



Next Generation Cancer Therapies

January 2020

Forward-looking statements

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Next-generation cancer therapies

Trilaciclib

First-in-class
myelopreservation
therapy

Rintodestrant

(G1T48)

Potential best-in-class
oral SERD

Lerociclib

Differentiated
oral CDK4/6
inhibitor

**Committed to improving lives
and outcomes of people living
with cancer**



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).”

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



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**

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

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.

Planning to submit MAA in 2H20

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

	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)
 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

Chemotherapy + trilaciclib



Chemotherapy + PD-1 + trilaciclib



AC = adriamycin and cyclophosphamide

Opportunity to improve patient outcomes across multiple indications

~1 million* patients in planned indications

68,000

Small Cell
Lung Cancer

>350,000

Adjuvant Breast
Cancer

>500,000

Colorectal Cancer

20,000

Metastatic
Triple-Negative
Breast Cancer

Next steps for trilaciclib across multiple indications

SCLC

- Complete NDA submission in 2Q20
- PDUFA date assigned in 3Q20 (pending acceptance)
- MAA submission in 2H20

Breast Cancer

- Initiate I-SPY2 trial in 2Q20
- Updated OS data from mTNBC trial in 2H20

Colorectal Cancer

- 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

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

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

Assessing the potential of rintodestrant

Phase 1/2a program
w/ ~100 patients
enrolled by YE20:
additional data 2H20

- ~65 patients enrolled in Phase 1/2a trial to **identify dose** (expansion cohorts of 600 mg and 1,000 mg monotherapy)
- Collecting PD data from biopsies to **confirm activity in the tumor**
- **Additional arm** to include another ~40 patients evaluating **rintodestrant + palbociclib combination**

Significant potential to improve ER+ breast cancer treatment

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

89,000

2L

139,000

1L

223,000

**Adjuvant
(Stage II / III)**

median duration
of therapy

14 months

33 months

60 months

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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 2H20 on 150mg and 200mg BID cohorts, enabling Phase 3 dose selection

Significant progress in 2019, setting up catalysts in 2020

Trilaciclib

- ✓ Breakthrough Therapy designation for SCLC
- ✓ Began rolling NDA submission for SCLC
- ✓ Preliminary OS improvement in TNBC

Rintodestrant (G1T48)

- ✓ Phase 1 data demonstrated POC and potential best-in-class profile
- ✓ Completed Phase 2a monotherapy enrollment

Lerociclib

- ✓ Demonstrated POC and differentiation from existing CDK4/6i
- ✓ Completed enrollment of BC and lung trials

2020: near-term clinical and regulatory milestones

Therapy	Indication	1H20	2H20
Trilaciclib	Small cell lung cancer	Complete NDA submission	PDUFA date assigned; MAA filing
	Breast cancer	Initiate I-SPY 2 trial	OS update from Phase 2 TNBC trial
	Metastatic colorectal cancer	FDA pre-Phase 3 meeting	Initiate Phase 3 trial
Rintodestrant (G1T48)	ER+, HER2- BC	Initiate Phase 2 expansion w/ palbociclib combination	Data update
Lerociclib	ER+, HER2- BC (+ fulvestrant)		Data update

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 2H21



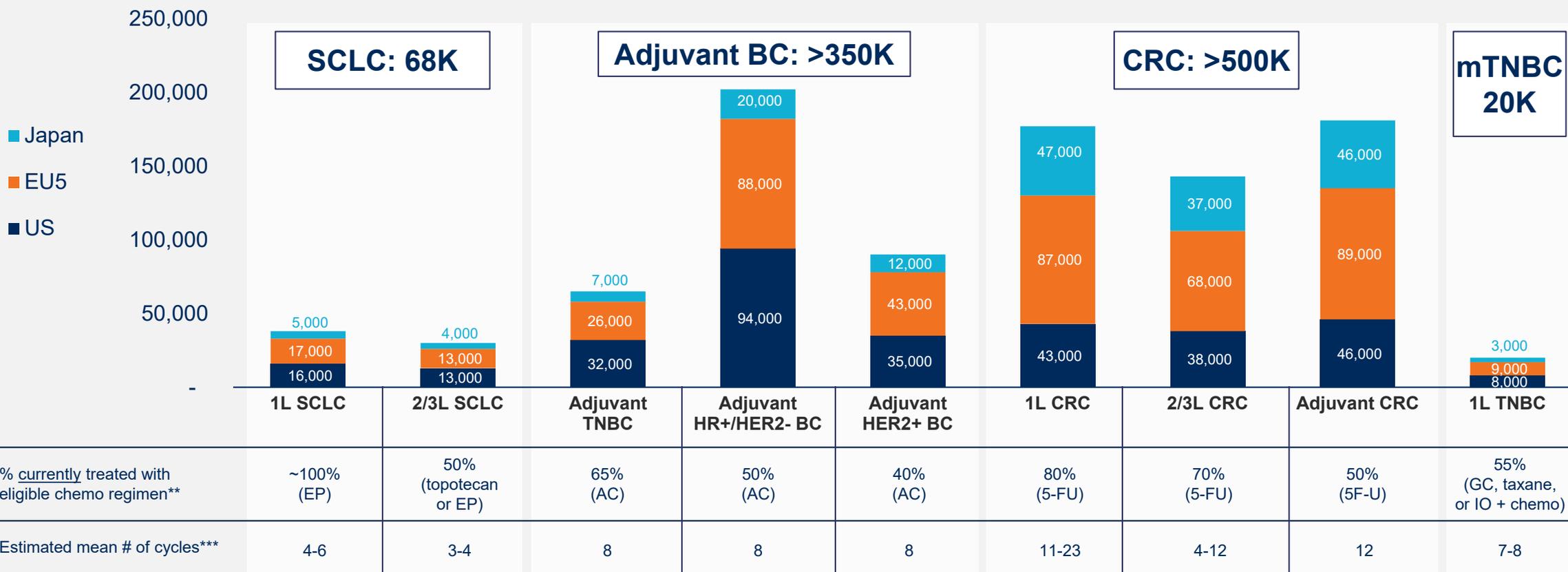
Appendix



Potential to improve outcomes across tumor types

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

Global Chemotherapy Treated Incident Patients (G7)*



*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)