Next Generation Cancer Therapies

October 2019

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 presentation include, but are not limited to, the therapeutic potential of trilaciclib, lerociclib and G1T48, the expected timing of data availability from ongoing clinical trials, the expected timing of initiation of future clinical trials, and the timing for the commencement and completion of marketing applications in the U.S. and Europe for trilaciclib in SCLC, 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.

Small molecule therapeutics for big oncology indications

G1 THERAPEUTICS

First-in-class therapy
to improve outcomes for patients treated with chemotherapy

Differentiated oral CDK4/6 inhibitor
for more effective combination treatment

Potential best-in-class
oral SERD
for the treatment of ER+ breast cancer

$325M cash and investments
at end of 2Q 2019

Small molecule therapeutics for big oncology indications

Trilaciclib

- ✓ Breakthrough Therapy Designation; begin rolling NDA submission for SCLC in 4Q19, expect to complete in 2Q20
- ✓ Preliminary OS benefit in mTNBC; initiating Phase 3 trial in 2H20
- ✓ Initiating Phase 3 mCRC trial in 2H20

Lerociclib

- ✓ Less neutropenia and favorable tolerability – advantages in breast cancer (BC) adjuvant setting
- ✓ Data + dose identification in 4Q19 to support pivotal trials
- ✓ Initiating Phase 3 1L BC trial in 2H20

G1T48

- ✓ Best-in-class potential
- ✓ Differentiated chemistry, favorable tolerability
- ✓ Initiating Phase 3 1L combo trial with CDK4/6i in 2H20

All three therapies have potential to **improve outcomes for women with breast cancer** in advanced/ metastatic and adjuvant settings

Catalysts across all programs in 2019/2020

	INDICATION/COMBO	4Q19	1H20	2H20
trilaciclib IV - CDK4/6i	1st-line SCLC (+ etop/carbo)	Begin rolling NDA submission for SCLC	Complete NDA submission for SCLC	MAA filing for SCLC
	1st-line SCLC (+ etop/carbo/Tecentriq)			
	2nd/3rd-line SCLC (+ topotecan)			
	Metastatic TNBC (+ gem/carbo)			Initiate Phase 3 TNBC trial
	Metastatic CRC (5-FU regimens)			Initiate Phase 3 mCRC trial
lerociclib Oral - CDK4/6i	ER+, HER2- BC (+ Faslodex)	Present additional Phase 1b/2a data		Initiate Phase 3 BC trial
	EGFRm NSCLC (+ Tagrisso)			
G1T48 Oral - SERD	ER+, HER2- BC			Initiate Phase 3 CDK4/6i combination trial + Present additional data

Well funded with $325M cash at end of 2Q19; anticipate 2019 YE cash of $260-270M

TRILACICLIB

Hematopoietic stem and progenitor cells (HSPCs)

Trilaciclib: improving outcomes for patients on chemo

G1 THERAPEUTICS

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, burdens HC system

2

Phase 2 program: improved patient outcomes

- Less neutropenia *and* anemia in SCLC
- Reduced G-CSF usage *and* transfusions in SCLC
- Topline OS benefit in mTNBC; data featured in ESMO oral presentation and published in *The Lancet Oncology*

3

Next steps

- SCLC myelopreservation NDA/MAA filings in 2020
- Initiating Phase 3 mCRC and mTNBC trials in 2H20
- Exploring partnerships to maximize access for patients globally

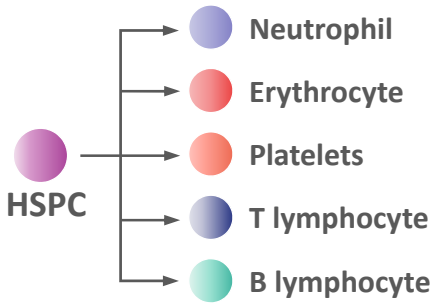
Trilaciclib: context-dependent efficacy

G1 THERAPEUTICS

SCLC trials: myelopreservation

Transient G1 arrest during chemotherapy

Proactive protection of HSPC prevent chemotherapy-induced myelosuppression

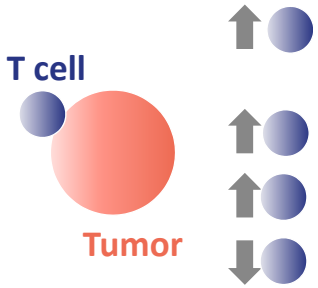


- A. Reduces occurrence and duration of severe neutropenia
- B. Reduces anemia and thrombocytopenia
- C. Reduces need for supportive care (growth factors, transfusions, chemotherapy dose reductions)
- D. Preserves lymphocytes

Weiss et al, Annals of Oncology 2019
He et al, Science Translational Medicine 2017
Bisi et al, Mol Cancer Ther., 2016

TNBC trial: OS improvement

Preserves immune cell function and potentially enhances anti-tumor immunity



- A. Alters the proliferation kinetics and composition of intratumor T-cell subsets to favor increased effector function
- B. Enhances T-cell activation
- C. Increases antigen processing and presentation on tumor cells
- D. Reduces immunosuppressive function of regulatory cells

Tan et al, Lancet Oncology 2019
Zhang et al, Nature 2018
Jerby-Arnon et al, Cell 2018
Goel et al, Nature 2017
Deng et al, Cancer Discovery 2017

Trilaciclib benefits linked to setting

	Primary Benefit: Myelopreservation	Primary Benefit: Anti-Tumor Efficacy
Chemotherapy schedule	Multi-day regimens	Single-day regimens
Tumor type	---	Tumor microenvironments more favorable to immune modulation
Settings/indications:	✓ **SCLC (etoposide + platinum, topotecan)** ✓ **1L mCRC (5-FU regimens)** ✓ **Neoadjuvant TNBC (doxorubicin + cyclophosphamide + taxane)**	✓ **1L mTNBC (TBD +/- anti-PD-L1)** ✓ **1L mBC (taxane)**

Two-pronged development strategy: myelopreservation and anti-tumor efficacy

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

G1 THERAPEUTICS

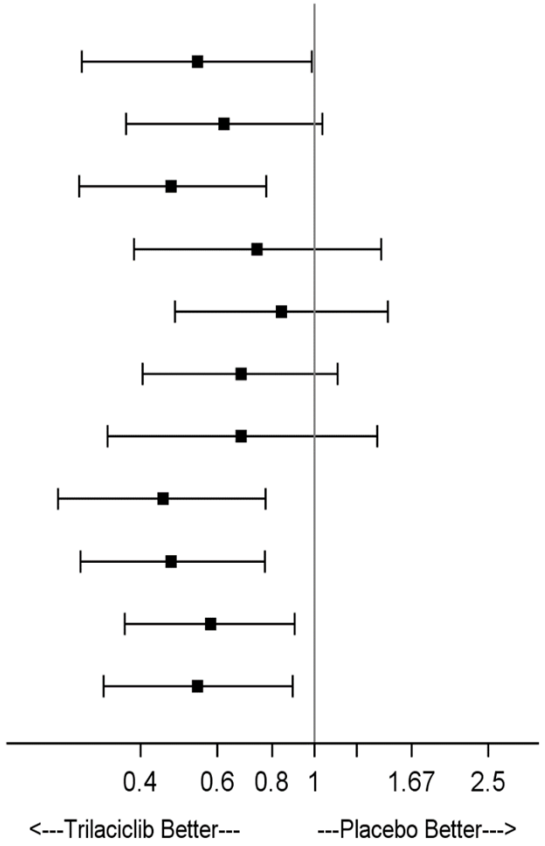
	PLACEBO + CHEMOTHERAPY	TRILACICLIB + CHEMOTHERAPY	
Patients (intent-to-treat population)	120	125	**P-VALUE[+]**
Mean duration (in days) of severe neutropenia in cycle 1 (SD)	4 (5.2)	1 (2.3)	**<0.0001**
Occurrence of severe neutropenia	64 (53.3%)	16 (12.8%)	**<0.0001**
Occurrence of RBC transfusions on/after 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**

primary endpoints

[+] 2-sided p-value; data presented at MASCC 2019

PRO data in SCLC: trilaciclib improves the patient experience

Domain	No. of Events TRI/PLA	Median TTD, Months TRI/PLA	Hazard Ratio [95% CI]
FACT-G	23/40	NYR/NYR	0.54 [0.29;0.99]
PWB	32/51	NYR/5.16	0.62 [0.37;1.04]
FWB	31/55	7.62/3.78	0.47 [0.29;0.78]
EWB	23/27	NYR/NYR	0.74 [0.39;1.42]
SWB	32/34	7.85/NYR	0.84 [0.48;1.47]
FACT-L	31/45	NYR/7.16	0.68 [0.41;1.13]
LCS	20/27	NYR/NYR	0.68 [0.34;1.39]
L-TOI	24/48	NYR/5.62	0.45 [0.26;0.77]
FACT-An	31/58	NYR/3.48	0.47 [0.29;0.77]
Fatigue	39/61	7.03/2.33	0.58 [0.37;0.90]
Anemia TOI	33/55	7.20/3.78	0.54 [0.33;0.89]



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

- Trilaciclib improves symptoms and functions across multiple parameters over time compared to placebo
- Statistically significant improvements shown in:
  - fatigue
  - anemia
  - functional wellbeing

*Pooled analysis across all three SCLC studies; data presented at MASCC 2019

Trilaciclib mTNBC randomized Phase 2 trial: key findings

G1 THERAPEUTICS

- 102-patient three-arm trial; all groups received gemcitabine/carboplatin (GC), a single-day regimen
  - Group 1 – GC only
  - Group 2 – GC + trilaciclib on day of GC
  - Group 3 – GC + trilaciclib on day prior to and day of GC
- ***Both trilaciclib arms showed significant OS improvement compared to control***
- Endpoints for myelopreservation were not achieved in this trial
- Trilaciclib was well tolerated with improvement in anemia-related PRO measures

THE LANCET Oncology

Trilaciclib plus chemotherapy versus chemotherapy alone in patients with metastatic triple-negative breast cancer: a multicentre, randomised, open-label, phase 2 trial

Antoinette R Tan, Gail S Wright, Anu R Thummala, Michael A Danso, Lazar Popovic, Timothy J Pluard, Hyo S Han, Željko Vojnović, Nikola Vasev, Ling Ma, Donald A Richards, Sharon T Wilks, Dušan Milenković, Zhao Yang, Joyce M Antal, Shannon R Morris, Joyce O'Shaughnessy

Lancet Oncol 2019; September 28, 2019
http://dx.doi.org/10.1016/S1470-2045(19)30616-3
Now **Online First** at TheLancet.com: 10.15 CEST, September 28, 2019

ESMO 2019: Trilaciclib improves overall survival when given with gemcitabine/carboplatin (GC) in patients with metastatic triple negative breast cancer (mTNBC) in a randomized Phase 2 trial; Abstract #6255

Significant overall survival benefit with trilaciclib

ITT population	Control (GC only) (Group 1)	Trilaciclib + GC (Group 2)	Trilaciclib + GC (Group 3)	Trilaciclib + GC (Group 2+3)
	N = 34	N = 33	N = 35	N = 68
Median OS (months)	12.6	20.1	17.8	20.1
HR		0.33	0.34	0.36
p-value		0.028	0.0023	0.0015
Median PFS (months)	5.7	9.4	7.3	8.8
HR		0.60	0.59	0.59
p-value		0.13	0.12	0.063

Overall Response Rate (ORR): 33% (Group 1), 50% (Group 2), 37% (Group 3)

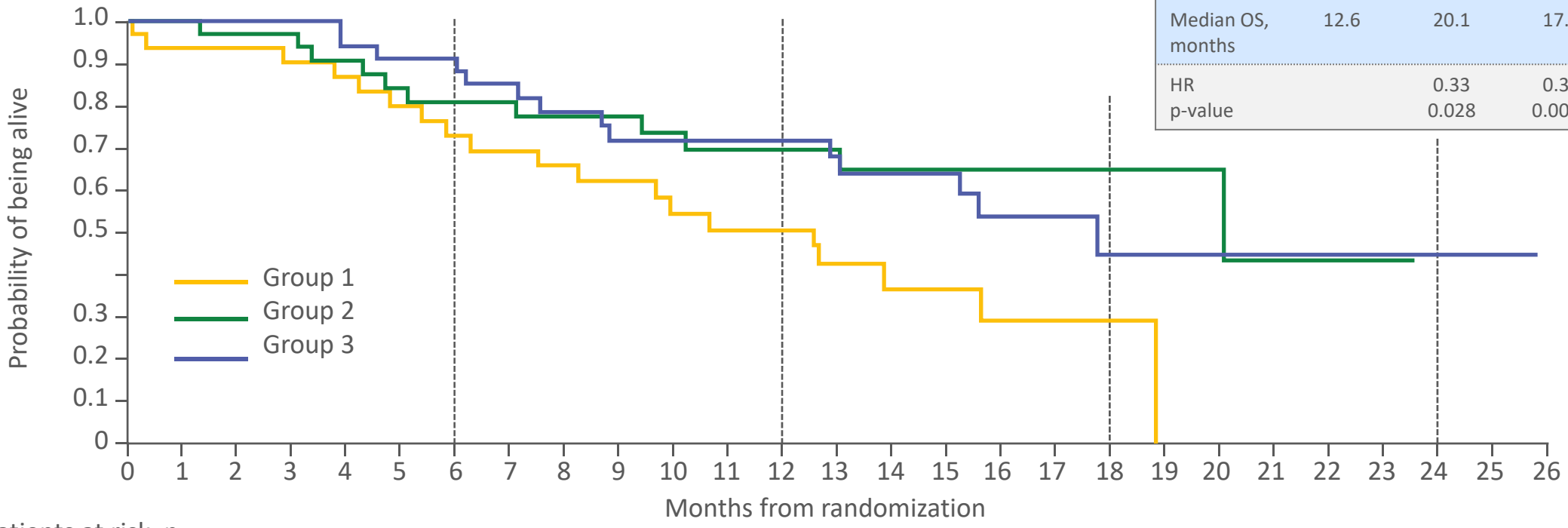
Patients with death - Group 1: 20/34 (58.8%); Group 2: 11/33 (33.3%); Group 3: 14/35 (40.0%)

Group 1: GC only (Day 1/8) (n=34); Group 2: trilaciclib + GC (Day 1/8) (n=33); Group 3: trilaciclib + GC (Day 1/2/8/9) (n=35)

ESMO 2019: Trilaciclib improves overall survival when given with gemcitabine/carboplatin (GC) in patients with metastatic triple negative breast cancer (mTNBC) in a randomized Phase 2 trial; Abstract #6255

Results published concurrently in *The Lancet Oncology*

Significant overall survival benefit with trilaciclib



	Group 1	Group 2	Group 3
Median OS, months	12.6	20.1	17.8
HR		0.33	0.34
p-value		0.028	0.0023

Patients at risk, n

Group 1	34	27	27	26	25	23	21	19	18	16	14	13	13	9	6	6	3	2	1	0	0	0	0	0	0	0	0
Group 2	33	33	32	31	28	26	24	22	20	20	19	17	17	15	13	13	12	10	8	5	3	2	1	1	0	0	0
Group 3	35	35	35	35	32	31	30	26	23	21	21	20	19	17	13	13	9	8	5	3	3	1	1	1	1	1	0

OS benefit greater than PFS suggests immune-mediated effect

Based on data as of 17 May 2019
Group 1: GC only (Day 1/8) (n=34); Group 2: trilaciclib + GC (Day 1/8) (n=33); Group 3: trilaciclib + GC (Day 1/2/8/9) (n=35)
ESMO 2019: Trilaciclib improves overall survival when given with gemcitabine/carboplatin (GC) in patients with metastatic triple negative breast cancer (mTNBC) in a randomized Phase 2 trial; Abstract #6255
Results published concurrently in *The Lancet Oncology*

Trilaciclib regulatory update

Small cell lung cancer

- Breakthrough Therapy Designation (BTD)
- Pre-NDA meeting with Hematology Division completed
- **Will begin rolling NDA submission in 4Q19; expect to complete submission in 2Q20**
- Anticipate MAA submission in 2H20

Triple-negative breast cancer

- Productive interactions with Oncology Division
- Received feedback on Phase 2 data and comments on preliminary Phase 3 trial design
- **Expect to initiate Phase 3 trial in 2H20**

Development plan targets broad myelopreservation label and anti-tumor efficacy label for specific tumors

G1 THERAPEUTICS

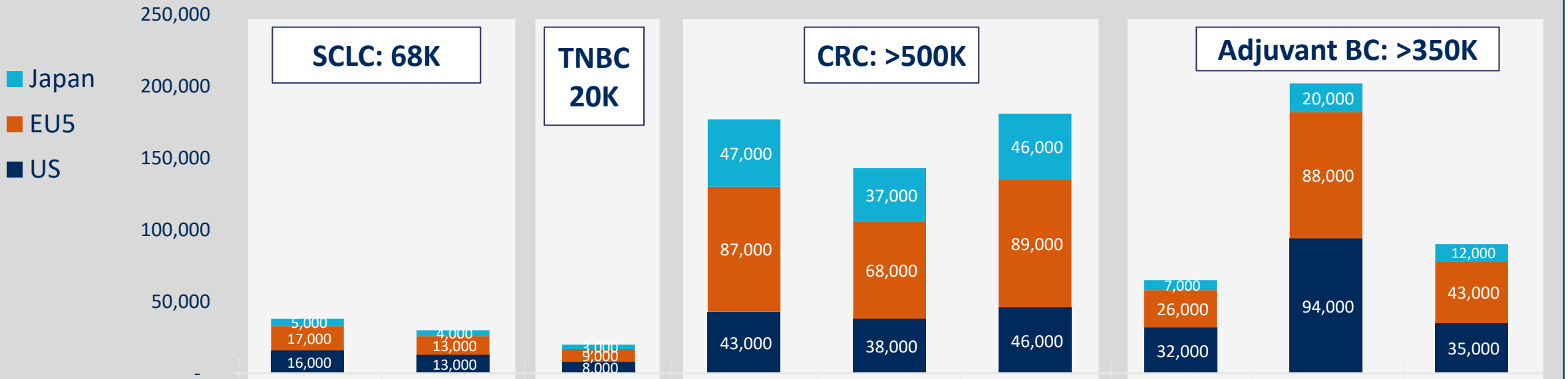
DISEASE OF INTEREST	CHEMO REGIMENS	2020	2021	2022	2023	2024	2025
Myelopreservation							
1L SCLC	Etoposide + platinum, topotecan		☆				
1L mCRC	5-FU regimens					☆	
Neoadj TNBC	Doxo + cyclo + taxane					☆	
Anti-tumor efficacy							
1L mTNBC	TBD +/- anti-PD-L1					☆	
1L mBC	Taxane						

Partnering to enable expansion in other tumor types: e.g. NSCLC

☆ Denotes timing for completion of FDA review and potential U.S. approval; RoW is ~2Q later for all indications except SCLC. End of shading highlights data readout; dashed box indicates preparing, filing and regulatory review period.

~1 million chemo-treated patients in planned indications

Global Chemotherapy Treated Incident Patients (G7)*



	1L SCLC	2/3L SCLC	1L TNBC	1L CRC	2/3L CRC	Adjuvant CRC	Adjuvant TNBC	Adjuvant HR+/HER2- BC	Adjuvant HER2+ BC
% currently treated with eligible chemo regimen**	~100% (EP)	50% (topotecan or EP)	55% (GC, taxane or IO + chemo)	80% (5-FU)	70% (5-FU)	50% (5-FU)	65% (AC)	50% (AC)	40% (AC)
Estimated mean # of cycles***	4-6	3-4	7-8	11-23	4-12	12	8	8	8

Potential to be used for myelopreservation in the same patient across multiple lines of therapy

*Source: Secondary epi sources, 2027 estimates

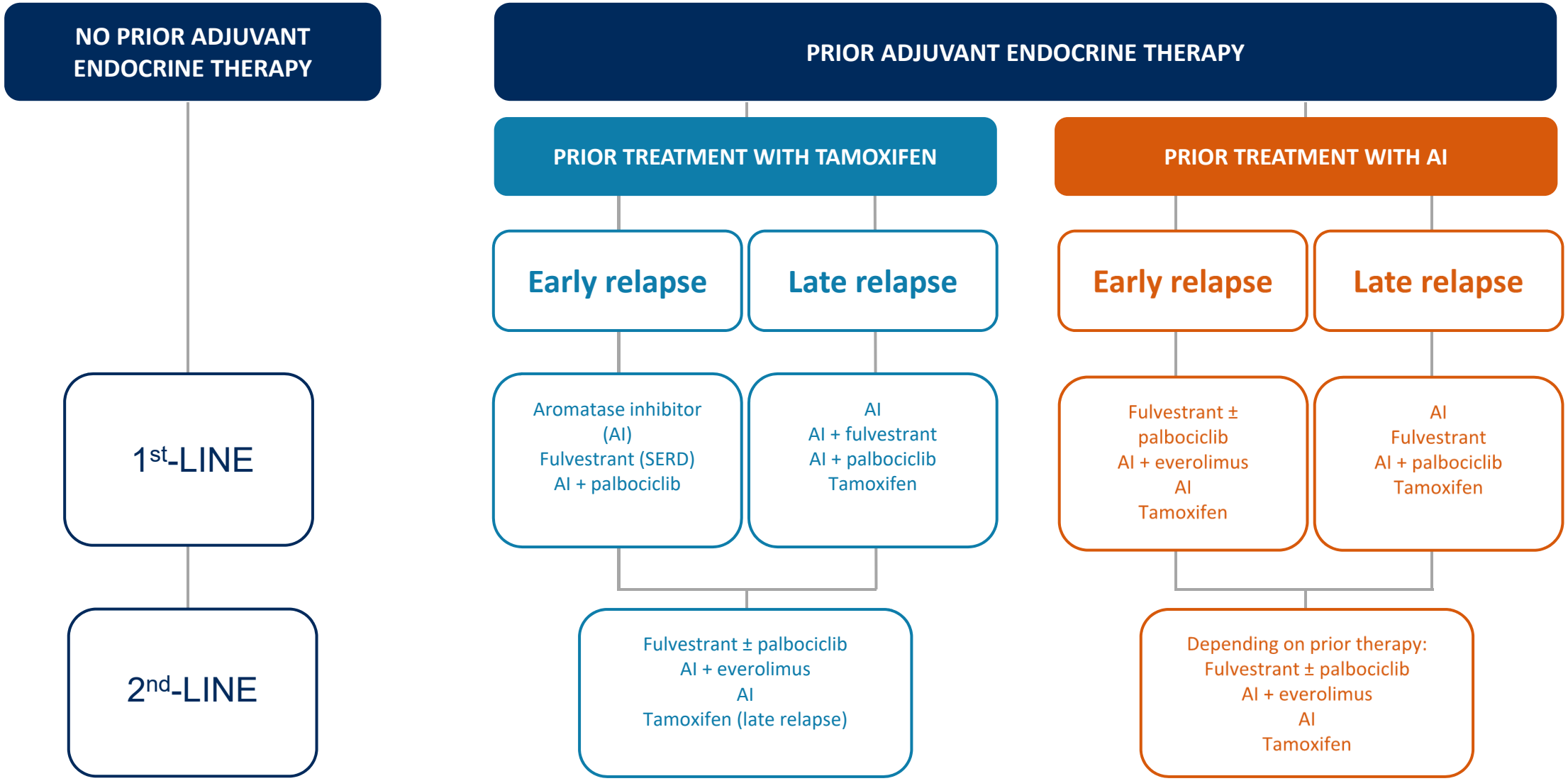
**EP refers to any regimen that includes etoposide + platinum; GC refers to gemcitabine/carboplatin; AC refers to any regimen that includes Adriamycin and cyclophosphamide; 5-FU refers to any regimen that includes fluorouracil (e.g., FOLFOX). In addition to CRC, pancreatic cancer, gastroesophageal cancer and squamous cell carcinoma of the head and neck (SCCHN) are also treated with 5-FU regimens (% currently treated with 5-FU regimens varies by tumor type and region)

***Source: SCLC and TNBC: G1 Therapeutics' completed trials; CRC and Adjuvant BC: number of cycles for eligible chemo regimens from Decision Resources Group Treatment Landscape and Forecast Assumptions 2018 Reports (CRC and BC)

LEROCICLIB & G1T48:
Early lines of treatment in breast cancer

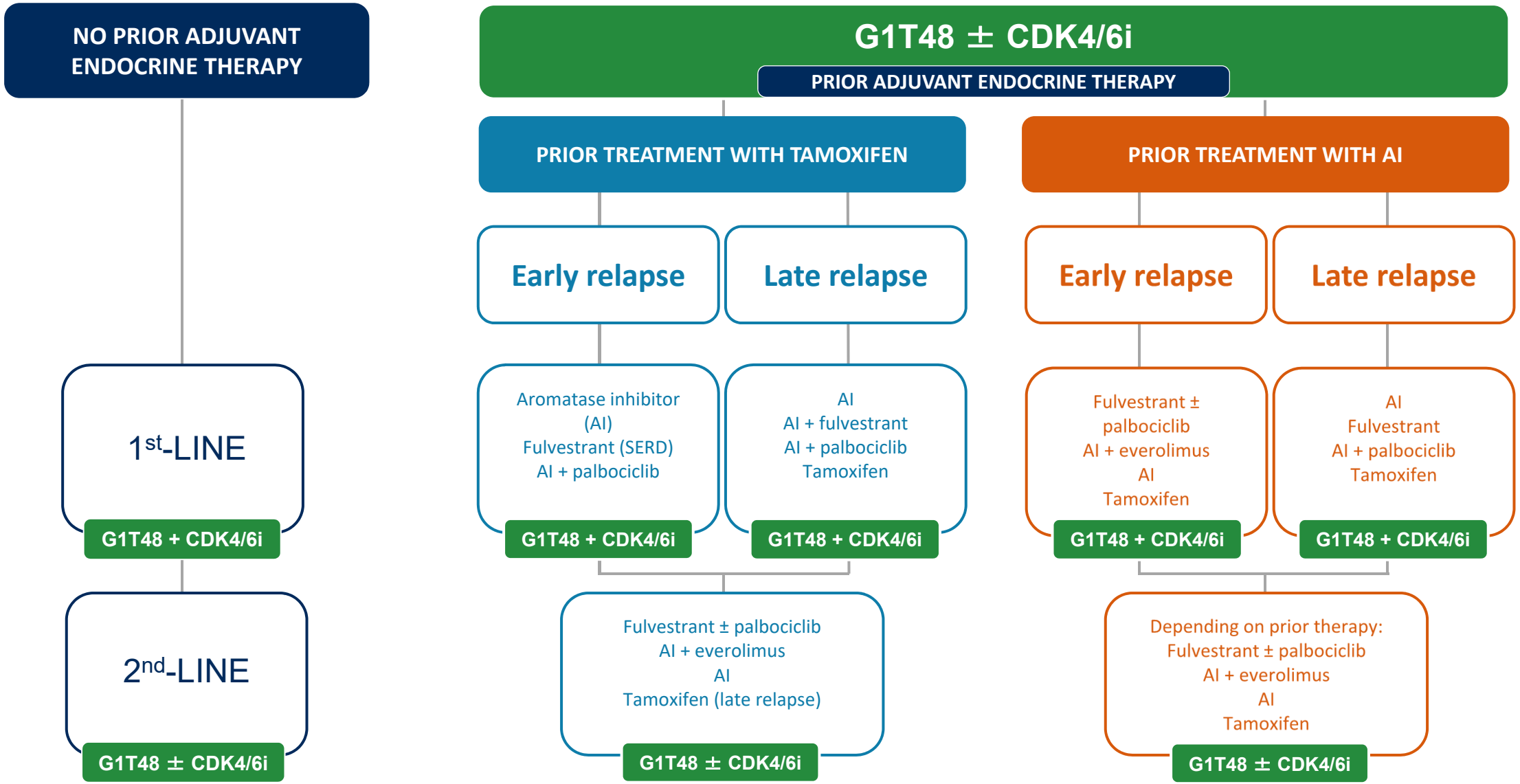
Tumor cell proliferation

Current ASCO guidelines for ER+ mBC



*Adapted from Rugo et al JCO 2016

Opportunity across multiple lines, including adjuvant



*Adapted from Rugo et al JCO 2016

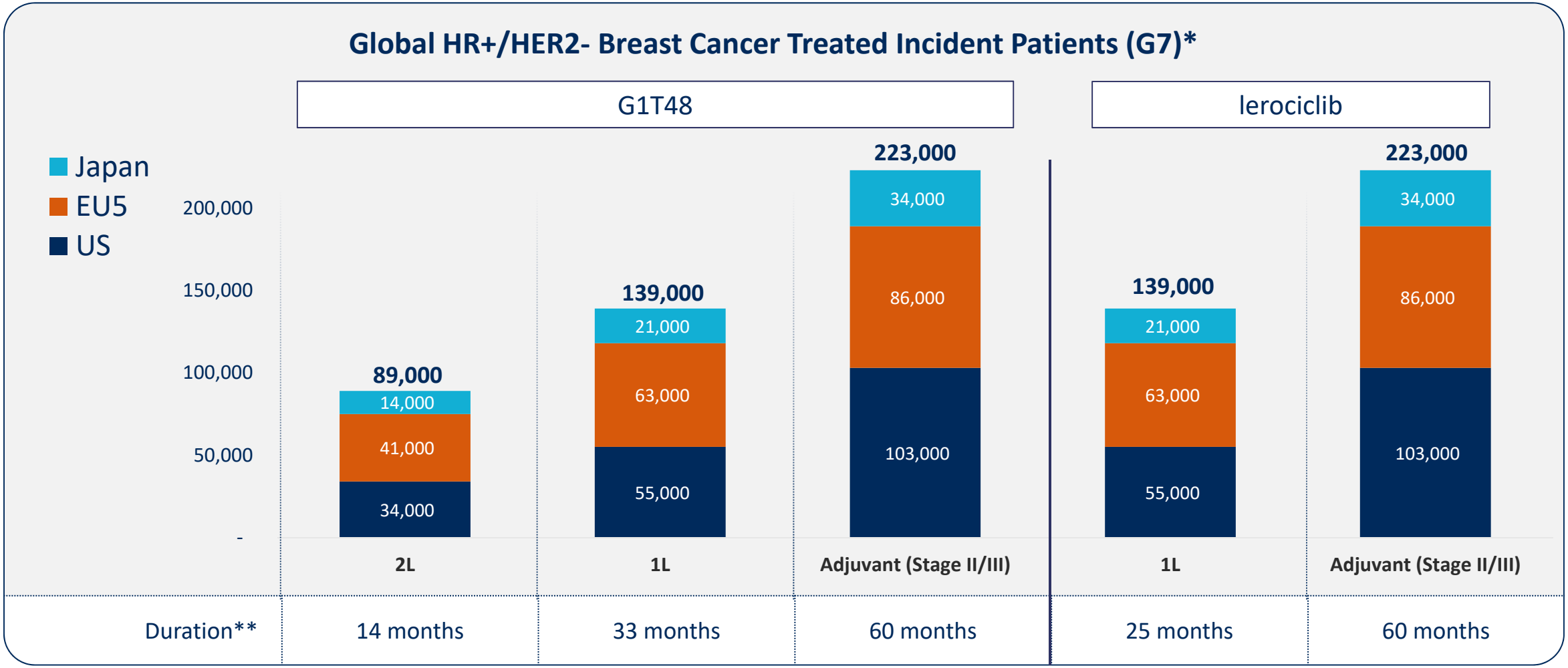
Lerociclib and G1T48: improving patient care in advanced/metastatic and adjuvant settings

DISEASE OF INTEREST	COMBO DRUG	2020	2021	2022	2023	2024	2025	2026	2027
G1T48									
1L ER+ mBC	CDK4/6i								
2L ER+ mBC	Everolimus								
Neoadjuvant BC*	N/A								
Adjuvant ER+ BC	NA								
lerociclib									
1L ER+ mBC	Fulvestrant								
Adjuvant ER+ BC	Aromatase inhibitor								

G1T48 and lerociclib partnering to enable expansion in other indications

★ Denotes timing for completion of FDA review and potential U.S. approval; RoW is ~2Q later for all indications. End of shading highlights data readout; dashed box indicates preparing, filing and regulatory review period.
* Neoadjuvant trial enables adjuvant trial

G1T48 and lerociclib: >350,000 1L and adjuvant BC patients



Adjuvant use: long treatment duration requires well tolerated profile

*Source: Secondary epi sources, 2027 estimates
**Duration estimates based on similar trial results in the same or similar patient populations as planned trials

LEROCICLIB

Tumor cell proliferation

Lerociclib: differentiated profile in CDK4/6 inhibitor landscape

G1 THERAPEUTICS

- 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®	+	+	+	–	–	–	–
Kisqali®	+	+	+	+	+	–	–
Verzenio®	+	+	–	–	+	+	+

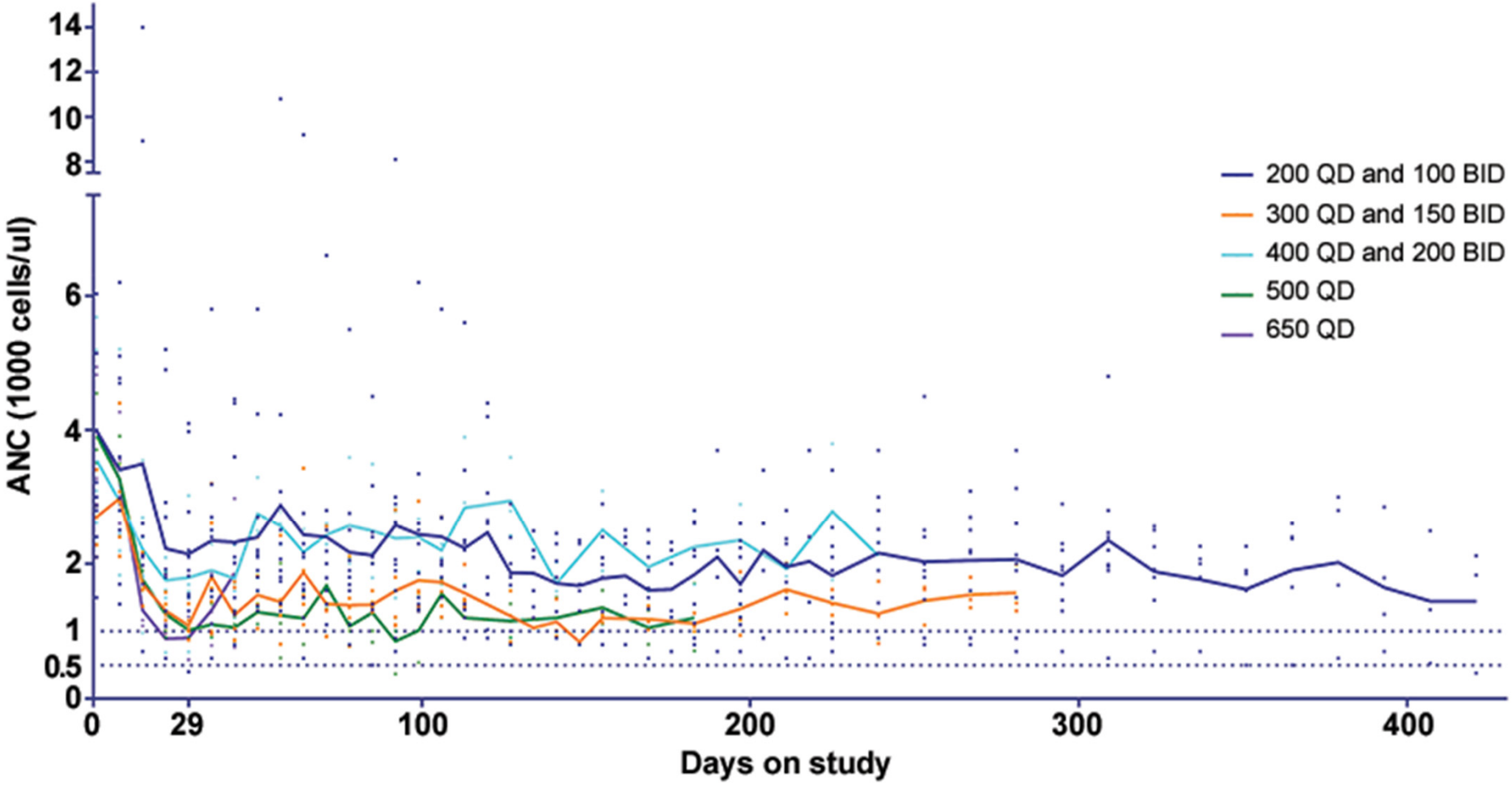
ER+, HER2- breast cancer lerociclib/fulvestrant combination Phase 1b/2a trial: enrollment completed – data 4Q19

G1 THERAPEUTICS

PRIMARY ENDPOINTS	• Assess safety and dose-limiting toxicities • Identify dose for pivotal trial
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	• Preliminary Phase 1b data presented at ASCO 2018 • Phase 2a enrollment completed • **Anticipate reporting Phase 1/2 data and dose selection in 4Q19**

Continuously dosed lerociclib: less neutropenia

Less Gr 4 neutropenia: opportunity to reduce patient monitoring

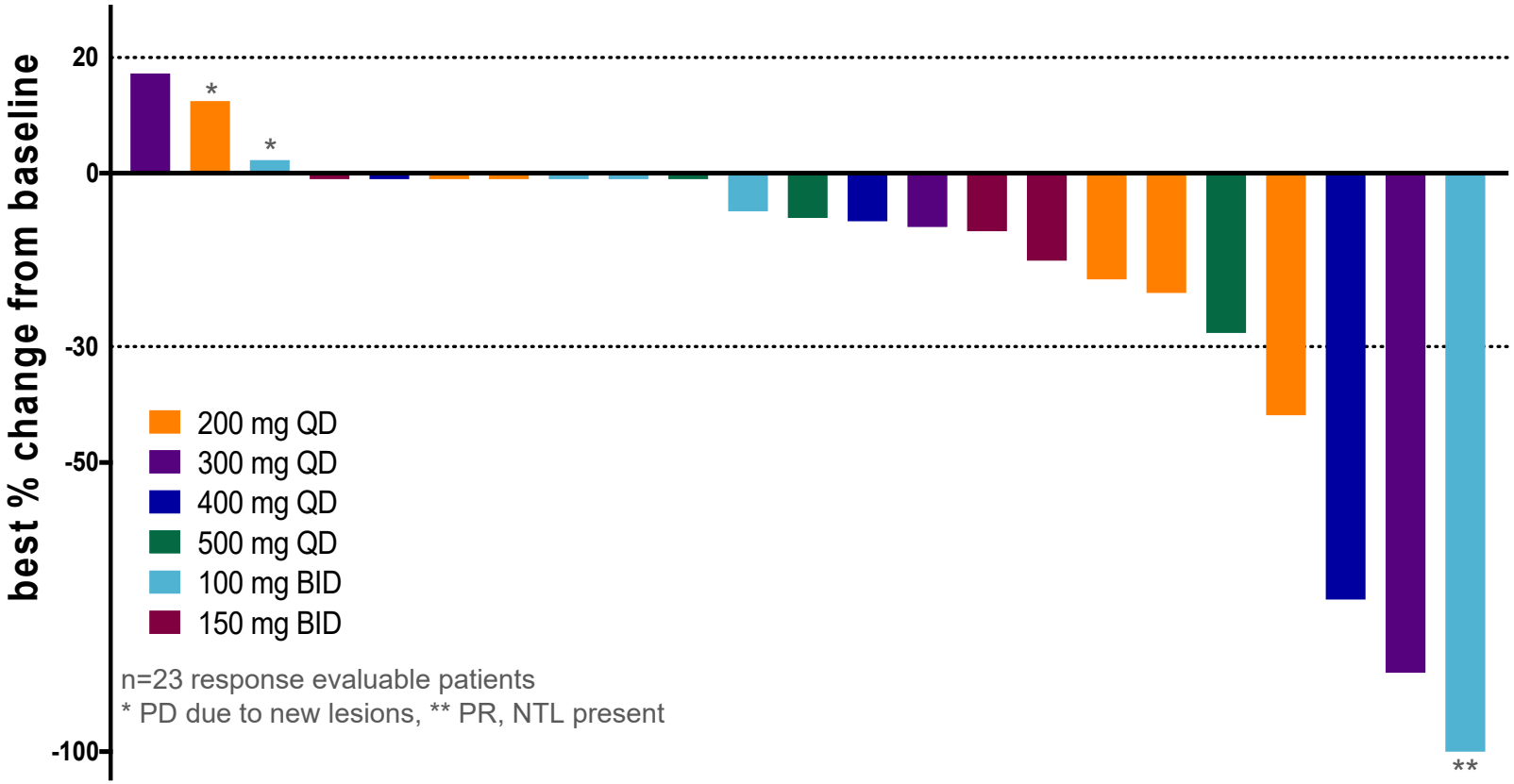


Data presented at 2018 ASCO Annual Meeting

Continuously dosed lerociclib: promising efficacy

G1 THERAPEUTICS

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

Lerociclib: key takeaways

G1 THERAPEUTICS

1

Differentiated oral CDK4/6i

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

2

Opportunity in BC and other indications

- Additional data and dose selection in 4Q19
- Initiating pivotal BC trial in 2H20
- Ongoing trial in EGFRm NSCLC in combination with Tagrisso

3

Efficient BC clinical/ regulatory pathway

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

G1T48 (ORAL SERD)

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 indicated for adjuvant setting

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 Phase 1 data presented @ ESMO 2019
- Initiating Phase 3 combination trial with CDK4/6i in 2H20

G1T48 Phase 1 trial: key findings

G1 THERAPEUTICS

✓ Well tolerated; favorable safety profile at all dose levels

✓ No dose-limiting toxicities observed; maximum tolerated dose not reached

✓ AEs mostly Grade 1

✓ ^{18}F-FES PET scans – ER occupancy ≥ 80% in doses ≥ 400 mg

✓ Preliminary evidence of anti-tumor activity in heavily pre-treated population

✓ Phase 1 completed; 600 mg and 1,000 mg dose expansion cohorts enrolling

Dose-escalation study of G1T48, an oral selective estrogen receptor degrader (SERD), in postmenopausal women with ER+/HER2- locally advanced or metastatic breast cancer (ABC); Abstract #3587

Favorable tolerability and safety profile; AEs mostly Grade 1

G1 THERAPEUTICS

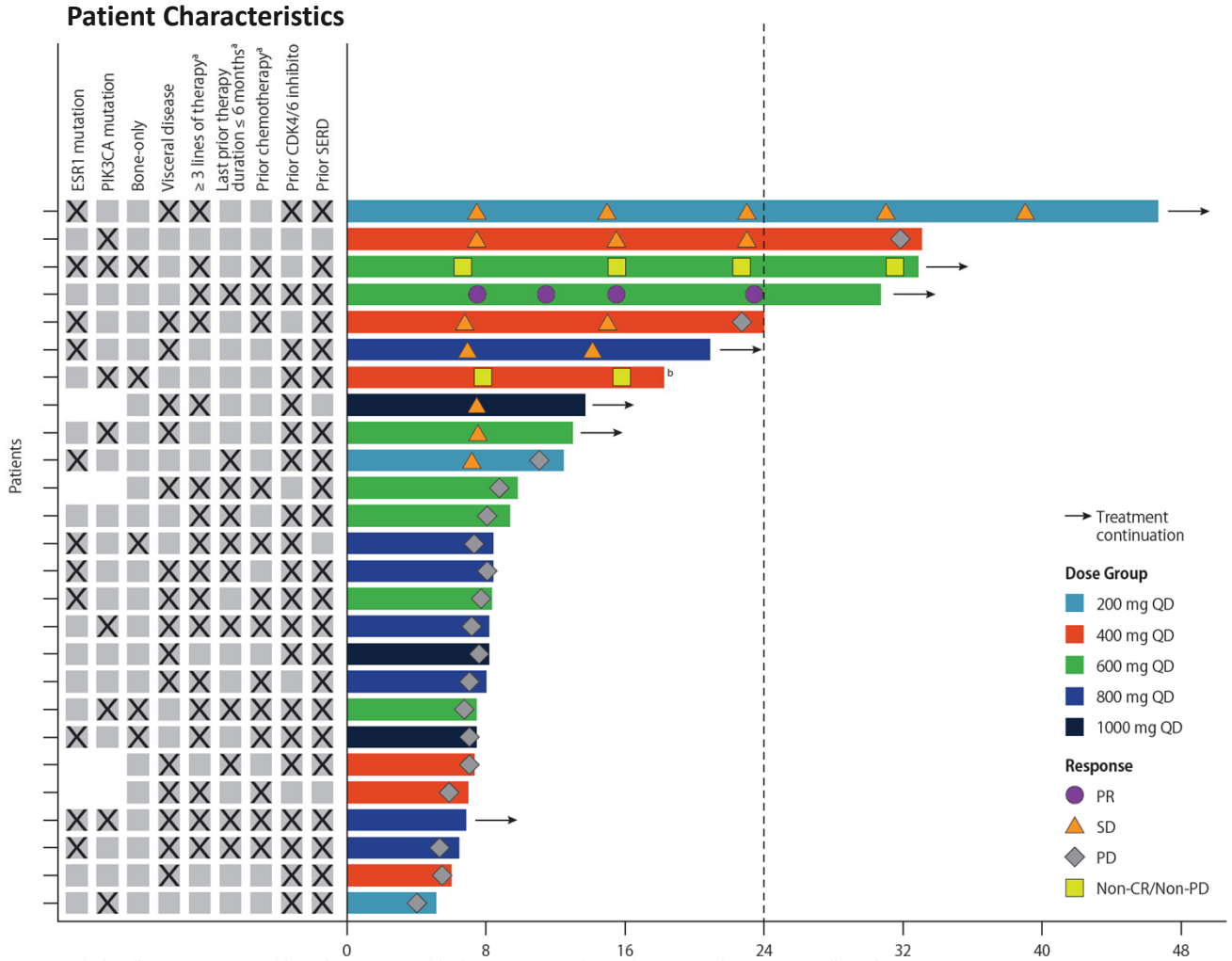
Drug-related adverse event	Grade 1	Grade 2	Grade 3	Grade 4	Total (N=26)
Fatigue	6 (23.1%)	1 (3.8%)	1 (3.8%)	0	8 (30.8%)
Hot flush	5 (19.2%)	2 (7.7%)	0	0	7 (26.9%)
Diarrhea	6 (23.1%)	1 (3.8%)	0	0	7 (26.9%)
Headache	4 (15.4%)	0	0	0	4 (15.4%)
Nausea	4 (15.4%)	0	0	0	4 (15.4%)
Muscle spasms	2 (7.7%)	1 (3.8%)	0	0	3 (11.5%)
Myalgia	3 (11.5%)	0	0	0	3 (11.5%)
Abdominal distension	1 (3.8%)	1 (3.8%)	0	0	2 (7.7%)
Musculoskeletal stiffness	1 (3.8%)	1 (3.8%)	0	0	2 (7.7%)
Cough	0	1 (3.8%)	0	0	1 (3.8%)
Hypoglycemia	0	1 (3.8%)	0	0	1 (3.8%)
Lymphopenia	0	1 (3.8%)	0	0	1 (3.8%)
Pain (musculoskeletal chest)	0	1 (3.8%)	0	0	1 (3.8%)

AEs occurring in ≥3 patients or ≥CTCAE Grade 2; All TEAEs; AEs regardless of causality

Data cut: 12 August 2019

Dose-escalation study of G1T48, an oral selective estrogen receptor degrader (SERD), in postmenopausal women with ER+/HER2- locally advanced or metastatic breast cancer (ABC); Abstract #3587

Efficacy demonstrated in heavily pre-treated population



Includes all patients (measurable and non-measurable disease). No grey box indicates samples were not collected.
[a] In advanced/metastatic setting; [b] One patient discontinued treatment due to Grade 2 gastrointestinal symptoms.
CDK, cyclin-dependent kinase; CR, complete response; ESR1, estrogen receptor 1; PD, progressive disease; PIK3CA, phosphatidylinositol 4,5-bisphosphate 3-kinase catalytic subunit alpha; PR, partial response; QD, once daily; SD, stable disease; SERD, selective estrogen receptor degrader.

Response evaluable pts (N=19)	
ORR	1 (5.3%)
CBR	3 (15.8%)

ORR=(CR+PR); CBR=(CR+PR+SD≥24 weeks)

- Patient characteristics associated with PD by 8 weeks:
  - Visceral disease
  - ≥ 3 lines of prior therapy
  - ≤ 6 months on most recent prior therapy
  - Prior chemotherapy in metastatic setting

Dose-escalation study of G1T48, an oral selective estrogen receptor degrader (SERD), in postmenopausal women with ER+/HER2- locally advanced or metastatic breast cancer (ABC); Abstract #3587

Catalysts across all programs in 2019/2020

	INDICATION/COMBO	4Q19	1H20	2H20
trilaciclib IV - CDK4/6i	1st-line SCLC (+ etop/carbo)	Begin rolling NDA submission for SCLC	Complete NDA submission for SCLC	MAA filing for SCLC
	1st-line SCLC (+ etop/carbo/Tecentriq)			
	2nd/3rd-line SCLC (+ topotecan)			
	Metastatic TNBC (+ gem/carbo)			Initiate Phase 3 TNBC trial
	Metastatic CRC (5-FU regimens)			Initiate Phase 3 mCRC trial
lerociclib Oral - CDK4/6i	ER+, HER2- BC (+ Faslodex)	Present additional Phase 1b/2a data		Initiate Phase 3 BC trial
	EGFRm NSCLC (+ Tagrisso)			
G1T48 Oral - SERD	ER+, HER2- BC			Initiate Phase 3 CDK4/6i combination trial + Present additional data

Well funded with $325M cash at end of 2Q19; anticipate 2019 YE cash of $260-270M

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