G1 Therapeutics:
Next Generation Cancer Therapies

June 2019

www.g1therapeutics.com

NASDAQ: GTHX

Forward-looking statements

This presentation contains 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 news release include, but are not limited to, the therapeutic potential of trilaciclib, lerociclib and G1T48 and the timing for next steps with regard to the trilaciclib marketing applications, and are based on the Company's expectations and assumptions as of the date of this presentation. Each of these forward-looking statements involves risks and uncertainties. Factors that may cause the Company's actual results to differ from those expressed or implied in the forward-looking statements in this presentation are discussed in the Company's filings with the U.S. Securities and Exchange Commission, including the "Risk Factors" sections contained therein and include, but are not limited to, the Company's ability to complete clinical trials for, obtain approvals for and commercialize any of its product candidates; the Company's initial success in ongoing clinical trials may not be indicative of results obtained when these trials are completed or in later stage trials; the inherent uncertainties associated with developing new products or technologies and operating as a development-stage company; the Company's development of a CDK4/6 inhibitor to reduce chemotherapy-induced myelosuppression is novel, unproven and rapidly evolving and may never lead to a marketable product; and market conditions. Except as required by law, the Company assumes no obligation to update any forward-looking statements contained herein to reflect any change in expectations, even as new information becomes available.

Robust oncology pipeline addressing large indications

Three wholly-owned clinical-stage therapeutic candidates

Trilaciclib

First-in-class myelopreservation agent

- ✓ NDA/MAA submissions for SCLC planned for 2020
- ✓ **Topline OS benefit in mTNBC**
- ✓ Randomized trials in additional tumor types/chemo regimens in 2020

Lerociclib

Differentiated CDK4/6 inhibitor

- ✓ POC in Ph1b ER+ BC trial
- ✓ **Less neutropenia and favorable tolerability compared to marketed CDK4/6is**
- ✓ Initiating randomized trials in 2020

G1T48

Potential best-in-class oral SERD for breast cancer (BC)

- ✓ Differentiated chemistry, favorable tolerability
- ✓ **Accelerating program: data in ER+ BC in 3Q19**
- ✓ Initiating randomized trials in 2020
- ✓ Opportunity across multiple lines, including adjuvant

Catalysts across all programs in 2019/2020

	INDICATION/COMBO	3Q19	4Q19	2020
trilaciclib IV - CDK4/6i	1st-line SCLC (+ etop/carbo)			NDA/MAA submissions for myelopreservation in SCLC + randomized trials for additional tumor types and chemo regimens
	1st-line SCLC (+ etop/carbo/Tecentriq)	Present additional Phase 2 data		
	2nd/3rd-line SCLC (+ topotecan)			
	Metastatic TNBC (+ gem/carbo)		Present additional Phase 2 data	
lerociclib Oral - CDK4/6i	ER+, HER2- BC (+ Faslodex)		Present additional Phase 1b/2a data	Additional data presentations + randomized trials
	EGFRm NSCLC (+ Tagrisso)	Present preliminary Phase 1b data		
G1T48 Oral - SERD	ER+, HER2- BC	Present preliminary Phase 1 data		Initiate randomized monotherapy and CDK4/6i combination trials

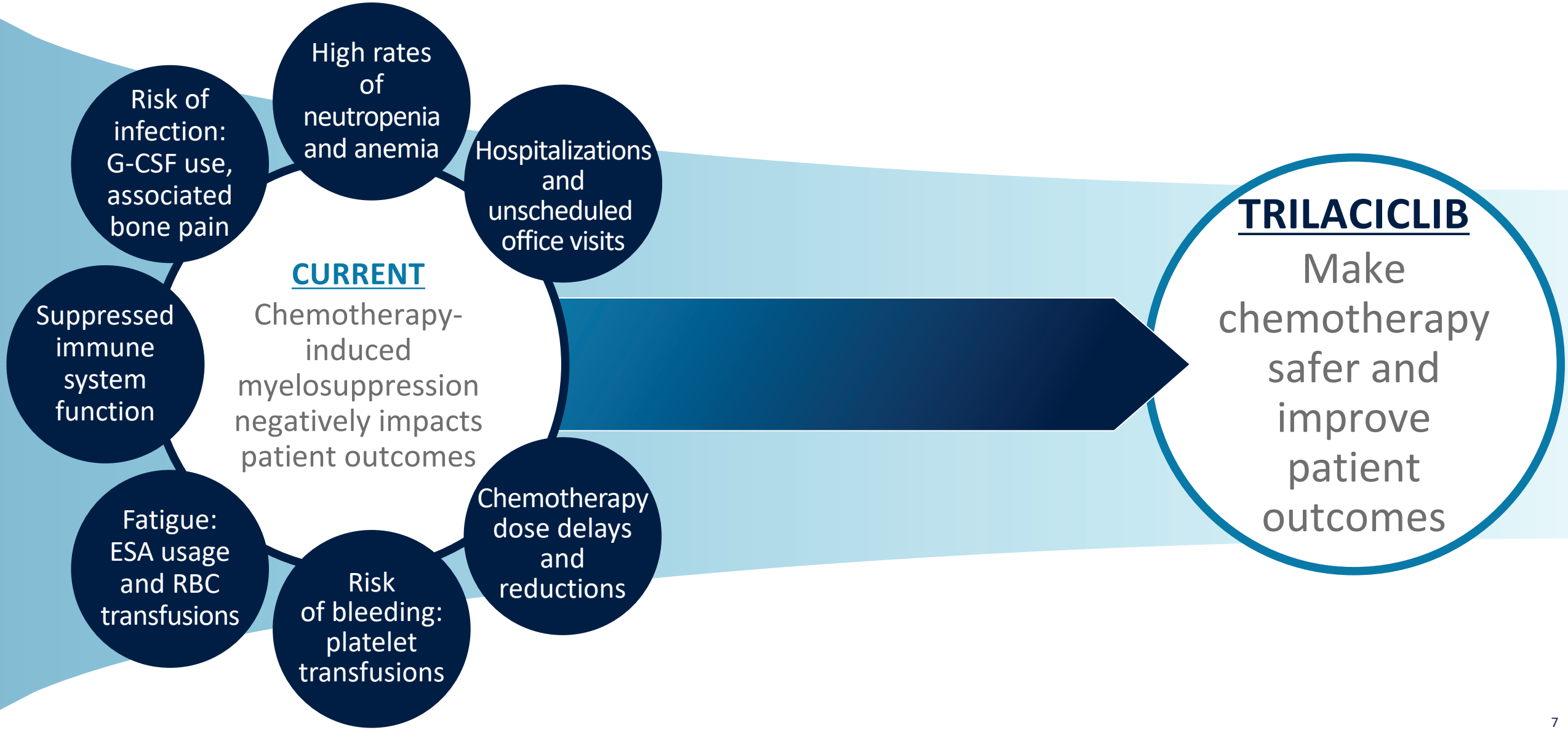
Strong financial position to execute on development plans

- Cash position at end of 1Q19: $348M
- Expected cash position at end of 2Q19: $322-327M
- Expected cash position at end of full-year 2019: $260-270M

TRILACICLIB DEVELOPMENT UPDATE

Hematopoietic stem and progenitor cells (HSPCs)

Trilaciclib: first-in-class myelopreservation agent



Trilaciclib: improving outcomes for patients on chemo

1

Substantial need

- ~1 million patients in U.S. receive chemotherapy each year
- **Chemo to remain a cornerstone of cancer treatment**
- Myelosuppression is common; impacts QoL and burdens HC system

2

Phase 2 program: improved safety and patient outcomes

- Less neutropenia *and* anemia in SCLC
- Reduced G-CSF usage *and* transfusions in SCLC
- **Topline OS benefit in mTNBC**

3

Next steps

- **Anticipate 2020 SCLC myelopreservation NDA/MAA filings**
- Initiate randomized trials in additional tumor types/chemo regimens in 2020
- Exploring partnerships to maximize access for patients globally

Integrated analysis for three randomized SCLC trials: robust myelopreservation - neutrophils, RBCs, platelets

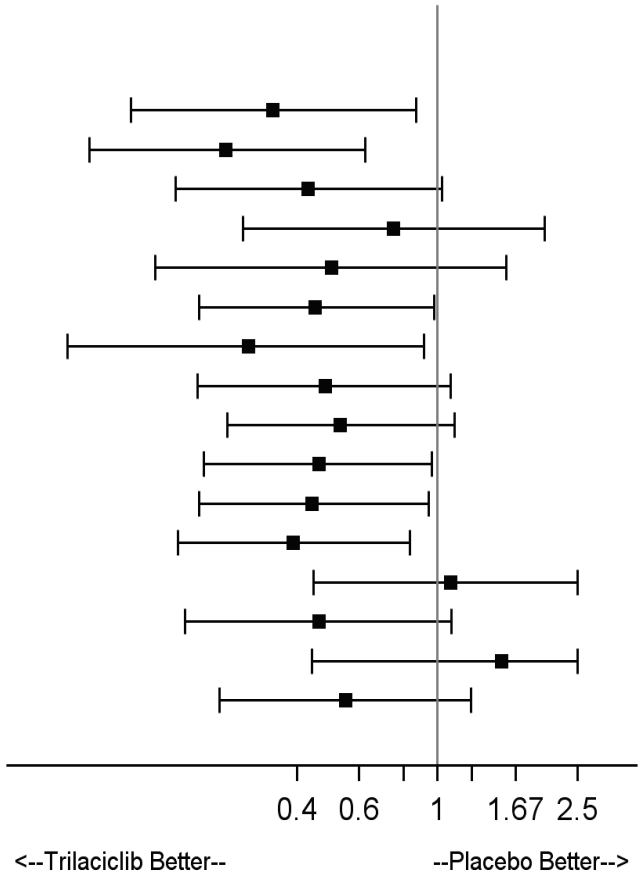
	PLACEBO + CHEMOTHERAPY	TRILACICLIB + CHEMOTHERAPY	
Patients (intent-to-treat population)	120	125	P-VALUE[+]
primary endpoints: Mean duration (in days) of severe neutropenia in cycle 1 (SD)	4 (5.2)	1 (2.3)	**<0.0001**
primary endpoints: Occurrence of severe neutropenia	64 (53.3%)	16 (12.8%)	**<0.0001**
Occurrence of RBC transfusions on/after 5 weeks	32 (26.7%)	19 (15.2%)	**0.0207**
Cumulative incidence RBC transfusions on/after 5 wks: event rate per 100 wks	3.2	1.5	**0.0020**
Occurrence of Grade 3/4 anemia	39 (32.5%)	26 (20.8%)	**0.0188**
Occurrence of Grade 3/4 thrombocytopenia	44 (36.7%)	26 (20.8%)	**0.0081**

[+] 2-sided p-value

PRO data: trilaciclib improves the patient experience

G1T28-03: 2L/3L SCLC, topotecan +/- trilaciclib

Domain	No. of Events Trilaciclib/Placebo	Median TTD, Months Trilaciclib/Placebo	Hazard Ratio [95% CI]
FACT-G	7/13	NYR/2.86	0.34 [0.14;0.87]
PWB	7/16	NYR/1.64	0.25 [0.10;0.62]
FWB	10/13	8.84/2.23	0.43 [0.18;1.03]
EWB	8/8	NYR/NYR	0.75 [0.28;2.02]
SWB	6/8	6.70/NYR	0.50 [0.16;1.57]
FACT-L	12/16	4.40/2.10	0.45 [0.21;0.98]
LCS	4/11	NYR/10.02	0.29 [0.09;0.92]
Lung TOI	10/14	NYR/2.10	0.48 [0.21;1.09]
FACT-An	14/16	3.75/1.02	0.53 [0.25;1.12]
Fatigue	14/17	3.09/0.95	0.46 [0.22;0.96]
Anemia TOI	13/17	3.09/1.02	0.44 [0.21;0.94]
GP1: Energy	12/17	3.75/1.41	0.39 [0.18;0.83]
GP4: Pain	11/9	NYR/NYR	1.09 [0.45;2.66]
GP5: Side effects	9/13	NYR/2.53	0.46 [0.19;1.09]
B5: Hair loss	7/4	NYR/NYR	1.52 [0.44;5.23]
An: Tired	11/13	NYR/1.48	0.55 [0.24;1.24]



Threshold=3 for PWB,SWB,EWB,FWB,LCS and Fatigue, =6 for FACT-L total, L-TOI and An-TOI, =7 for FACT-G total and FACT-An total, =1 for items
NYR=Not yet reached

- Patient-reported outcomes (PRO) data from 2nd/3rd-line SCLC trial (ASCO 2019)
- Trilaciclib improves symptoms and functions across multiple parameters
- Pooled data to be presented at MASCC 2019

Updated anti-tumor efficacy results in metastatic TNBC: statistically significant improvement in overall survival (OS)

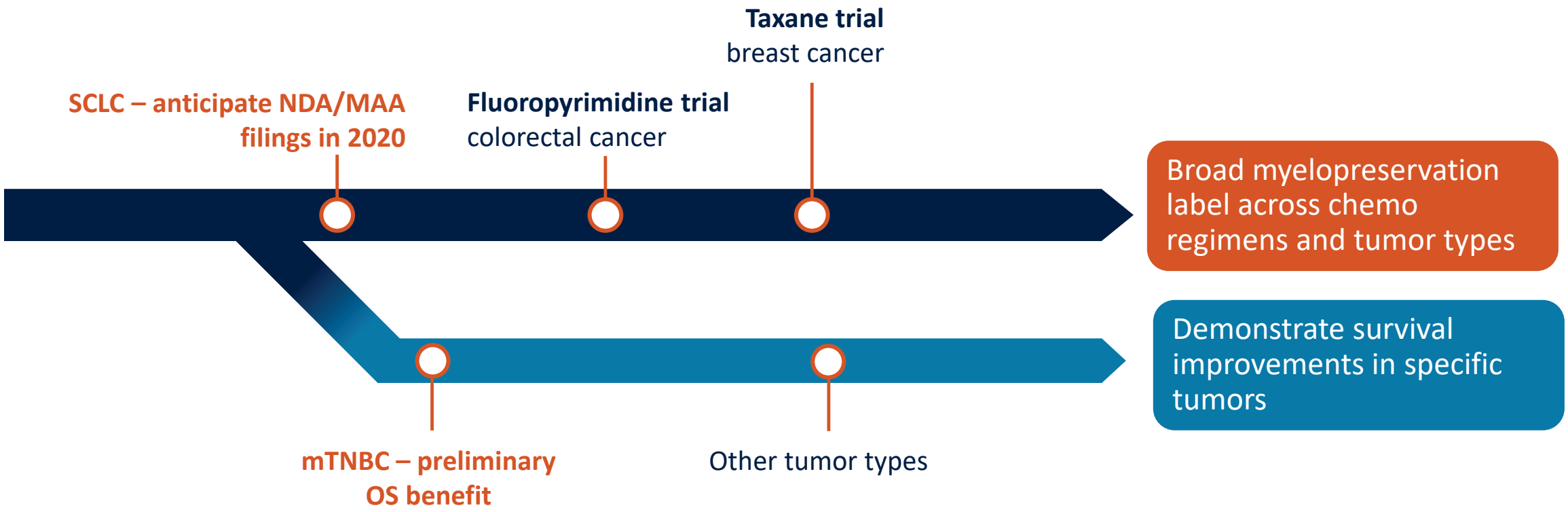
TRIAL DESIGN: 102 patients, randomized, open-label; gemcitabine/carboplatin (GC) +/- trilaciclib (two dose schedules)

Preliminary data showed statistically significant OS improvement for patients receiving GC + trilaciclib compared with GC alone

- ORR and PFS data were consistent with results presented at SABCS 2018
- Safety and tolerability consistent with previously reported data; no serious adverse events attributed to treatment with trilaciclib
- Data to be presented at medical meeting later this year

Advancing multiple tumor/chemo regimens

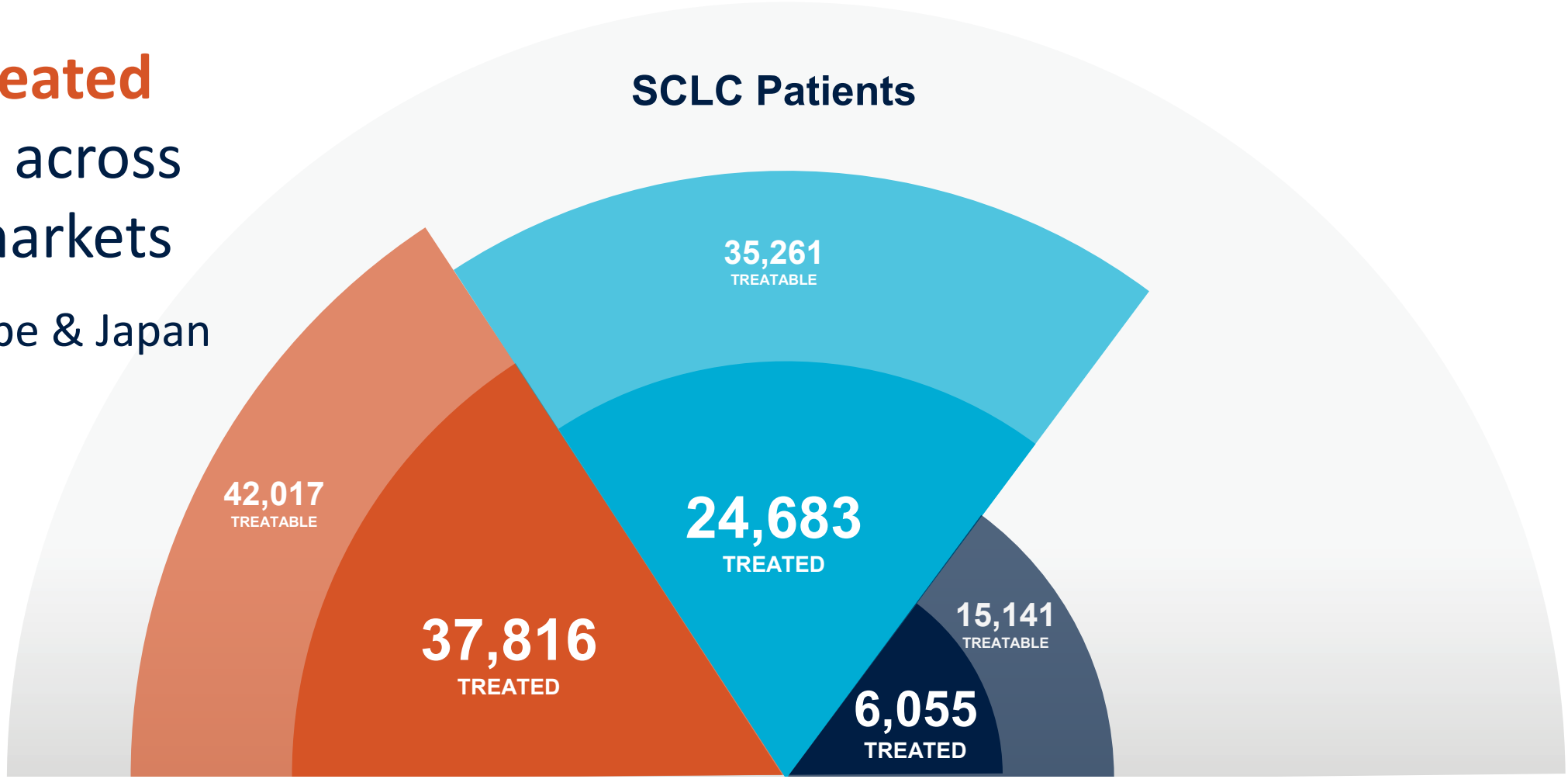
Establish trilaciclib as first-in-class myelopreservation agent



Trilaciclib could benefit a significant number of SCLC patients

~68k treated patients across major markets

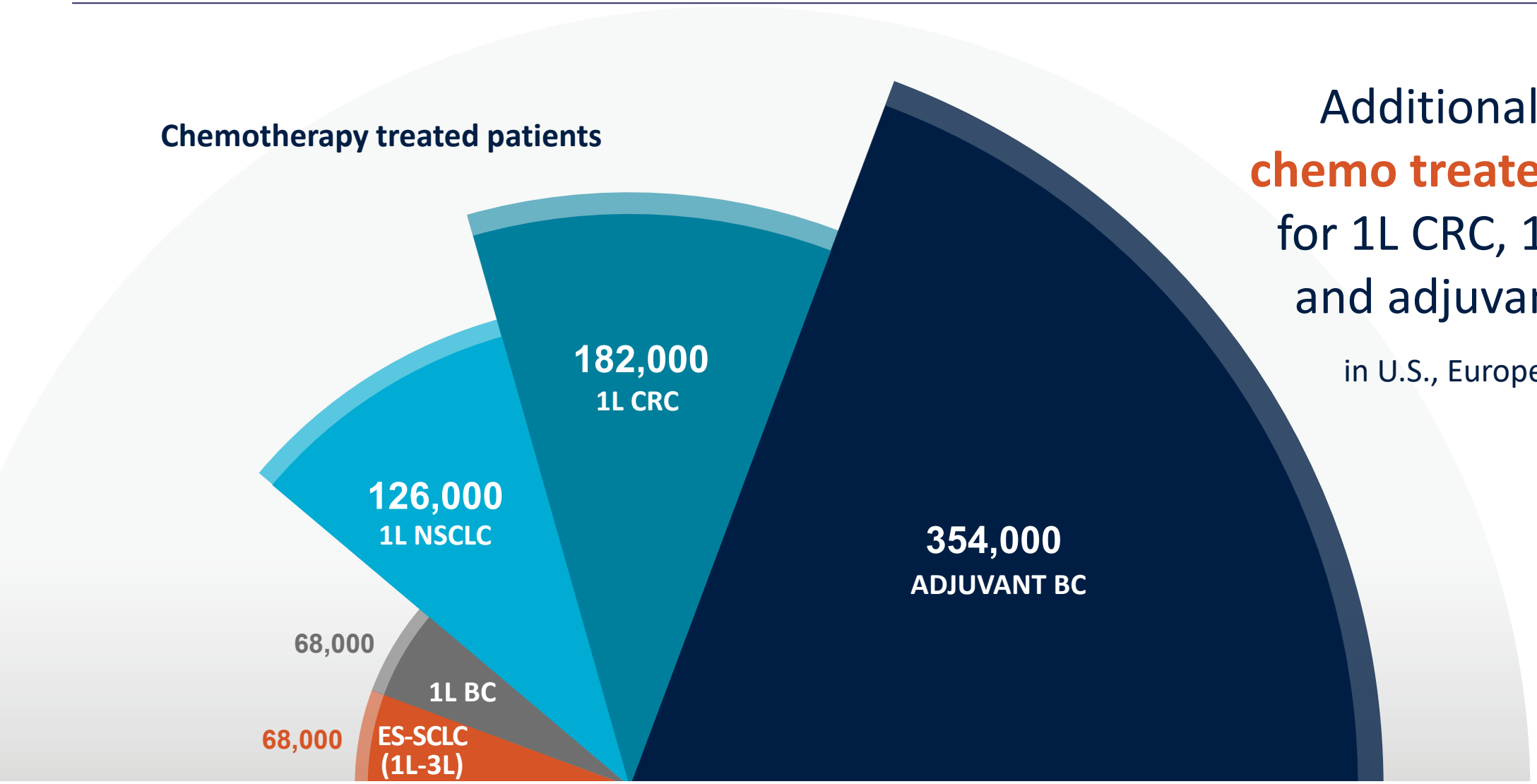
in U.S., Europe & Japan



1L 90% TREATMENT RATE **2L** 70% TREATMENT RATE **3L** 40% TREATMENT RATE

2030 estimates, secondary epi source & ZS forecast model

Potential to benefit a significant number of patients beyond SCLC

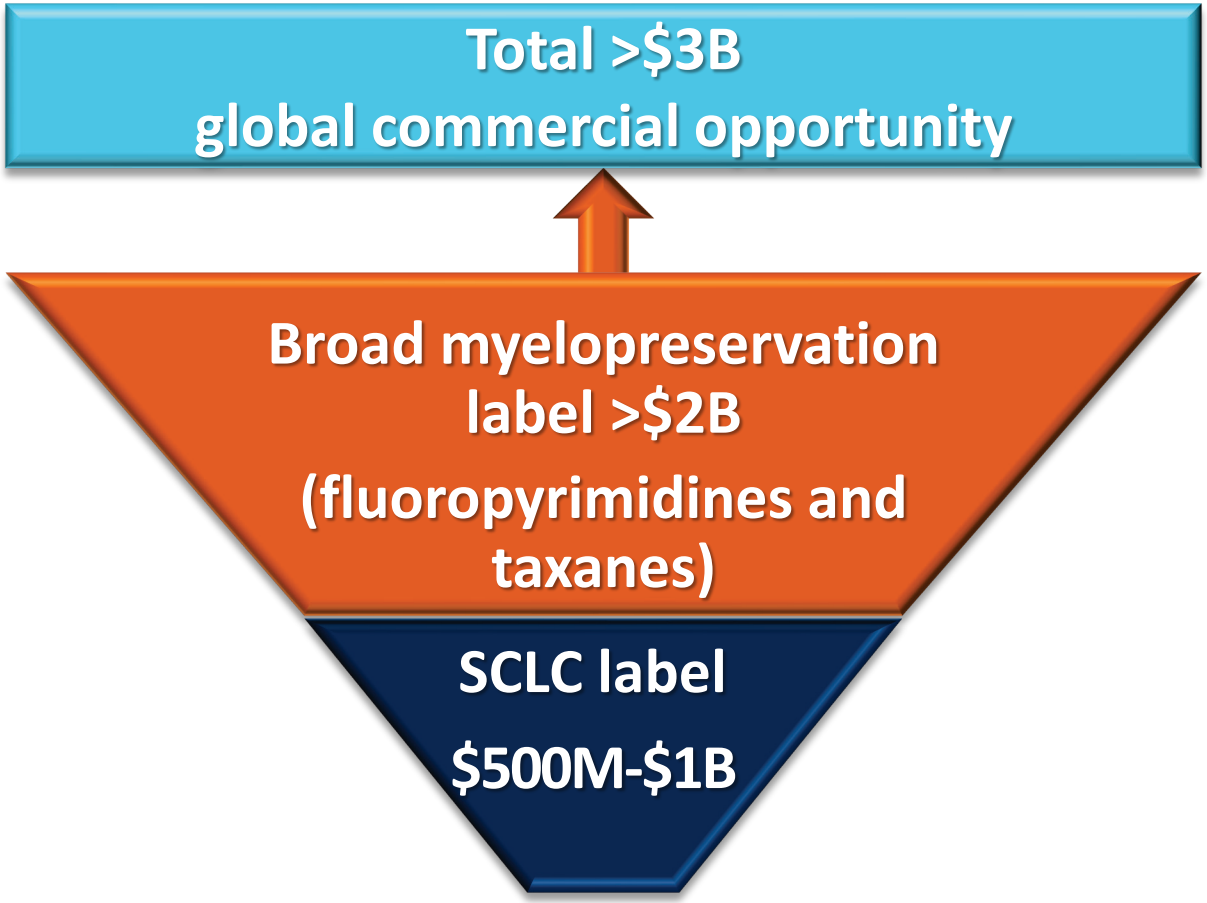


Additional **>730K chemo treated** patients for 1L CRC, 1L NSCLC, and adjuvant/1L BC

in U.S., Europe & Japan

1. Decision Resources Group, 2027 estimates

Substantial global opportunity* to help patients



- ***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 and will provide access to patients

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

LEROCICLIB DEVELOPMENT UPDATE

Tumor cell proliferation

Lerociclib profile differentiated in CDK4/6i landscape

- Differentiated PK and tolerability profile
- Continuous dosing (no holiday) with fewer dose-limiting toxicities
- Potential for less CBC monitoring, reducing patient & physician burden

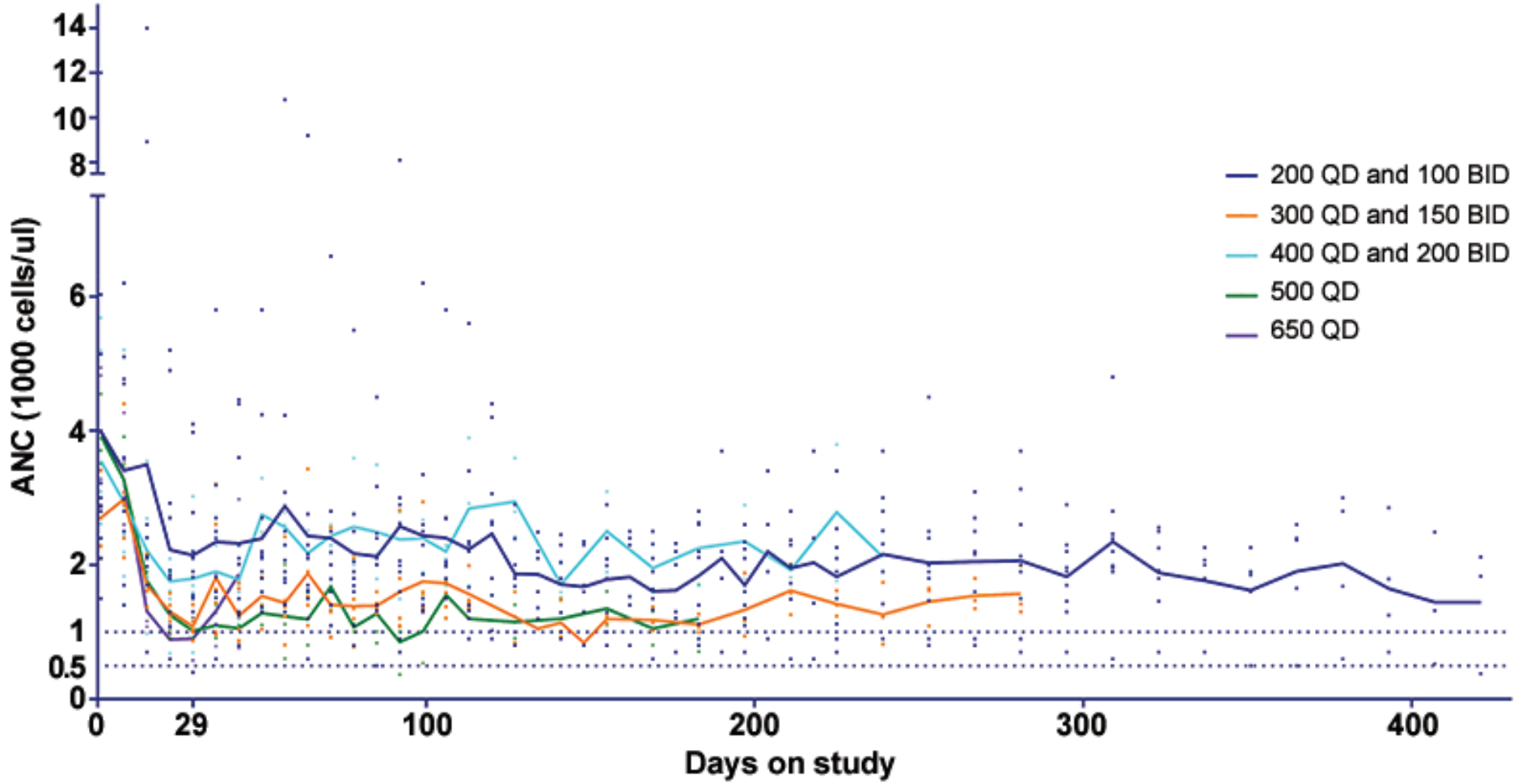
	DOSE-LIMITING NEUTROPENIA	MONITORING REQUIREMENT	DOSING HOLIDAY	QT PROLONGATION	DILI	GRADE 3/4 DIARRHEA	VTE
lerociclib	–	**Potential for less monitoring**	–	–	–	–	–
Ibrance®	X	X	X	–	–	–	–
Kisqali®	X	X	X	X	X	–	–
Verzenio®	X	X	–	–	X	X	X

ER+, HER2- breast cancer fulvestrant combination Phase 1b/2a trial

PRIMARY ENDPOINTS	• Assess safety and dose-limiting toxicities • Identify dose for randomized studies
SECONDARY ENDPOINTS	• PK, PD • ORR, PFS and OS
DESIGN	• Open-label, single-arm; continuous dosing of lerociclib + fulvestrant in ER+, HER2- breast cancer • Phase 1b: dose escalation (QD and BID schedules), 3+3 design • Phase 2a: dose expansion/selection
MILESTONE TIMING	• Phase 1b dose escalation completed; preliminary data presented at ASCO 2018 • **Anticipate reporting additional data and dose selection in 4Q19**

Continuously dosed lerociclib: less neutropenia

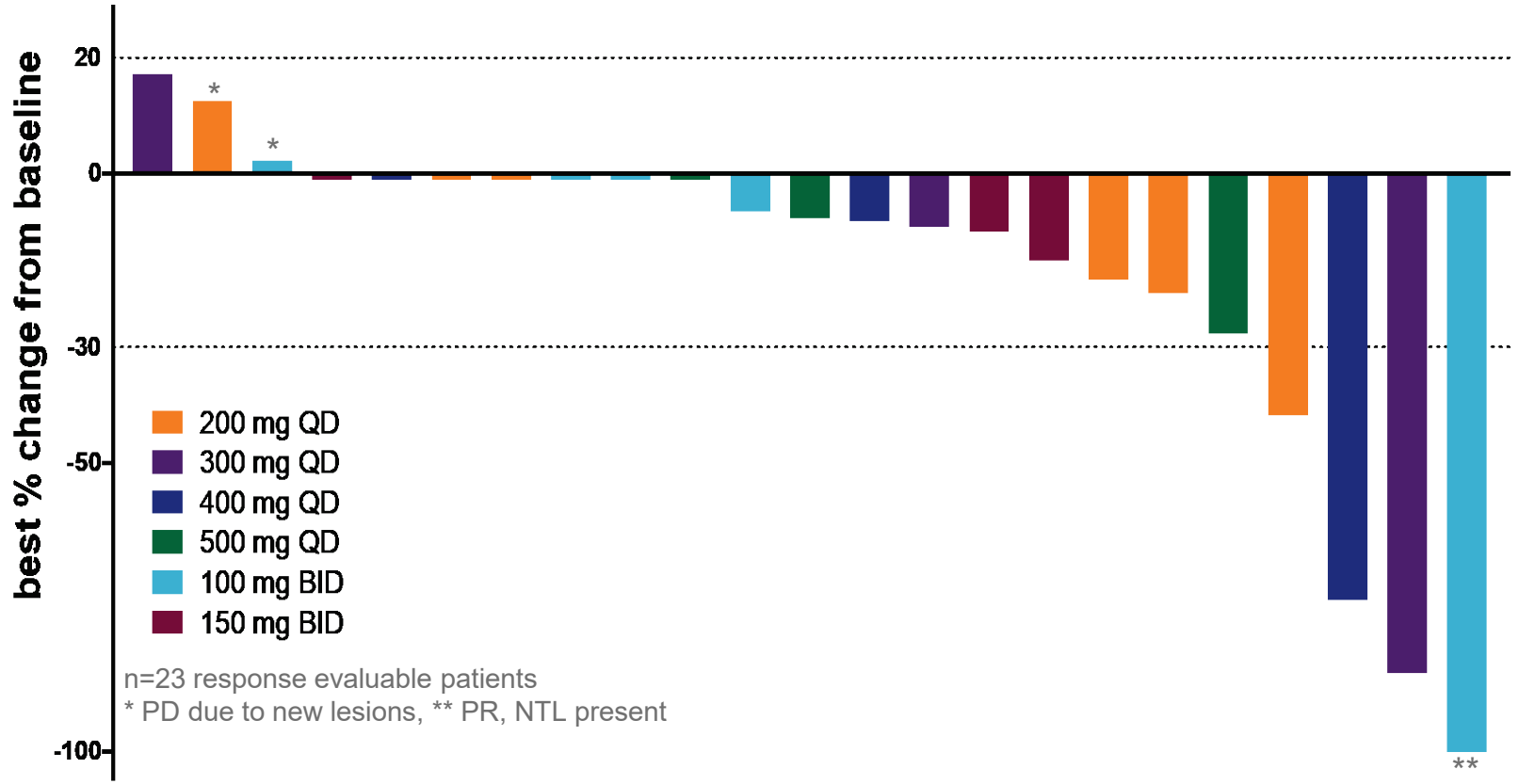
Less Gr 4 neutropenia: opportunity to reduce patient monitoring



Data presented at 2018 ASCO Annual Meeting

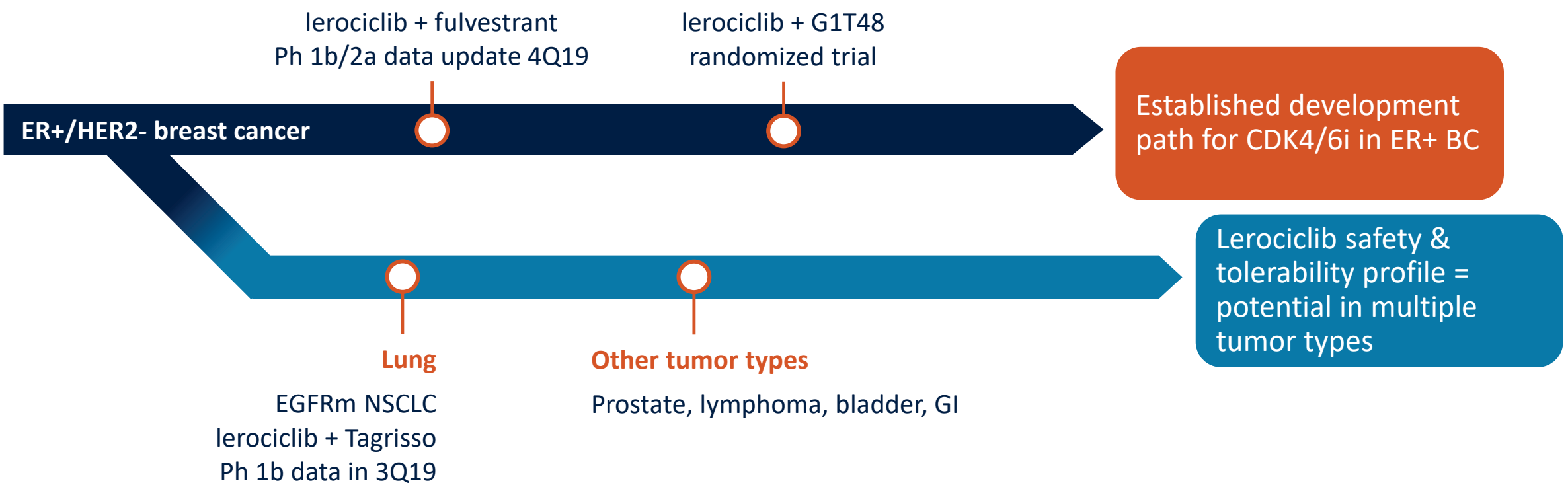
Continuously dosed lerociclib: promising efficacy

Anti-tumor activity at all dose levels



Data presented at 2018 ASCO Annual Meeting; efficacy data updated to account for one patient with non-measurable disease at baseline

Potential combination regimens in multiple indications



Lerociclib: key takeaways

1

Differentiated oral CDK4/6i

- Less dose-limiting neutropenia; potential for less frequent blood count monitoring
- **Favorable GI tolerability profile: advantages in the adjuvant setting**

2

Opportunity in BC and other indications

- **Additional data and dose selection anticipated in 4Q19**
- Randomized BC trial initiating in 2020
- Ongoing trial in EGFRm NSCLC in combination with Tagrisso

3

Efficient clinical/ regulatory pathway

- Established development parameters for CDK4/6i therapies in breast cancer

G1T48 (ORAL SERD) UPDATE

Tumor cell dissolution

G1T48: key takeaways

1

Established need for oral SERD

- > 300,000 women in U.S. and Europe diagnosed with ER+, HER2- BC each year
- Intramuscular (IM) SERD fulvestrant is effective but not optimal treatment

2

Potential for oral SERD

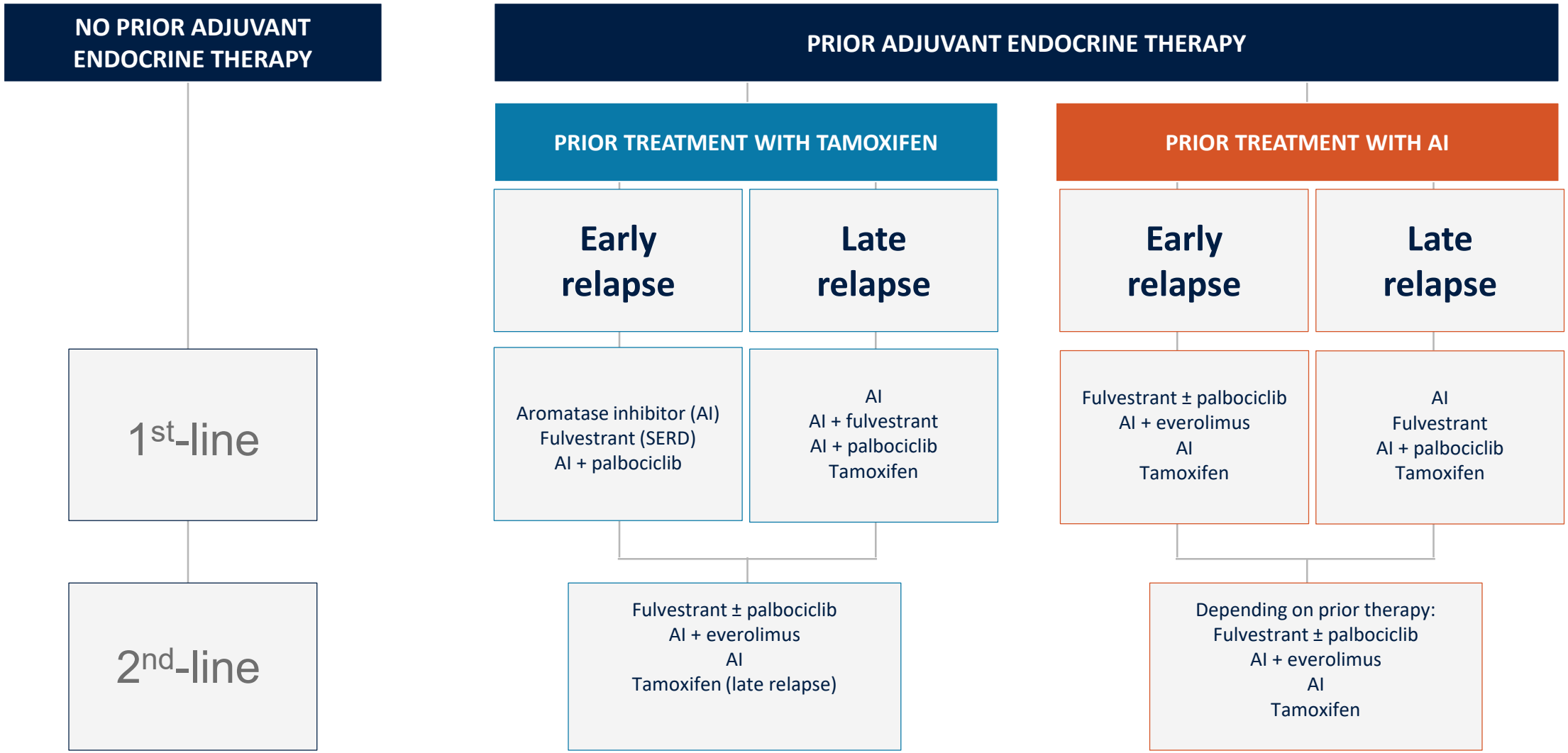
- **Oral delivery provides opportunity to move SERD into earlier lines of therapy, including adjuvant settings**
- Monotherapy and combination regimens

3

G1T48: potential best-in-class oral SERD

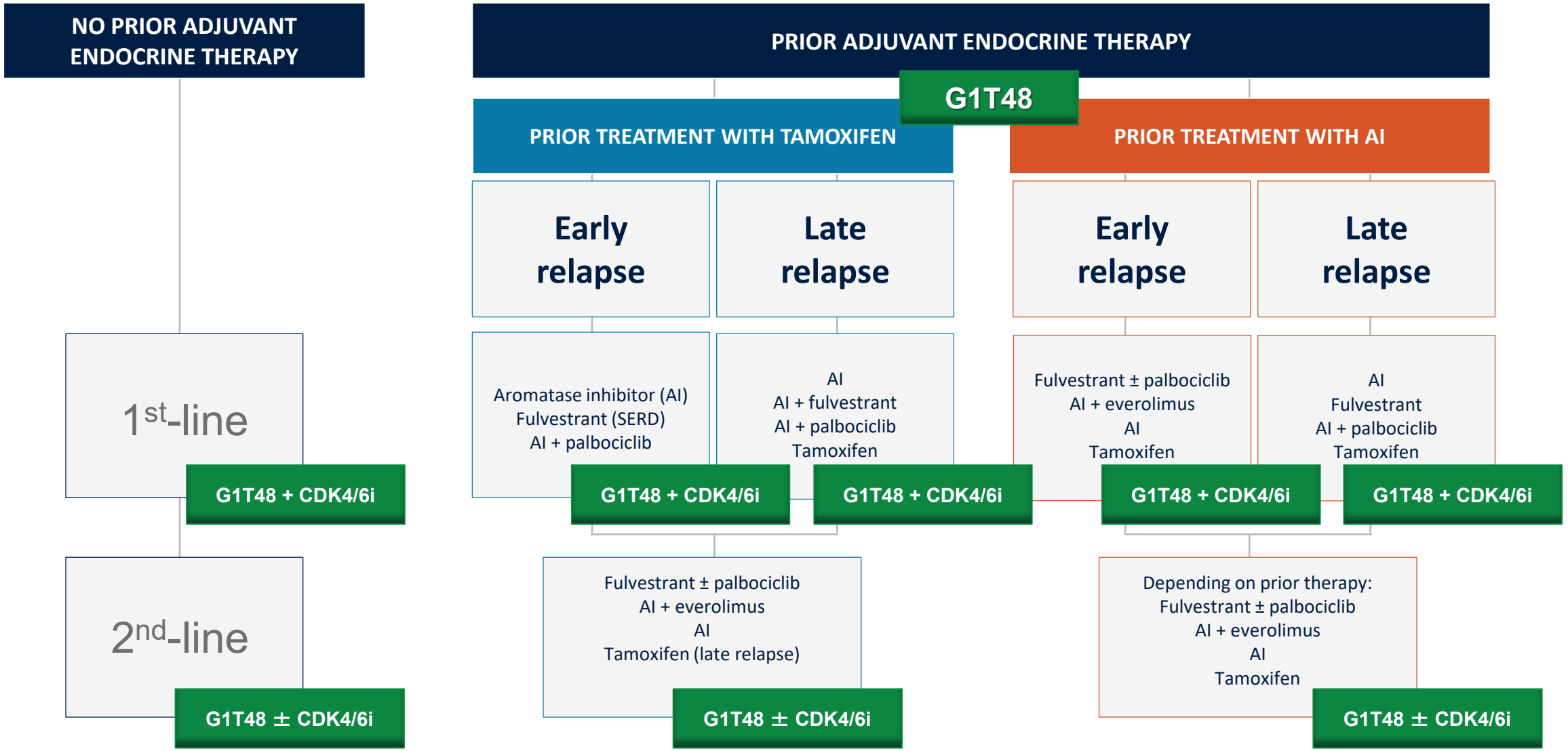
- Differentiated chemistry, favorable tolerability
- **Encouraging early data – accelerating program**
- Expect to initiate randomized monotherapy and CDK4/6i combination trials in 2020

ASCO guidelines for ER+ mBC: opportunity across multiple lines of therapy



Adapted from Rugo et al JCO 2016

ASCO guidelines for ER+ mBC: opportunity across multiple lines of therapy

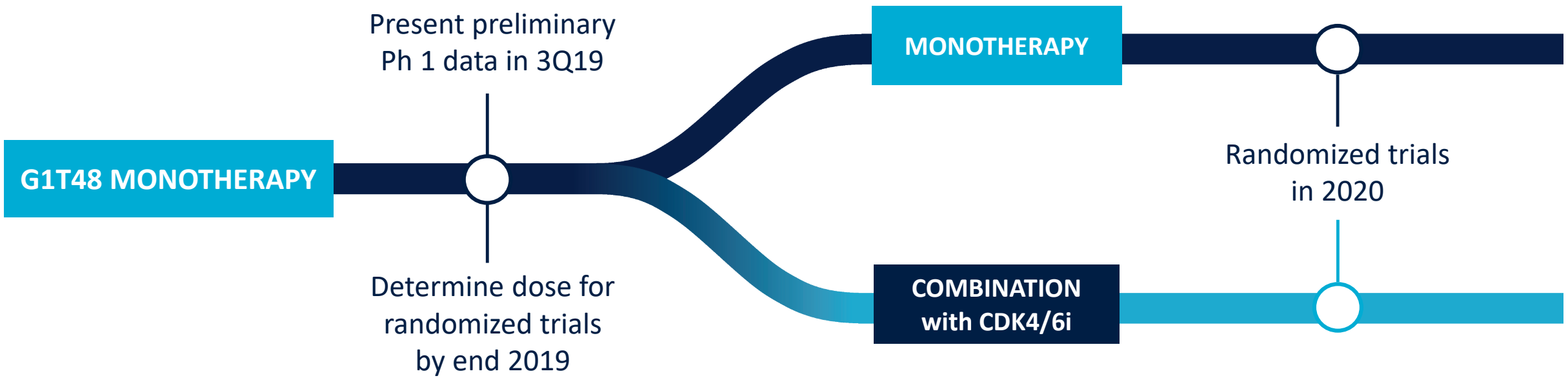


Adapted from Rugo et al JCO 2016

ER+, HER2- breast cancer
Phase 1/2a trial

PRIMARY ENDPOINTS	• Assess safety and dose-limiting toxicities • Identify dose for randomized studies
SECONDARY ENDPOINTS	• PK, PD (ctDNA, [18F] FES PET, CTCs) • ORR, PFS and OS • Food effect on bioavailability
DESIGN	• Open-label, ER+, HER2- breast cancer, enrolling up to 104 patients • Phase 1: dose-finding, G1T48 monotherapy in 2nd/3rd-line setting • Phase 2a: dose expansion/selection
MILESTONE TIMING	• Phase 1 enrollment ongoing • **Anticipate POC Ph 1 data 3Q19**

Development pathways leading to a standard-of-care label



- ✓ *Potential to benefit ER+BC patients across multiple lines of therapy*
- ✓ *Opportunity for use in earlier lines of therapy, including adjuvant*

Catalysts across all programs in 2019/2020

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G1T48 Oral - SERD	ER+, HER2- BC	Present preliminary Phase 1 data		Initiate randomized monotherapy and CDK4/6i combination trials

Strong balance sheet: $348M at end of 1Q19; anticipate 2019 YE cash of $260-270M

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