BeyondSpring

Plinabulin DUBLIN-3 NSCLC Topline Data

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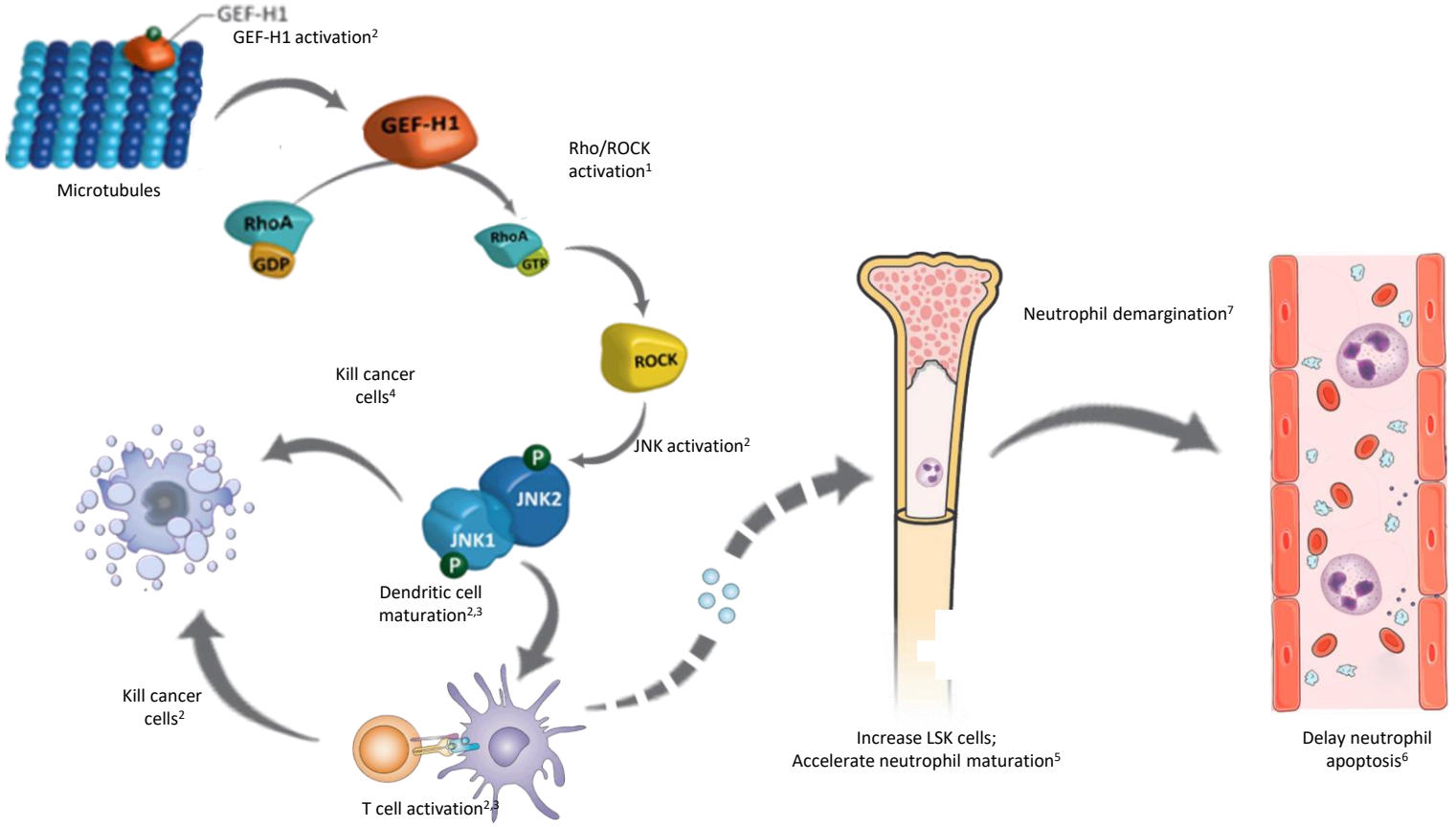
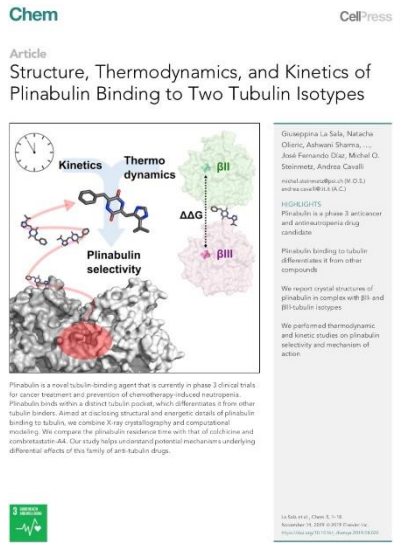
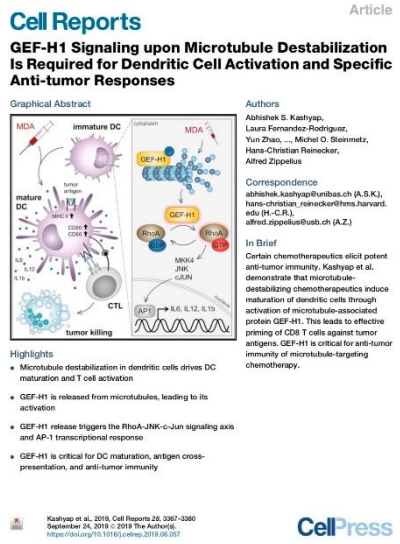
By attending this presentation, you acknowledge that you will be solely responsible for your own assessment of the market and our market position and that you will conduct your own analysis and be solely responsible for forming your own view of the potential future performance of our business.

Plinabulin: First-in-Class, *Selective Immunomodulating Microtubule-Binding Agent* (*SIMBA*) - Potent Antigen Presenting Cell (APC) inducer

Plinabulin[1]







Plinabulin Novel Target: Immune Defense Protein GEF-H1

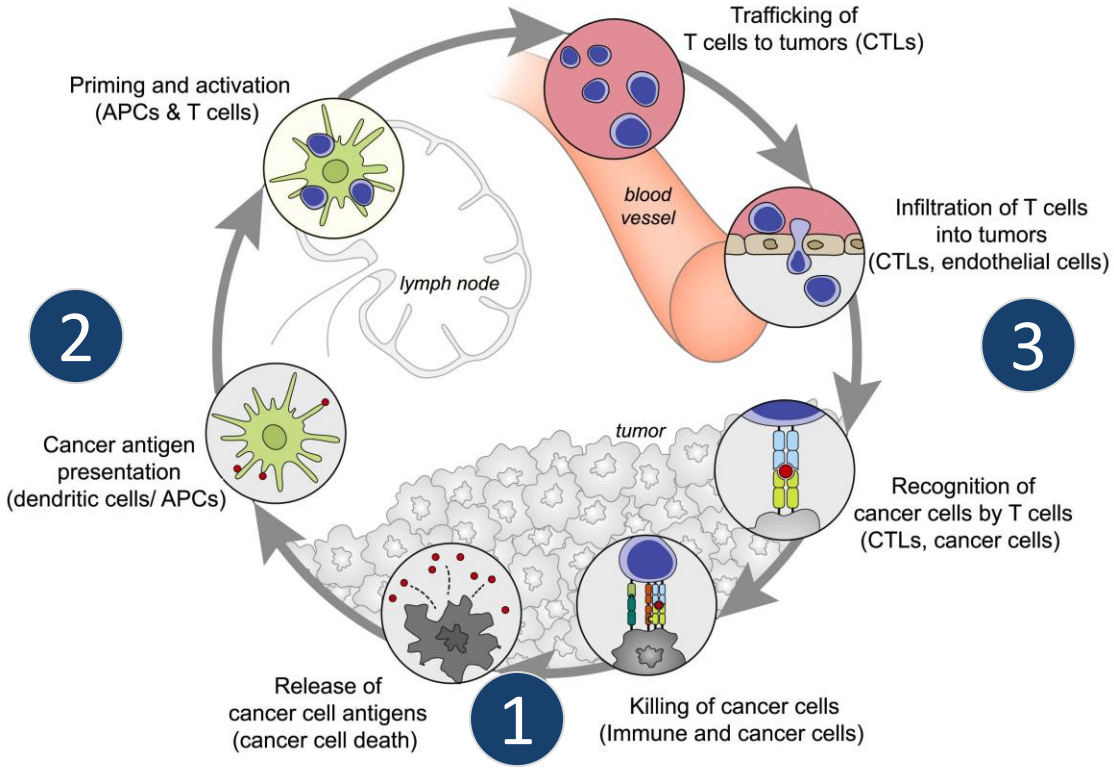
Note: [1] La Sala et al., 2019 Chem. [2] Kashyap et al., 2019 Cell Reports. [3] Zhang et al., 2005 Mol Cell Biol. [4] Singh et al., 2011 Blood. [5] Suwa et al., 2000 Am J Physiol Heart Circ Physiol; Ghosh et al., 2018 ACR Annual Conference; Blayney et al., Society of Leukocyte Biology. [6] Asensi et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

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

2 Plinabulin

Stimulate maturation of dendritic cells to increase antigen presentation

Dendritic cells are the most important antigen-presenting cells



1 Radiation/Chemotherapy/ Plinabulin

Release Tumor Antigens

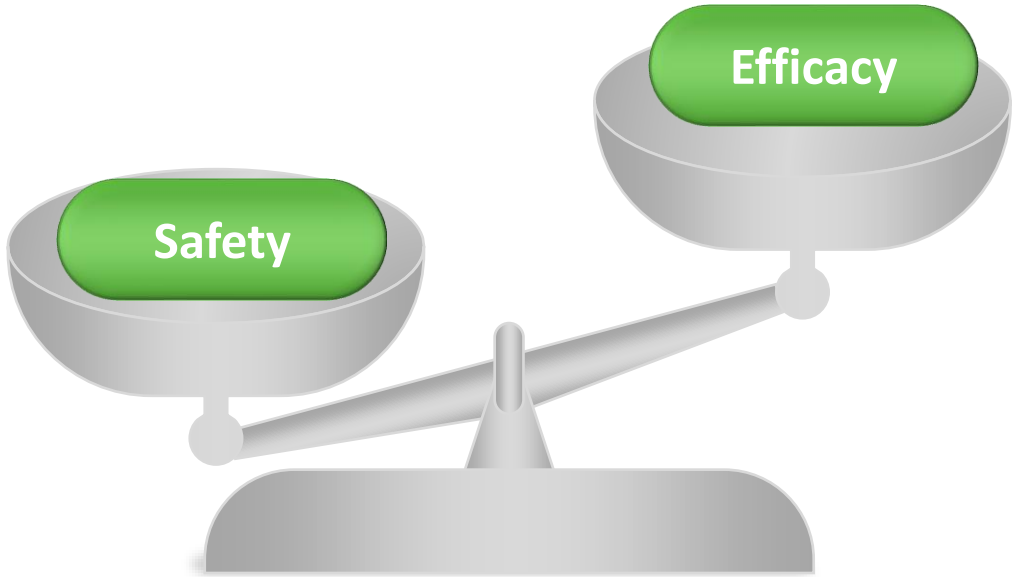
For more potent anti-cancer effect

3 Checkpoint Inhibitors

Optimize T cell response

1 + 2 + 3 → Optimal Immuno-Oncology Response

Severely Unmet Medical Need – 2nd/3rd Line NSCLC, EGFR Wild Type



- Large patient population with limited treatment options
  - EGFR wild type: ~85% western NSCLC and ~70% of Asian NSCLC patients
  - With immunotherapies moved to first line, Docetaxel-based therapies are the mainstay therapy
  - TKIs are worse than docetaxel[1]
- 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.

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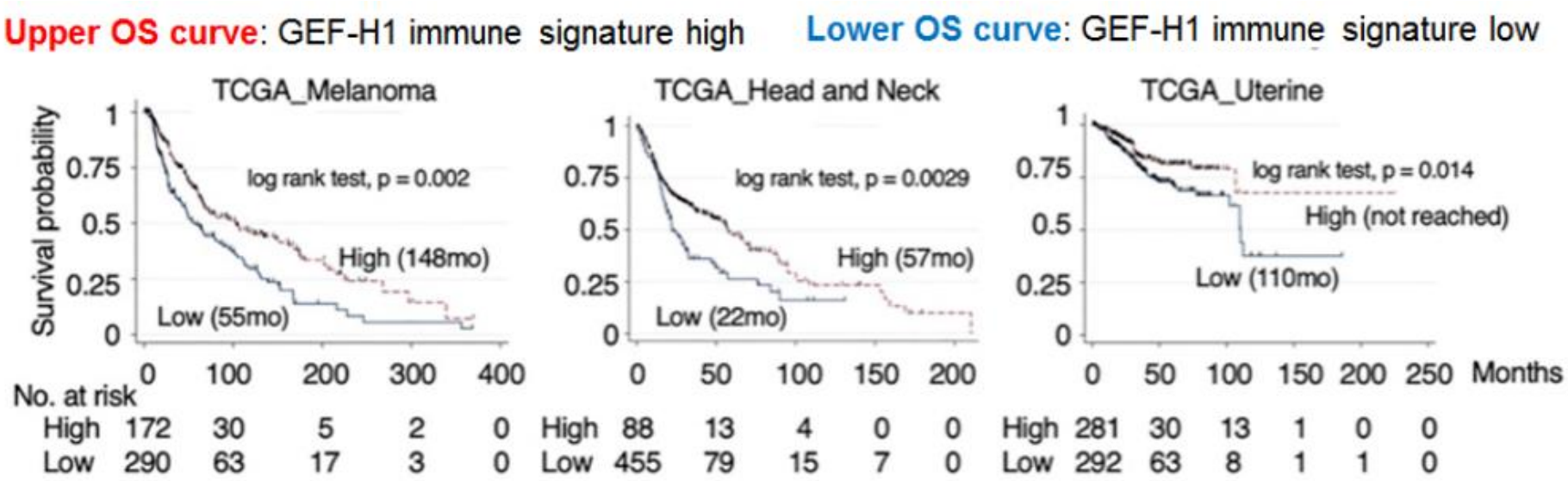
[1] Lancet Oncol. 2013 Sep;14(10):981-8.

Scientific Rationale – Patients with High GEF-H1 Live Longer

Plinabulin Activates GEF-H1[1]

Patients with High GEF-H1 Immune Signature Live Longer in Various Cancers[1]



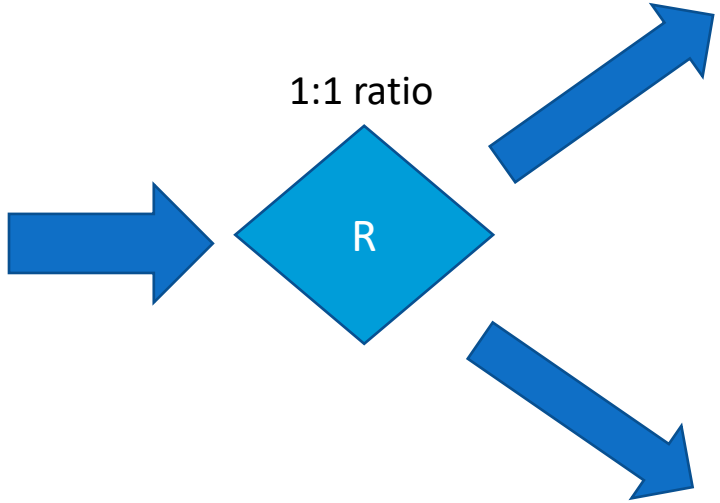
Based on Plinabulin's Immune MOA, patients with measurable lung lesion were selected prospectively for Dublin-3 Study.

[1] Kashyap et al., 2019 Cell Reports

Docetaxel + Plinabulin Compared to Docetaxel + Placebo in Patients With 2nd/3rd line NSCLC, EGFR wild type (DUBLIN-3)

Global, Randomized, Single-Blinded (blinding for patients only)
Stratified for: Region (Asia/non-Asia), Prior Line, ECOG score
60 sites: U.S., China, and Australia

- Non-squamous or squamous **NSCLC**
- Stage IIIb/IV
- ECOG performance status ≤ 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



Docetaxel + Plinabulin

Docetaxel + Placebo

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

Dublin-3 Phase 3 Topline Data

- Significant Improvement in OS, PFS, ORR, 24 M, 36 M OS Rate (Combo vs. Docetaxel)
- Significant Reduction in Grade 4 Neutropenia (Combo vs. Docetaxel)

Primary Endpoint	Docetaxel (75 mg/m2) N=281	Plinabulin (30 mg/m2) + Docetaxel (75 mg/m2) N=278
OS (months or M)		Mean OS, p=0.03 OS Log-rank p<0.04; HR = 0.82

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	Docetaxel N=281	Plinabulin (30 mg/m2) + Docetaxel (75 mg/m2) N=278
ORR (%)		P <0.03
PFS (months or M)		P<0.01
Grade 4 neutropenia, cycle 1 Day 8 (%)	27.8%	5.3%; p<0.0001
24 Month OS Rate (%)	12.5%	22.1%; p<0.01
36 Month OS Rate (%)	5.3%	11.7%; p<0.04
48 Month OS Rate (%) - exploratory	0%	10.6%; p value cannot be calculated

OS Analysis Method Based on Relevance

1. Mean OS p value – Most Relevant for immune agent with more longer survival patients

- **Analysis method stated in Statistical Analysis Plan (SAP); the data will be included in Clinical Study Report (CSR)**

Mean OS takes into consideration all patients' overall survival time and censoring time. It is stated in SAP to use restricted mean survival time (RMST) methods to analyze the mean OS; the expected survival time for the two treatments were compared, restricted to the maximum follow-up time for the study.

2. OS Log-rank p value – Relevant as it takes into account the whole OS K-M curve

- **Analysis method stated in SAP; the data will be included in CSR**
- **OS log-rank p value needs to be $p < 0.046$, 2-sided test, to meet statistical significance due to adjustment for prespecified interim looks**

OS Log rank method is one of the most popular methods of comparing the survival for treatments, which takes the whole follow-up period into account. It is a nonparametric method and has the considerable advantage that it does not require knowing anything about the shape of the survival curve or the distribution of survival times.

3. OS Hazard Ratio (HR) – Not Relevant for immune agent with more longer survival patients

- **Per the SAP, HR would not be presented in the CSR if it fails Cox proportional hazard ratio assumption. Since Plinabulin is an immune agent with treatment effects that vary over different time points, the assumption failed; thus, the HR will not be included in the CSR.**

Hazard ratio (e.g., hazard under active treatment/hazard under control) is often used to characterize the treatment effects for survival data. It is derived under Cox proportional hazard ratio (HR) assumptions. Under this assumption, the HR is the same at all timepoints (i.e., the treatment effect in terms of improving hazard is the same at all timepoints). The assumption fails to hold if the HR varies over timepoints (i.e., the treatment effects vary over different timepoints). In fact, Cox proportional hazard ratio assumption often fails for immune anticancer treatments, including plinabulin, as these treatments have greater effects in the later part of the survival curve than in the earlier part. Clearly, in this situation, the single HR number derived under Cox proportional hazard ratio assumption is not relevant to consider.

Product Profile (Plinabulin + Docetaxel for 2nd/3rd line NSCLC, EGFR wild type)

Next steps: Discuss filing plan with FDA & NMPA in 2021 with potential filing 1H 2022

Docetaxel (Current SOC)	Plinabulin - Docetaxel Combination
• Modest survival benefit	• Survival benefit, with longer survival due to GEF-H1 I/O MOA
• Severe safety concerns, e.g., CIN	• Favorable safety profile, including significant CIN reduction
• Poor Quality of Life	• Improved quality of life

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

Plinabulin: potential as the "Cornerstone" Therapy to Add onto Current IO Therapies to Address Severe Unmet Medical Needs

PD-1/PD-L1 Inhibitors
- $30 B 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

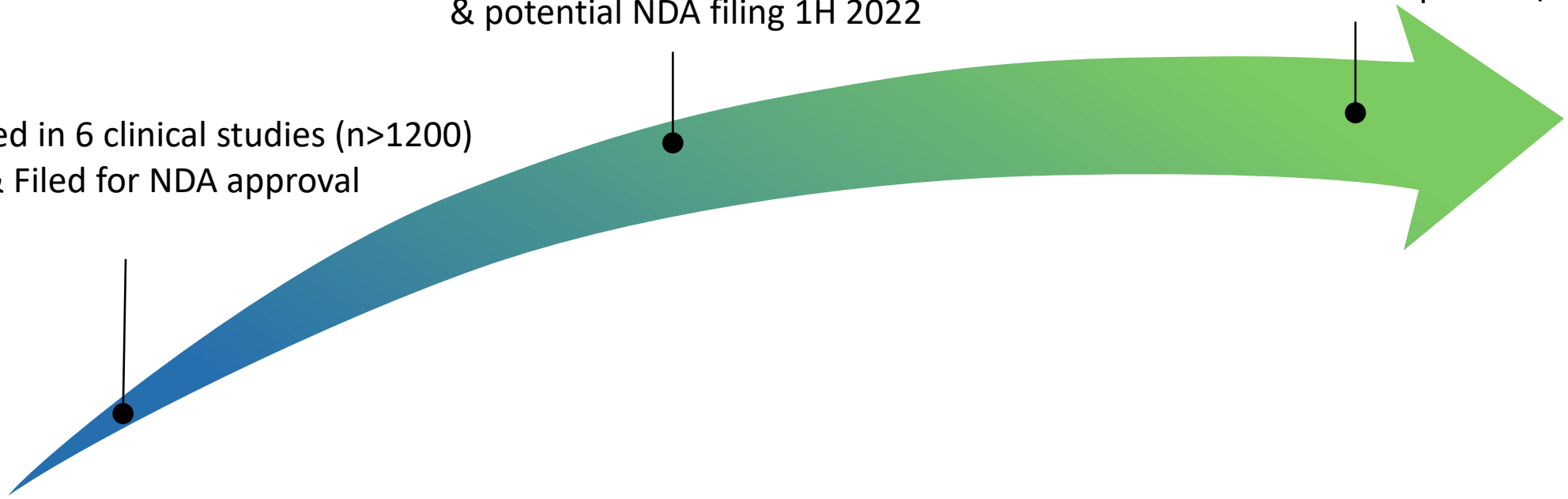
Plinabulin Franchise: Pipeline in a Drug

Clinical Confirmation → **Expand** → **Transform**

Confirmed in 6 clinical studies (n>1200)
& Filed for NDA approval

Positive Phase 3 Topline OS data (n=559)
& potential NDA filing 1H 2022

Promising early clinical efficacy data
– 7 different cancers in phase 1/2 study



CIN (BTD & Priority Review)
Superior Regimen vs. SOC
PDUFA 11/30/2021

NSCLC
Strong MOA Rationale &
Successful DUBLIN-3 phase 3 Study

Multiple Cancers (I/O Combo)
Synergistic MOA with Checkpoint Inhibitors & Promising Preclinical & Early Clinical Efficacy Data

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