NASDAQ: GTHX

G1 THERAPEUTICS

Next Generation Cancer Therapies

September 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. 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, our reliance on partners to develop and commercial licensed products, and the impact of pandemics such as COVID-19 (coronavirus), 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; 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.

Committed to improving lives and outcomes of people living with cancer

G1 THERAPEUTICS

Next-generation cancer therapies under development

Trilaciclib

First-in-class myelopreservation therapy

Rintodestrant

Potential best-in-class oral SERD

Lerociclib

Differentiated oral CDK4/6 inhibitor

Preparing for next stage of growth

R&D and commercial expertise
to bring trilaciclib to patients in the U.S.

Trilaciclib launch 1Q21
co-promotion with Boehringer Ingelheim

Rintodestrant data 2H21
combination with palbociclib

Strong cash position
funds operations into 2022

G1 THERAPEUTICS

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

G1 THERAPEUTICS

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)."

*Epstein et al, *Patient Burden and Real-World Management of Chemotherapy-Induced Myelosuppression: Results from an Online Survey of Patients with Solid Tumors*; Advances in Therapy, July 2020

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

Phase 2 trial findings*:

- **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
- 30-minute IV infusion prior to chemo; **given first time and every time** chemo is administered

- ✓ **NDA: Priority Review with 2/15/21 PDUFA date**
- ✓ **Breakthrough Therapy Designation for SCLC**
- ✓ **U.S. co-promotion with Boehringer Ingelheim**

* Based on data from four randomized, trials in: 1st-line SCLC (+ etop/carbo), 1st-line SCLC (+ etop/carbo/Tecentriq), 2nd/3rd-line SCLC (+ topotecan), and 1st-, 2nd, 3rd-line mTNBC (+gemcitabine/carboplatin)

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 35 for detail

First potential indication: small cell lung cancer (SCLC)

In three randomized trials, trilaciclib reduced 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***
- ✓ Feb. 15, 2021 PDUFA date (Priority Review)

* Based on pooled data from three randomized, placebo-controlled, double-blind trials in: 1st-line SCLC (+ etop/carbo), 1st-line SCLC (+ etop/carbo/Tecentriq), 2nd/3rd-line SCLC (+ topotecan)

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	

Updated from data presented at MASCC 2019

*Epstein et al, *Patient Burden and Real-World Management of Chemotherapy-Induced Myelosuppression: Results from an Online Survey of Patients with Solid Tumors*; Advances in Therapy, July 2020

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**

*Adapted from: Myelopreservation and reduced use of supportive care with trilaciclib in patients with small cell lung cancer ASCO 2020 Congress Poster: Weiss et al, Poster #384 or Smart Poster (mobile optimized)

**2-sided p-value; pooled data from three randomized, placebo-controlled, double-blind SCLC trials

Roadmap to establish new standard of care

Barriers	Critical Success Factors	
Myelosuppression under-recognized as unmet need	**Increase Awareness of Impact of Chemo Induced Myelosuppression on Lives of Patients**	• Increase awareness of impact on patients • Build strong KOL and other critical stakeholders
Entrenched “rescue” behaviors	**Establish Trilaciclib’s Multi-Lineage, Myelopreservation Benefit as SOC in SCLC**	• Advance inclusion across all relevant guidelines • Drive rapid awareness among early adopters • Demonstrate value
Access environment for supportive care especially challenging	**Optimize Early Experience**	• Minimize access barriers at launch • Ensure swift adoption to formularies, pathways, EMR systems and order sets at key accounts

Executional Excellence at Launch

- Field Sales Force
- Medical Affairs
- Marketing Strategy
- Market Access

Bringing trilaciclib to SCLC patients in the U.S.

Key functional capabilities at G1: Marketing, Market Access, Medical Affairs

Co-promotion agreement with experienced Boehringer Ingelheim oncology sales force

Commercial Objectives

Increase awareness of impact of chemo-induced myelosuppression on lives of patients

Establish trilaciclib's multi-lineage, myelopreservation benefit as SOC in SCLC

Optimize early experience by ensuring access

Bringing trilaciclib to patients

Boehringer Ingelheim

3-year co-promotion in U.S. for first potential indication of SCLC

先声药业 Simcere

Development and commercialization rights in Greater China

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*; final data in 4Q20

* 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 ESMO 2019 Oral Presentation: O'Shaugnessey et al, Abstract #6255; results published concurrently in *The Lancet Oncology*

Preliminary overall survival benefit in mTNBC

	Control (GC only) (Group 1)	Trilaciclib + GC (Group 2)	Trilaciclib + GC (Group 3)	Trilaciclib + GC (Group 2+3)
ITT population	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

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)

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 ESMO 2019 Oral Presentation: O'Shaugnessey et al, Abstract #6255; results published concurrently in *The Lancet Oncology*

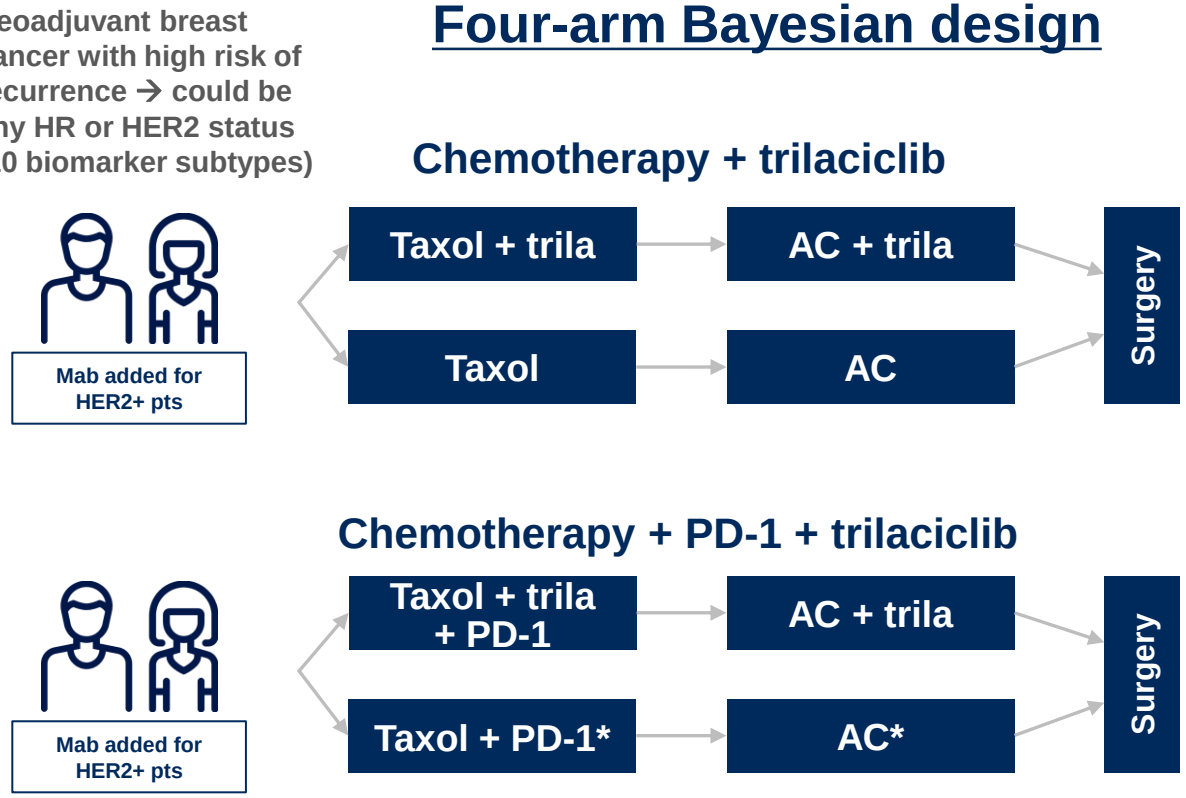
Breast cancer neoadjuvant trial: I-SPY 2 initiated in 2Q20

Goals of Phase 2 trial

- Evaluate trilaciclib in a broadly-used chemo regimen (Taxol + AC)
- Evaluate trilaciclib in all breast cancer sub-types (ER+, HER2+, TNBC)
- Endpoints: pathological complete response (pathCR), myelopreservation
- Data in 2023

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

Pursuing additional indications: metastatic colorectal cancer (mCRC)

Primary endpoints: myelopreservation measures

- ✓ Initiating Phase 3 trial in 4Q20
- ✓ Trial design incorporates FDA feedback
- ✓ Myelopreservation, PRO, and survival endpoints
- ✓ Data in 2023

Next steps for trilaciclib across multiple indications

SCLC

- ✓ **Feb. 15, 2021 PDUFA date (Priority Review)**
- Launch-ready 1Q21

Breast Cancer

- ✓ **Initiated I-SPY2 trial in 2Q20**
- Final OS data from mTNBC trial in 4Q20

Colorectal Cancer

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

G1 THERAPEUTICS

Next-generation cancer therapies

Trilaciclib

First-in-class myelopreservation therapy

Rintodestrant

Potential best-in-class oral SERD

Lerociclib

Differentiated oral CDK4/6 inhibitor

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

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

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). ESMO 2019 Poster: Dees et al, Abstract #3587

Assessing the potential of rintodestrant

Phase 1/2a program w/ ~110 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
- **800 mg QD selected as dose for further development**
- **Initiated additional arm** in 2Q20 (~40 patients) to evaluate **rintodestrant (800 mg) + palbociclib**

Next-generation cancer therapies

Trilaciclib

First-in-class myelopreservation therapy

Rintodestrant

Potential best-in-class oral SERD

Lerociclib

Differentiated oral CDK4/6 inhibitor

Lerociclib: differentiated oral CDK4/6 inhibitor in development

	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

* drug-induced liver injury

Global agreements accelerate further development

EQRx™
REMAKING MEDICINE

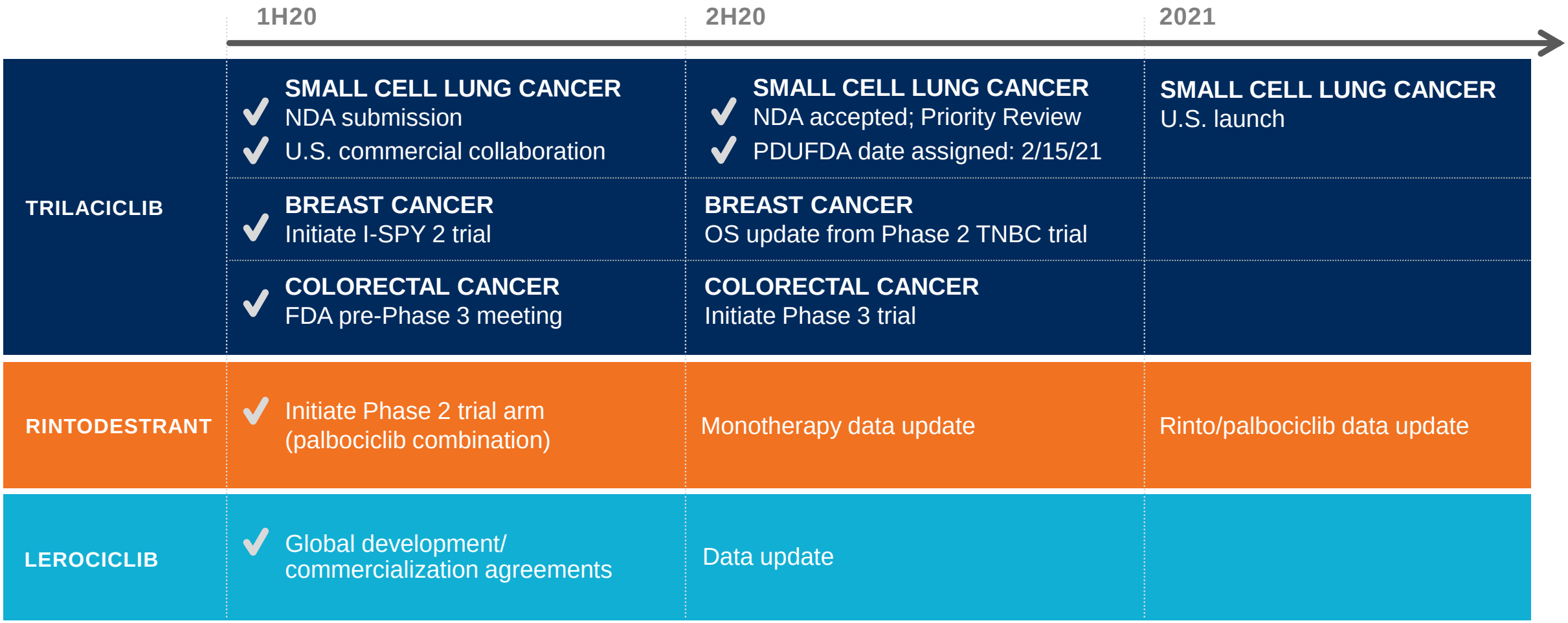
Development and commercialization rights in U.S., EU, Japan and other markets

GENOR BIOPHARMA

Development and commercialization rights in Asia-Pacific (except Japan)

G1 THERAPEUTICS

2020 – 2021: key milestones



Preparing for next stage of growth

R&D and commercial expertise
to bring trilaciclib to patients in the U.S.

Trilaciclib launch 1Q21
co-promotion with Boehringer Ingelheim

Rintodestrant data 2H21
combination with palbociclib

Strong cash position
funds operations into 2022

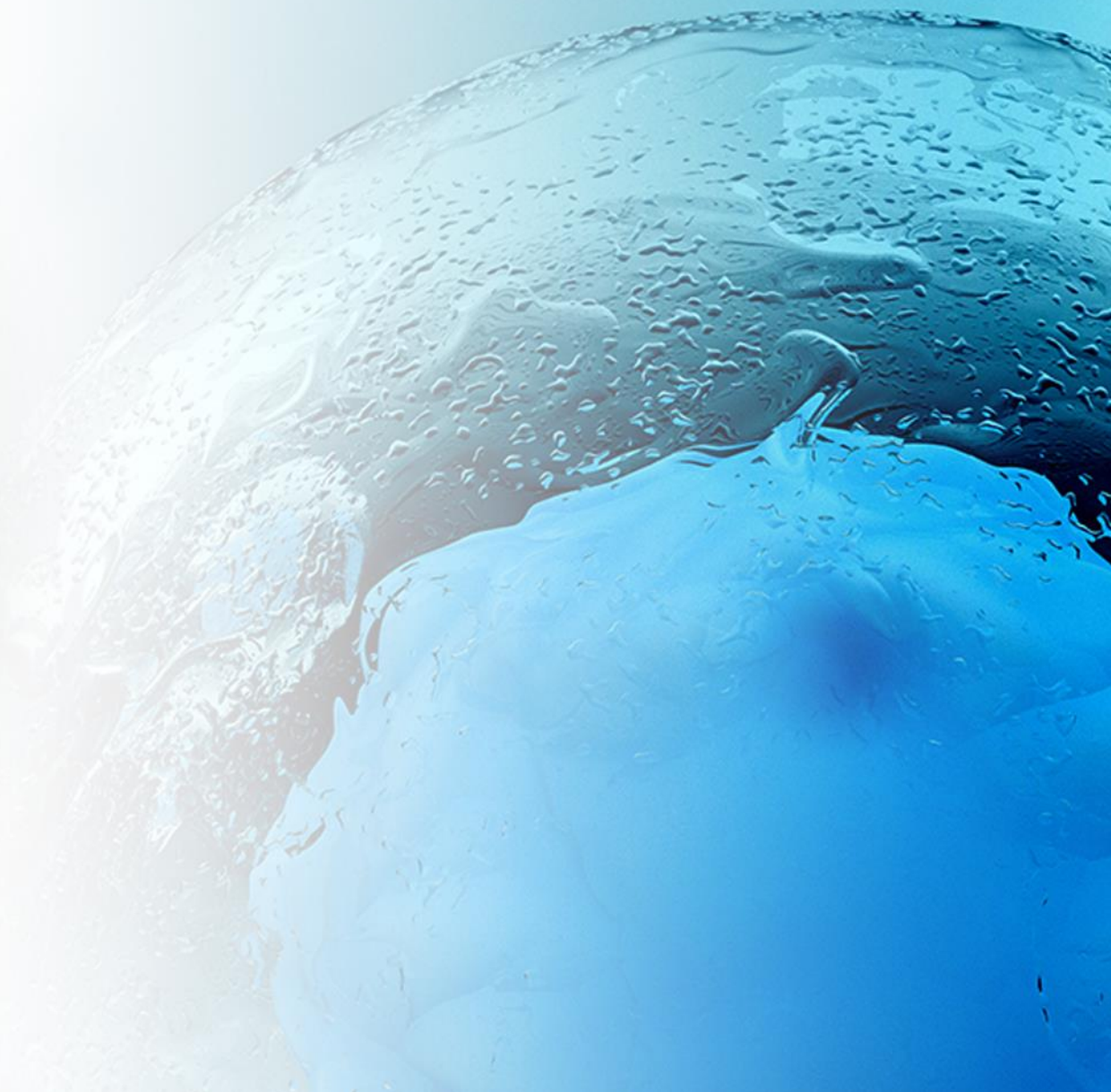
G1 Therapeutics: improving outcomes in cancer treatment

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

Rintodestrant: potential best-in-class oral SERD

Global rights to trilaciclib (ex-China) and rintodestrant provide options for additional value-creating partnerships

Well funded with cash runway into 2022

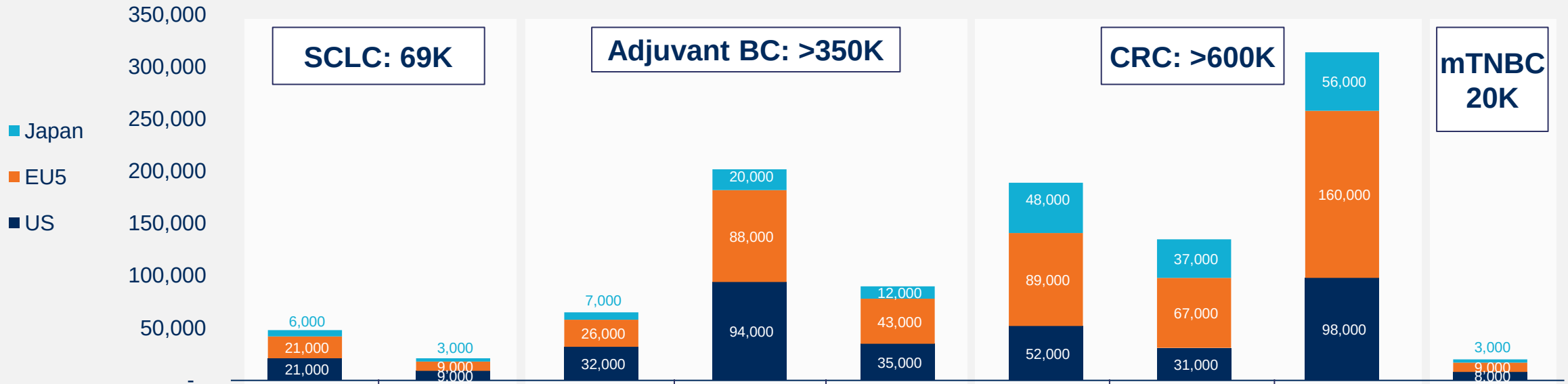


Appendix

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)