NASDAQ: GTHX

G1 THERAPEUTICS

Next Generation Cancer Therapies

May 2020

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, those relating to the therapeutic potential of trilaciclib, rintodestrant and lerociclib, the timing of marketing applications in the U.S. and Europe for trilaciclib in SCLC, trilaciclib's possibility to improve patient outcomes across multiple indications, rintodestrant's potential to be best-in-class oral SERD, lerociclib's differentiated safety and tolerability profile over other marketed CDK4/6 inhibitors and the impact of pandemics such as COVID-19 (coronavirus), 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; 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.

Next-generation cancer therapies

Trilaciclib

First-in-class myelopreservation therapy

Rintodestrant

Potential best-in-class oral SERD

Lerociclib

Differentiated oral CDK4/6 inhibitor

Committed to improving lives and outcomes of people living with cancer

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Current chemotherapy landscape

~1M
U.S. patients
receive
chemotherapy
annually

Chemotherapy
remains the cornerstone
of treatment
for most cancers

Myelosuppression

is currently an unavoidable consequence of chemo that impacts patient safety, QoL and costs to the HC system

Neutropenia and anemia	Risk of infection: G-CSF use, associated bone pain	RBC transfusions and ESA rescue
Impaired anti-tumor immunity		Fatigue
Hospitalizations and unscheduled office visits	Chemotherapy dose delays and reductions	Risk of bleeding: platelet transfusions

Patient experience of myelosuppression: burdensome and far-reaching

89%

OF CANCER PATIENTS

with myelosuppression rate it as having a moderate to major impact on their life*

"…the overall fatigue was the worst. It stole my energy and joy for both life and family. It made me want to quit chemo numerous times."

"I don't feel like doing ANYTHING some days. It's like depression but completely physical. Of course, everyone's trying to be supportive. And I have my own obligations, but I feel like a burden."

"…it so happened I had a father dying in the hospital and I was strictly forbidden from entering a hospital (except my own)."

*Sterling IRB-reviewed online survey in 4Q19 of 301 patients treated with chemotherapy within past 12 months who experienced myelosuppression; respondents: 51% breast cancer; 33% lung cancer; 16% colorectal cancer; manuscript in preparation

What if we can improve the chemo experience for people living with cancer?

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Our solution:

Trilaciclib

First-in-class

myelopreservation therapy that has the potential to make chemotherapy safer, improve the patient experience, and in some settings, help patients live longer

Our solution: trilaciclib

- 30-minute IV infusion prior to chemo; **given first time and every time** chemo is administered
- **Preserves** bone marrow and immune system function from damage by chemo
- **Protects** patients from the dangerous side effects of myelosuppression
- In some settings, may help **patients live longer**
- Can be **incorporated into multiple chemo regimens**, including I/O + chemo

FDA Breakthrough Therapy Designation for SCLC

*As observed in clinical trials to date

Body of evidence in SCLC: three randomized trials

Trilaciclib reduces chemotherapy-related toxicity and need for rescue interventions

- ✓ Significant improvement in patient experience, notably **less fatigue**
- ✓ **Less neutropenia** and **anemia**
- ✓ **Reduced G-CSF usage** and **transfusions**

Three randomized, placebo-controlled, double-blind trials in:
1st-line SCLC (+ etop/carbo), 1st-line SCLC (+ etop/carbo/Tecentriq), 2nd/3rd-line SCLC (+ topotecan)

Improved treatment experience in SCLC

Patient survey findings*
(patients not enrolled in trilaciclib trials)

- 88% of SCLC respondents reported that myelosuppression **had moderate to major impact on their life**
- Of those, 63% noted fatigue as their biggest myelosuppressive issue
- Of those who noted fatigue, average rating of 8.4 on 10-point scale of how bothersome fatigue was

Patient Reported Outcomes data (n=235)
(pooled from three randomized, placebo-controlled, double-blind trials)

Subscale	<<Trilaciclib Better Placebo Better>>	Hazard Ratio (95% CI)
Fatigue		0.56 (0.37, 0.85)
Functional Well-being		0.44 (0.28, 0.70)
Physical Well-being		0.62 (0.39, 0.97)
Anemia – Trial Outcome Index		0.53 (0.34, 0.83)
Functional Assessment of Cancer Treatment - Anemia		0.46 (0.29, 0.72)
	1	

*Sterling IRB-reviewed online survey in 4Q19

Updated from data presented at MASCC 2019

Significant multi-lineage myelopreservation benefits support improved patient experience

		PLACEBO + CHEMO	TRILA + CHEMO	
	Patients (intent-to-treat population)	**119**	**123**	**P-VALUE***
Neutrophils	Mean duration (days) of severe neutropenia in cycle 1 (SD)	4 (5.1)	0 (1.8)	**<0.0001**
	Occurrence of severe neutropenia	63 (52.9%)	14 (11.4%)	**<0.0001**
	Occurrence of G-CSF administration	67 (56.3%)	35 (28.5%)	**<0.0001**
	Incidence of G-CSF administration (event rate per 100 cycles)	40.6	16.4	**<0.0001**
Red Blood Cells	Occurrence of Grade 3/4 anemia	38 (31.9%)	25 (20.3%)	**0.0279**
	Occurrence of ESA administration	14 (11.8)	4 (3.3%)	**0.0254**
	Occurrence of RBC transfusions on/after 5 weeks	31 (26.1%)	18 (14.6%)	**0.0252**
	Incidence of RBC transfusions on/after 5 weeks (event rate per 100 weeks)	3.1	1.5	**0.0027**
Platelets	Occurrence of Grade 3/4 thrombocytopenia	43 (36.1%)	24 (19.5%)	**0.0067**

*2-sided p-value; pooled data from three randomized, placebo-controlled, double-blind SCLC trials, updated from data presented at MASCC 2019

Preparing to bring trilaciclib to SCLC patients

U.S.

Rolling NDA submission initiated 4Q19; expect to complete submission 2Q20

Building strong, functional capabilities in U.S.

Ex-U.S.

Evaluating partnership opportunities to commercialize trilaciclib ex-U.S.

Pursuing additional indications: breast cancer

Preliminary survival benefit observed in mTNBC randomized trial

- ✓ Patients able to tolerate more cycles of chemo, without increased toxicity
- ✓ Reduced rate of RBC transfusions
- ✓ Patient-reported outcomes data support improved patient experience
- ✓ Significant improvement in OS

Preliminary overall survival benefit in mTNBC

ITT population	Control (GC only) (Group 1) N = 34	Trilaciclib + GC (Group 2) N = 33	Trilaciclib + GC (Group 3) N = 35	Trilaciclib + GC (Group 2+3) 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

Hypothesis: trilaciclib's preservation of immune system function during chemo drives OS benefit

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

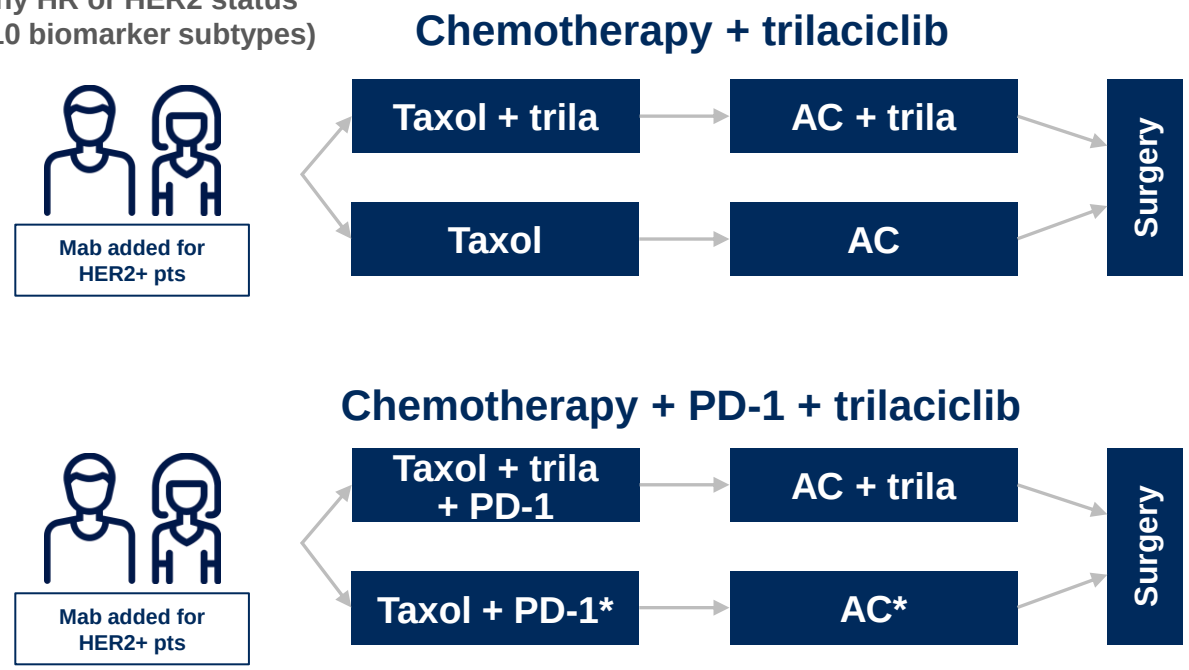
Next step in breast cancer: I-SPY 2 neoadjuvant trial

Goals of Phase 2 trial

- Evaluate trilaciclib in broadly-used chemo regimens (e.g. Taxol + AC)
- Evaluate trilaciclib in all breast cancer sub-types (ER+, HER2+, TNBC)
- Evaluate impact of trilaciclib on tumor immune microenvironment +/- PD-1
- Endpoints: biomarkers, efficacy and myelopreservation

Neoadjuvant breast cancer with high risk of recurrence → could be any HR or HER2 status (10 biomarker subtypes)

Four-arm Bayesian design



AC = adriamycin and cyclophosphamide
* Taxol + PD-1 followed by AC will potentially be historical data

Opportunity to improve patient outcomes across multiple indications

~1 million* patients in planned indications

69,000
Small Cell Lung Cancer

>350,000
Adjuvant Breast Cancer

>600,000
Colorectal Cancer

20,000
Metastatic Triple-Negative Breast Cancer

*Includes U.S., EU5 and Japan; Decision Resources Group estimate for chemo-treated patients in 2027; see Slide 30 for detail

Next steps for trilaciclib across multiple indications

SCLC

- Complete NDA submission in 2Q20
- PDUFA date assigned in 3Q20 (pending acceptance)

Breast Cancer

- Initiate I-SPY2 trial in 2Q20
- Updated OS data from mTNBC trial in 4Q20

Colorectal Cancer

- Completed FDA pre-Phase 3 meeting
- Initiate Phase 3 trial in 4Q20

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Improving options for ER+, HER2- breast cancer

- ER degradation shown to be most effective means of blocking estrogen signaling in ER+, HER2- breast cancer
- Only available SERD is fulvestrant – painful intramuscular injections

Opportunity to improve options in first-line and adjuvant settings with oral SERD

Rintodestrant Phase 1 data: well tolerated with proof-of-concept anti-tumor activity

Well tolerated; favorable safety profile observed at all dose levels

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

AEs mostly Grade 1, no bradycardia or cytopenias

^{18}F-FES PET scans: **ER occupancy ≥ 80%** in doses ≥ 600 mg

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

ESMO 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

Assessing the potential of rintodestrant

Phase 1/2a program w/ ~100 patients enrolled by YE20: additional data 4Q20

- 67 patients enrolled in Phase 1/2a trial, including expansion cohorts of 600 mg and 1,000 mg monotherapy
- Based on totality of data, **800 mg QD selected as dose for further development**
- **Initiating additional arm** in 2Q20 (~40 patients) to evaluate **rintodestrant (800 mg) + palbociclib**

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Significant potential to improve ER+ breast cancer treatment

>450,000 2L, 1L, and adjuvant ER+ BC patients globally

	2L	1L	Adjuvant (Stage II / III)
	89,000	**139,000**	**223,000**
median duration of therapy	14 months	33 months	60 months

*Source: secondary epi sources, Decision Resources Group 2027 estimates for U.S., EU5 and Japan
**Duration estimates based on similar trial results in the same or similar patient populations as planned trials

Next-generation cancer therapies

Trilaciclib

First-in-class myelopreservation therapy

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Potential best-in-class oral SERD

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Differentiated oral CDK4/6 inhibitor

Lerociclib: differentiated oral CDK4/6 inhibitor

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

Differentiated PK and tolerability profile

Continuous dosing (no holiday) with fewer dose-limiting toxicities

Potential for less CBC monitoring, reducing patient & physician burden

Clinical overview: improved safety and tolerability profile

Phase 1b/2 trial: 110 patients lero + fulvestrant (similar entry criteria to PALOMA 3)

Low rates of Grade 4 neutropenia **without a drug holiday**

Low rates of stomatitis and alopecia across all dose levels

65.2% clinical benefit rate; median progression-free survival of 15 months (immature)

Updated data 3Q20 supporting 150 mg BID as go forward dose

SABCS 2019: Dose escalation and expansion study of lerociclib (G1T38), an oral CDK4/6 inhibitor, dosed with no drug holiday in combination with fulvestrant in patients with HR+/HER2- advanced breast cancer; Abstract #P1-19-17

2020: near-term clinical and regulatory milestones

Therapy	Indication	2Q20	3Q20	4Q20
Trilaciclib	Small cell lung cancer	Complete NDA submission	PDUFA date assigned	
	Breast cancer	Initiate I-SPY 2 trial		OS update from Phase 2 TNBC trial
	Metastatic colorectal cancer	Completed FDA pre-Phase 3 meeting		Initiate Phase 3 trial
Rintodestrant	ER+, HER2- BC	Initiate Phase 2 expansion w/ palbociclib combination		Data update
Lerociclib	ER+, HER2- BC (+ fulvestrant)		Data update	

COVID-19 impact statement

Trilaciclib

- SCLC NDA filing on track for 2Q20
- CRC Phase 3 trial on track for initiation in 4Q20
- I-SPY 2 initiation on track for 2Q20; initial enrollment will be affected by COVID-19

Rintodestrant

- Monotherapy trial fully enrolled; G1 clinical operations team/external CROs are in contact with sites regularly to confirm ongoing participation and minimize disruption
- Rintodestrant/palbociclib combination trial on track for initiation in 2Q20; initial enrollment will be affected by COVID-19 - plan to bring on additional sites this summer to hit full enrollment target of YE20

General

- Across all programs, we do not anticipate significant supply chain delays or shortages
- Lerociclib trials: continuing to collect data and explore partnership opportunities

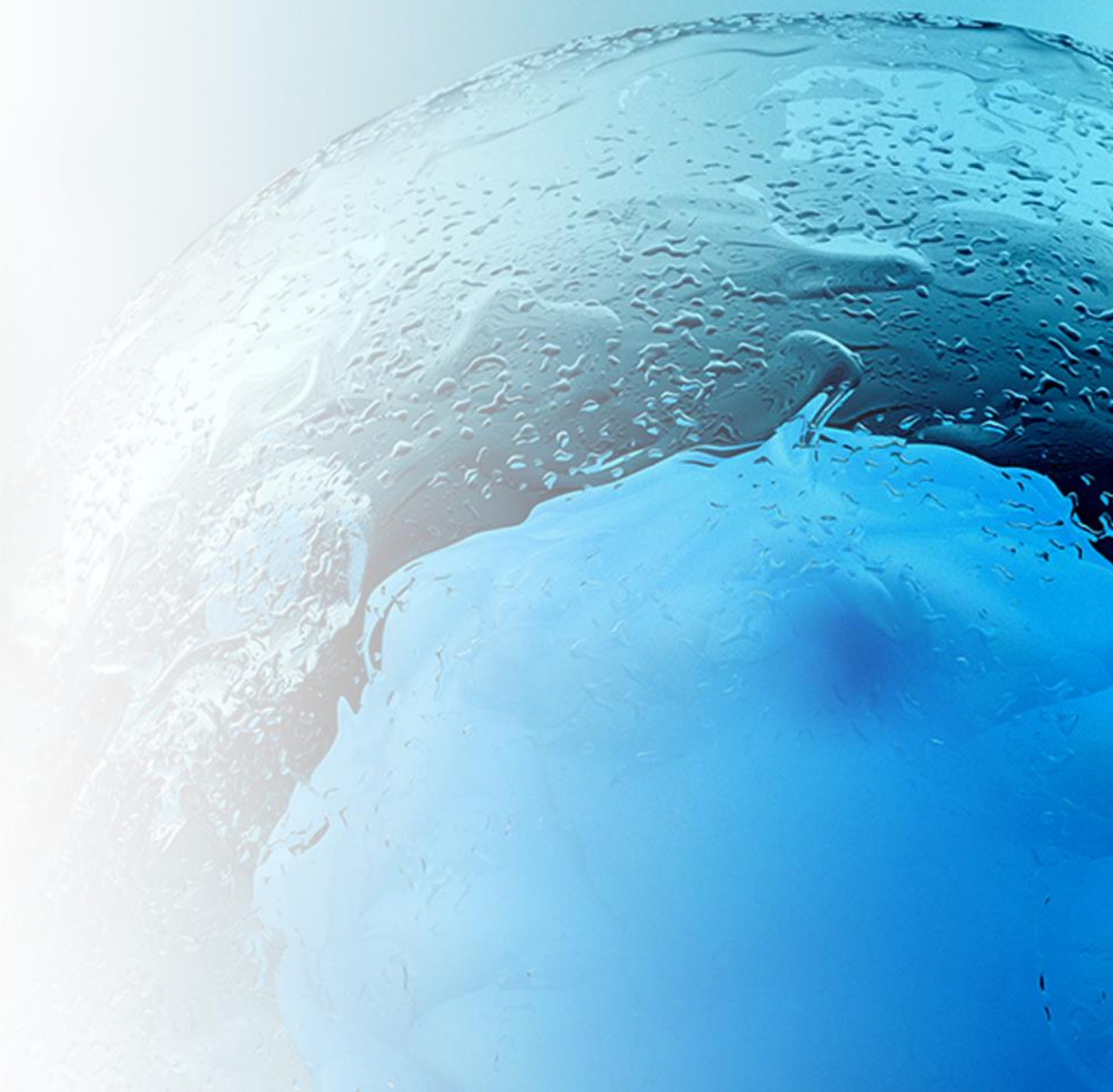
G1 Therapeutics: improving outcomes in cancer treatment

Trilaciclib: near-term opportunity to improve outcomes for patients receiving chemo

Rintodestrant: potential best-in-class oral SERD

Global rights to all compounds provides multiple options for value-creating partnerships

Well funded with cash runway into 4Q21

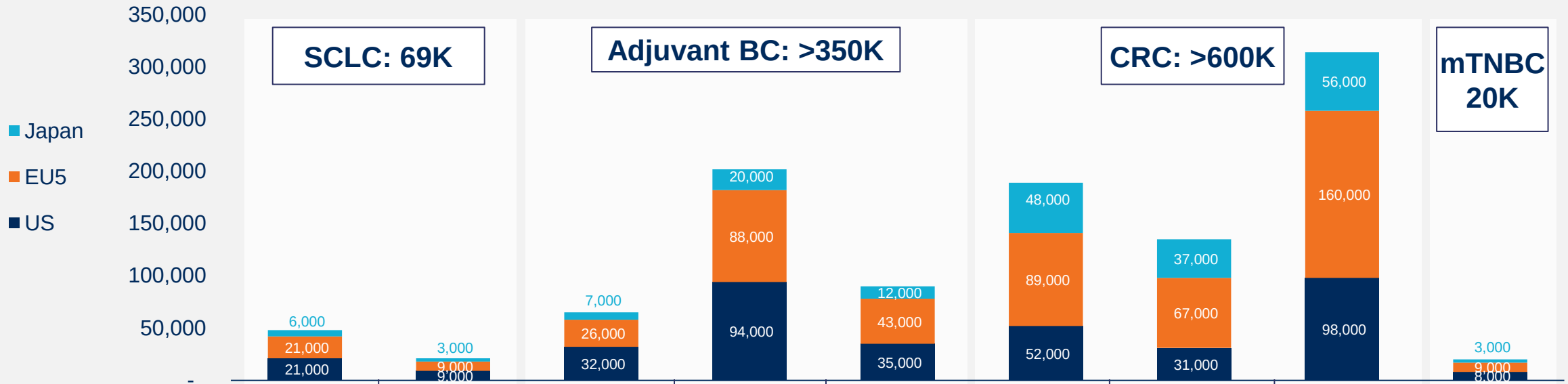


Appendix

Potential to improve outcomes across tumor types

Trilaciclib used first time, and every time, patient receives chemotherapy

Global Chemotherapy Treated Incident Patients (G7)*



	1L SCLC	2/3L SCLC	Adjuvant TNBC	Adjuvant HR+/HER2- BC	Adjuvant HER2+ BC	1L CRC	2/3L CRC	Adjuvant CRC	1L TNBC
% currently treated with eligible chemo regimen**	~95% (EP)	50% (topotecan or EP)	75% (Taxol AC)	50% (Taxol AC)	35% (Taxol AC)	80% (5-FU)	70% (5-FU)	50% (5-FU)	55% (GC, taxane, or IO + chemo)
Estimated mean # of cycles***	4-6	3-4	8	8	8	11-23	4-12	12	7-8

*Source: Secondary epi sources, 2027 estimates
**EP refers to any regimen that includes etoposide + platinum; GC refers to gemcitabine/carboplatin; Taxol AC refers to Taxol + 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 2019 Reports (CRC and BC)