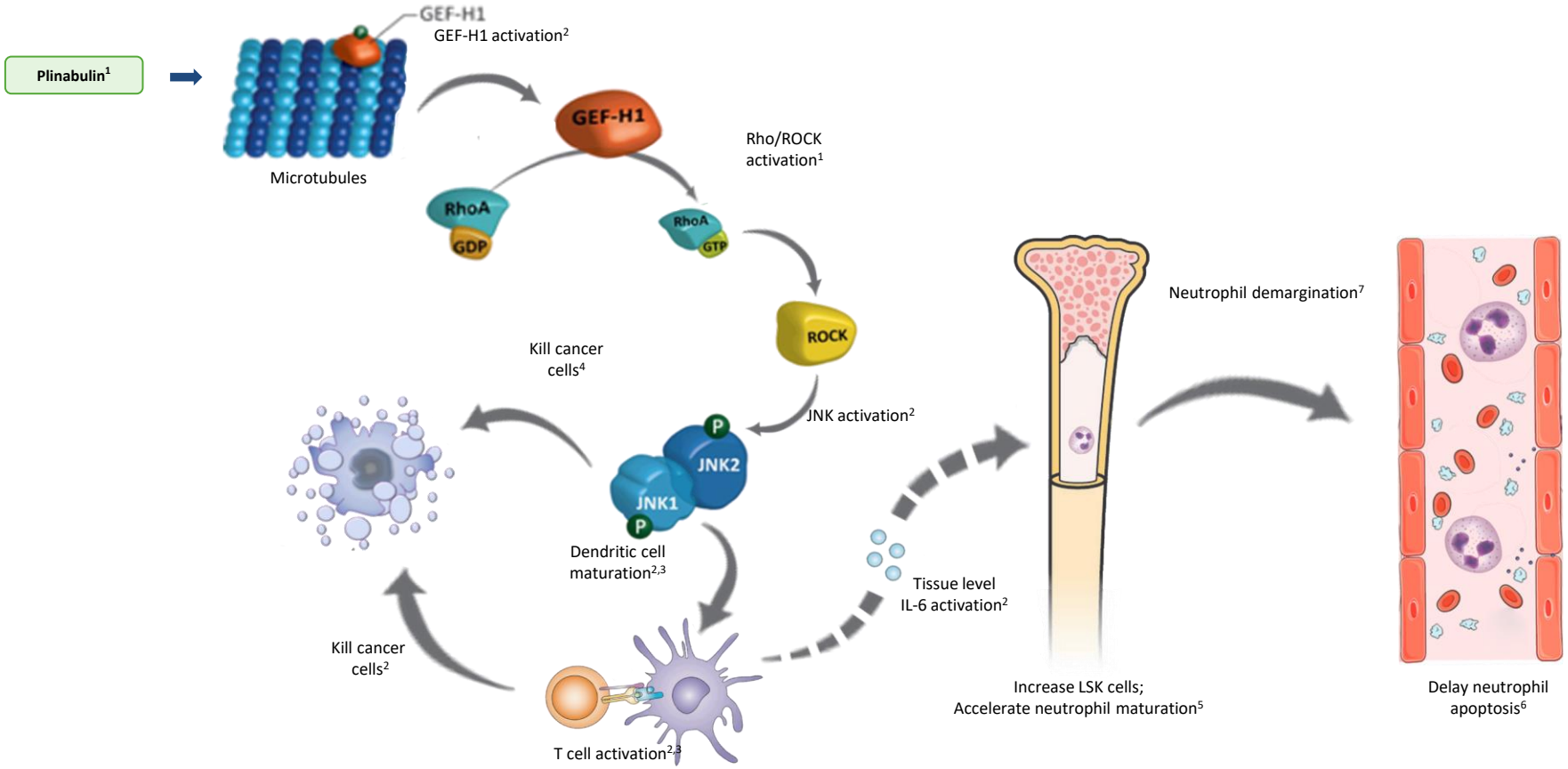
Note: [1] Rolling submission basis in China. [2] Global rights to Plinabulin ex-China. 58% ownership of Chinese subsidiary, Dalian Wanchunbulin Pharmaceuticals Ltd., which owns Chinese rights to Plinabulin. [3] Seed Therapeutics is a subsidiary of BeyondSpring Therapeutics.

Plinabulin: first-in-class agent, stimulating innate and adaptive immune system (Proven Target: Immune Defense Protein GEF-H1)

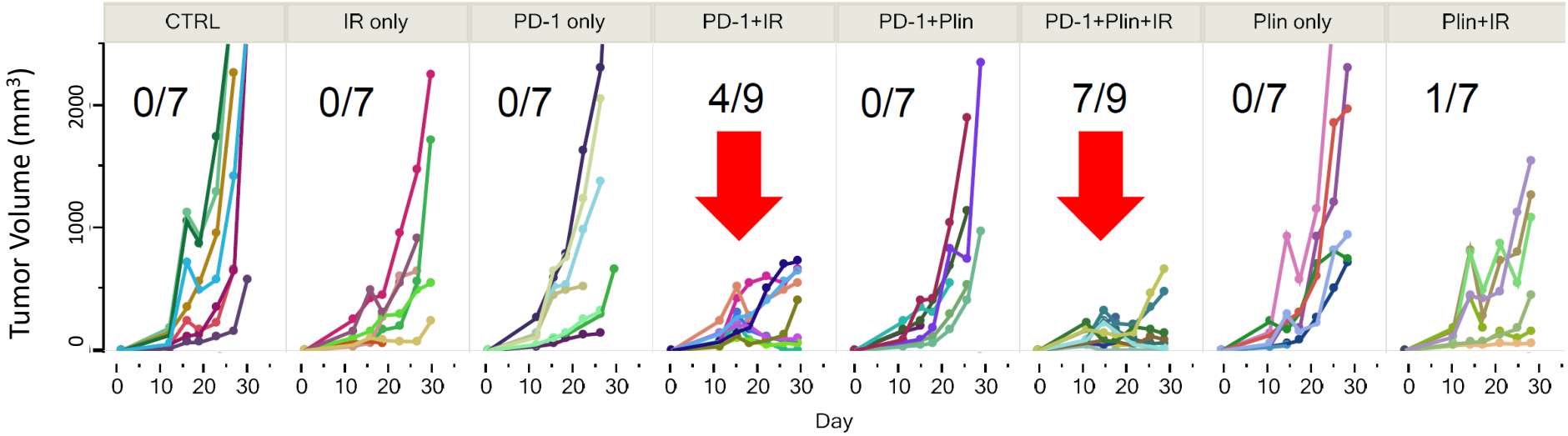


Plinabulin's immune mechanism designed to enable its effects in multiple cancer indications:

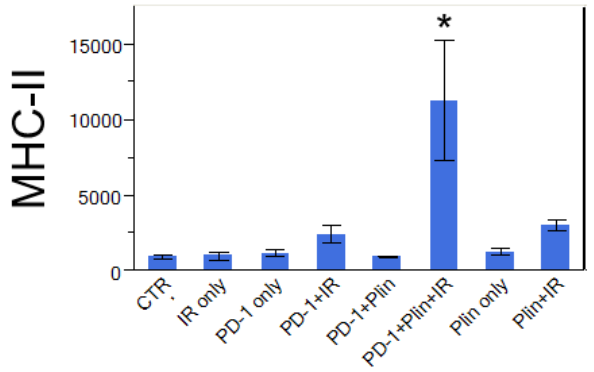
- **Chemotherapy Induced Neutropenia (CIN):** Designed to protect progenitor cells from chemo assault in bone marrow with week 1 benefit, which compliments G-CSF week 2 benefit for improved benefit potential
- **NSCLC:** Chemo (e.g. docetaxel) introduces real time tumor antigen, Plinabulin is designed 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: [1] La Sala et al., 2019 Chem. [2] Kashyap et al., 2019 Cell Reports. [3] Zhang et al., 2005 Mol Cell Biol. [4] Singh et al., 2011 Blood. [5] Suwa et al., 2000 Am J Physiol Heart Circ Physiol; Ghosh et al., 2018 ACR Annual Conference; Blayney et al., Society of Leukocyte Biology. [6] Asensi et al., 2004 Infection and Immunity.

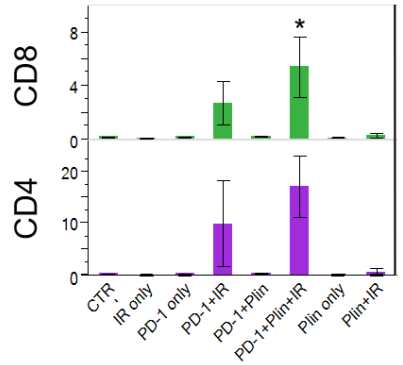
Triple Combo: Plinabulin + PD-1 + Radiation the Best Tumor Response in PD-1 non-responsive tumor model (MD Anderson)



DC activation within the tumor (Day 30)



T cell analysis within the tumor (Day 30)



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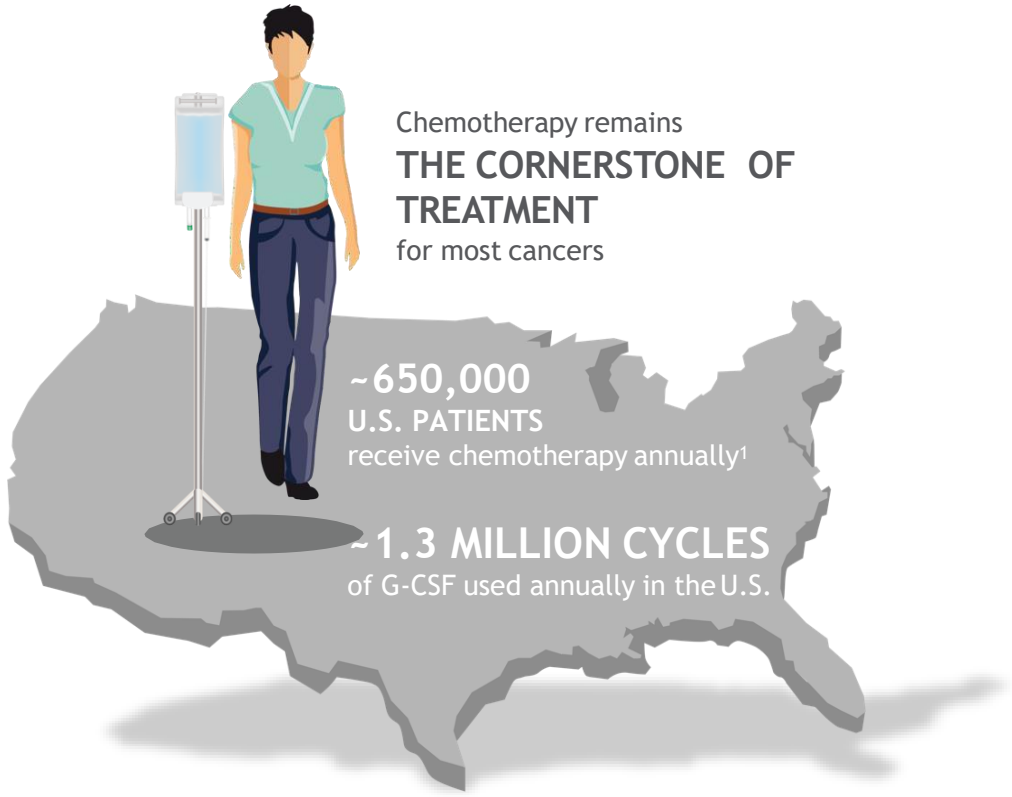
Breakthrough Therapy Designation (US & China FDA) - NDA submission Q1 2021

Plinabulin + G-CSF

in Chemotherapy-Induced Neutropenia (CIN)

Plinabulin will add value to a large and growing CIN market - PD-1 + chemo approved, so chemo will not go away

Plinabulin + G-CSF in each cycle of chemo in non-myeloid cancers prevented or reduced the severity of neutropenia



U.S. Sales -- $4.5 Billion[2]

As a combination therapy Plinabulin's base of business is G-CSF units

G-CSF cycles/year:

- U.S.: 1.3 million[2]
- Global: 4 million[3]

Unit growth (U.S.):[2]

- MAT Aug '19: 6.8%
- MAT Aug '20: 1.1%*

50%+ growth expected in use of first-line chemotherapy by 2040 worldwide[4]

Note: [1] Centers for Disease Control and Prevention. Information for Health Care Providers. Available at: www.cdc.gov/cancer/preventinfections/providers.htm. Accessed February 21, 2020; [2] NSP IQVIA July '20; [3]G-CSF market size based on IQVIA data (MIDAS for ex-U.S. and DDM MD for U.S.; Q3 '16 to Q2 '18. Standardized G-CSF units. 4. Wilson B, Jacob S, Yap ML, et al. Estimates of global chemotherapy demands and corresponding physician workforce requirements for 2018 and 2040: a population-based study. Lancet Oncology 2019; 20(6): 769-780.

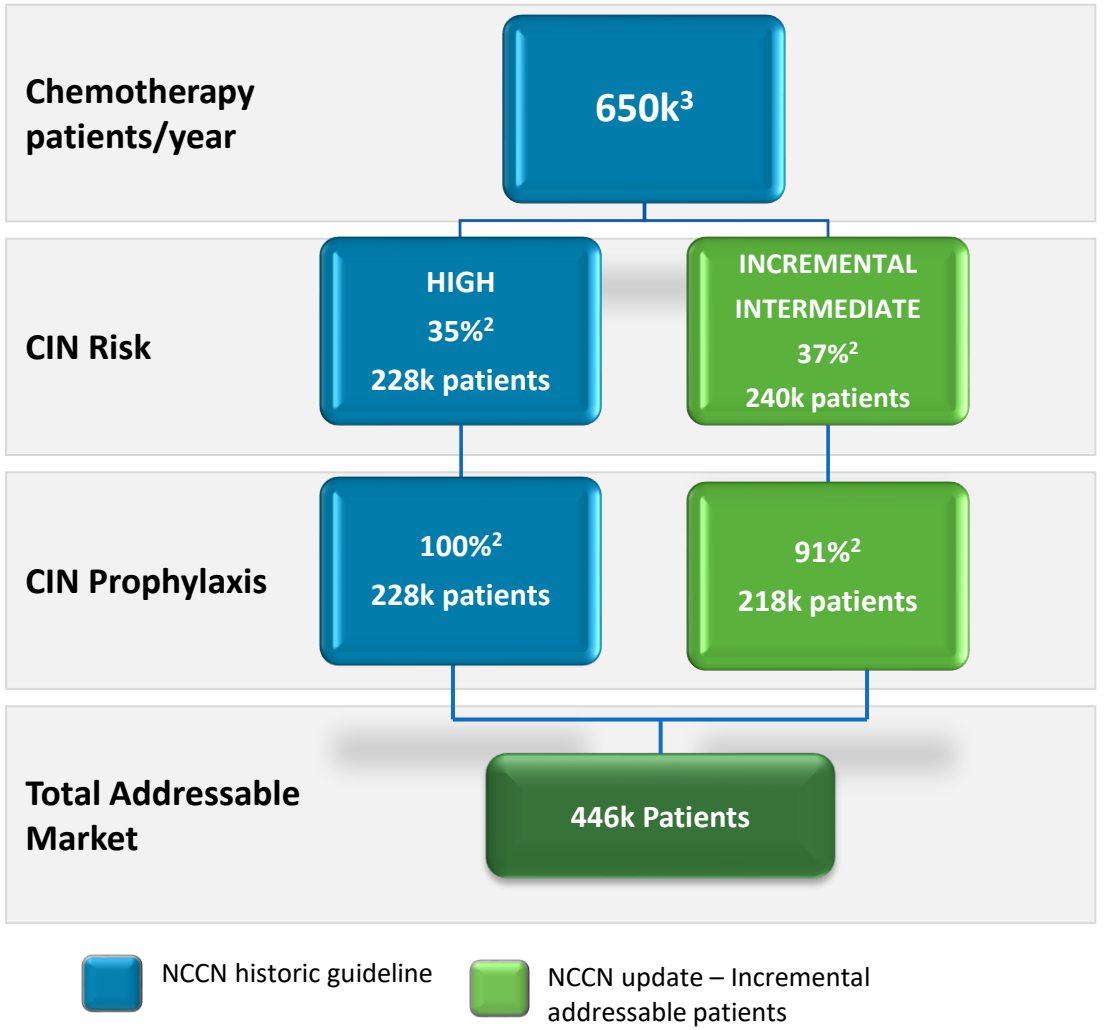
* Growth despite a 20% decline in chemotherapy cycles nationwide from March – June '20 due to the pandemic.

New CIN guidelines double the Addressable US Market

- **CIN guidelines modified in early 2020:**
  - COVID-19 recognized as a universal risk factor
  - Prophylaxis now recommended for both high and intermediate risk patients

- **The addressable population increased by 100%:**
  - **2019:** 30% of intermediate risk patients received prophylaxis for CIN[1]
  - **2020**: 90% - dramatic jump in approach to preventing CIN[2]

CIN Prophylaxis Market dynamics post-guideline update



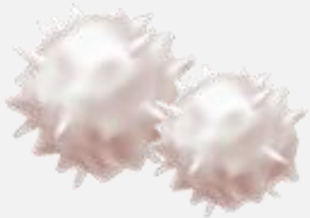
1 BYSI qual market research Sept 2019, 2 BYSI qual Market research Aug 2020, 3 https://www.cdc.gov/cancer/preventinfections/providers.html

High unmet medical need even with SOC G-CSF

CIN is a dangerous decrease in a patient's white blood cell count.
If Grade 4 neutropenia (ANC < 0.5x109 cells/L) is not treated, patients could die in first cycle of chemotherapy

Short-term Outcome Benefit

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



CIN

#1 reason for FN, hospitalization, sepsis, mortality and chemotherapy disruption[1]

Long-term Outcome Benefit

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

Slight Changes in Dosing or Delivery Can Have A Devastating Impact on Survival[2]

15% = 50%

Reduction in Relative Dose Intensity

Reduction in Overall Survival

More than 75% of negative clinical consequences occur in Week 1 after chemo; G-CSF cannot prevent week 1
Plinabulin + G-CSF has the potential to address this important unmet clinical need[3]

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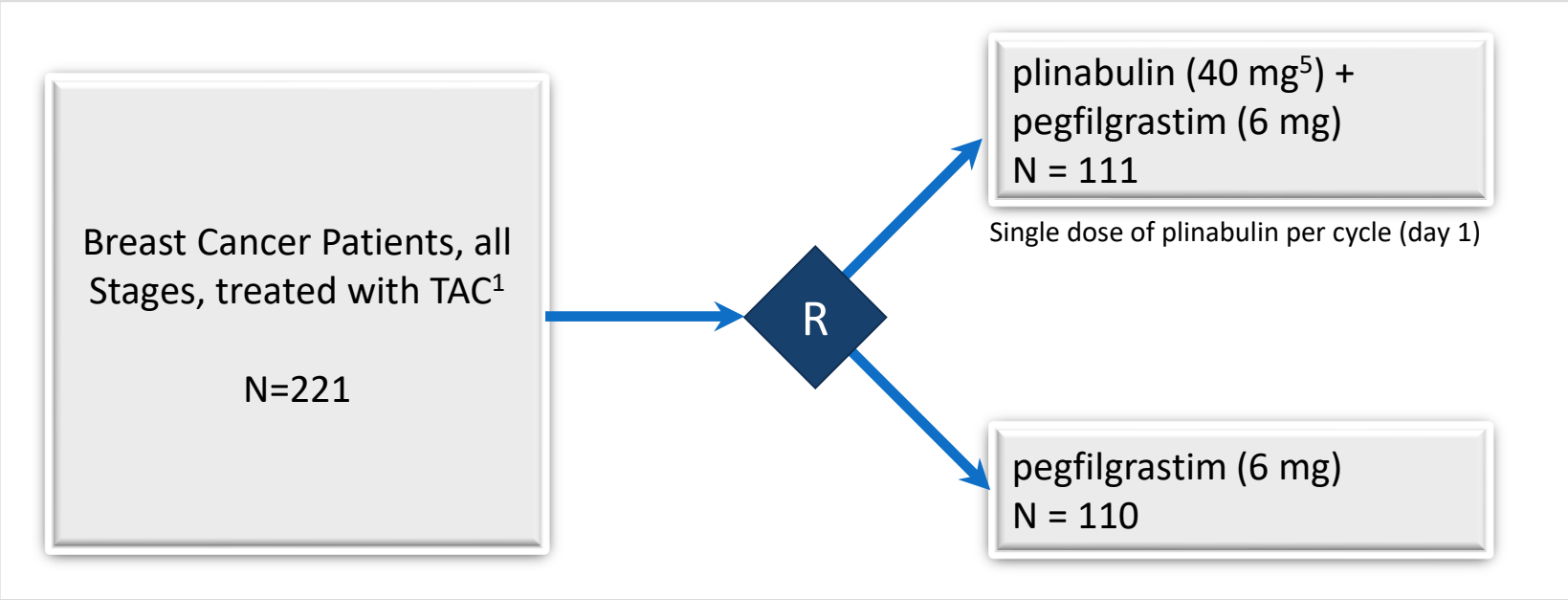
Source: [1] Lalami Y, Klastersky J.. Crit. Rev Oncol Hematol. 2017; 120:163-179. [2] Bonadonna G, Valagussa P, Moliterni A et al. Adjuvant cyclophosphamide, methotrexate, and fluorouracil in node-positive breast cancer. N Engl J Med 1995;332:901-906. [3] Cancer, Volume: 98, Issue: 11, Pages: 2402-2409, First published: 17 November 2003, DOI: (10.1002/cncr.11827)

Plinabulin trials designed to maximize broad potential: Plinabulin + G-CSF for all chemo in non-myeloid cancers

Protective-2 Phase 3 Design （4 cycles of chemo treatment）



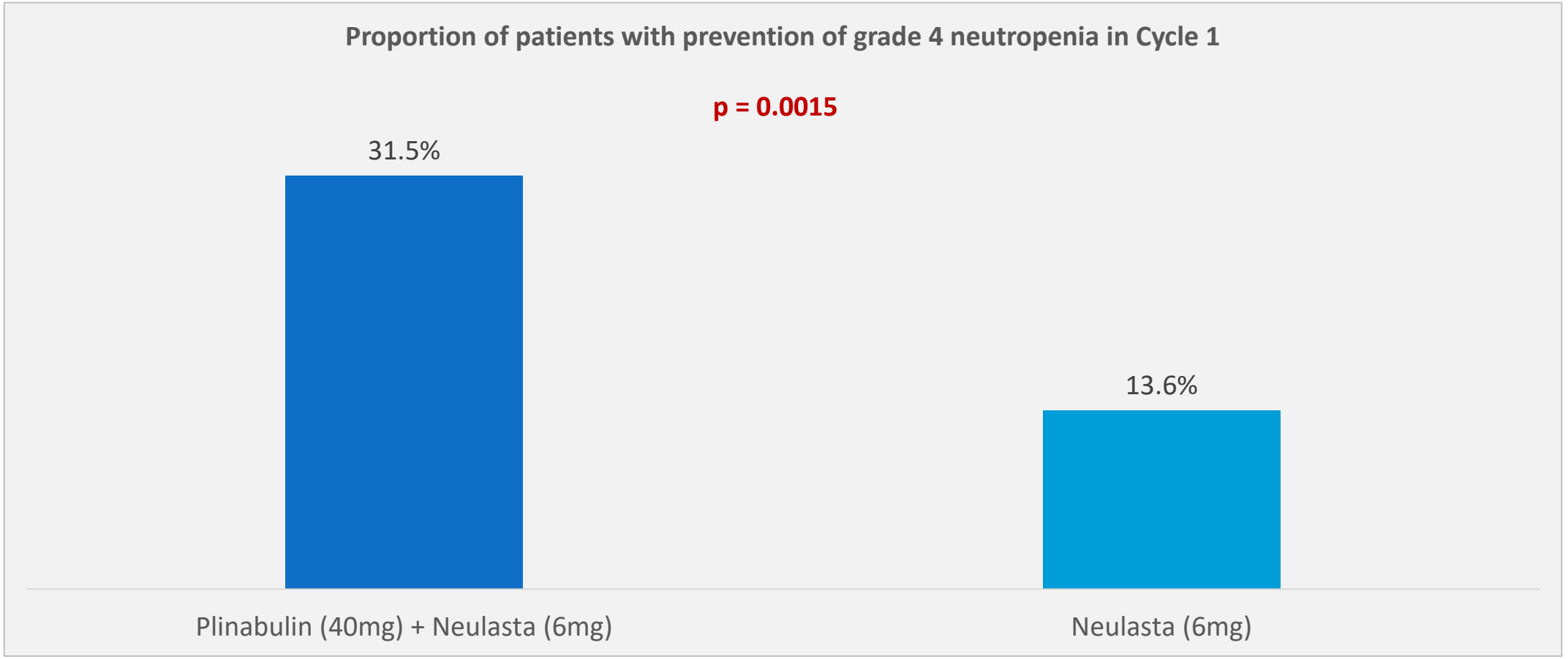
Double blinded, active controlled, global trial (CRO & central lab: Covance)

Primary Endpoint:
- % prevent Grade 4 neutropenia (Cycle 1)

Secondary Endpoints:
- Mean DSN[2] (Cycle 1, Day 1-8)
- Mean ANC[3] nadir (Cycle 1)
- % of prevention of grade 3 and 4 neutropenia (Cycle 1)
- DSN (Cycle 1)
- % of bone pain (Cycle 1)
- Composite risk
- % of RDI[4] < 85%

[1]TAC=Docetaxel, doxorubicin and cyclophosphamide.
[2]Duration of Severe (Grade 4) Neutropenia
[3]Absolute Neutrophil Count
[4]Relative Dose Intensity
[5]Fixed dose, equivalent to 20 mg/m^2

Plinabulin – G-CSF combination demonstrated over 100% better prevention of grade 4 neutropenia in Cycle 1



PROTECTIVE-2 Phase 3 data: positive topline results with statistical significance favoring the combination

Key Efficacy Endpoints	Results (combo n=111, pegfilgrastim n=110)
Primary endpoint:	
Proportion of patients with prevention of grade 4 neutropenia in Cycle 1	• 31.5% vs. 13.6%, p=0.0015 • **>100% better prevention rate** in combination of plinabulin + G-CSF
Key secondary endpoints (based on ANC):	
Mean DSN in Cycle 1, Day 1-8	• p = 0.0065 • Plinabulin's MoA of early onset in Week 1
Mean DSN in Cycle 1 (severe neutropenia: ANC < 0.5 x 10^9 cells/L)	• p = 0.0324 • Combination is better in CIN benefit vs. G-CSF in cycle 1
Mean ANC Nadir (x 10^9 cells/L)	• 0.538 vs. 0.308, p = 0.0002 • The combination helps to lift patients away from grade 4 danger zone
Mean Duration of Profound Neutropenia in cycle 1 (Profound Neutropenia: ANC < 0.1 x 10^9 cells/L)	• p = 0.0004 • Combo better than G-CSF alone in CIN benefit

Better safety profile in the combination vs. SoC

- **>20% less grade 4 AEs** in the combination (**58.6%**), compared to pegfilgrastim alone **(80.0%)**

Profound Neutropenia leads to 80% death in first week of infection[1], 48% FN and 50% Infection[2].

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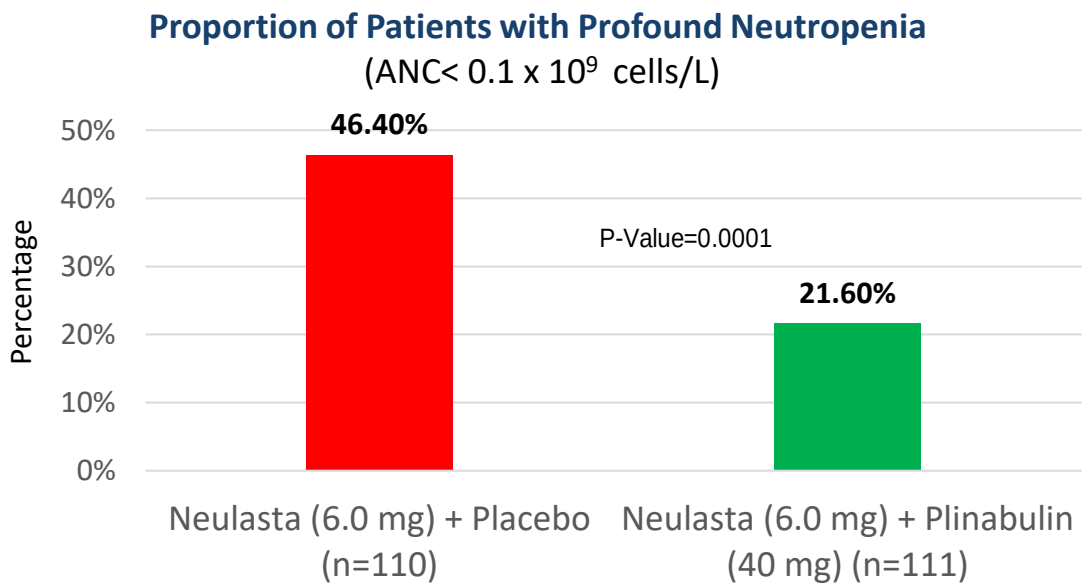
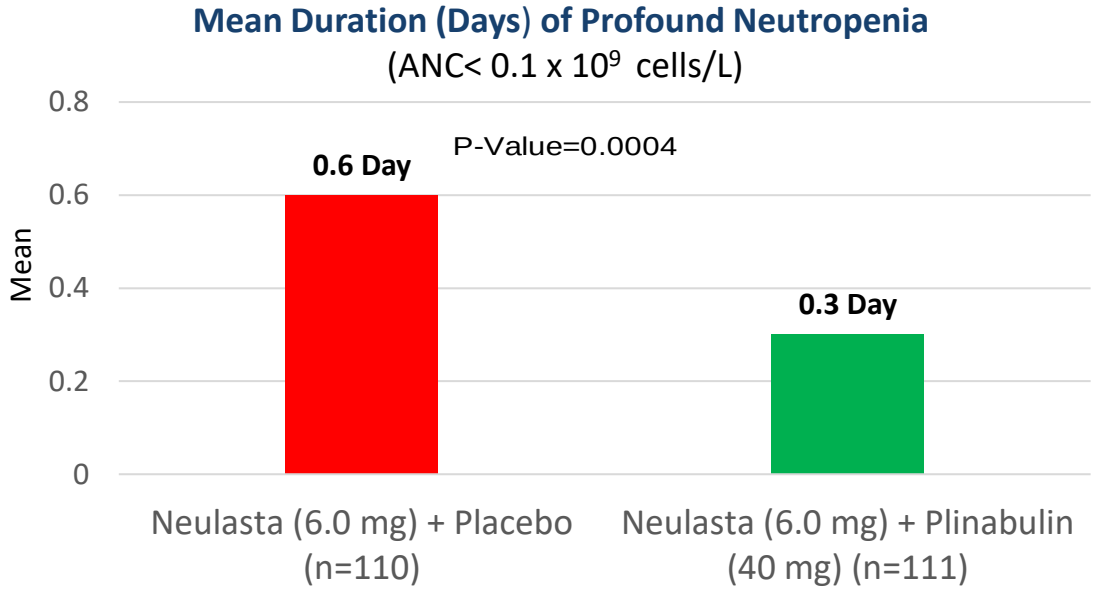
1. Bodey et al. Ann Intern Med 64(2): 328 (1966); 2. Bodey et al. Cancer 41(4): 1610 (1978)

Protective-2 (Phase 3): Superior prevention of Profound Neutropenia with Combination vs G-CSF alone





The combination reduces the incidence of Profound Neutropenia by >50% Compared to G-CSF Alone, which correlates to >40% FN risk reduction in the combo vs. G-CSF.

Plinabulin+ G-CSF for CIN, NDA Submission in Q1 2021: Superior profile in a broad label: all chemo, non-myeloid solid tumor

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

Supporting Study

Plinabulin vs. placebo

- 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)

- Superior response in primary and key secondary endpoints with statistical significance
- Effect size correlate with clinical meaningful endpoints

MOA support from 5 studies: Plinabulin early onset in Week 1, G-CSF effect in Week 2

Supporting Study

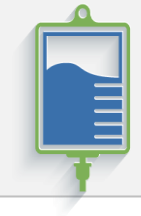
Plinabulin vs. G-CSF (Protective-1)

- Non-inferior CIN activity
- Superior adverse event profile: limited bone pain, limited platelet reduction, and limited immune suppression[1]

700+ cancer patients treated with Plinabulin (various doses)

1. Blayney et al. JAMA Oncology 6(11): e204429 (2020)

Chemotherapy without compromise: Turning the **4 Ds** into the **4 Ss**



DECREASED
recommended dose

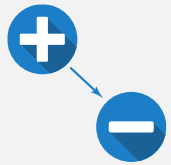
STABLE DOSE
maintaining ≥85%

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

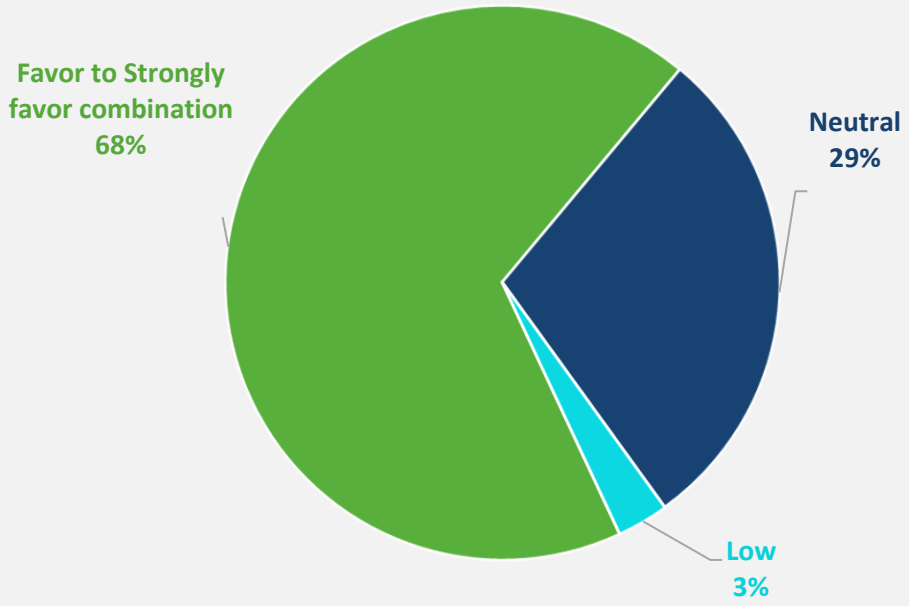
- Differentiated clinical profile, potential to improve SOC
- Greater clinical control
- Improved outcomes

Oncologists understand Plinabulin's potential to raise the SoC in CIN

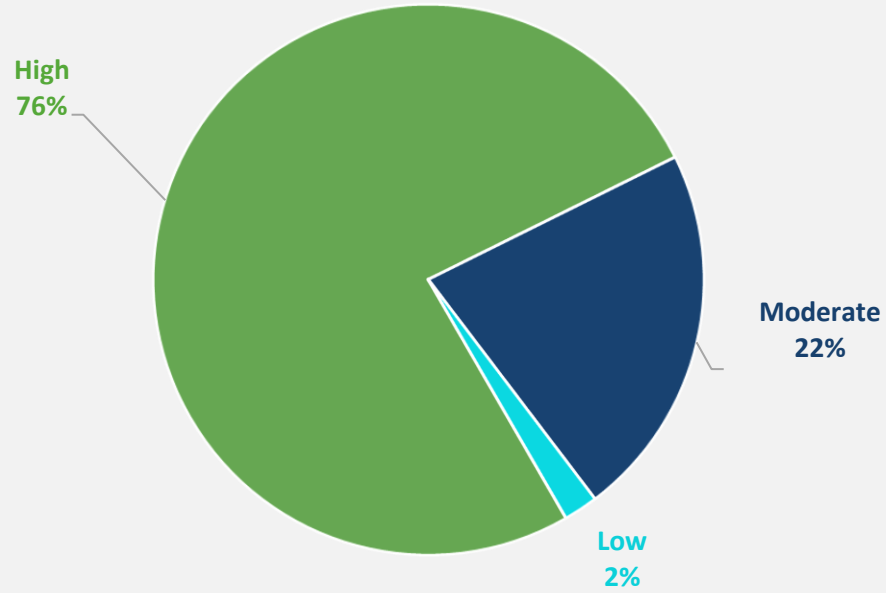
Survey of 102 Board-certified U.S. Oncologists

- Understanding of combination therapy: **High**
- Likelihood to prescribe: **High**

Comfort with COMBINATION THERAPY



Likelihood to use Plinabulin + G-CSF COMBINATION THERAPY



Market research conducted Sep '20; n = 102 board certified U.S. oncologists; data on file BeyondSpring
C01 Based on the product information you have just seen, how likely are you to prescribe the Product N + G-CSF combo for CIN in non-myeloid malignancies?
C02 How would you rate your comfort with using a combination treatment (e.g. Product N + G-CSF combo) for CIN in non-myeloid malignancies

Plinabulin + G-CSF: “Breakthrough Therapy” with potential to set a new SOC for 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)
- ✓ Monotherapy G-CSF not effective
- ✓ 4Ds result in reduced OS

Product differentiation

Plinablulin + G-CSF addresses 3 oncologist needs:

- ✓ Maintains chemo regimen
- ✓ Keeps ANC out of the danger zone and thus less FN and less hospitalization
- ✓ Improved A/E profile

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

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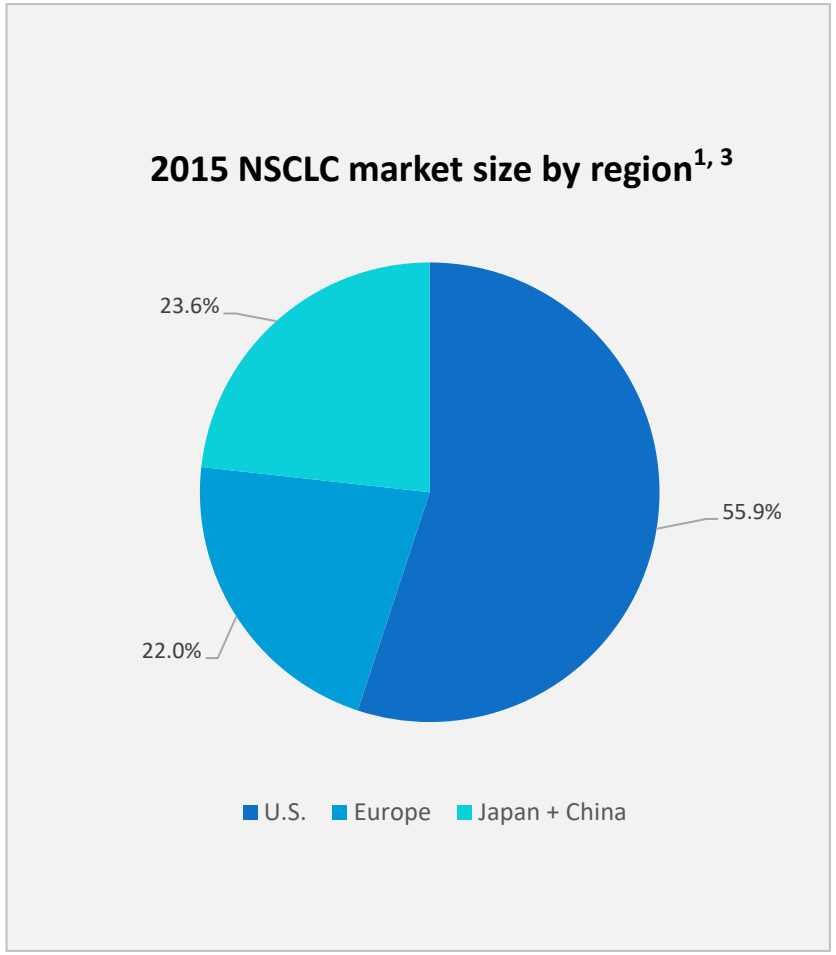
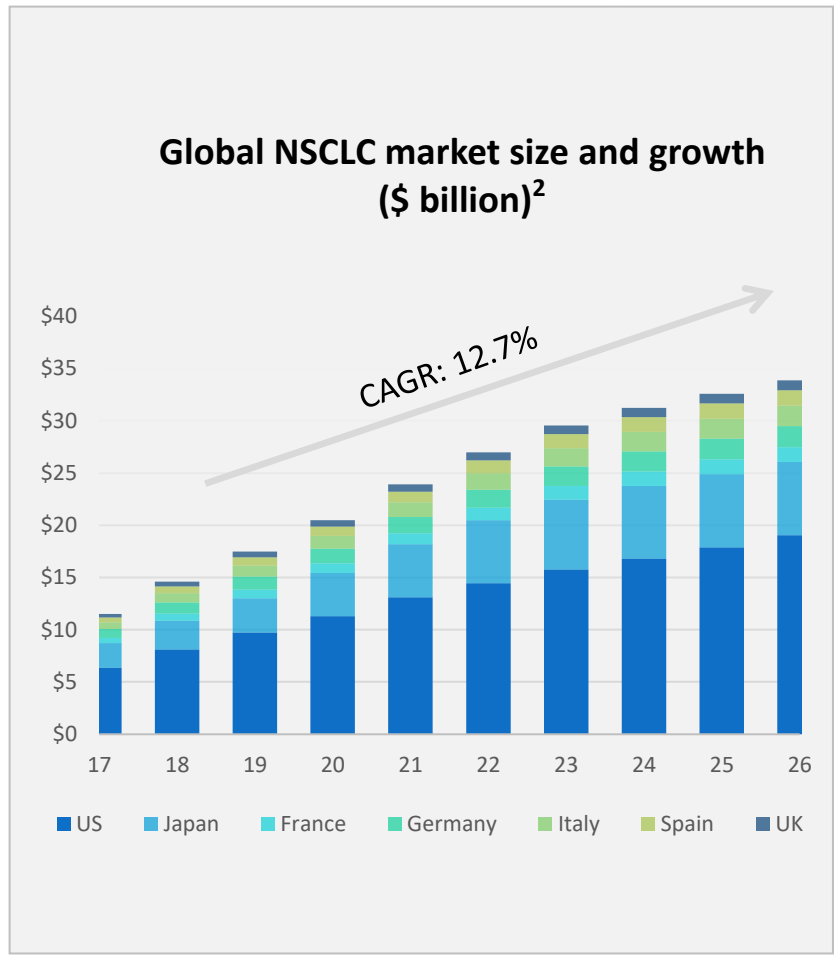
Plinabulin in NSCLC
- Final phase 3 topline anti-cancer data in 1H 2021

Increasing incidence of non-small cell lung cancer (NSCLC)

Key Investment Highlights:

- ~1.5M NSCLC diagnoses globally
- Key NSCLC drug sales (U.S., Japan, and major EU markets):
  - $11.5B in 2017
  - Increasing to $33.9B by 2026
- Primary drivers of growth:
  - Increasing incidence of NSCLC
  - Premium-priced checkpoint inhibitor usage, particularly in the 1st line setting





Source: GlobalData;
Note: [1] Market share by regions broken out into the 8 major markets for NSCLC: France, Germany, Italy, Japan, Spain, UK and U.S. [2]Datamonitor [3] China NSCLC market forecast.

Approved therapies fail to address EGFR wild type NSCLC (85% of Western patients) in 2nd and 3rd line treatment

Only four therapies currently approved: Severe Unmet Medical Needs

	Moving into 1st line		2nd and 3rd lines	
	Nivolumab (PD-1) vs. docetaxel[1]	**Pemetrexed vs. docetaxel[2]**	**Ramucirumab + docetaxel vs. docetaxel[3]**	**Plinabulin + docetaxel vs. Docetaxel[4]**
mOS	+2.8 months (12.2 vs. 9.4) HR = 0.73	+0.4 months (8.3 vs. 7.9) HR = 0.99	+1.4 months (10.5 vs. 9.1) HR = 0.86	+4.6 months (11.3 vs. 6.7) HR < 0.75[5]
ORR	19% vs.12%	9.1% vs. 8.8%	23% vs. 14%	18.4% vs.10.5%
Grade 3/4 neutropenia	0% vs. 27%	5% vs. 40%	49% vs. 39%	7% vs. 26%
DOR	17 vs. 6 months	4.6 vs. 5.3 months		12.7 vs. 1 months
Conclusion	▪ Introduces potential cytokine storm leading to inflammation ▪ Moved into 1st line	▪ No efficacy improvement ▪ Approved based on low neutropenia rate	▪ Modest efficacy benefit ▪ Higher severe neutropenia rate than docetaxel	✓ **Superior efficacy** ✓ **Superior CIN benefit** ✓ **Durable anti-cancer benefit** ✓ **Safety benefit**

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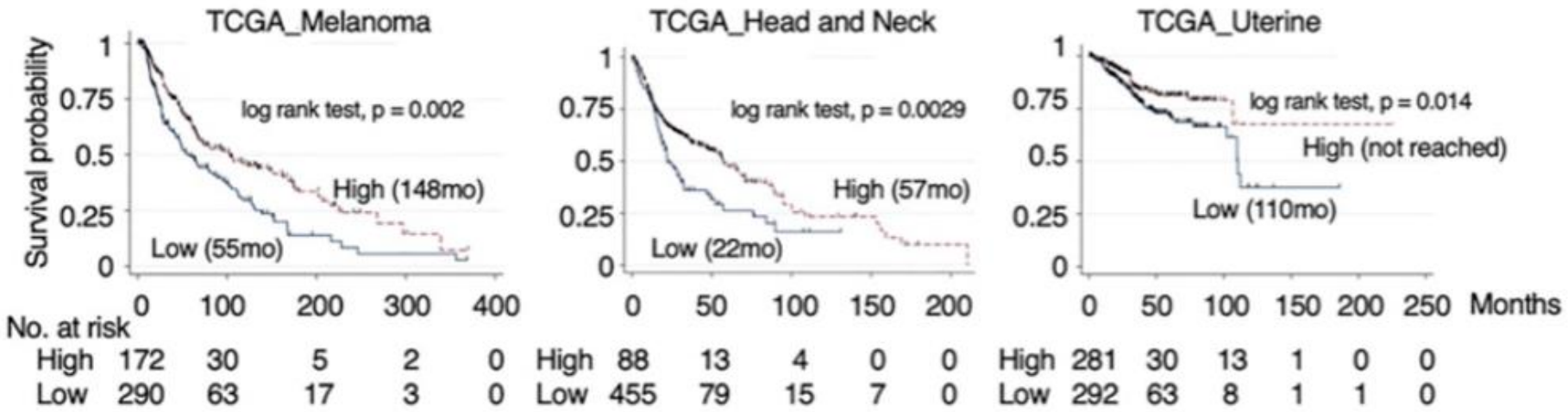
Note: [1] NEJM 373: 1627-1639 (2015). [2] JCO 22(9): 1589-1597 (2004). [3] Lancet 384 (9944): 665-673 (2014). [4] Based on Study 101. [5] Based on first interim look of DUBLIN-3.

DUBLIN-3 (Study 103): Phase 3 in NSCLC hypothesis based on Plinabulin IO mechanism on activating GEF-H1, a proven target

GEF-H1 - higher GEF-H1 immune signatures associated with longer OS in cancer patient [1]

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

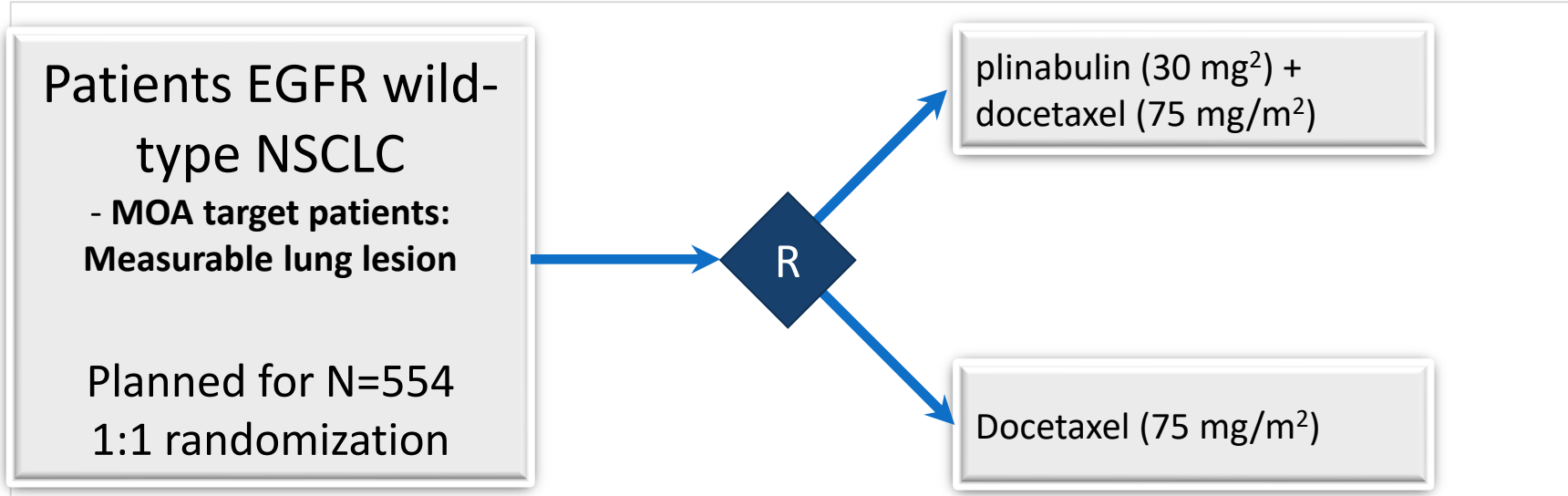


- Anti-cancer activity
- Augmentation of IO effect in combo with chemo or radiation, as antigen generator
- GEF-H1 mechanism driven OS benefit

[1] Kashyap et al., 2019 Cell Reports.

DUBLIN-3 (Study 103): Phase 3 in NSCLC – second interim analysis completed; DSMB recommended trial to continue

DUBLIN-3 Phase 3 in NSCLC Trial Design



Primary Endpoint:
- Overall Survival

Secondary Endpoints:
- Grade 4 neutropenia, ORR, PFS, DOR, QoL

One active controlled, randomized global study with robust p value in primary endpoint is required for approval.

- First interim analysis completed in Q1 2019 at 1/3 patient mortality. DSMB recommended trial to continue without modification (HR < 0.75 based on mOS)
- Second interim analysis completed in Q2 2020 at 2/3 patient mortality. DSMB recommended trial to continue without modification
- **Final analysis: 439 patient mortality; study succeeds if p < 0.046 for mOS 1H 2021**

[1]TAC=Docetaxel, doxorubicin and cyclophosphamide. [2]Duration of Severe (Grade 4) Neutropenia
[3]Absolute Neutrophil Count [4]Relative Dose Intensity Fixed dose, equivalent to 20 mg/m²

Plinabulin: “pipeline in a drug” for multiple cancer indications

Foundation

CIN

CIN indication (broad label)

- 6 clinical trials confirm benefit
- CIN benefit in multiple chemo

Next Milestone

- U.S. & China NDA submission: Q1 2021 for CIN

NSCLC

NSCLC indication (+ docetaxel)

- 2 clinical trials show anti-cancer activities

Next Milestone

- Global final topline data in NSCLC H1 2021

Translation

+ additional solid tumors

Safety demonstrated in >700 patients

- Plinabulin potentially adds OS and reduces CIN of any chemo
- Expand in additional cancer indications in combo with docetaxel and other chemo

Transformation

triple combo with IO + radiation/chemo

The “attractive” triple combo

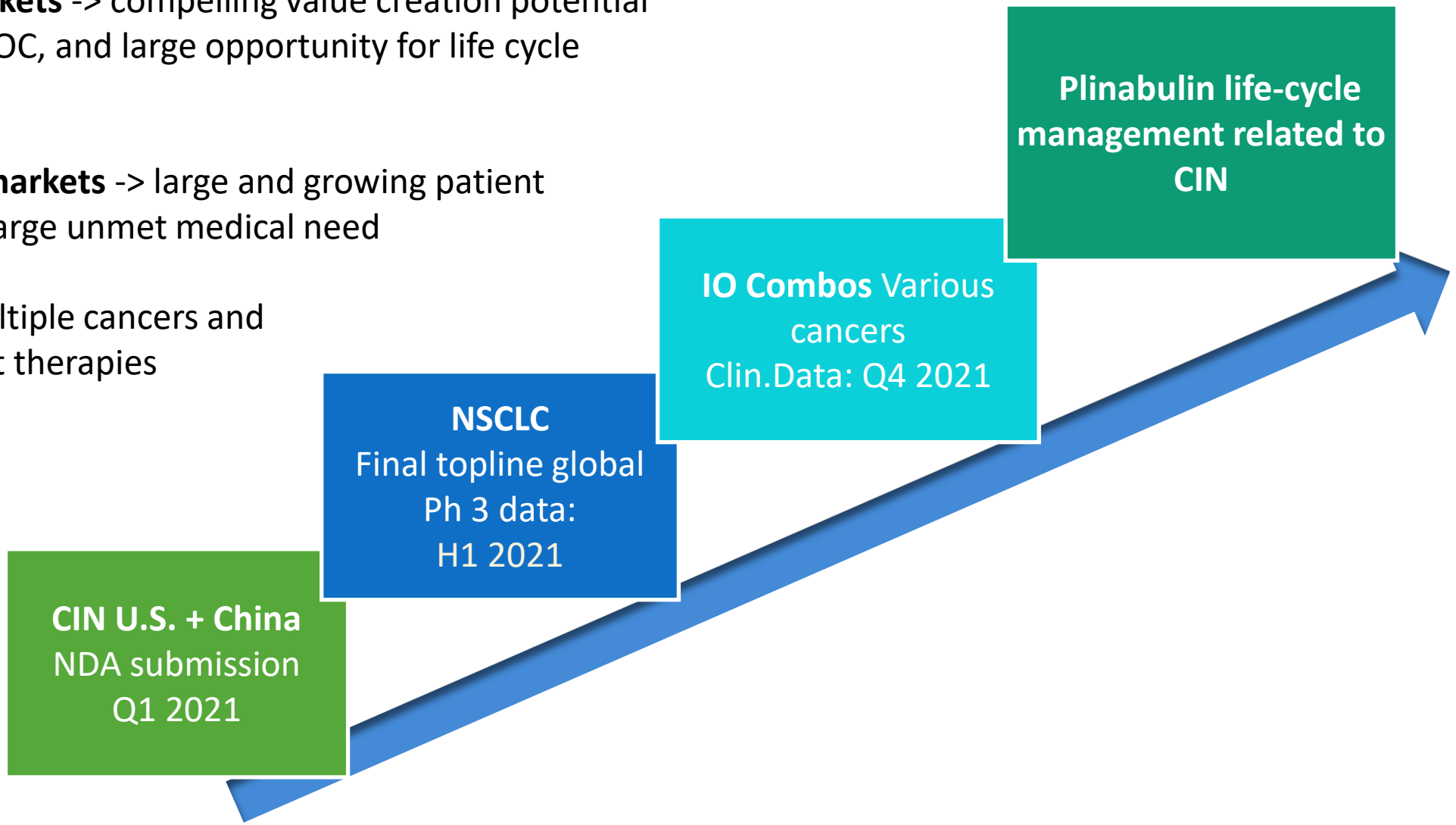
- MOA and pre-clinical data support combo approach and benefits from triple therapy
- Plinabulin: induces tumor antigen specific T cells
- PD-1/PD-L1 Ab: release brake for T cells to target and kill cancers

$100+ billion market opportunity for IO therapies[1]

Note: [1] Based on data from Evaluate Pharma.

Near-term milestones will create significant value for Plinabulin in the next 12 to 36 months

- **CIN in global markets** -> compelling value creation potential from improving SOC, and large opportunity for life cycle management
- **NSCLC in global markets** -> large and growing patient population with large unmet medical need
- **IO Combos** -> multiple cancers and improving current therapies



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SEED THERAPEUTICS

SEED is a majority-owned subsidiary pursuing "Molecular Glue" targeted protein degradation to degrade disease-causing proteins previously believed to be undruggable

- $800M collaboration with 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

2 near-NDA Assets Global Market Opportunities

PLINABULIN: Raising SOC in CIN & NSCLC

- ✓ First-in-Class immune agent
- ✓ New Chemical Entity
- ✓ IP through 2036 in 36 jurisdictions

CIN: Combo with G-CSF

- ✓ Final Ph 3 topline data Nov 2020
- ✓ NDA submission early 1Q 2021
- ✓ Market: $4.5B (US)
- ✓ Breakthrough Designation (US, China)

NSCLC: Combo with docetaxel

- ✓ Final Ph 3 data 1H2021
- ✓ Early 2022 NDA submission
- ✓ $30B+ global market

Broad Pipeline

PLINABULIN: A pipeline in a drug

- ✓ Triple combo w/IO agents and radiation/chemo
- ✓ Expansion to additional solid tumors

Targeted Protein Degradation Platform

- ✓ Seed Therapeutics (Subsidiary)
- ✓ Collaboration with Eli Lilly

Three Pre-Clinical IO Agents

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

Commercialization Planning Underway

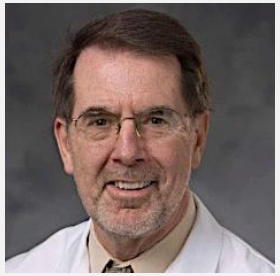
Appendix

Strong network of advisors

Douglas Blayney, M.D.

Principal Investigator, CIN Study 105 & Study 106

- Founding member and former Board Member of the NCCN Guidelines for Neutropenia Management in U.S.
- Former president of ASCO
- Former member of FDA's Oncologic Drugs Advisory Committee
- Medical Director of Stanford Cancer Institute



Jeffrey Crawford, M.D.

DSMB Chairman, CIN Study 105 & Study 106

- Chairman of NCCN Guidelines for Neutropenia Management in U.S.
- Lead investigator of the U.S. multicenter, randomized trial of Filgrastim (G-CSF, Neupogen), leading to FDA approval
- Professor of Medicine at Duke University

Yuankai Shi, M.D.

Principal Investigator, CIN Study 105 & 106 China

- Chairman of the NCCN Guidelines for Neutropenia Management in China
- Director of Oncology Department at Cancer Hospital Chinese Academy of Medical Sciences

David Ettinger, M.D.

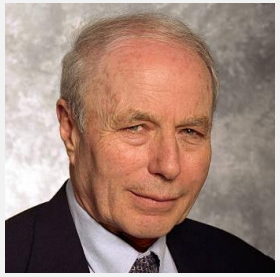
SAB Member, NSCLC Study 103

- Chairman of NCCN Guideline for NSCLC and Board of Directors of NCCN Guideline
- Alex Grass Professor of Oncology, Sidney Kimmel Comprehensive Cancer Center at Johns Hopkins University

Yan Sun, M.D.

Principal Investigator, NSCLC Study 103 China

- Chairman of the NCCN Guidelines for NSCLC in China
- Co-founder of the Steering Committee of the Chinese Society of Clinical Oncology (CSCO)
- Director of GCP Center at Cancer Hospital of Chinese Academy of Medical Sciences



Avram Hershko, M.D.

SAB Member, Ubiquitination Platform

- Nearly 50 years of research leadership in ubiquitination pathway
- 2004 Nobel Prize in Chemistry for discovery of ubiquitin-mediated protein degradation
- Distinguished Professor at Rappaport Faculty of Medicine at Technion in Haifa

Plinabulin – first-in-class agent (a 20-year journey)

2000-2005: NCE discovered 20 years ago from sea microbes, then optimized

- In 2000, new chemical entity (NCE) Halamide class compound was discovered from sea microbes by Nereus Pharmaceuticals based in San Diego, CA
- 300+ derivatives were made and screened through colon cancer cell lines, and Plinabulin was found to be most efficacious and safe compound to enter clinics

2005-2010: Early clinical studies showed unique clinical profile for Plinabulin, a tubulin binder; but did not know why

- Early clinical studies in NSCLC in Plinabulin + docetaxel showed durable anti-cancer benefit, and serendipitous finding of CIN benefit
- Mechanism as a tubulin binder cannot explain clinical profile

2010-2020: Research collaboration with experts in protein structure, immune and CIN field shed light on Plinabulin's unique MOA, leading to targeted clinical development and extended/strong patent protection to 2036

- Four MOA papers published in 2019, collaborating with leading scientists from Univ. of Basel, Fred Hutch, Mass General and MD Anderson
- Data from additional manufacturing and research provide strong basis for extended and strong patent protection to 2036 in 36 jurisdictions
- Design registration studies in CIN and NSCLC based on Plinabulin MOA and chart targeted clinical development programs.

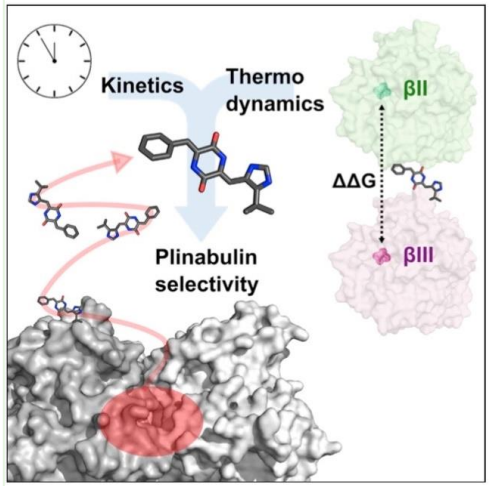
Plinabulin differentiated tubulin binding and its effect in DC maturation and GEF-H1 release published in Chem and Cell Reports

Chem

CellPress

Article

Structure, Thermodynamics, and Kinetics of Plinabulin Binding to Two Tubulin Isotypes



Giuseppina La Sala, Natacha Olieric, Ashwani Sharma, ..., José Fernando Díaz, Michel O. Steinmetz, Andrea Cavalli

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andrea.cavalli@iit.it (A.C.)

HIGHLIGHTS

Plinabulin is a phase 3 anticancer and antineutropenia drug candidate

Plinabulin binding to tubulin differentiates it from other compounds

We report crystal structures of plinabulin in complex with βII- and βIII-tubulin isotypes

We performed thermodynamic and kinetic studies on plinabulin selectivity and mechanism of action

Plinabulin is a novel tubulin-binding agent that is currently in phase 3 clinical trials for cancer treatment and prevention of chemotherapy-induced neutropenia. Plinabulin binds within a distinct tubulin pocket, which differentiates it from other tubulin binders. Aimed at disclosing structural and energetic details of plinabulin binding to tubulin, we combine X-ray crystallography and computational modeling. We compare the plinabulin residence time with that of colchicine and combretastatin-A4. Our study helps understand potential mechanisms underlying differential effects of this family of anti-tubulin drugs.

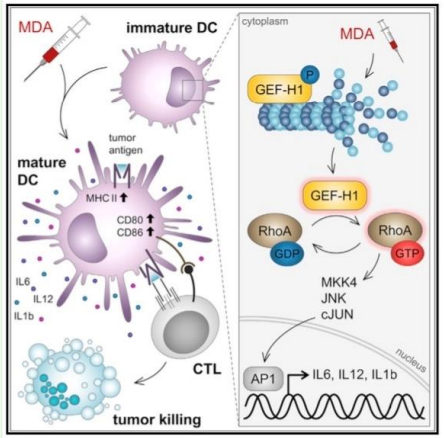
La Sala et al., Chem 5, 1–18
November 14, 2019 © 2019 Elsevier Inc.
https://doi.org/10.1016/j.chempr.2019.08.022

Cell Reports

Article

GEF-H1 Signaling upon Microtubule Destabilization Is Required for Dendritic Cell Activation and Specific Anti-tumor Responses

Graphical Abstract



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In Brief

Certain chemotherapeutics elicit potent anti-tumor immunity. Kashyap et al. demonstrate that microtubule-destabilizing chemotherapeutics induce maturation of dendritic cells through activation of microtubule-associated protein GEF-H1. This leads to effective priming of CD8 T cells against tumor antigens. GEF-H1 is critical for anti-tumor immunity of microtubule-targeting chemotherapy.

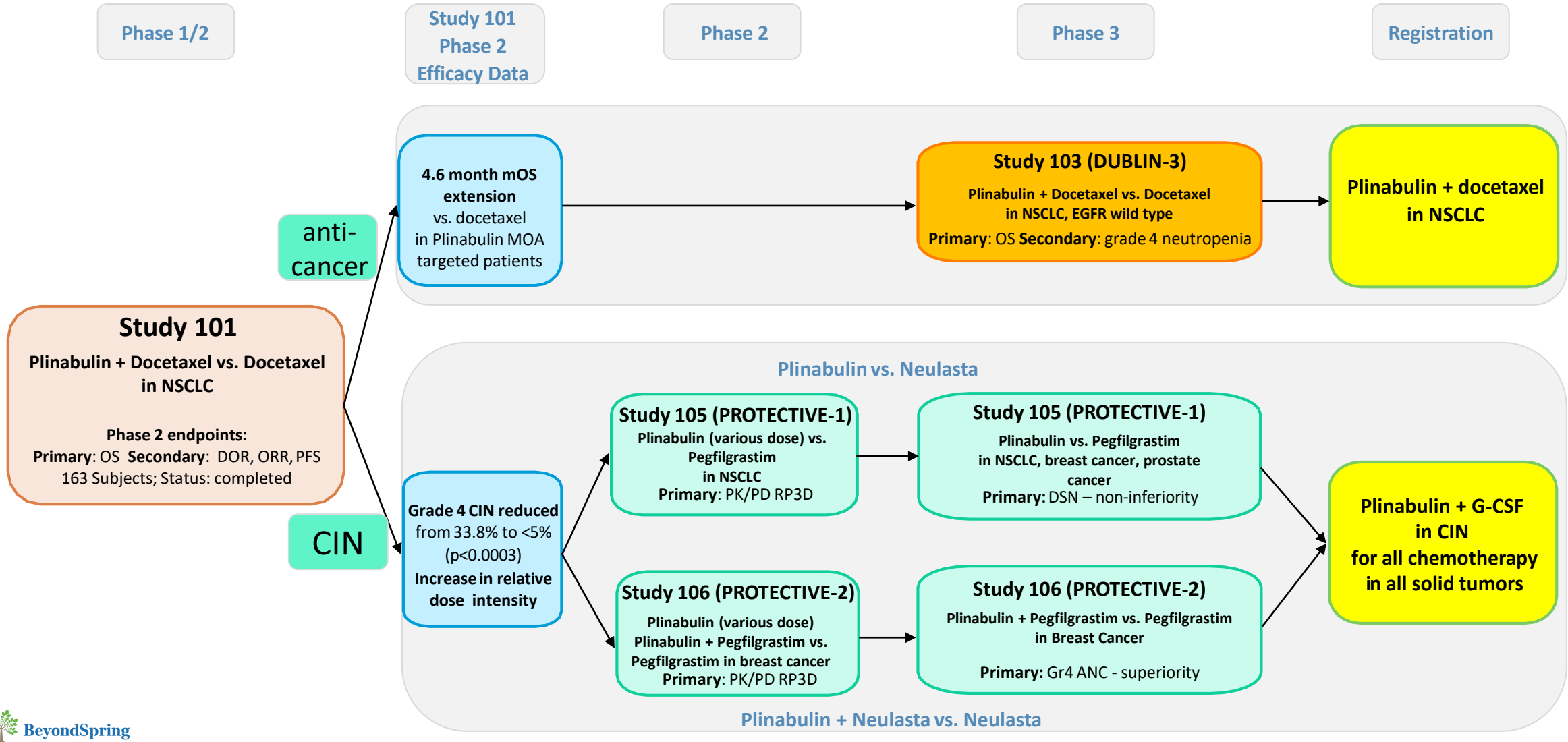
Highlights

- Microtubule destabilization in dendritic cells drives DC maturation and T cell activation
- GEF-H1 is released from microtubules, leading to its activation
- GEF-H1 release triggers the RhoA-JNK-c-Jun signaling axis and AP-1 transcriptional response
- GEF-H1 is critical for DC maturation, antigen cross-presentation, and anti-tumor immunity

Kashyap et al., 2019, Cell Reports 28, 3367–3380
September 24, 2019 © 2019 The Author(s).
https://doi.org/10.1016/j.celrep.2019.08.057

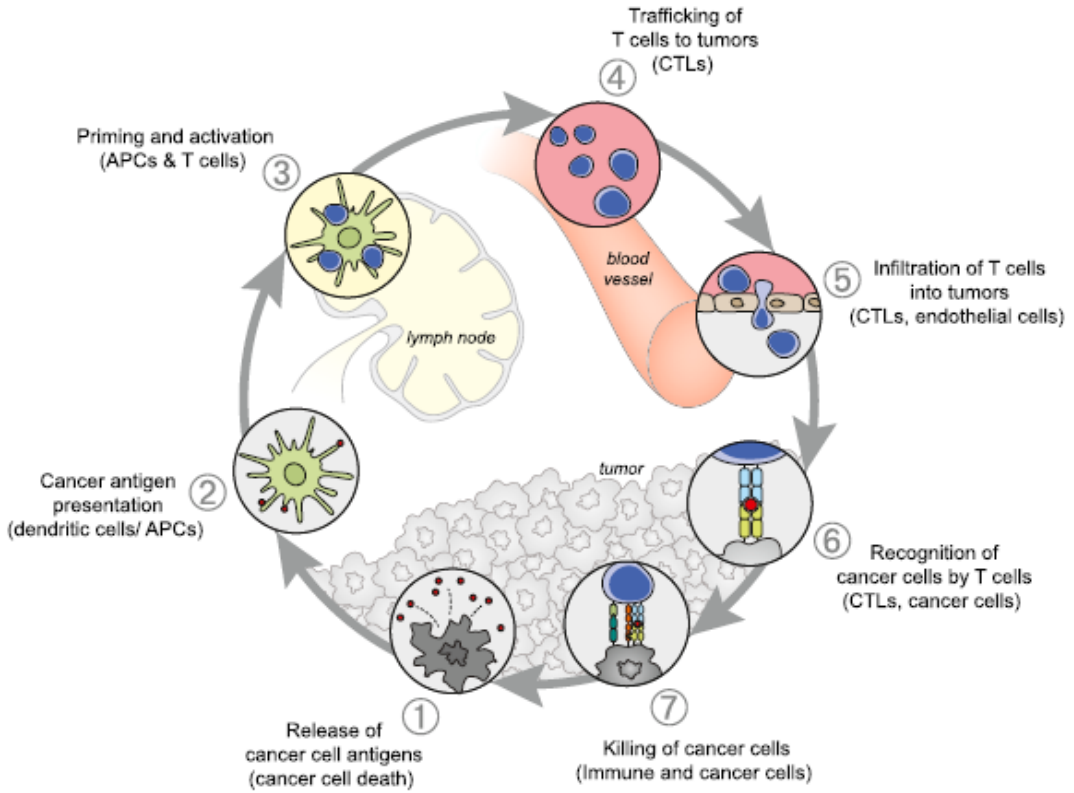
CellPress

Plinabulin Registration Studies



Plinabulin induces dendritic cell DC maturation, a key step in initiating anti-cancer immunotherapy

- The generation of cancer immunity is a cyclic process. In principle, the response of T cells to tumor cells should be amplified and expanded
- Initiating anti-cancer immunity includes antigen release, presentation and activation of cancer antigen-specific T cells. Dendritic cells are the most important antigen-presenting cells



Global neutropenia market

- CIN market = $7 billion in 2017 (mainly used with high risk chemo)
- China and the U.S. represent 2/3 of all G-CSF global therapy
- Plinabulin positioning: Plinabulin as mono or combo therapy improves on the standard of care in the treatment of Chemotherapy Induced Neutropenia; potential for improved chemotherapy outcome

Addressable market

- Combination with G-CSF to
  - Improved neutropenia
  - Reduced bone pain
  - Improve compliance & persistency with chemo

Global

- G-CSF cycles/year = 4.3 million[1]
- G-CSF market value = $7 billion
- Plinabulin + G-CSF: reduced neutropenia and improved bone pain; potential for improved compliance and persistency with chemo
- Plinabulin: reduced bone pain; improved thrombocytopenia and immune function

Canada
$140M/yr G-CSF market
80K G-CSF cycles/yr

EU 5
$870M/yr G-CSF market
850K G-CSF cycles/yr

South Korea
$46M/yr G-CSF market
18% peg growth YoY
78K G-CSF cycles/yr

China
$350M/yr G-CSF market
20% cycle growth YoY
33% $ G-CSF growth YoY
1.6M G-CSF cycles/yr

United States
$5+B/yr G-CSF market
1.3M G-CSF cycles/yr

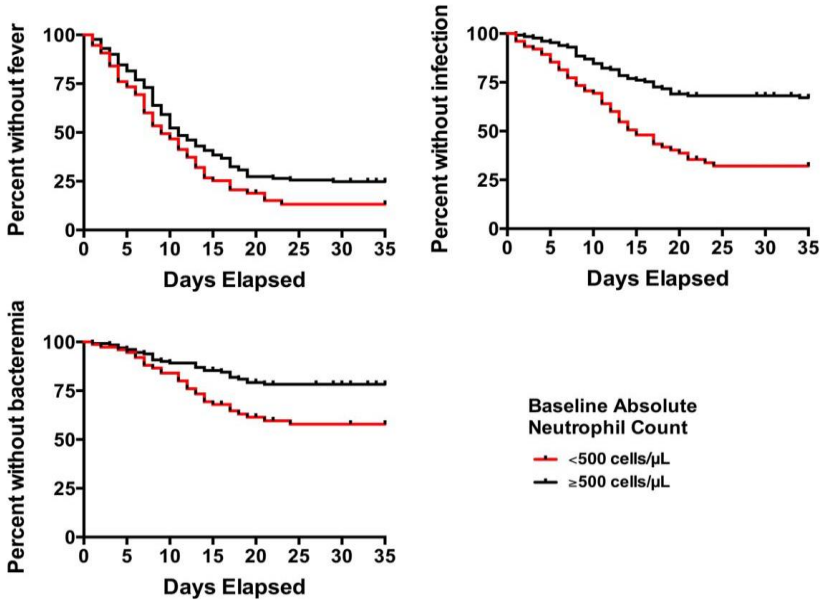
Australia
$40M/yr G-CSF market
53K G-CSF cycles/yr

Japan
$240M/yr G-CSF market
7% peg growth YoY
330K G-CSF cycles/yr

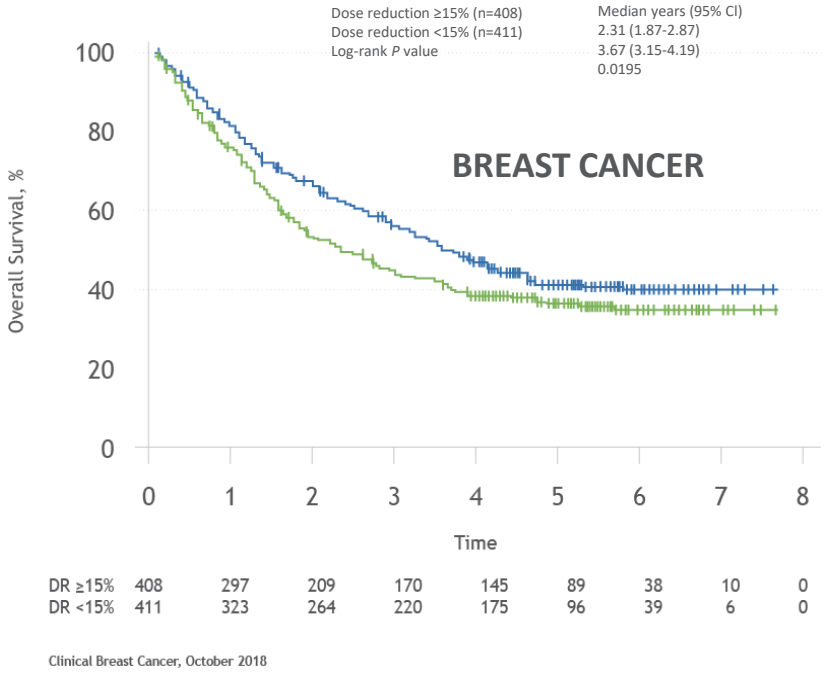
Note: [1] https://onlinelibrary.wiley.com/doi/full/10.3322/caac.21338. G-CSF market growth based on IQVIA data and DDM MD data Q3 '16 to Q2 '18. Standardized G-CSF units

Grade 4 neutropenia leads to development of fever and infection; and to chemo dose reduction and less survival

Grade 4 neutropenia was associated with fever (p = 0.04), documented infection (p < 0.0001), and bacteremia (p = 0.002)[1]



Grade 4 neutropenia leads to dose reduction to <85% of optimum dose → lower OS[2]



Note: [1]Buckley SA et al., "Prediction of adverse events during intensive induction chemotherapy for acute myeloid leukemia or high-grade myelodysplastic syndromes." American J. Hematology 2014; 89(4): 423-28. 2. Denduluri N et al., Clinical Breast Cancer 18(5): 380-386 (2018); Lalami et al. Critical Reviews in Oncology / Hematology 120: 163-179 (2017).

Potential for a broad Prevention of CIN label: Plinabulin + G-CSF for all chemo in non-myeloid solid tumors

The Premise

- Chemo kills fast dividing cells, which includes cancer cells, and white blood cells in bone marrow
- CIN is a problem with bone marrow, and not a problem with a specific type of cancer
- All bio-similar filgrastim or pegfilgrastim approval was based on TAC and breast cancer, which is an example of high-risk chemotherapy.

Broad Label Potential for Plinabulin – G-CSF Combination

- G-CSF class provides a base protection from severe neutropenia in week 2 following chemotherapy use.
- Plinabulin has MoA of protecting neutrophil in week 1 after chemotherapy, which has been consistently shown in five (5) trials that includes various chemotherapies, and in various non-myeloid cancer trials.
- Thus, the combination provides increased protection for the complete cycle 1 following chemotherapy.

Proposed Label

Plinabulin when combined with G-CSF is indicated for concurrent administration with a myelosuppressive chemotherapeutic regimen in patients with non-myeloid solid tumor for the prevention of chemotherapeutic induced neutropenia (CIN).

2nd and 3rd line NSCLC (EGFR wild type): severe unmet clinical need

2nd/3rd line NSCLC patients

	EGFR mutant	EGFR wild type	In EGFR wild type patients
% of 2L/3L NSCLC patients (western)	15%	85%	Much larger population
mOS SoC	18.3 months (TKI)	6-8 months (docetaxel)	Much shorter OS
mOS TKI vs docetaxel[1]		5.4 vs 8.2 months	TKI worse than docetaxel
Currently available therapies		PD-1 Pemetrexed Ramucirumab + docetaxel Docetaxel	All with significant limitations

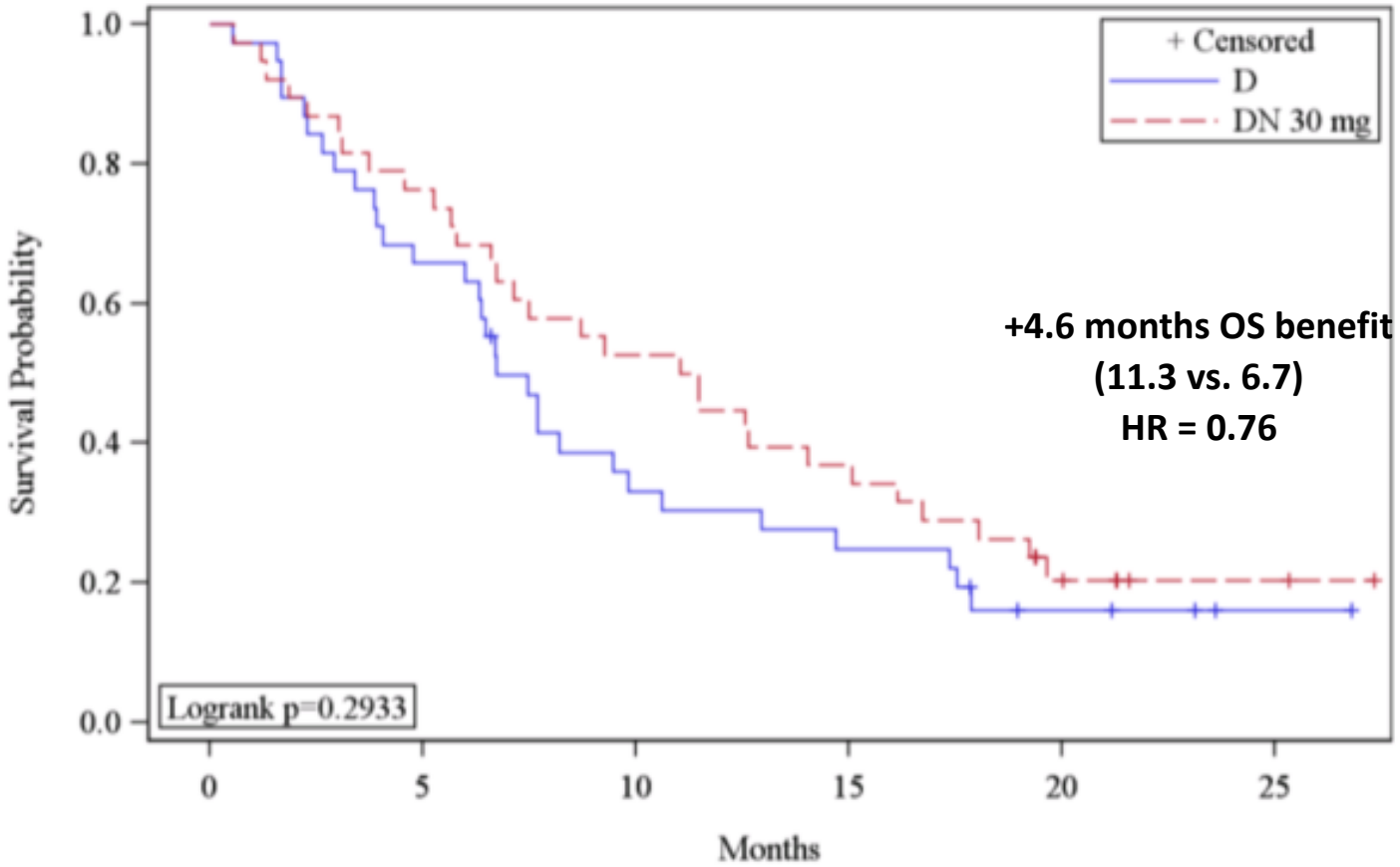
Severe unmet clinical need

For lung cancer patients infected by COVID-19, death rate is 55%[2]

BeyondSpring

Note: [1] Lancet Oncol. 2013 Sep;14(10):981-8. [2] Mehta V et al., Cancer Discovery May 1, 2020 online; DOI: 10.1158/2159-8290.CD-20-0516.

Post-hoc Phase 2 data from Plinabulin in NSCLC in mechanism targeted patients shows overall survival benefit



+4.6 months OS benefit
(11.3 vs. 6.7)
HR = 0.76

	Subjects	Event	Censored	Median Survival	95% CL
D	38	31(82%)	7(18%)	6.733	(6, 9.833)
DN 30 mg	38	30(79%)	8(21%)	11.25	(6.733, 15.07)

- **Plinabulin MoA- targeted patients: Measurable lung lesion with RECIST 1.1 (CT scan > 1 cm in lung); 70% of NSCLC**
- **Improved QoL and well tolerated safety profile**

Note: ASCO-SITC 2017 meeting oral presentation

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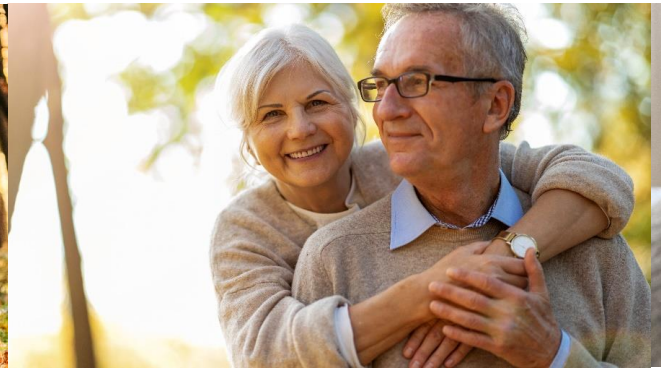

www.beyondspringpharma.com