Optimizing Chemotherapy, Advancing Survival

39th Annual J.P. Morgan Healthcare Conference

January 13, 2021

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, 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. Trilaciclib, rintodestrant and lerociclib are not approved by the FDA. The safety or effectiveness of trilaciclib, rintodestrant and lerociclib have not been established by the FDA. 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.

G1 THERAPEUTICS

Transformed Company Heading into a Pivotal 2021

2020

- Trilaciclib
- Rintodestrant
- Lerociclib — OUT-LICENSED (EQRx, GENOR BIOPHARMA)
- CDK2 Discovery Platform — OUT-LICENSED (ARC THERAPEUTICS)

2021

Trilaciclib is a cornerstone therapy:

- Near-term U.S. launch in SCLC (Priority Review)
- Pipeline-in-a-molecule development opportunity

Simcere Partner for Greater China

Rintodestrant + palbociclib Phase 2 data expected 2Q

$207M cash on hand (as of December 31, 2020)

Streamlined company focused on maximizing the development and commercialization of trilaciclib

G1 THERAPEUTICS

Chemo to Remain Mainstay Therapy Despite Shortcomings

Over 1 million cancer patients receive chemo in the U.S. each year

- Cost-efficient and effective treatment option expected to remain backbone of SoC
- Established high water-mark that has proven difficult to exceed head-to-head
- Immunotherapy with chemo has demonstrated the best results in many tumors

Two Critical Areas of Unmet Need

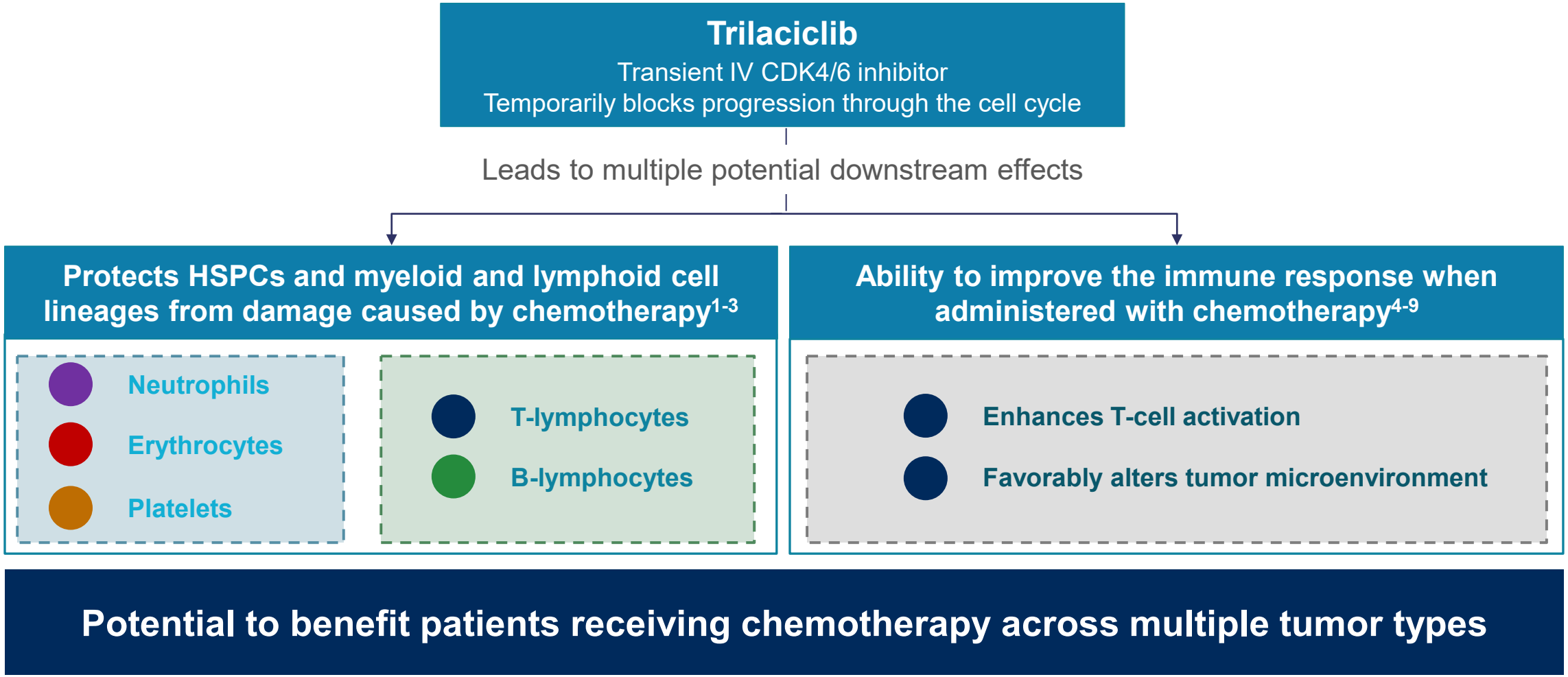
1 Proactively reducing the damaging consequences of chemotherapy

2 Meaningfully improving overall survival in broad populations

High unmet need for new therapies that can significantly reduce myelosuppression and meaningfully improve efficacy across patient populations

G1 THERAPEUTICS

Trilaciclib: Novel Approach to Address Shortcomings of Chemo



1. Weiss J, et al. Ann Oncol. 2019 Oct; 30(10): 1613–1621. 2. He S, et al. Sci Transl Med. 2017;9:eaal3986. 3. Bisi JE, et al. Mol Cancer Ther. 2016;15:783-93. 4. Tan A, et al. Lancet Oncol. 2019 Sep 28. 5. Zhang J, et al. Nature. 2018;553:91-95. 6. Jerby-Arnon L, et al. Cell. 2018;175:984-997. 7. Goel S, et al. Nature. 2017;548:471-475. 8. Deng J, et al. Cancer Discov. 2018;:216-233. 9. O'Shaugnessy et al., 2020 San Antonio Breast Cancer Symposium (SABCS), Poster #PD1-06.

Trilaciclib Demonstrated Meaningful Benefits Across Studies

Myelopreservation Impact[1-5]

- **Reduces** rate of hematologic adverse events (less neutropenia, anemia, thrombocytopenia)
- **Decreases** rescue interventions and costs (less transfusions, G-CSF, hospitalizations)
- **Improves** patients' quality of life (well-being and less fatigue)

Protects myeloid cell lineages

Protects lymphoid cell lineages

Improves immune response

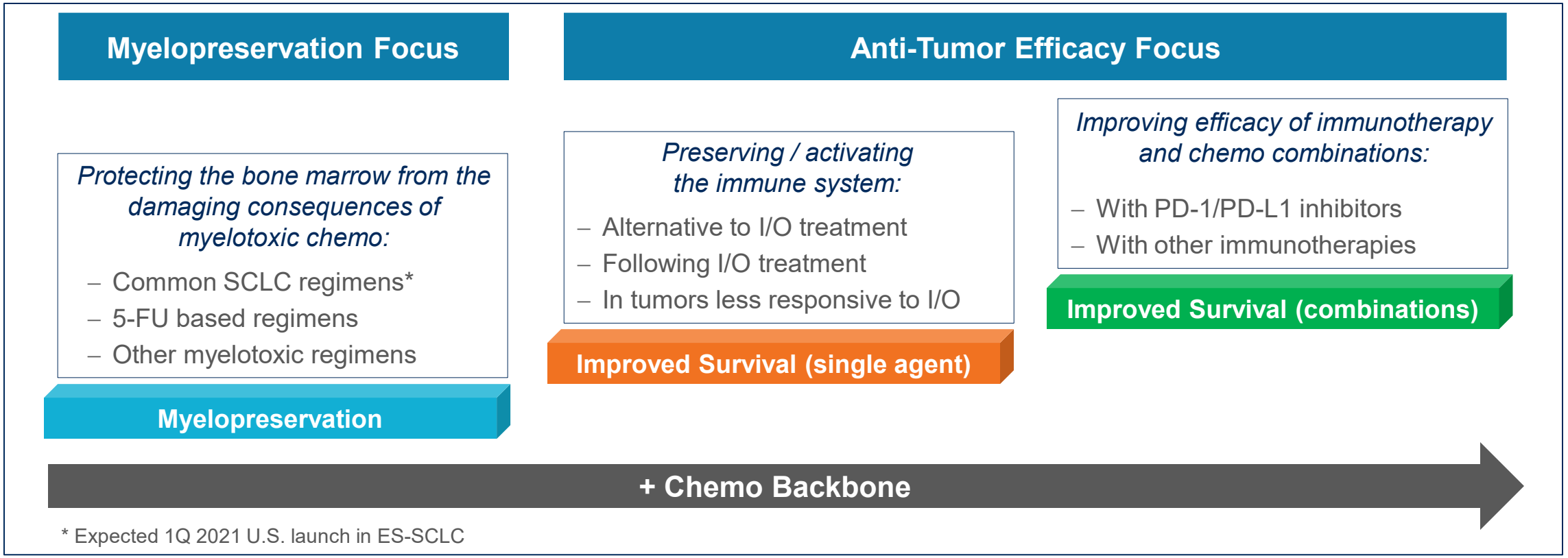
Anti-Tumor Efficacy Impact[6-11]

- **Increases** patients' ability to receive longer duration of chemotherapy-based regimens
- **Protects** the immune system from damage by chemotherapy
- **Enhances** T-cell activation and favorably alters the tumor microenvironment

Potential to provide myelopreservation and/or anti-tumor efficacy benefits in patients treated with chemotherapy

1. Weiss J, et al. Ann Oncol. 2019 Oct; 30(10): 1613–1621. 2. He S, et al. Sci Transl Med. 2017;9:eaal3986. 3. Bisi JE, et al. Mol Cancer Ther. 2016;15:783-93. 4. Weiss et al. MASCC Oral Presentation, Abstract #MASCC9-0845. 5. Tan A, et al. Lancet Oncol. 2019 Sep 28. 6. Ferrarotto et al., 2020 North America Conference on Lung Cancer (NACLC), Abstract # OA03.08. 7. Zhang J, et al. Nature. 2018;553:91-95. 8. Jerby-Arnon L, et al. Cell. 2018;175:984-997. 9. Goel S, et al. Nature. 2017;548:471-475. 10. Deng J, et al. Cancer Discov. 2018;:216-233. 11. O'Shaugnessy et al., 2020 San Antonio Breast Cancer Symposium (SABCS), Poster #PD1-06.

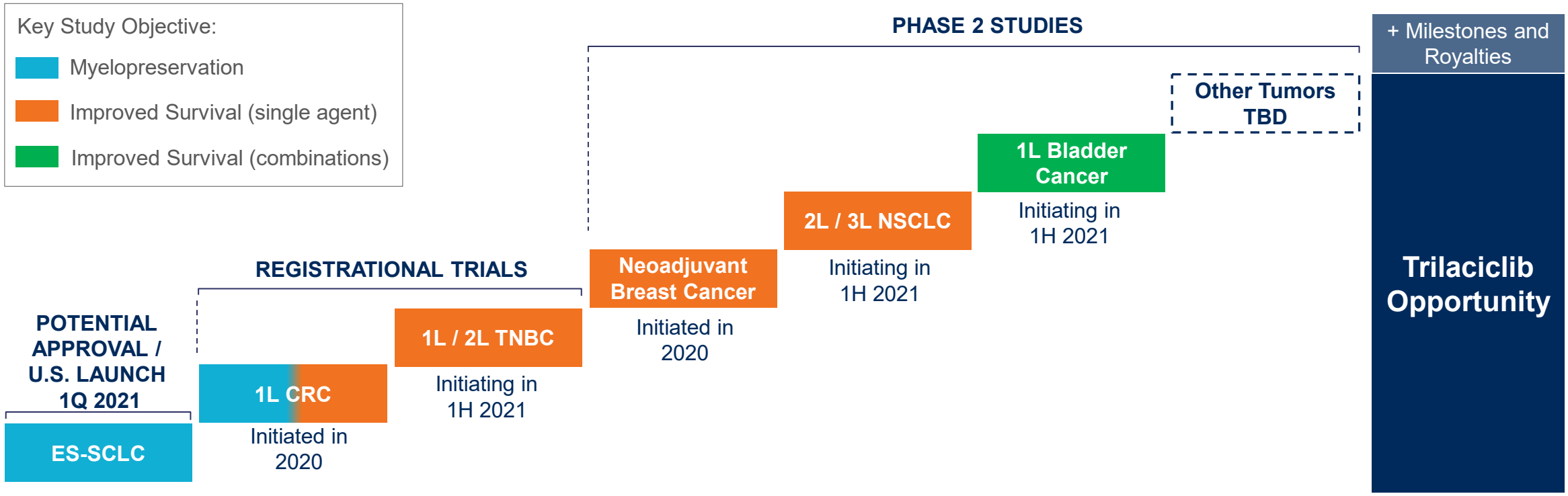
Significant Expansion Opportunities for Trilaciclib



Optimizing development plan across three core growth platforms will enable trilaciclib to benefit as many patients as possible

G1 THERAPEUTICS

Pipeline-in-a-Molecule Opportunity Beyond ES-SCLC Launch



Aggressively pursuing development in areas of high strategic importance where trilaciclib is most likely to provide meaningful benefits to patients

G1 THERAPEUTICS

2021 Key Objectives

1. Obtain U.S. approval for ES-SCLC and successfully launch trilaciclib in 1Q
2. Establish trilaciclib as Standard of Care for ES-SCLC patients in the U.S.
3. Maximize long-term value of trilaciclib by executing robust development plan
4. Evaluate partnership options for rintodestrant following combination data readout in 2Q
5. Continue managing investor capital efficiently

Focused on successfully launching trilaciclib in ES-SCLC and accelerating development into other areas where chemotherapy is used

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G1 THERAPEUTICS

Prepared for Trilaciclib Approval and U.S. Launch in 1Q21

NDA Discussions on Track

- PDUFA action date for SCLC indication: February 15th, 2021
- NDA under "Priority Review"
- Less complex CMC application given small molecule compound

Pre-Launch Activities Ongoing

- Identified HCP targets
- Profiled key accounts
- Engaged payors
- Educating leading patient advocacy organizations

Ready for 1Q Launch

- G1 infrastructure in place
  - ✓ Marketing
  - ✓ Market Access
  - ✓ Commercial Operations
  - ✓ Medical Affairs team
  - ✓ Manufacturing and supply chain
- Boehringer Ingelheim field sales team trained and ready[1]
  - ✓ Experienced lung cancer team
  - ✓ Incentivized structure (% net sales)

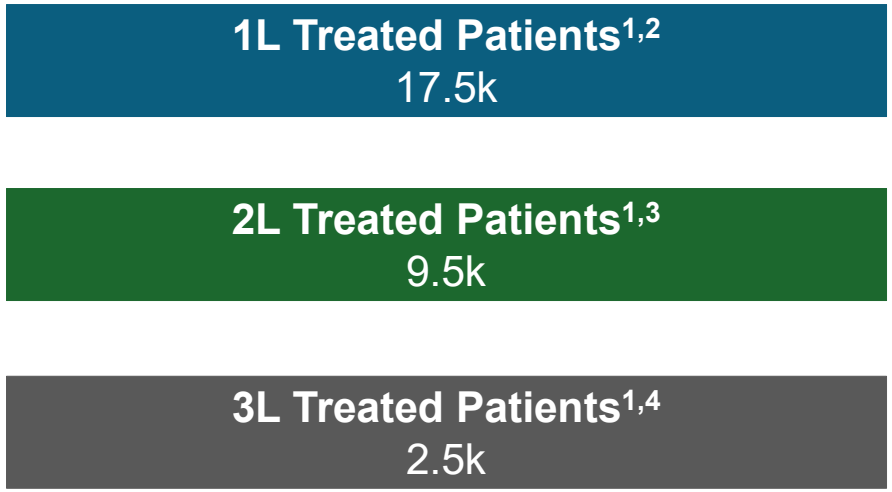
Following NDA approval, we are ready to make this important new treatment available to the majority of patients with ES-SCLC undergoing chemotherapy in the U.S.

1. Three-year agreement where Boehringer Ingelheim leads sales force engagement initiatives for trilaciclib in the U.S. for the initial ES-SCLC indication. The agreement does not extend to additional indications.

G1 THERAPEUTICS

Opportunity to Meaningfully Impact the Lives of Many Patients

~30k ES-SCLC Patients Treated Annually in the U.S.[1]



ES-SCLC patients predominately treated with highly myelosuppressive chemo regimens

- Limited successful innovation given aggressiveness of disease (1L median OS ~1 year[5])
- Standard treatment includes 4 to 6 cycles of chemo

Payor research and discussions indicate potential broad patient access to trilaciclib

- Anticipate pricing product above supportive care treatments and below therapeutics
- ~60% of ES-SCLC patients covered by Medicare (expect Medicare to cover label at launch)

Trilaciclib provides a meaningful improvement for SCLC patients and has potential to generate near-term revenue to further support ongoing development

1. Based on incidence of 25k for all SCLC with 81% of patients being diagnosed at Extensive Stage; *Decision Resources Group, Small Cell Lung Cancer Disease Landscape & Forecast, March 2020.*
2. Based on 22k 1L SCLC total patients (20K de novo ES-SCLC and 2K late relapse LS-SCLC) treated at an assumed 80% treatment rate (from 2020 internal primary market research).
3. Based on 12.5k 2L SCLC total patients (11k progressed 1L SCLC and 1.5k early relapse LS-SCLC) treated at an assumed 72% treatment rate (from 2020 internal primary market research).
4. Based on 5k 3L SCLC total patients treated at an assumed 50% treatment rate (from 2020 internal primary market research).
5. Demonstrated in trilaciclib G1T28-02 and G1T28-05 study control arms.

G1 THERAPEUTICS

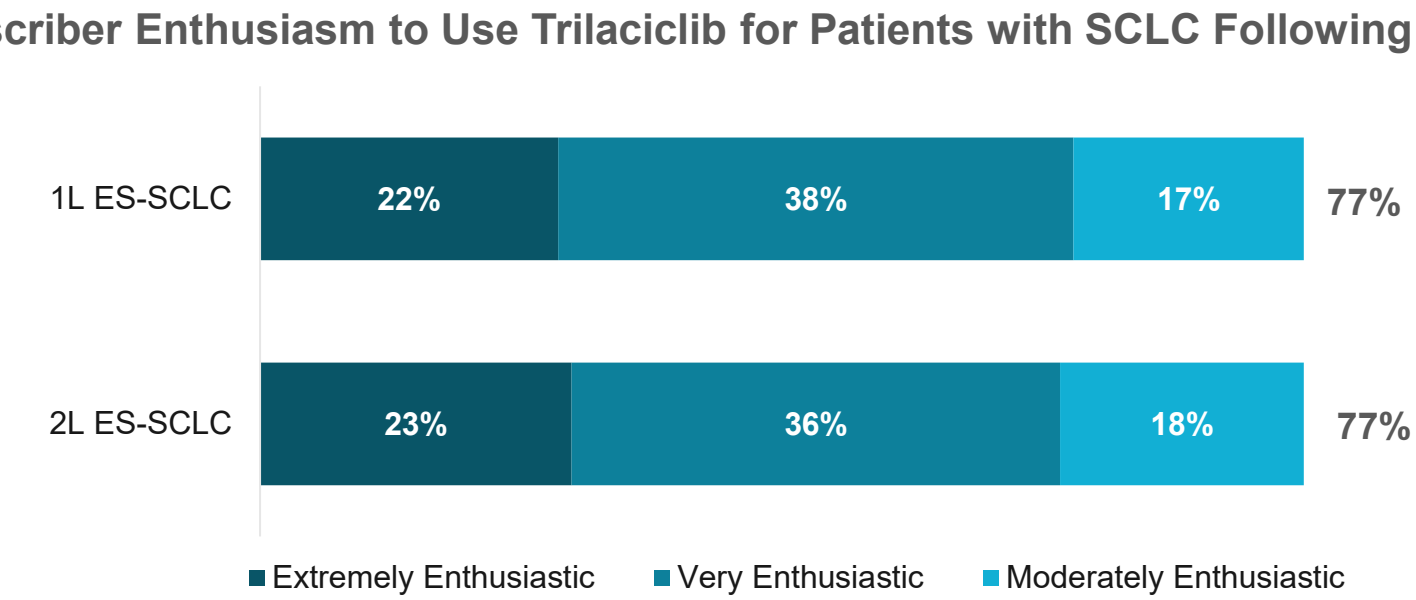
Three Core Goals for a Successful U.S. ES-SCLC Launch

1 Increase Awareness of Myelosuppression	Increase awareness of the significant multi-lineage impact of myelosuppression on clinical outcomes, costs, and patients' QoL
2 Communicate the Unique Benefits of Trilaciclib	Educate prescribers, payers, and patients on the benefits of trilaciclib's proactive multi-lineage protection
3 Optimize Early Experience	Gain inclusion into relevant guidelines / pathways; enable broad patient access; and ensure ease of use for prescribers / nurses / staff

Focused on ensuring patients with ES-SCLC can benefit from trilaciclib first time and every time they are treated with chemotherapy

G1 THERAPEUTICS

Prescribers are Enthusiastic to Use Trilaciclib



Source: internal market research conducted July 2020 (n=153 oncologists)

Education will be key to establish trilaciclib as a Standard of Care for patients with ES-SCLC receiving chemotherapy

G1 THERAPEUTICS

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G1 THERAPEUTICS

The Burden of Chemotherapy

MYELOSUPPRESSION

An unavoidable consequence of chemo that impacts patient safety, healthcare system costs and QoL

HEMATOLOGIC EVENT:	**NEUTROPENIA**	**ANEMIA**	**THROMBOCYTOPENIA**
CONSEQUENCE:	Risk of infection	Fatigue	Risk of bleeding
RESPONSE:	G-CSF use (associated bone pain)	RBC transfusions and ESA rescue	Platelet transfusions
	Increased healthcare costs	**Chemotherapy dose reductions and delays**	**Hospitalizations and unscheduled patient care**

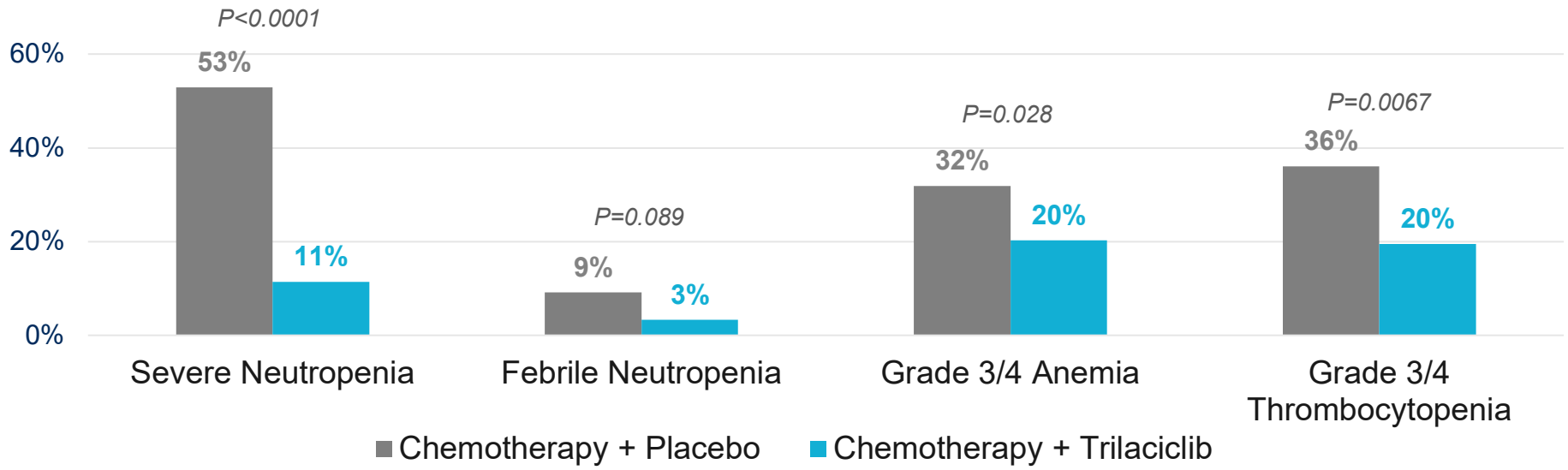
Myelosuppression has a significant negative impact on clinical outcomes, healthcare costs, and overall patient quality of life

G1 THERAPEUTICS

Trilaciclib Meaningfully Reduces Myelosuppression in SCLC

Reduced Incidence of Multi-lineage Myelosuppression in 1L–3L SCLC[1]

(pooled data across our 3 randomized placebo-controlled double-blind trials)



Clinical Results: Trilaciclib consistently demonstrated meaningful reductions in hematologic adverse events across multiple randomized SCLC studies

1. Weiss et al., 2020 American Society of Clinical Oncology (ASCO), Abstract #384.

G1 THERAPEUTICS

Trilaciclib Expected to Drive Significant Payor/Hospital Savings

Average Total Annual Cost Per Patient with a Grade 3/4 Hematologic Event (Jan 2016 – Dec 2019)[1]

Neutropenia	$131,047
Anemia	$95,954
Thrombocytopenia	$90,053

Average total annual cost per patient *without a* grade 3/4 hematologic event: $67,802

Cost savings from less hematologic events largely driven by:

- Reduced interventions (e.g., G-CSF, ESA)
- Fewer required transfusions
- Fewer complications and hospitalizations

Payor Impact: Trilaciclib's ability to reduce the severe hematologic consequences of chemotherapy expected to result in a budget-neutral to savings-positive impact

1. Epstein et al, *Journal of Clinical Oncology* May 25, 2020; 38, no. 15_suppl

G1 THERAPEUTICS

Trilaciclib Improves Patients' Quality of Life

89% of cancer patients with myelosuppression rate it as having a moderate to major impact on their life[1]:

"…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."

"**Did not get out as much, not able to work**,
always feeling tired."

Trilaciclib helps patient functioning in ES-SCLC patients:

Median Time to Deterioration[2]

(pooled data from three randomized, placebo-controlled, double-blind trials)

Measure	Placebo (months)	Trilaciclib (months)	Improvement (months)
Fatigue	2.3	7.0	**4.7**
Anemia –TOI (Trial Outcome Index)	3.8	7.2	**3.4**
Functional Well Being	3.8	7.6	**3.8**

Patient Benefit: Trilaciclib's proactive protection enables better quality of life for patients in this palliative treatment setting

1. 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
2. Weiss et al., MASCC Oral Presentation 2019, Abstract #MASCC 9-0845

Opportunity for Trilaciclib to Become Standard of Care in SCLC

Clinical Results: Meaningfully reduces the hematologic adverse events in SCLC

Payer Impact: Provides cost savings for system (trilaciclib expected to be budget neutral or better)

Patient Benefits: Improves the overall quality of life for patients

Heightened awareness of myelosuppression due to the COVID pandemic may further encourage adoption of trilaciclib as a Standard of Care

G1 THERAPEUTICS

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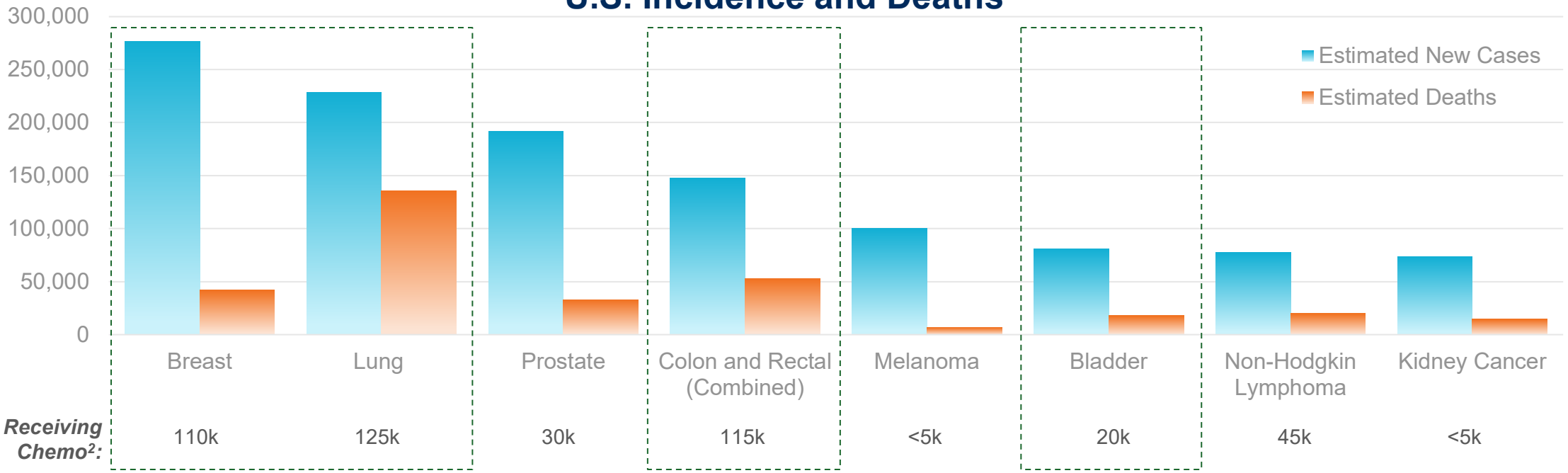
G1 THERAPEUTICS

Aggressively Pursuing Development in Common Tumor Types

U.S. Incidence and Deaths[1]



G1 has / will soon initiate sponsored studies in many of the most common and deadly tumor types

1. Estimated new cases and deaths from National Cancer Institute for 2020.
2. Estimated patients receiving chemotherapy from Kantar Health CancerMPact Patient Metrics, 2019 data based on IQVIA BrandImpact regimen shares and Kantar Health Treatment Architecture 2019 survey data for patients receiving chemo (rounded to nearest 5,000 patients).

Broad Portfolio of Impactful Studies Across Tumor Types

Cancer Type	Indication	Study Size	Phase 2	Pivotal	Approval
Lung	SCLC	NA	Under Priority Review with FDA		
	2L / 3L NSCLC (Post-checkpoint treatment)	TBD	Starting 1H 2021		
Colorectal	1L CRC	~300	Ongoing		
Breast	1L TNBC[1]	~170	Starting 1H 2021		
	2L TNBC[1] (Post-checkpoint treatment)	~80	Starting 1H 2021		
	Neoadjuvant	Adaptive	Ongoing		
Bladder	1L Bladder (Checkpoint combination)	TBD	Starting 1H 2021		

Two registrational studies will be ongoing by mid 2021 in addition to multiple Phase 2 studies to evaluate trilaciclib in several treatment settings / tumor types

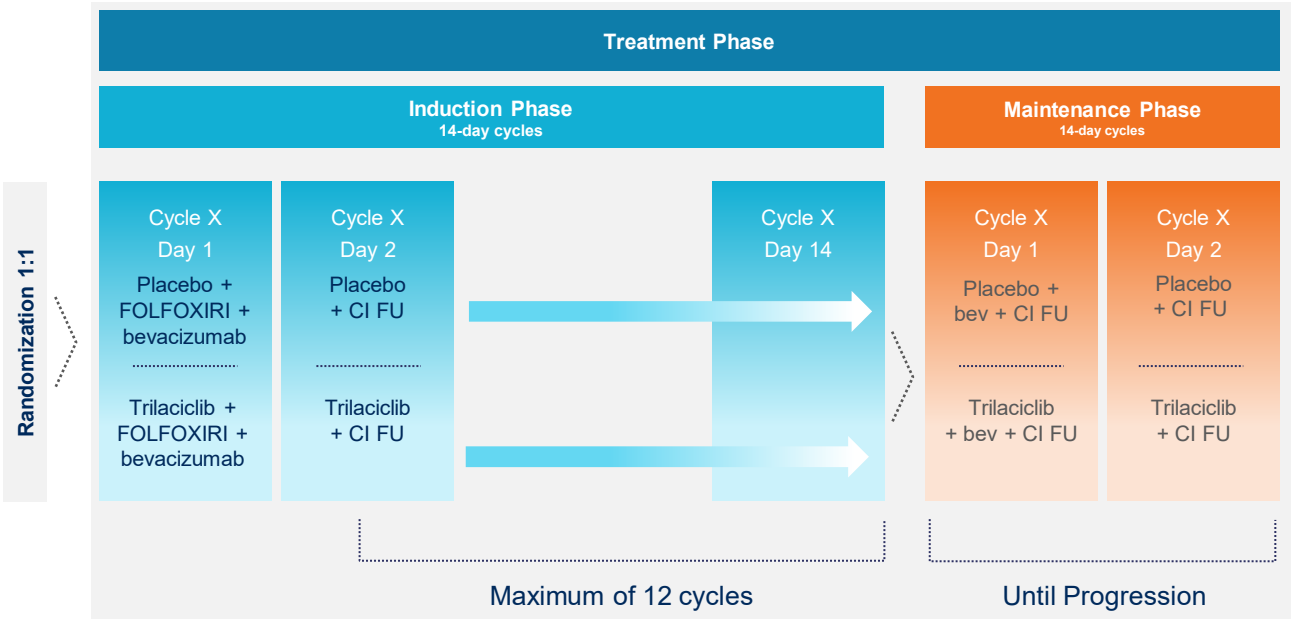
1. 1L TNBC and 2L TNBC cohorts being conducted under one study protocol.

G1 THERAPEUTICS

Ongoing First-Line CRC Pivotal Trial

FOLFOXIRI: most efficacious chemo regimen but highly myelosuppressive

Ability to significantly expand FOLFOXIRI usage supported by market research



PRIMARY ENDPOINT:
Myelopreservation

SECONDARY ENDPOINTS:
PFS/OS, PRO

TARGET ENROLLMENT:
~300 participants

PATIENTS TREATED UNTIL PROGRESSION

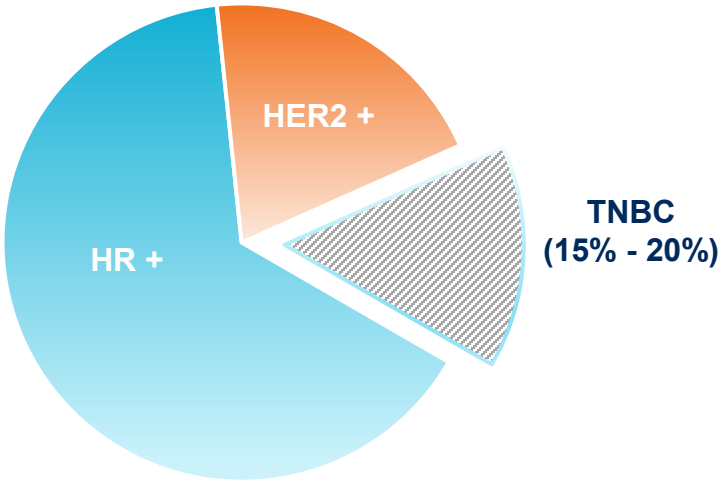
MULTI-DAY CHEMO REGIMEN

Strong support from preclinical models for the benefits of trilaciclib in combination with 5-FU-based chemo regimens

G1 THERAPEUTICS

Metastatic TNBC is an Area of High Unmet Need

Breast Cancer Subtypes



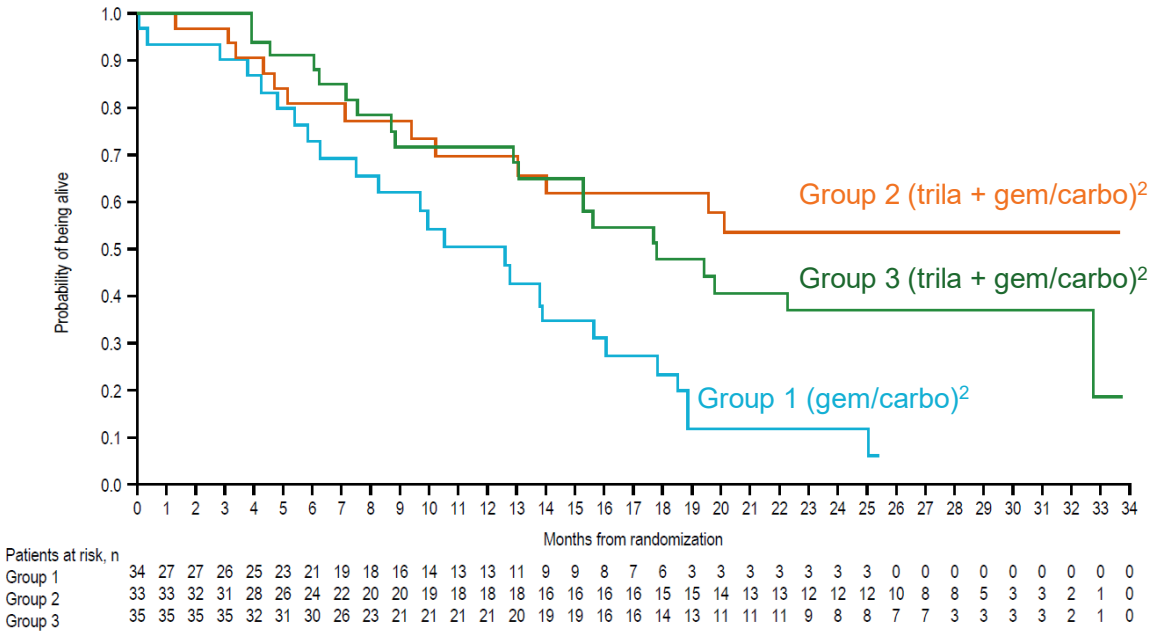
- TNBC tumors categorized by lack of HR expression and HER2 gene amplification
- Tumors are aggressive and difficult to treat
- Targeted therapies only demonstrated benefit in subpopulations (e.g., PD-L1 agents, PARPs)
- Antibody Drug Conjugates (ADCs) demonstrated OS improvement in 3L to date, but have associated toxicity

Urgent need for new therapies that extend Overall Survival with decreased toxicity

G1 THERAPEUTICS

Observed Robust OS Improvement in mTNBC Phase 2

Overall Survival in Intent-to-Treat Population[1]



Treatment Group[2]	Median OS, months	Hazard Ratio (95% CI)	*P* Value
Group 1: (gem/carbo)	12.6	-	-
Group 2: (gem/carbo + trilaciclib)	Not Reached	**0.31** (0.15-0.63)	0.0016
Group 3: (gem/carbo + trilaciclib)	17.8	**0.40** (0.22-0.74)	0.0004

Observed a robust statistically significant improvement in Overall Survival for both trilaciclib schedules

1. O'Shaughnessy et al., 2020 San Antonio Breast Cancer Symposium (SABCS), Poster #PD1-06. Note: primary endpoints relating to reduction in severe neutropenia not achieved in this study.
2. Patients randomized to receive gem/carbo chemotherapy only (Group 1) or gem/carbo plus one of two dosing schedules of trilaciclib: trilaciclib administered on the day of chemotherapy (Group 2) or trilaciclib administered the day prior to and the day of chemotherapy (Group 3).

OS Improvement Regardless of PD-L1 Status

Overall Survival for PD-L1 Positive Tumors[1]

Treatment Group[2]	Patients	Median OS (95% CI), Months	Hazard Ratio (95% CI)	*P* Value
Group 1: (gem/carbo)	17	10.5 (6.3 – 18.8)	-	-
Group 2 and 3: (gem/carbo + trilaciclib)	32	**32.7** (17.7 – NR)	**0.34** (0.2 – 0.7)	0.004

Overall Survival for PD-L1 Negative Tumors[1]

Treatment Group[2]	Patients	Median OS (95% CI), Months	Hazard Ratio (95% CI)	*P* Value
Group 1: (gem/carbo)	10	13.9 (12.6 – NR)	-	-
Group 2 and 3: (gem/carbo + trilaciclib)	26	**17.8** (13.1 – NR)	**0.48** (0.2 – 1.2)	0.093

Overall Survival improvement was observed regardless of tumor PD-L1 status (greater effect in PD-L1 positive tumors)

1. O'Shaughnessy et al., 2020 San Antonio Breast Cancer Symposium (SABCS), Poster #PD1-06. Note: primary endpoints relating to reduction in severe neutropenia not achieved in this study.
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G1 THERAPEUTICS

Initiating TNBC Pivotal Trial (1L and 2L Cohorts) in 1H 2021

Strong evidence of efficacy across subsets and line of treatment in Phase 2 trial Evaluating 1L checkpoint-naïve and 2L checkpoint-experienced patients

PRIMARY ENDPOINT:
Overall survival

SECONDARY ENDPOINTS:
PRO, myelopreservation measures, PFS/ORR

TARGET ENROLLMENT:
~170 1L and ~80 2L participants

Pivotal study evaluating trilaciclib in mTNBC (PD-L1 positive and negative patients) complements ongoing I-SPY 2 Phase 2 Neoadjuvant BC study

G1 THERAPEUTICS

Initiating Two Additional Trilaciclib Phase 2 Trials in 1H 2021

1L Bladder Study (anti-PD-L1 combination)

Strong rationale for trilaciclib + chemo + I/O in 1L bladder cancer

- Known immunogenic tumor responsive to chemo + I/O
- Data suggests synergistic effect of trilaciclib + checkpoint[1-3]
- Similar chemo as TNBC study (gemcitabine/platinum)
- Benefits of treating patients until progression

Interim data expected in late 2022

- Primary aim to evaluate anti-tumor efficacy
- Randomized open-label study design

2L / 3L NSCLC Study (post-checkpoint)

Important area to demonstrate benefits of trilaciclib in post-checkpoint setting

- Known immunogenic tumor
- Trilaciclib mechanism is distinct from checkpoints
- High unmet need as treatment options limited in 2L / 3L
- Complementary commercial fit with SCLC indication

Interim data expected in early 2023

- Primary aim to evaluate anti-tumor efficacy
- Randomized double-blind study

Important future expansion areas for trilaciclib with data available in next 2 – 3 years

1. Lai et al., Journal for ImmunoTherapy of Cancer 2020; 8:e000847. doi:10.1136/jitc-2020-000847.
2. Deng et al., Cancer Discov. 2018;8(2):216- 33.
3. Daniel et al., 2019 European Society for Medical Oncology (ESMO), Abstract # 1742PD

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5. Continue managing investor capital efficiently

G1 THERAPEUTICS

Rintodestrant Demonstrates a Favorable Oral SERD* Profile

Fulvestrant is currently only SERD available

- Proven approach but painful intramuscular injections limit use to 2L and preclude use in earlier lines of therapy
- An oral SERD has potential to move into earlier lines of ER-positive breast cancer therapy

Rintodestrant monotherapy Phase 1b findings to date:

- Favorable tolerability - AEs mostly Grade 1 or Grade 2
- Strong ER target engagement/occupancy with evidence of anti-tumor activity in heavily pre-treated patients

40-patient Phase 2 combination trial with CDK4/6 inhibitor palbociclib ongoing; data in 2Q21

Phase 2 combination data will be important to help secure partner to fund Phase 3 investment

* SERD = Selective Estrogen Receptor Degrader

Next steps will be evaluated following data readout expected in 2Q21

G1 THERAPEUTICS

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5. **Continue managing investor capital efficiently**

G1 THERAPEUTICS

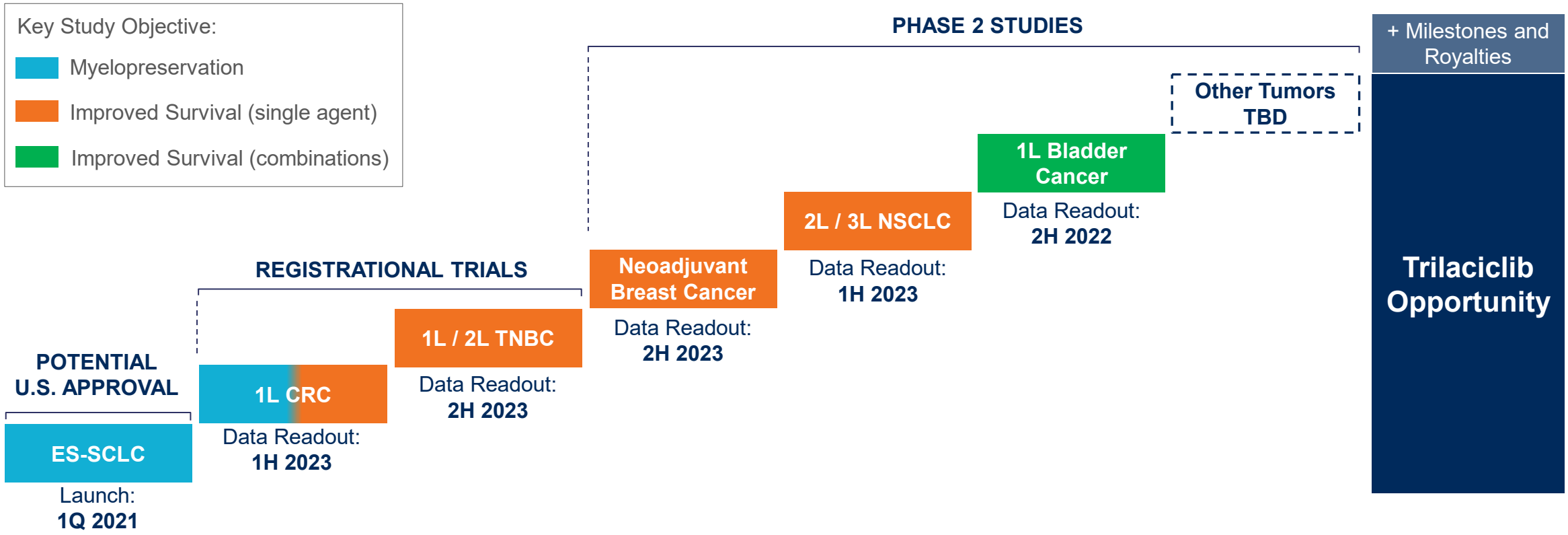
Continue to Efficiently Manage Capital

- **~$207M cash at year-end 2020 provides runway into second half of 2022**
- **Efficiently executing plan with lean organization of ~125 FTEs**
  - Utilizing capital efficient promotion arrangement with Boehringer Ingelheim for trilaciclib U.S. launch in SCLC
  - Expect to leverage co-development opportunities with partner Simcere for potential cost and timing efficiencies
- **Access to debt facility up to $100M total ($20M drawn to date)**
- **Potential future milestones (up to $486M) and royalties from licensing agreements**

Efficiently managing capital with a lean organization and benefiting from existing partnership arrangements

G1 THERAPEUTICS

Maximizing Value of Trilaciclib



Expect ES-SCLC launch in 1Q 2021 and multiple data readouts to drive expansion and long-term growth

G1 THERAPEUTICS