



Cowen and Company  
39<sup>th</sup> Annual Healthcare Conference  
March 11, 2019

[www.g1therapeutics.com](http://www.g1therapeutics.com)

NASDAQ: GTHX

# Forward-looking statements

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This presentation and the accompanying oral commentary contain “forward-looking” statements within the meaning of the Private Securities Litigation Reform Act of 1995. Words such as “may,” “will,” “expect,” “plan,” “anticipate,” “estimate,” “intend” and similar expressions (as well as other words or expressions referencing future events, conditions or circumstances) are intended to identify forward-looking statements. Forward-looking statements in this presentation include, but are not limited to the following: the therapeutic potential of trilaciclib, lerociclib and G1T48; initial success in our ongoing clinical trials may not be indicative of results obtained when these trials are completed or in later stage trials; our development of trilaciclib to reduce chemotherapy-induced myelosuppression is novel, unproven and rapidly evolving and may never lead to a marketable product; our product candidates may cause undesirable side effects that could delay or prevent their marketing approval, limit the commercial profile of an approved label, or result in significant negative consequences following marketing approval, if any; we may not have the ability to recruit, enroll and complete clinical trials for, obtain approvals for, or commercialize any of our product candidates; we face substantial competition, which may result in others discovering, developing or commercializing competing products before or more successfully than we do; we may incur additional costs or experience delays in completing clinical trials; future legislation may increase the difficulty and cost for us to obtain marketing approval of and commercialize our product candidates and affect the prices we may obtain; and market conditions. Each of these forward-looking statements involves risks and uncertainties and are based on our expectations and assumptions as of the date of this presentation. Factors that may cause our actual results to differ from those expressed or implied in the forward-looking statements in this presentation are further discussed in our filings with the U.S. Securities and Exchange Commission (SEC), including the “Risk Factors” section in our annual report on Form 10-K for the fiscal year ended December 31, 2018 filed with the SEC. Such factors may be amended or updated from time to time in our subsequent periodic and other filings with the SEC, which are accessible on the SEC’s website at [www.sec.gov](http://www.sec.gov). We assume no obligation to update any forward-looking statement after the date of this presentation to reflect any change in expectations or future developments, even as new information becomes available.

# Vision: improve the lives of those affected by cancer

1

**Three wholly-owned investigational therapies with potential to improve patient care and generate significant value for shareholders**

2

**Relentless focus on patients, operational efficiency and financial discipline**

3

**Explore value-creating partnerships as we move toward commercialization of our product candidates**

# Robust clinical-stage pipeline

## Three wholly-owned product candidates addressing distinct multi-billion dollar markets

### Trilaciclib

First-in-class  
myelopreservation therapy

- ✓ Backbone with chemo
- ✓ 2018: positive SCLC data in three randomized Ph 2 trials

Next milestone in 2Q19:  
regulatory update

### Lerociclib

Oral CDK4/6  
inhibitor

- ✓ Combine with targeted Rx
- ✓ 2018: demonstrated POC in ER+ BC Ph 1 trial

Next milestones in 2H19:  
Clinical data updates in ER+ BC  
and EGFRm NSCLC trials

### G1T48

Oral SERD  
ER+ breast cancer

- ✓ Monotherapy & lero combo
- ✓ 2018: initiated ER+ BC Ph 1 trial

Next milestone in 4Q19:  
Phase 1 data

# Delivered on all clinical milestones in 2018

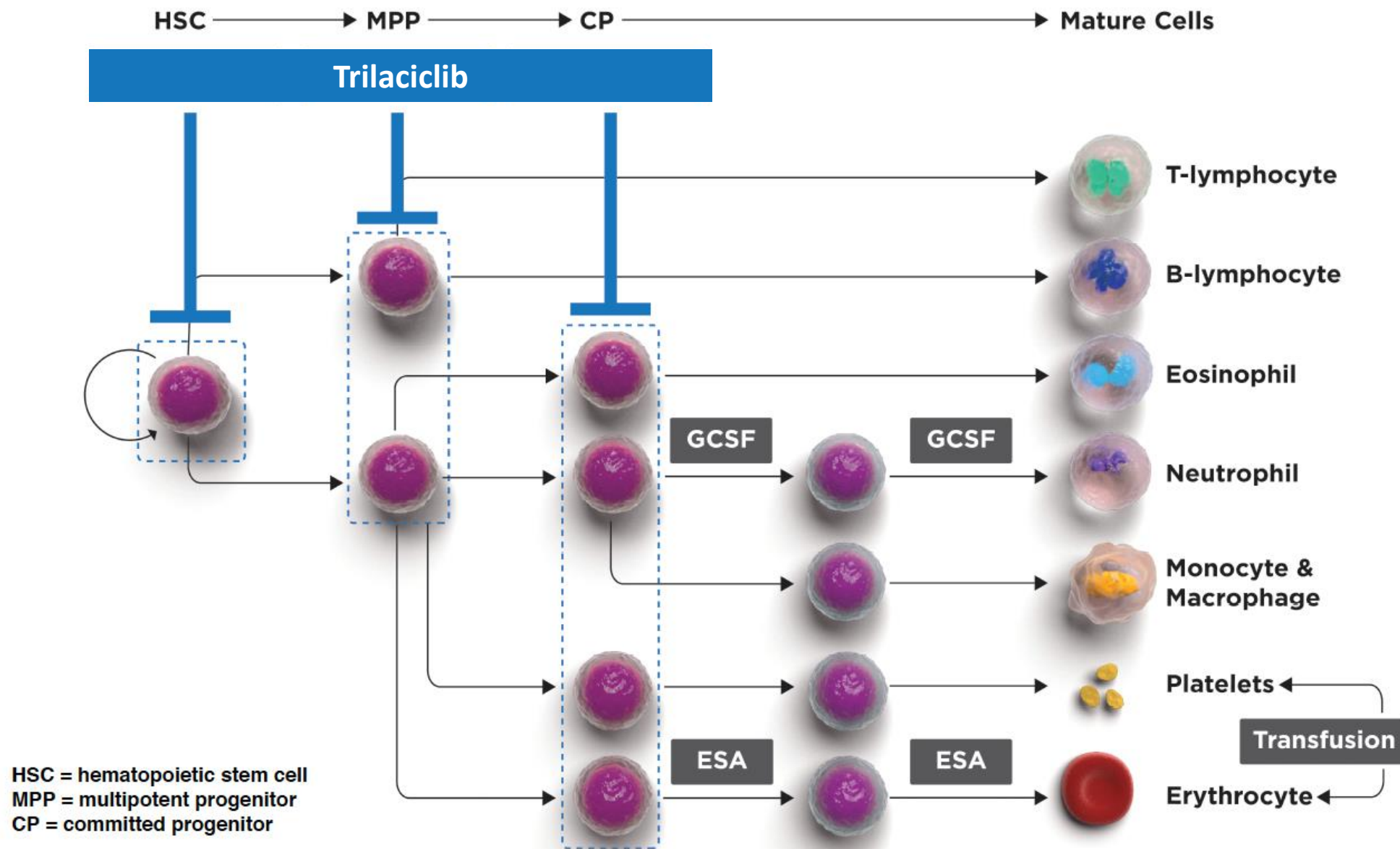
	INDICATION/COMBO	PHASE 1	PHASE 2	PHASE 3
trilaciclib IV CDK4/6i	1 <sup>st</sup> -line SCLC (+ etop/carbo)			
	1 <sup>st</sup> -line SCLC (+ etop/carbo/Tecentriq®)			
	2 <sup>nd</sup> /3 <sup>rd</sup> -line SCLC (+ topotecan)			
	Metastatic TNBC (+ gem/carbo)			
Ierociclib oral CDK4/6i	ER+, HER2- BC (+ Faslodex®)			
	EGFRm NSCLC (+ Tagrisso®)			
G1T48 oral SERD	ER+, HER2- BC (monotherapy)			

# TRILACICLIB DEVELOPMENT UPDATE

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Hematopoietic stem and progenitor cells (HSPCs)

# Trilaciclib's MOA provides multi-lineage benefits vs. current lineage-specific interventions

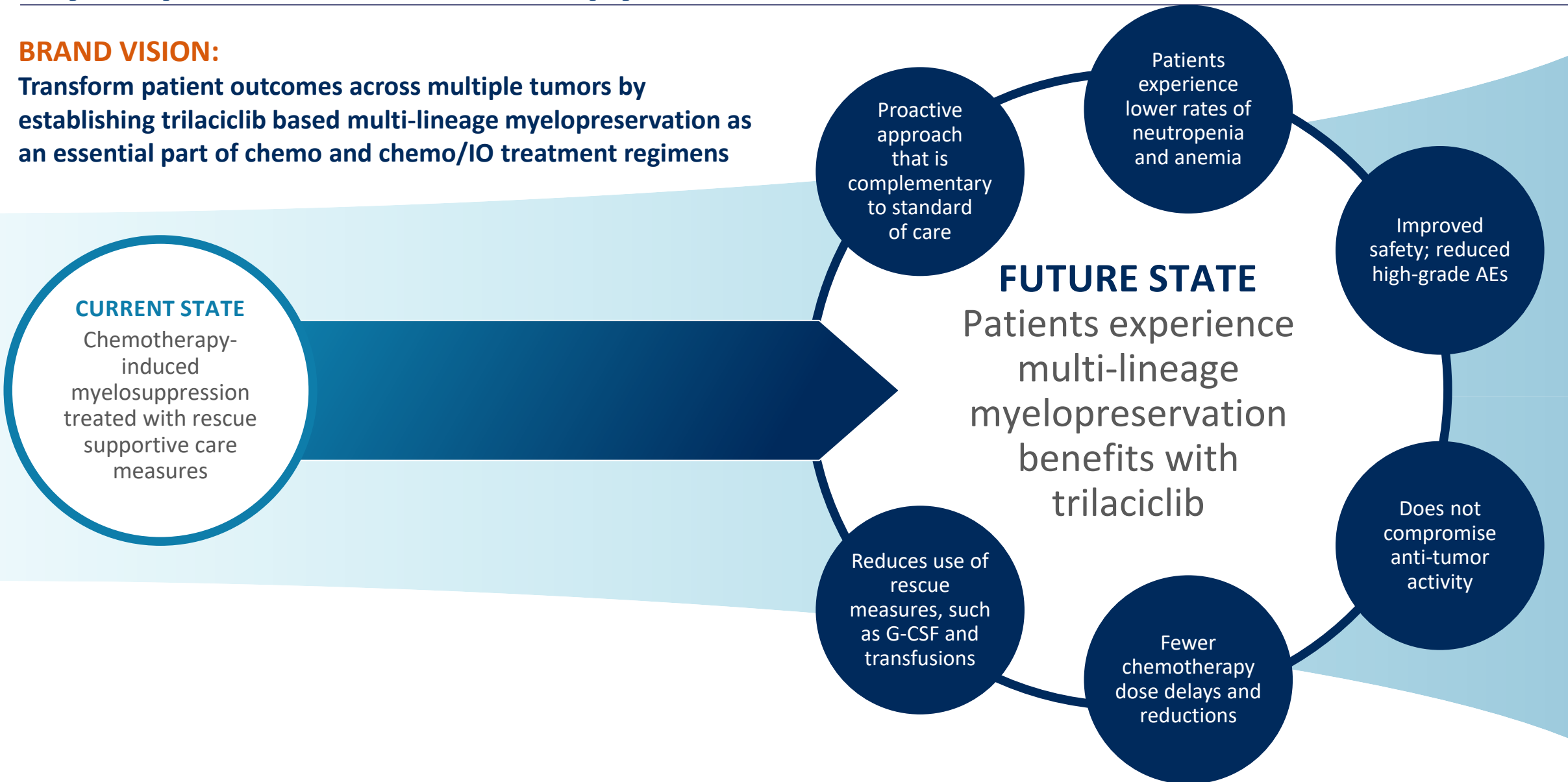


# Trilaciclib: first-in-class multi-lineage myelopreservation therapy



**BRAND VISION:**

Transform patient outcomes across multiple tumors by establishing trilaciclib based multi-lineage myelopreservation as an essential part of chemo and chemo/IO treatment regimens





# Trilaciclib development: key takeaways

1

## Substantial unmet need

- ~1 million patients in U.S. receive chemotherapy each year
- chemo to remain a cornerstone of cancer treatment
- myelosuppression still prevalent

2

## Phase 2 program showed benefits across different indications, lines of therapy and chemotherapy regimens

- myelopreservation in SCLC
- PFS in mTNBC

3

## Next steps in trilaciclib development

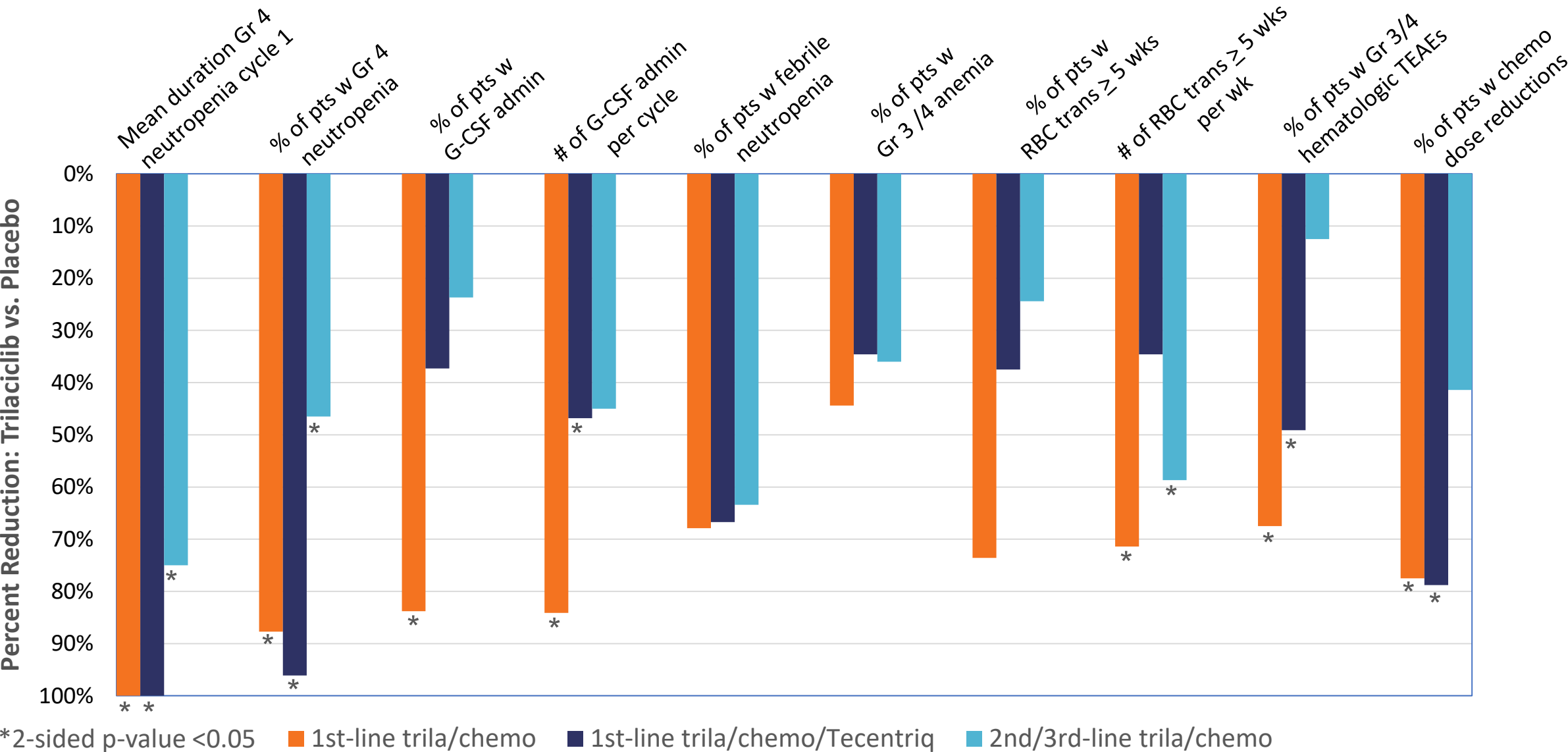
- meet with U.S. and European regulators
- target initial indication: SCLC
- additional trials initiating in 2H19

# Positive multi-lineage myelopreservation results from three randomized SCLC Phase 2 trials in 2018



TRIAL/TUMOR TYPE	REGIMEN	TRIAL DESIGN
1 <sup>st</sup> -line Small Cell Lung Cancer (G1T28-02)	+ etoposide/ carboplatin (EP)	• 77 patients, randomized, placebo-controlled, double-blind
1 <sup>st</sup> -line Small Cell Lung Cancer (G1T28-05)	+ EP/Tecentriq <sup>®</sup>	• 107 patients, randomized, placebo-controlled, double-blind
2 <sup>nd</sup> /3 <sup>rd</sup> -line Small Cell Lung Cancer (G1T28-03)	+ topotecan	• 92 patients, randomized, placebo-controlled, double-blind

# Myelopreservation benefits consistently demonstrated in three randomized, placebo-controlled SCLC studies



# Trilaciclib does not impair efficacy of chemotherapy

	trila/chemo 1 <sup>st</sup> -line			trila/chemo/Tecentriq 1 <sup>st</sup> -line			trila/chemo 2 <sup>nd</sup> /3 <sup>rd</sup> -line		
	placebo N = 37	trila N = 38	HR* or historical RR	placebo N = 53	trila N = 54	HR* or historical RR	placebo N = 29	trila N = 32	HR* or historical RR
Median OS (months)	10.6	10.9	<b>HR=0.87</b>	immature			immature		
Median PFS (months)	5.0	6.1	<b>HR=0.71</b>	5.4	5.9	<b>HR=0.78</b>	4.2	4.2	<b>HR=0.85</b>
Overall Response Rate	56.8%	66.7%	52%	63.5%	56.0%	60.2 - 64.4%	23.1%	16.7%	10.1 - 16.9%
Clinical Benefit Rate	86.5%	91.7%	75%	90.4%	96.0%	81.1 - 85.7%	61.5%	60.0%	61.5 - 73.4%

- Lack of efficacy impairment measured by HR (“do no harm”)

- Trilaciclib achieves comparable OS and PFS

- Response rates (RR) within historical ranges<sup>\*\*</sup>

\*HR=hazard ratio

\*\* Socinski et al. *J Clin Oncol* 2009; 27: 4787-92; Horn et al. *N Engl J Med* 2018; 379:2220-2229; von Pawel et al. *J Clin Oncol* 2014; 32:4012-4019; Evans et al. *J Thorac Oncol* 2015; 10: 1221–1228

Data cut: December 21, 2018

# Trilaciclib does not impair efficacy of chemotherapy

	trila/chemo 1 <sup>st</sup> -line			trila/chemo/Tecentriq 1 <sup>st</sup> -line			trila/chemo 2 <sup>nd</sup> /3 <sup>rd</sup> -line		
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Data cut: December 21, 2018

# Preliminary results in randomized mTNBC Phase 2 trial demonstrated trilaciclib improved PFS

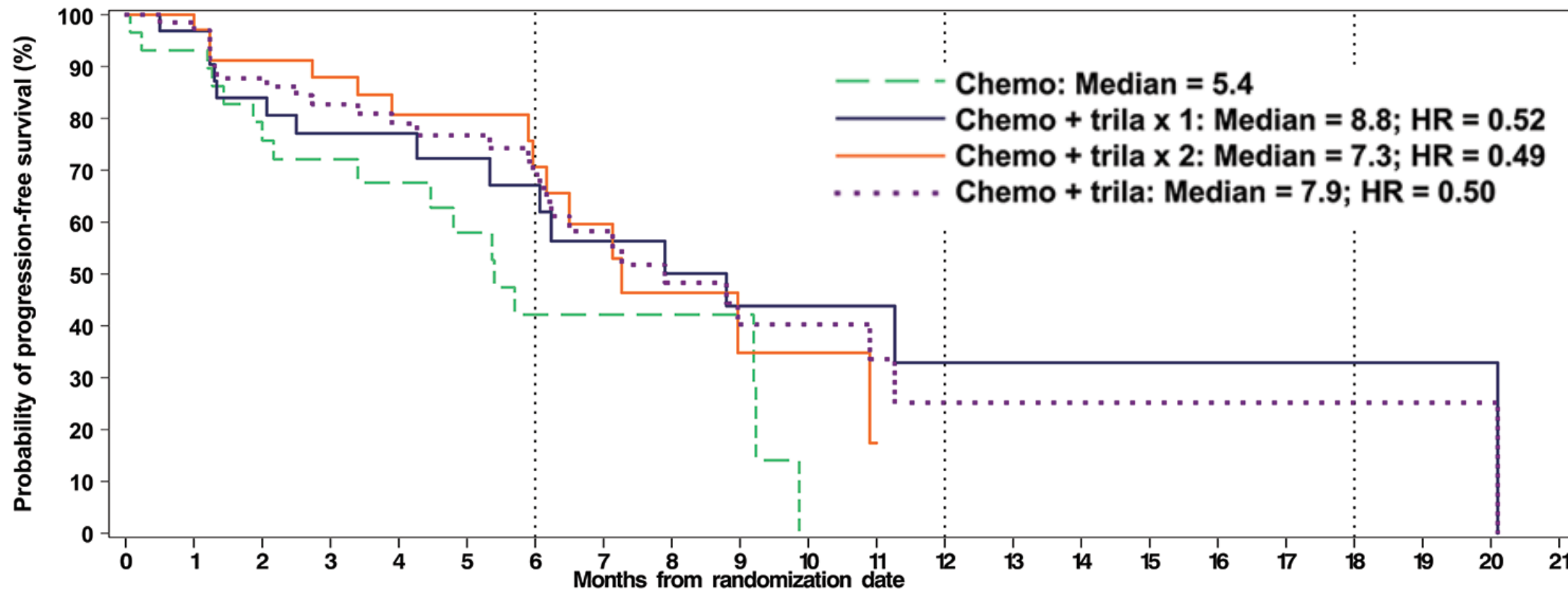


TRIAL/TUMOR TYPE	REGIMEN	TRIAL DESIGN
Metastatic Triple-Negative Breast Cancer (G1T28-04)	+ gemcitabine/ carboplatin	102 patients, randomized, open-label

- Patients on trilaciclib received more chemotherapy cycles than those in the control arm

- Safety profile consistent with previously reported trials; no trilaciclib-related serious adverse events reported

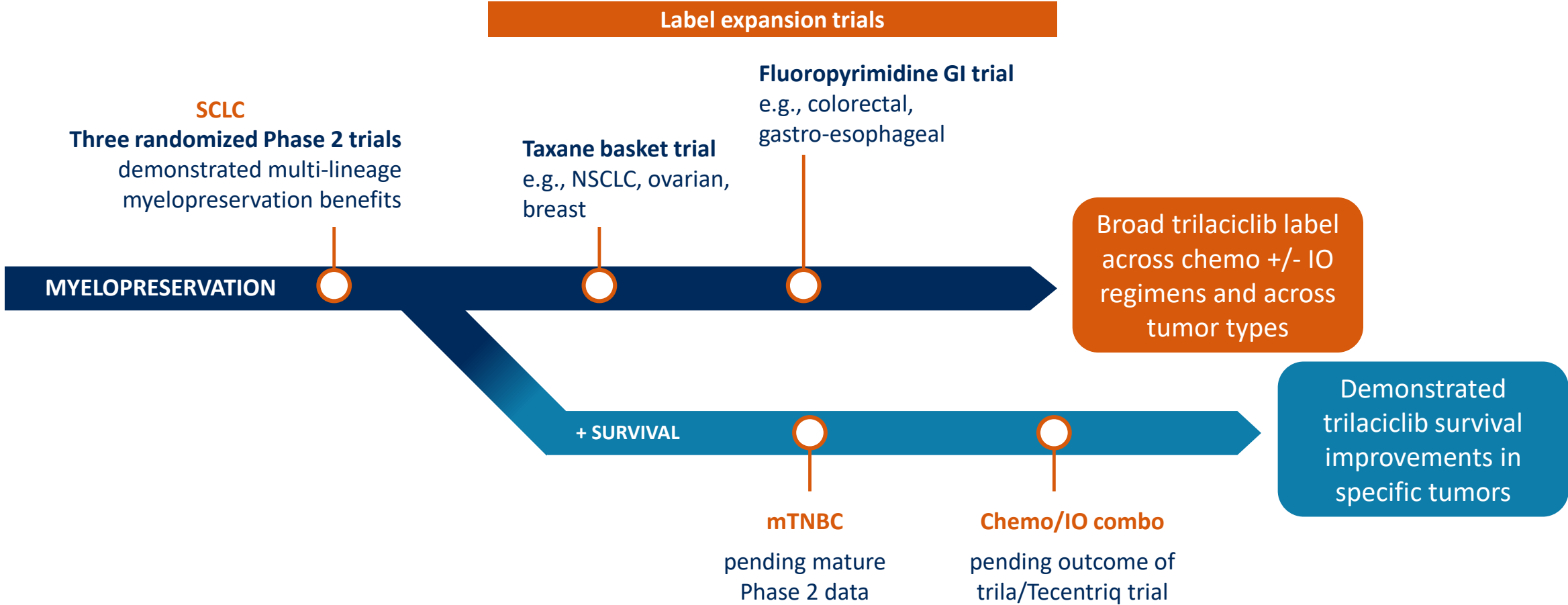
# Preliminary results demonstrated median PFS is longer when trilaciclib is added to chemotherapy



# Development strategy: two pathways to establish trilaciclib as an essential part of chemo and chemo/IO treatment



Establish trilaciclib as first-in-class myelopreservation therapy





# TRILACICLIB COMMERCIAL STRATEGY

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Hematopoietic stem and progenitor cells (HSPCs)

# Trilaciclib commercial strategy: key takeaways

1

**There is still substantial unmet need for patients experiencing myelosuppression, despite the availability of rescue interventions like G-CSF, ESAs and transfusions**

- no significant innovations for chemotherapy-induced myelosuppression
- chemotherapy will remain the backbone of treatment

2

**Multi-lineage myelopreservation in SCLC represents an advance for patients and a significant opportunity:  
\$500M - \$1B WW at peak**

- physicians see proactive myelopreservation as a better approach and anticipate significant use
- payers value the patient benefits and are willing to pay without significant restrictions

3

**Expanding the label across tumors to a broad myelopreservation indication may add >\$2B to peak sales**

- myelopreservation launch in SCLC meets a substantial unmet need and serves as proof of concept in other tumor types
- efficacy enhancement, OS or PFS data, would provide additional patient benefit and revenue upside, but is not required to generate use in a high % of patients

# Trilaciclib market research\* highlights a substantial global commercial opportunity

> \$3 billion global commercial opportunity

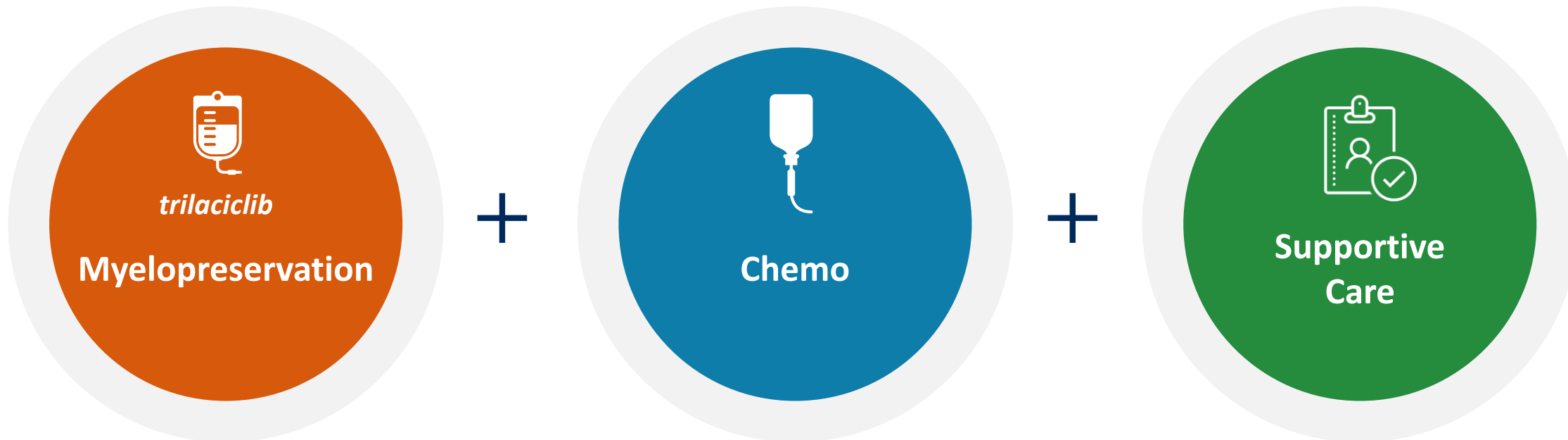
Broad myelopreservation label  
>\$2 billion  
(fluoropyrimidines and taxanes)

SCLC label  
\$500 million - \$1 billion

- ***Patients*** are better served with proactive myelopreservation
- ***Physicians*** anticipate significant use of trilaciclib based on its myelopreservation benefits alone
- ***Payers*** see the multi-lineage benefits of trilaciclib as unique

\* Using TPP defined by data from SCLC trials, interviewed:  
**100+ physicians and 15+ payors across 5 countries**

# Trilaciclib optimally positioned as first-in-class, multi-lineage myelopreservation therapy that is complementary to SOC



## Differentiating and motivating positioning

Proactively reduces myelotoxicity by preserving HSPC & immune system function

Does not compete with the current SOC

Potential for broad use across tumors/chemo

Convenient 30 min IV infusion prior to chemo

Rescue measures following chemotherapy

(G-CSF, ESAs and transfusions)

# LEROCICLIB DEVELOPMENT UPDATE

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Tumor cell proliferation



## Breast Cancer

- ✓ Differentiated profile
- ✓ Partnership opportunities to maximize value



## Combined with G1T48

- ✓ Wholly-owned all-oral CDK4/6i + SERD combination in ER+ breast cancer



## Beyond Breast Cancer

- ✓ Tolerability profile supports combination with other targeted agents
- ✓ Significant opportunity in multiple tumors

# Lerociclib profile differentiated in CDK4/6 landscape

- Differentiated PK and tolerability profile
- Continuous dosing (no holiday) with fewer dose-limiting toxicities
- Highly potent and selective with demonstrated anti-tumor POC

	DOSE-LIMITING NEUTROPENIA	MONITORING REQUIREMENT	DOSING HOLIDAY	QT PROLONGATION	DILI	GRADE 3/4 DIARRHEA	VTE
<b>lerociclib</b>	—	Potential for less monitoring	—	—	—	—	—
Ibrance®	X	X	X	—	—	—	—
Kisqali®	X	X	X	X	X	—	—
Verzenio®	X	X	—	—	X	X	X

# Lerociclib differentiated safety and tolerability profile: CDK4/6i partner of choice for combo regimens

CANCER	INDICATION	lerociclib +	STATUS
BREAST	ER+/HER2-	Faslodex® (fulvestrant)	Phase 2a enrolling; Phase 1b data update 4Q19
	ER+/HER2-	G1T48	Phase 1b/2 trial planned for 2019/2020
LUNG	EGFRm	Tagrisso	Phase 1b data in 3Q19
PROSTATE	CRPC	AR-antagonist	Exploring
LYMPHOMA	Mantle Cell	BTKi	Exploring
BLADDER	Urothelial	FGFRi	Exploring
GI	Pancreatic	MAPKi	Exploring



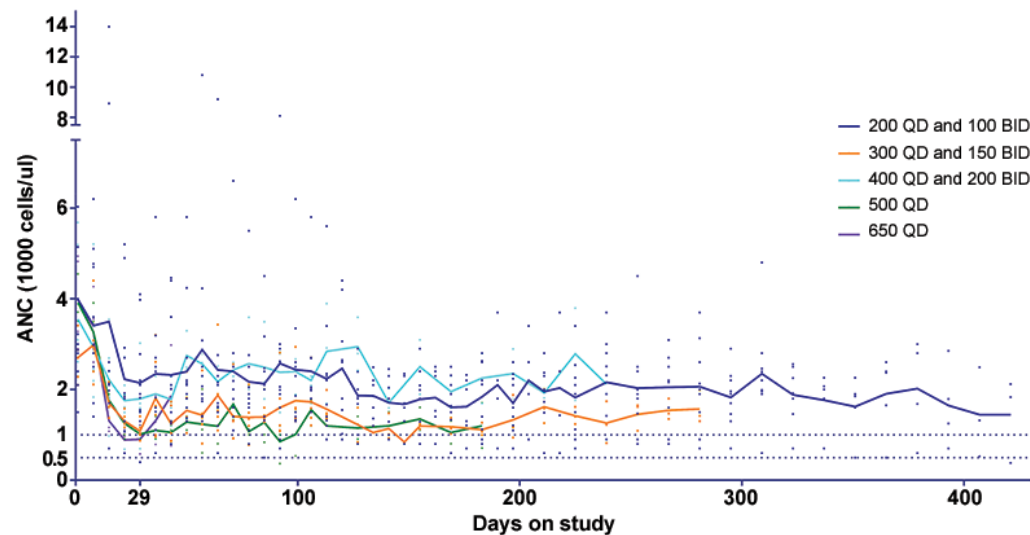
# ER+, HER2- breast cancer Faslodex<sup>®</sup> combination

## Phase 1b/2a trial

PRIMARY ENDPOINTS	<ul style="list-style-type: none"><li>• Assess safety, dose-limiting toxicities, and identify recommended Phase 2 dose/schedule</li></ul>
SECONDARY ENDPOINTS	<ul style="list-style-type: none"><li>• PK, PD</li><li>• ORR, PFS and OS</li></ul>
DESIGN	<ul style="list-style-type: none"><li>• Open-label, single-arm; continuous dosing of lerociclib + Faslodex in ER+, HER2- breast cancer</li><li>• Phase 1b: dose escalation (QD and BID schedules), 3+3 design</li><li>• Phase 2a: dose expansion at RP2D/schedule</li></ul>
MILESTONE TIMING	<ul style="list-style-type: none"><li>• Phase 1b dose escalation completed; preliminary data presented at ASCO 2018</li><li>• Enrolling expansion phase to identify differentiated clinical profile</li><li>• Anticipate reporting additional Phase 1b data in 4Q19</li></ul>

# Continuously dosed lerociclib: promising early data

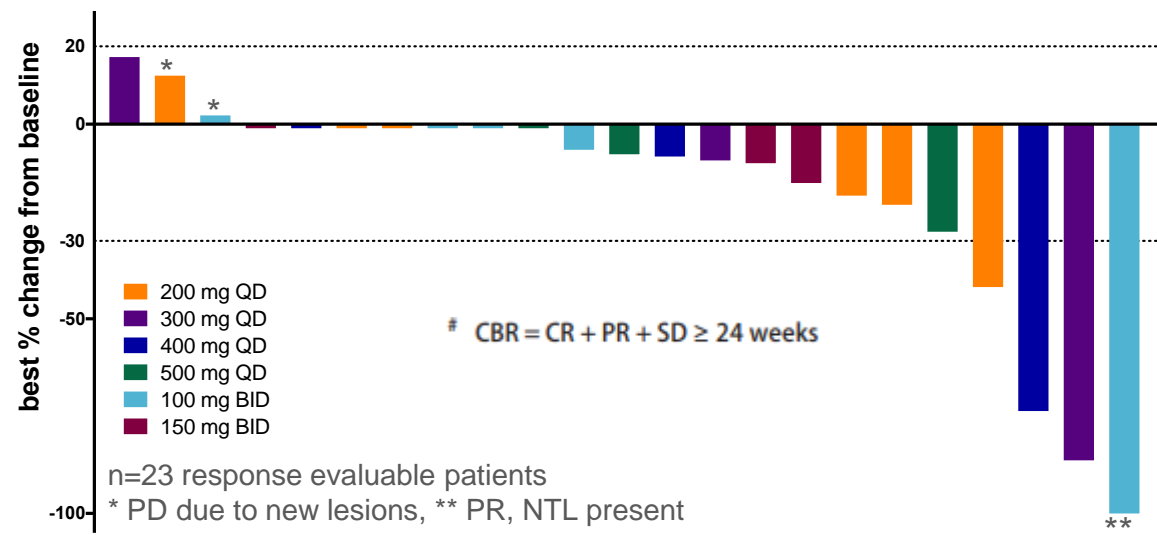
## Continuous dosing with less Gr 4 neutropenia



Dose	N	Day 29 mean % change
200mg QD	6	-48%
300mg QD	3	-66%
400mg QD	3	-50%
500mg QD	4	-74%
650mg QD	6	-76%

ANC decreases  
~50-60% for  
approved CDK4/6  
inhibitors

## Anti-tumor activity at all dose levels



Best Response lerociclib + fulvestrant (n=23)	
PR	4/23 (17%)
SD	16/23 (70%)
PD	3/23 (13%)
SD ≥ 24 weeks	11/23 (48%)
CBR 24	15/23 (65%)

CBR 24=CR+PR+SD≥24 weeks

# EGFRm NSCLC Tagrisso combination

## Phase 1b dose-finding/Phase 2 randomized trial

PRIMARY ENDPOINTS	<ul style="list-style-type: none"><li>• Assess safety, dose-limiting toxicities, and identify recommended Phase 2 dose</li><li>• PFS</li></ul>
SECONDARY ENDPOINTS	<ul style="list-style-type: none"><li>• PK, PD</li><li>• ORR and OS</li></ul>
DESIGN	<ul style="list-style-type: none"><li>• EGFRm NSCLC</li><li>• Phase 1b: single-arm dose-finding, lerociclib + Tagrisso in 1st/2nd-line setting</li><li>• Phase 2: lerociclib + Tagrisso, or Tagrisso; randomized (1:1)</li></ul>
MILESTONE TIMING	<ul style="list-style-type: none"><li>• Phase 1b enrollment ongoing</li><li>• Preliminary Phase 1b data expected in 3Q19</li></ul>

# Strong rationale for lerociclib + Tagrisso

1

**Goal is to extend time to resistance and improve PFS**

2

**In ER+ breast cancer, CDK4/6 inhibitors as a class extend PFS when added to endocrine therapy**

- addition of lerociclib to osimertinib follows this same paradigm of adding a CDK4/6 inhibitor to a growth signaling inhibitor as a means to extend progression free survival

3

**Lerociclib combined with osimertinib could extend time to resistance**

- osimertinib resistance mechanisms include activating mutations in PIK3CA, BRAF and KRAS; amplifications in MET, HER2, FGFR1, CCND, CDK4/6; and EGFR C797S mutation, many of which are “upstream” of CDK4/6
- preclinical data demonstrated prolongation of time to resistance by the addition of lerociclib to EGFR TKIs (Sorrentino et al 2018)

# G1T48 (ORAL SERD) UPDATE

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Tumor cell proliferation

# G1T48: strong strategic fit and patient need

1

**Selective estrogen receptor degrader (SERD):  
validated approach for ER+ breast cancer**

3

**All-oral lerociclib/G1T48 combination regimen  
offers potential competitive advantages**

2

**Faslodex (IM SERD): approved as monotherapy  
and in combination with CDK4/6i**

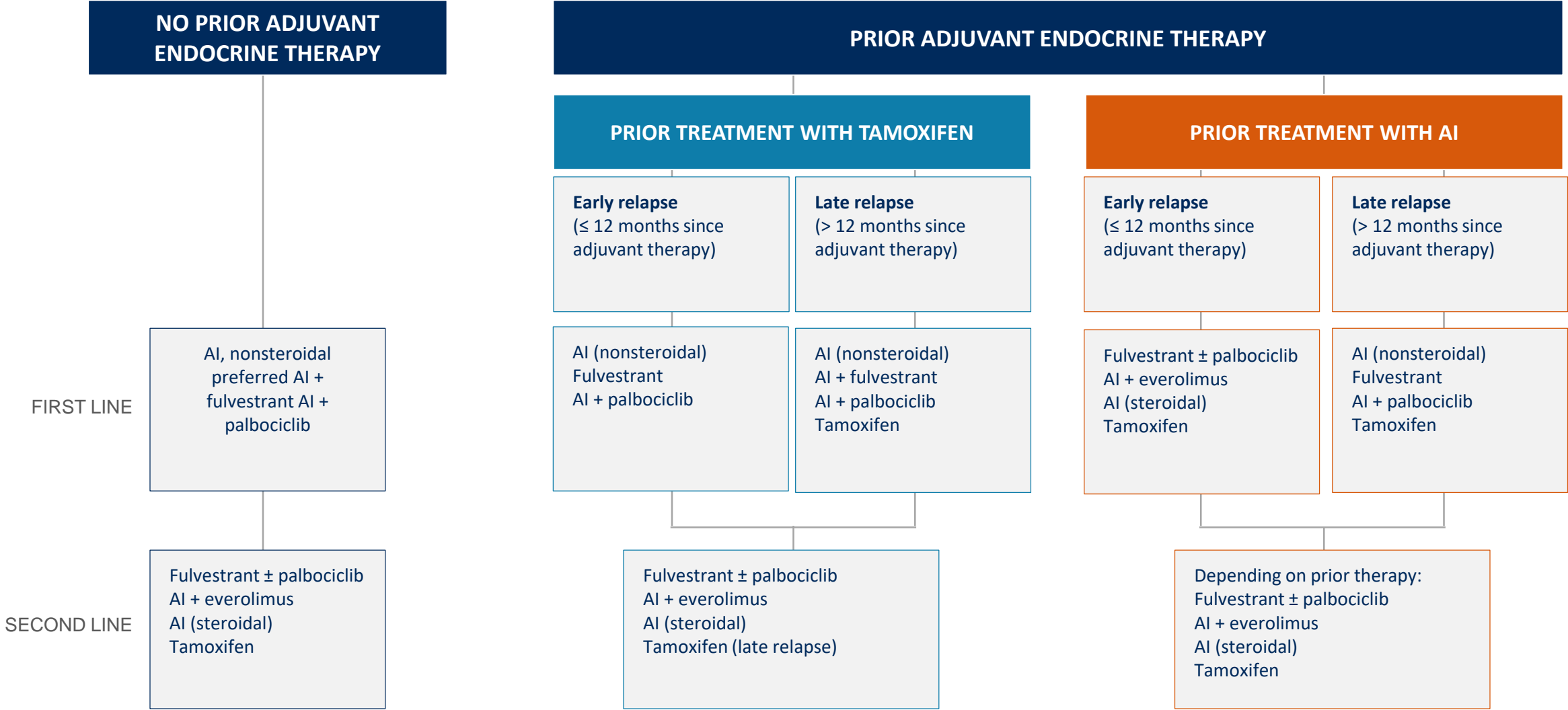
- > \$1B sales despite painful intramuscular (IM) injections; oral SERD addresses unmet patient need

4

**Phase 1 trial in ER+ breast cancer (G1T48  
monotherapy)**

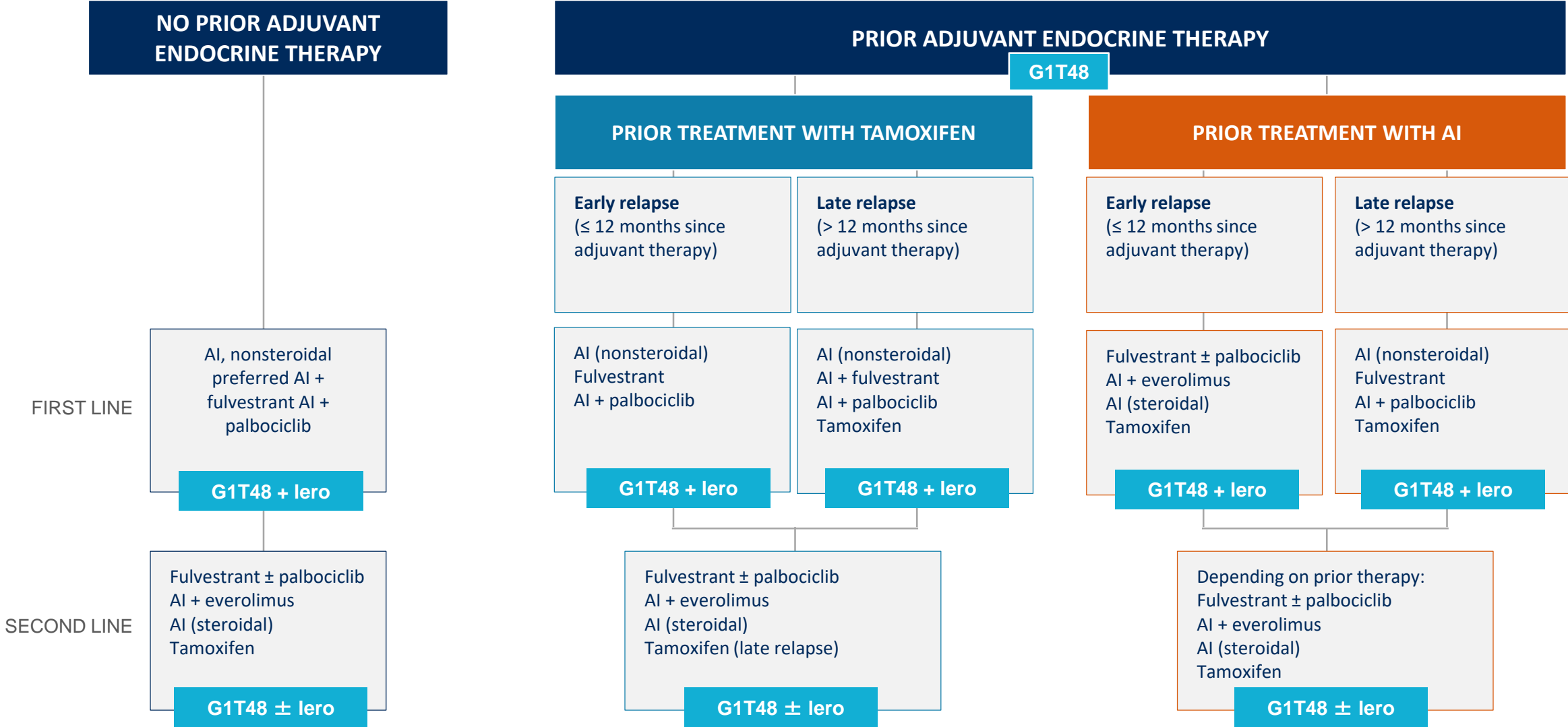
- initiated in 2018
- preliminary data expected in 4Q19
- plan to combine with lerociclib in 2019/2020, pending monotherapy trial results

# ASCO guidelines for HR+ mBC: Oral SERD creates opportunity across lines of therapy



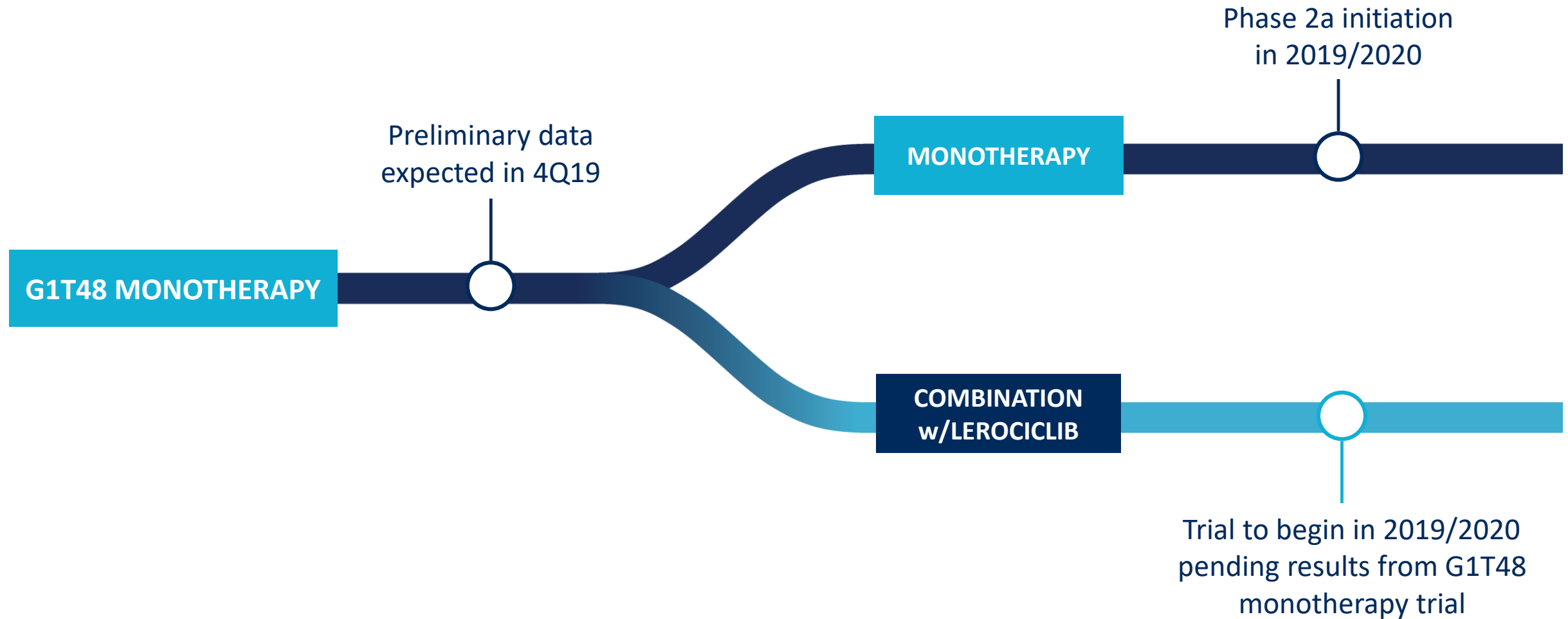
# ASCO guidelines for HR+ mBC:

## Oral SERD creates opportunity across lines of therapy





# Development pathways



# ER+, HER2- breast cancer

## Phase 1/2a trial

PRIMARY ENDPOINTS	<ul style="list-style-type: none"><li>• Assess safety, dose-limiting toxicities, and identify recommended Phase 2 dose</li></ul>
SECONDARY ENDPOINTS	<ul style="list-style-type: none"><li>• PK, PD</li><li>• ORR and OS</li><li>• Food effect on bioavailability</li></ul>
DESIGN	<ul style="list-style-type: none"><li>• Open-label, ER+, HER2- breast cancer, enrolling up to 104 patients</li><li>• Phase 1: dose-finding, G1T48 monotherapy in 2nd/3rd-line setting</li><li>• Phase 2a: dose expansion at RP2D</li></ul>
MILESTONE TIMING	<ul style="list-style-type: none"><li>• Phase 1 enrollment ongoing</li><li>• Report preliminary Phase 1 data in 4Q19</li></ul>

1

## Lerociclib – potential in multiple tumor types

- ongoing trials in breast and non-small cell lung cancer
- differentiated profile = “partner of choice” in CDK4/6i combo regimens

2

## G1T48 – oral SERD offers significant patient benefit

- oral delivery provides opportunity to move SERD into earlier lines of therapy
- monotherapy and combination regimens

3

## Lerociclib + G1T48 – all-oral BC regimen

- all-oral regimen offers significant differentiation in crowded breast cancer space

# Key anticipated milestones

	INDICATION/COMBO	2Q19	3Q19	4Q19
<b>trilaciclib</b> IV - CDK4/6i	1 <sup>st</sup> -line SCLC (+ etop/carbo)			
	1 <sup>st</sup> -line SCLC (+ etop/carbo/Tecentriq)		Present additional Phase 2 data (pending mature OS)	
	2 <sup>nd</sup> /3 <sup>rd</sup> -line SCLC (+ topotecan)	Present additional Phase 2 data	Provide regulatory update	
	Metastatic TNBC (+ gem/carbo)			Present additional Phase 2 data (pending mature PFS)
<b>Ierociclib</b> Oral - CDK4/6i	ER <sup>+</sup> , HER2- BC (+ Faslodex)			Report additional Phase 1b data
	EGFRm NSCLC (+ Tagrisso)		Report preliminary Phase 1b data	
<b>G1T48</b> Oral - SERD	ER <sup>+</sup> , HER2- BC (monotherapy)			Report preliminary Phase 1 data



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