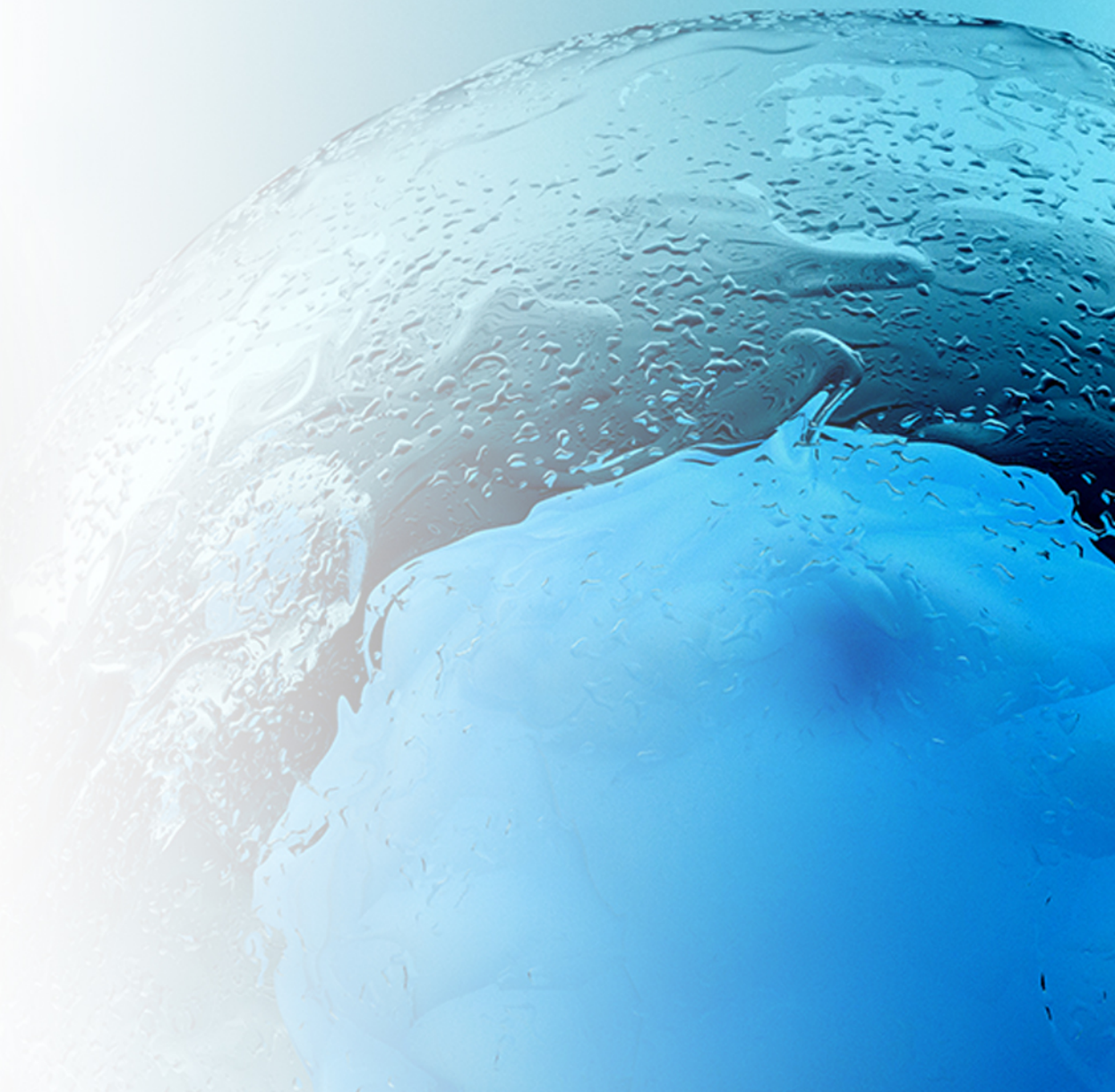
NOW APPROVED
COSELA™
trilaciclib for injection 300 mg

G1 THERAPEUTICS

Optimizing Chemotherapy, Advancing Survival

November 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 COSELA™(trilaciclib), rintodestrant and lerociclib, COSELA's possibility to improve patient outcomes across multiple indications, rintodestrant's potential as an 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. Rintodestrant and lerociclib are not approved by the FDA. The safety or effectiveness of 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

G1 Therapeutics
COSELA™ (trilaciclib) is a Cornerstone Therapy

- Launching COSELA in extensive-stage small cell lung cancer
  - No competition; no traditional headwinds
  - Experiencing a variety of tailwinds, including excellent reimbursement
  - Strategically priced to be budget neutral
- New G1 sales team to address execution & access at top tier accounts
- Deep pipeline of ongoing and planned trilaciclib clinical trials
  - Designed to maximize applicability to future treatment paradigms
  - Various chemo backbones / combination with other therapeutic agents
- Assessing synergies with other novel antitumor agents for future study
- Entering multi-year data-rich period with initial clinical data expected in:
  - 2H 2022: 1L bladder cancer, ADC combination, and MOA Phase 2 data
  - 1H 2023: 1L CRC Phase 3 data
  - 2H 2023: Phase 3 TNBC data
  - 2024+: Additional data from combination trials
- Cash runway into 2024

Trilaciclib is a pipeline-in-a-molecule development opportunity

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Chemo is a Mainstay of Cancer Therapy Despite Shortcomings

Over 1 million cancer patients receive chemo in North America 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

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COSELA: Novel Approach Designed to Address Shortcomings of Chemo-Based Therapies

COSELA
Transient IV CDK4/6 inhibitor
Temporarily blocks progression through the cell cycle

Leads to multiple potential downstream effects

Helps protect HSPCs and myeloid and lymphoid cell lineages from damage caused by chemotherapy[1-3]

- Neutrophils
- Erythrocytes
- Platelets
- T-lymphocytes
- B-lymphocytes

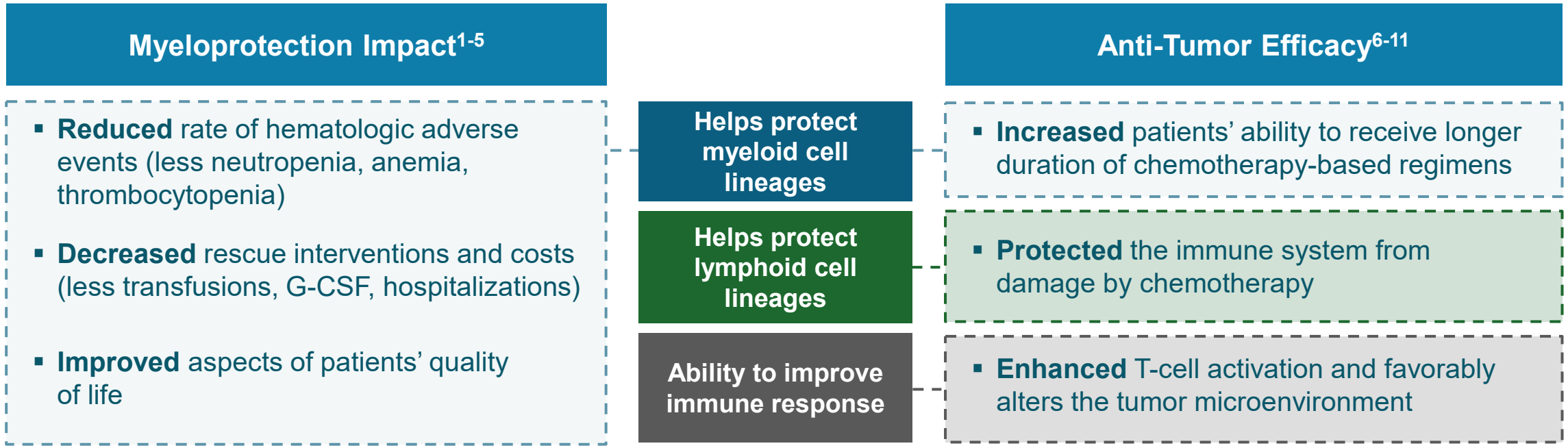
Ability to improve the immune response when administered with chemotherapy[4-9]

- Enhances T-cell activation
- Favorably alters tumor microenvironment

Potential to benefit patients receiving chemotherapy across multiple tumor types

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.

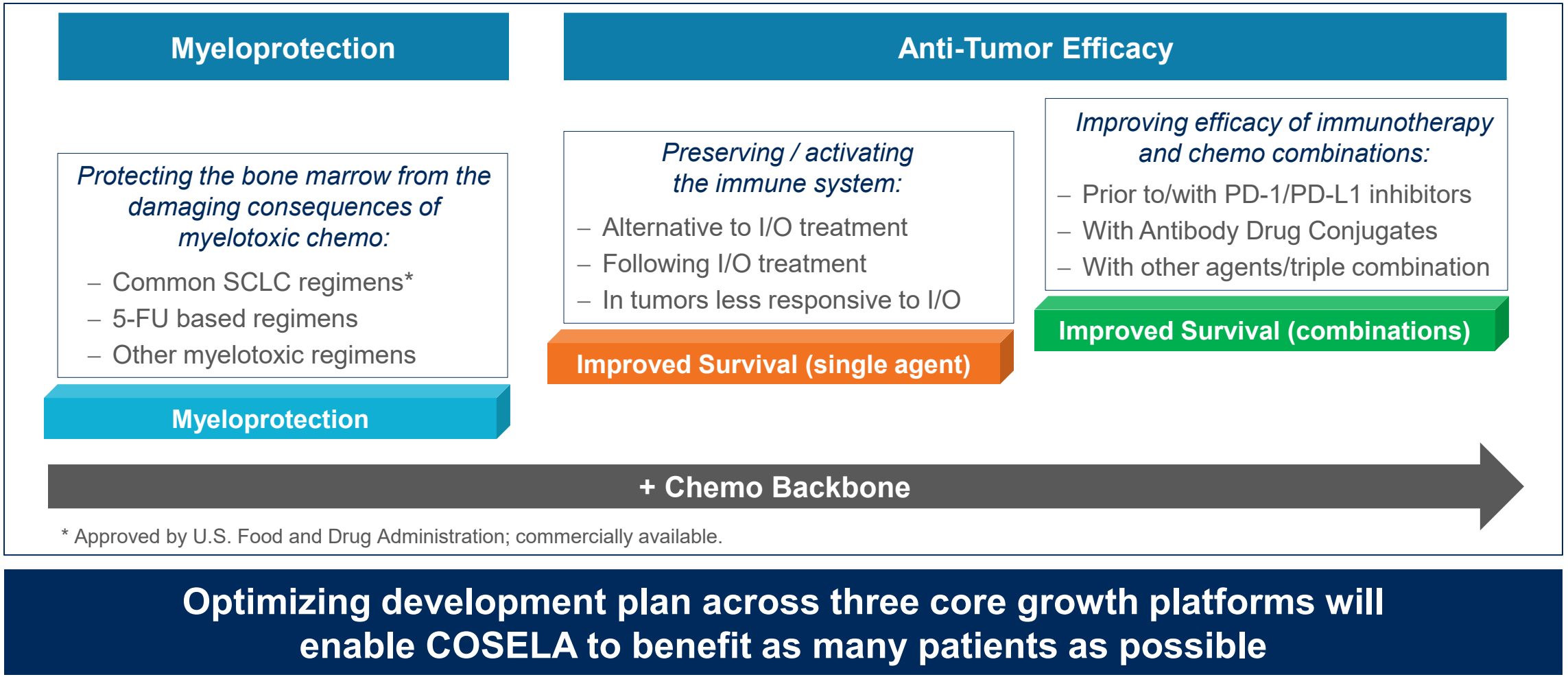
COSELA Demonstrated Meaningful Benefits Across Studies



Approved as myeloprotective therapy in ES-SCLC with most common chemotherapy regimens; increased anti-tumor efficacy being evaluated in additional trials

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 COSELA



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

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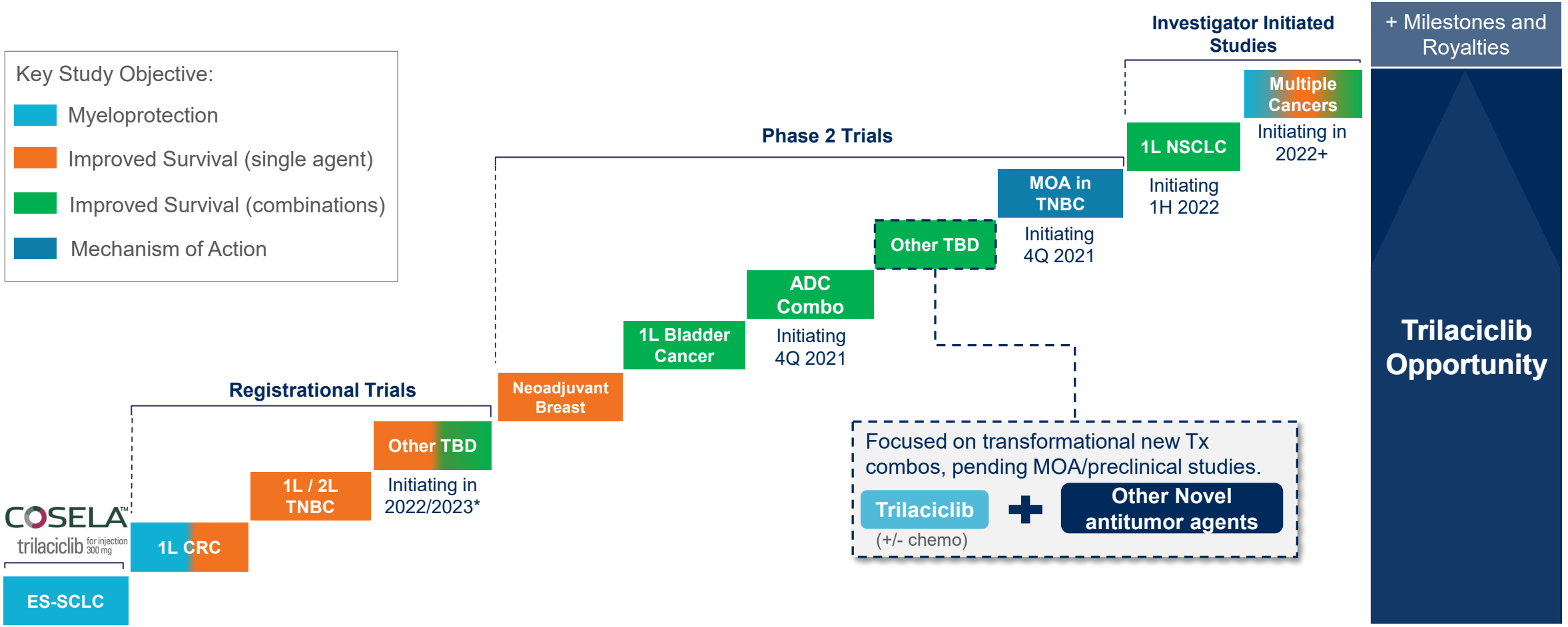
Pipeline-in-a-Molecule Opportunity Beyond ES-SCLC Launch

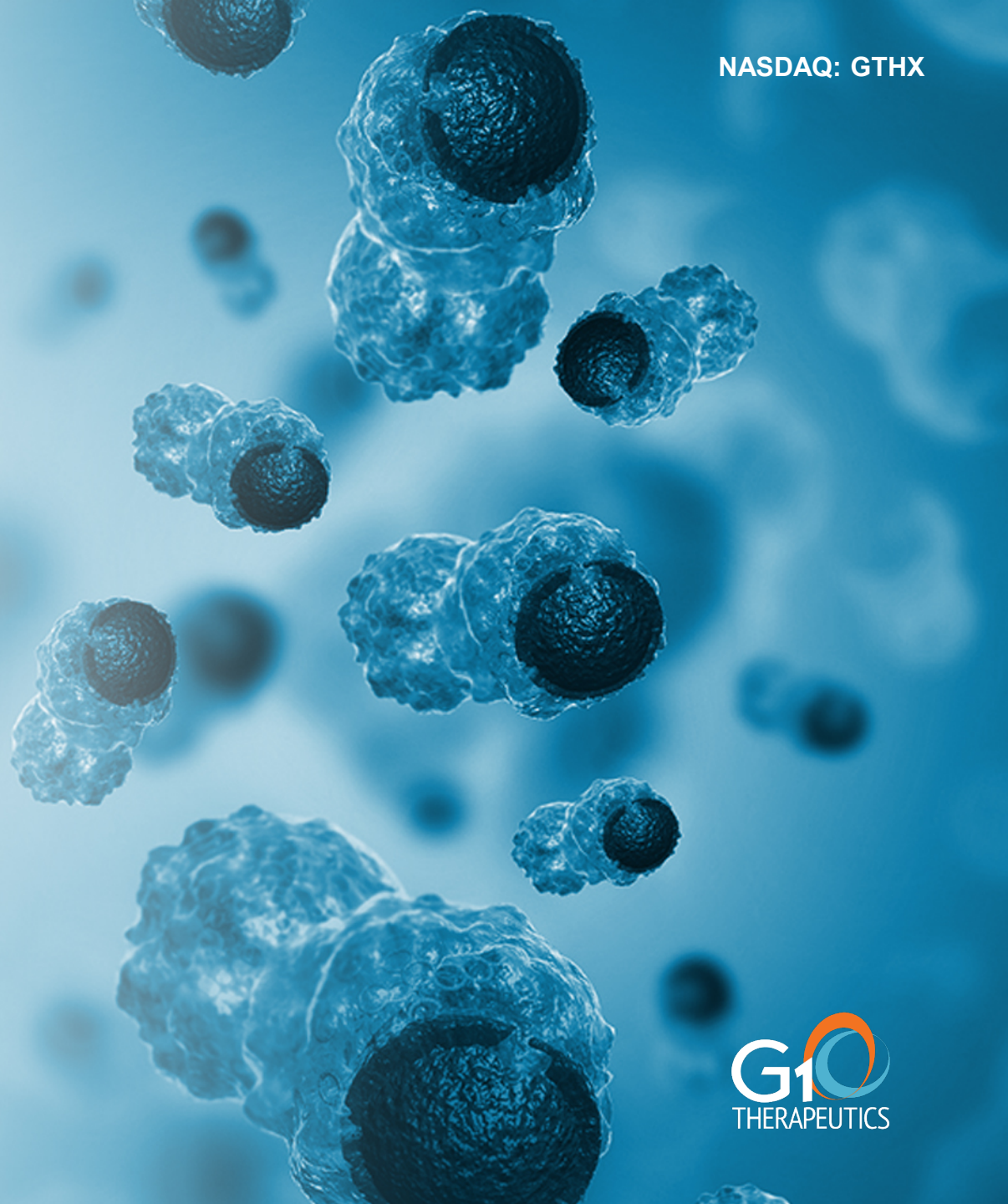


Aggressively pursuing development in areas of high strategic importance where trilaciclib is most likely to provide meaningful benefits to patients

*Assumes positive Phase 2 data readouts

NASDAQ: GTHX

COSELA™ (trilaciclib) Commercial Update



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Myelosuppression is Managed with Lineage Specific Interventions

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

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COSELA's Opportunity to Impact Many ES-SCLC Lives

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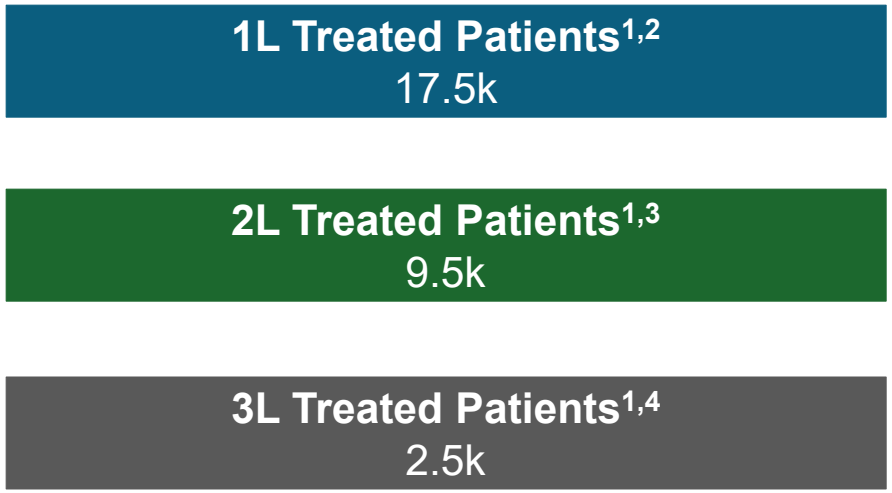
~30k ES-SCLC Patients Treated Annually in the U.S.[1]



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 COSELA

- ~60% of ES-SCLC patients covered by Medicare (expect Medicare to cover label at launch)

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

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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 COSELA G1T28-02 and G1T28-05 study control arms.

COSELA™

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Approved by U.S. Food and Drug Administration to decrease the incidence of chemotherapy-induced myelosuppression in adult patients when administered prior to a platinum/etoposide-containing regimen or topotecan-containing regimen for extensive-stage small cell lung cancer

First and only proactive multilineage myeloprotection therapy to decrease the incidence of chemotherapy-induced myelosuppression

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COSELA Helps Manage Multiple Myelosuppressive Consequences

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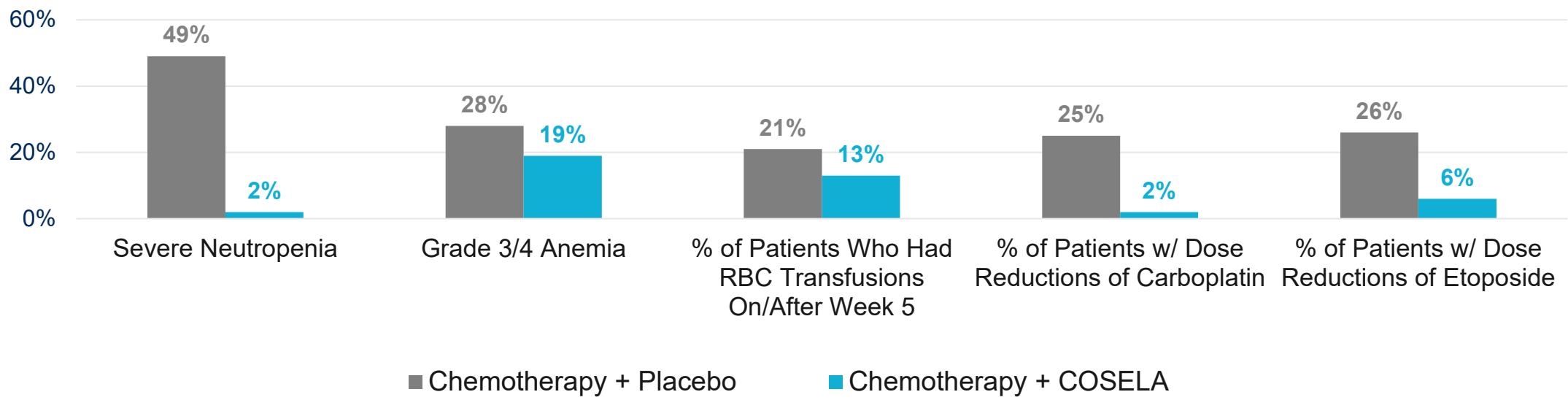
Reduced Incidence of Multi-lineage Myelosuppression in 1L SCLC Treated with Etoposide/Carboplatin/Atezolizumab[1]



Clinical Results: COSELA demonstrated reductions in multiple myelosuppressive consequences

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[1]COSELA™ (trilaciclib) label, 10003 Rev. 2/2021 US-2100006

COSELA's Hematologic Adverse Reactions Summary is Meaningful to HCPs

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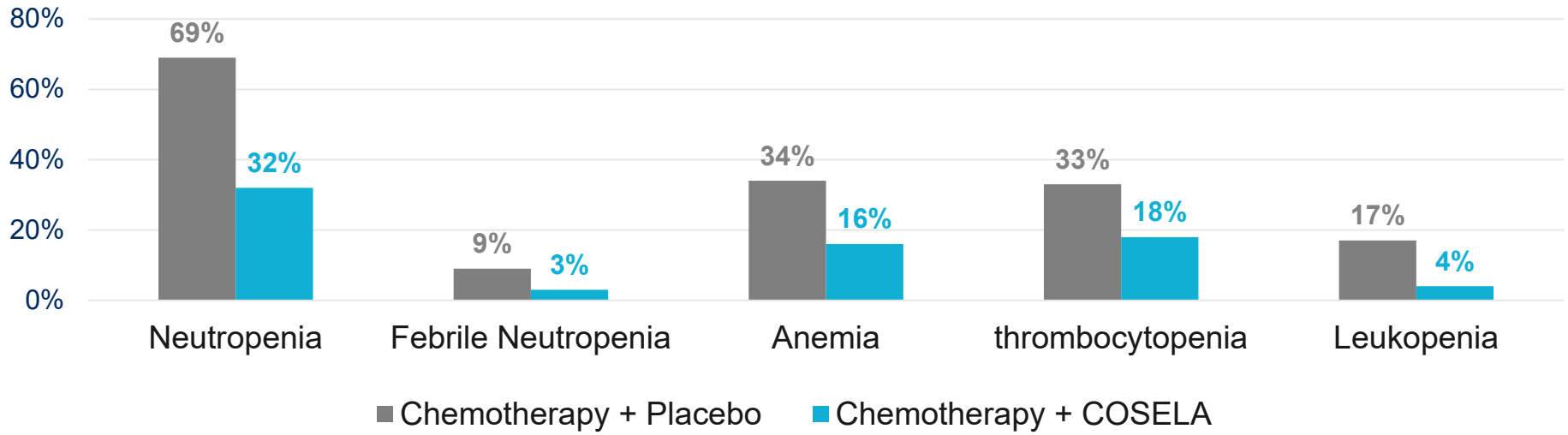
Grade 3/4 hematological adverse reactions occurring in patients treated with COSELA and placebo



COSELA demonstrated reductions in hematologic adverse events across multiple randomized SCLC studies

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

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Opportunity to Improve Quality of Life with COSELA

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."

COSELA may help patient functioning in ES-SCLC patients:

Median Time to Deterioration[2]

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

Measure	Placebo (months)	COSELA (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: Proactive protection enables better quality of life for patients in this palliative treatment setting

G1 THERAPEUTICS

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., Effects of Trilaciclib on Chemotherapy-Induced Myelosuppression and Patient-Reported Outcomes in Patients with Extensive-Stage Small Cell Lung Cancer: Pooled Results from Three Phase II Randomized, Double-Blind, Placebo-Controlled Studies; Clinical Lung Cancer, March 2021

COSELA's Label Includes Multi-Lineage Data
Important to Health Care Providers

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SIGNIFICANTLY REDUCED THE INCIDENCE AND DURATION OF SEVERE NEUTROPENIA (PRIMARY ENDPOINTS)

96% reduction in severe neutropenia with COSELA + E/P/A Regimen and **0 days** of severe neutropenia in cycle 1 vs **4** days without COSELA (P<0.0001)

Adjusted relative risk 0.038 (95% CI, 0.008, 0.195) and mean difference -3.6 (95% CI, -4.9, -2.3), respectively

DECREASED RATE OF DOSE REDUCTIONS (SECONDARY ENDPOINT)

The rate of all-cause chemotherapy dose reductions (events per 100 cycles) was significantly lower with COSELA: **2.1** vs **8.5** without COSELA (P=0.0195)

Adjusted relative risk 0.242 (95% CI, 0.079, 0.742)

INCIDENCE OF GRADE 3/4 ANEMIA AND RED BLOOD CELL (RBC) TRANSFUSIONS (SECONDARY ENDPOINTS)

The incidence of Grade 3/4 anemia was **28%** without COSELA vs **19%** with COSELA, and the incidence of RBC transfusions was **21%** without COSELA vs **13%** with COSELA

Adjusted relative risk 0.663 (95% CI, 0.336, 1.310) and 0.642 (95% CI, 0.294, 1.404), respectively

INTEGRATED SAFETY ACROSS STUDIES

The most common adverse reactions (≥10%) were fatigue, hypocalcemia, hypokalemia, hypophosphatemia, aspartate aminotransferase increased, headache, and pneumonia

G1 THERAPEUTICS

3Q2021: Commercial Tailwinds and Headwinds

Tailwinds

- Exceptional reimbursement with permanent J-code
- High awareness and intention to treat
- Strong user experience and reordering
- Strategically priced
- Fits within chemotherapy workflow to help manage CIM consequences
- Experience drives institutional depth

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Headwinds

- Lack of access to top tier accounts and high-quality relationships
- Variable geographic sales performance
- Slow return to in-person visits and external engagement outside the office

Decisively and actively addressing headwinds, including by hiring and deploying supplemental G1 sales force focused on top accounts

Actively Addressing Headwinds

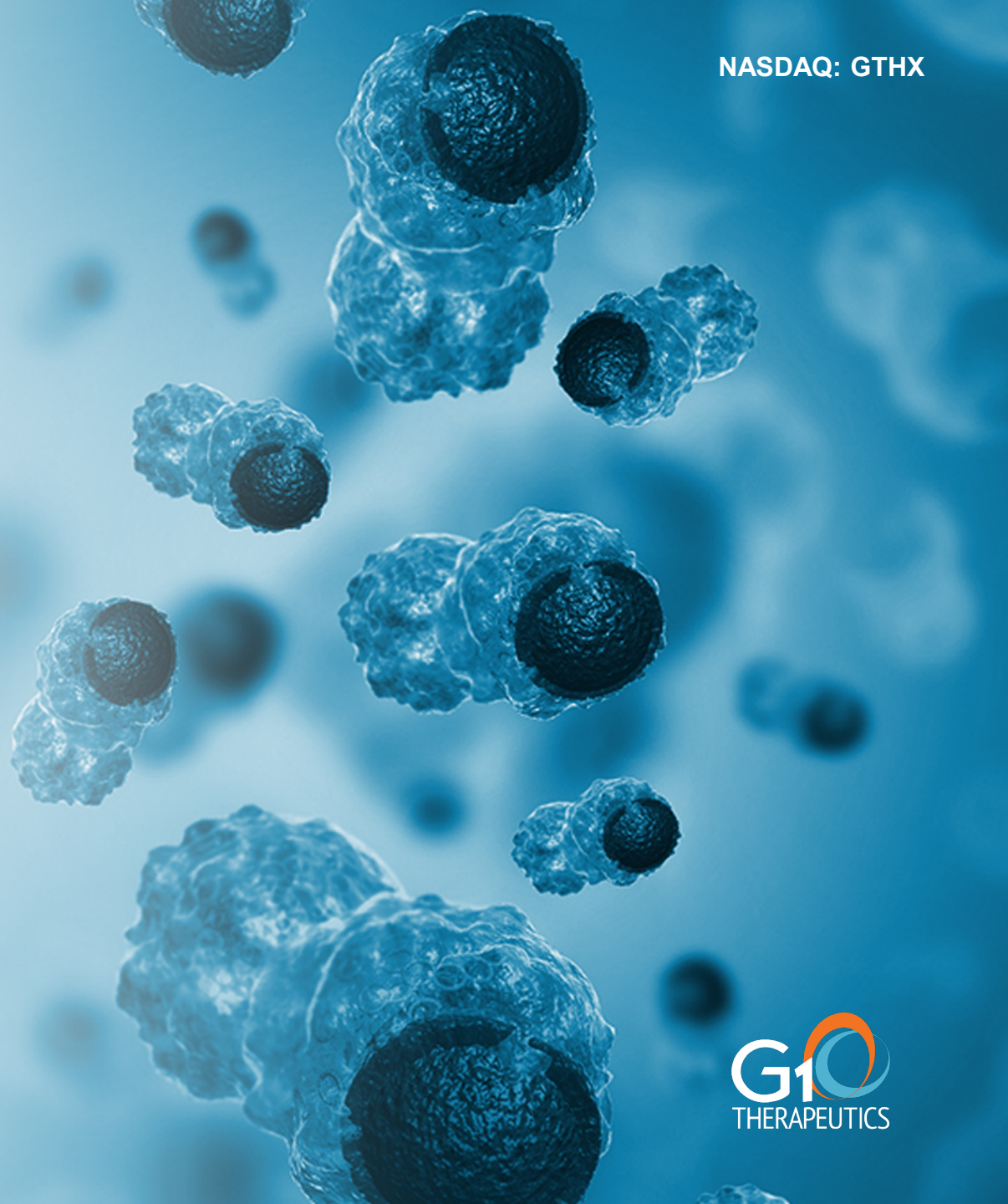
Hiring and Deploying 15-Person Sales Force to Supplement BI Oncology Sales Team

- Will allow G1 to target top accounts to accelerate sales activities and help maximize the adoption of COSELA
- Focus on execution / access / driving depth in largest accounts that provide care for 50%+ of patients
- Hiring, training, and deploying as they arrive; first hired in early November
  - Goal: majority hired by year end 2021
  - Should allow G1 to expedite impact on uptake and usage
- Strong interest in joining G1 based on innovation and opportunity:
  - COSELA is a novel, breakthrough therapy and priority-reviewed drug with a novel mechanism of action, dual committee endorsement from NCCN, strong reimbursement coverage, and no competition
  - Opportunity to participate in driving the growth and success of COSELA

New G1 sales force provides **opportunity to improve uptake and usage** to enable COSELA to impact the lives of many more patients with ES-SCLC

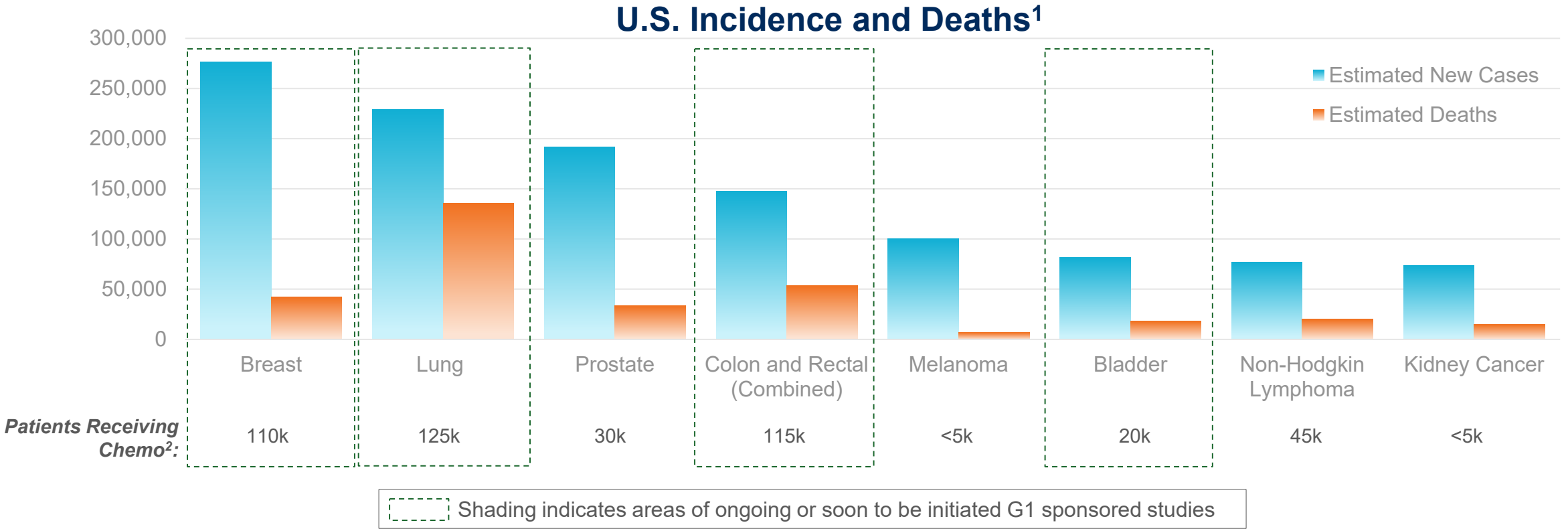
NASDAQ: GTHX

Trilaciclib Clinical Program



G1 THERAPEUTICS

Aggressively Pursuing Development in Common Tumor Types



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 Studies Across Common Tumor Types

Cancer Type	Indication	Study Size	Phase 2	Phase 3	Approval
Lung	ES-SCLC	NA			**Approved by U.S. Food and Drug Administration**
Colorectal	1L CRC	~300		**PRESERVE 1: Ongoing**	
Breast	1L TNBC[1]	~170		**PRESERVE 2: Ongoing**	
	2L TNBC[1] (Post-checkpoint treatment)	~80		**PRESERVE 2: Ongoing**	
	TNBC: MOA	TBA	**Initiating: 4Q 2021**		
	TNBC: ADC Combo	TBA	**Initiating: 4Q 2021**		
	Neoadjuvant	Adaptive	**I-SPY2: Ongoing**		
Bladder	1L Bladder (Checkpoint combination)	TBD	**PRESERVE 3: Ongoing**		

Registrational and Phase 2 trials ongoing; additional trials to develop data in combination with other agents to initiate in 4Q 2021

1/2L, first-/second-line; CRC, colorectal cancer; ES-SCLC, extensive-stage small cell lung cancer; TNBC, triple-negative breast cancer; MOA, mechanism of action

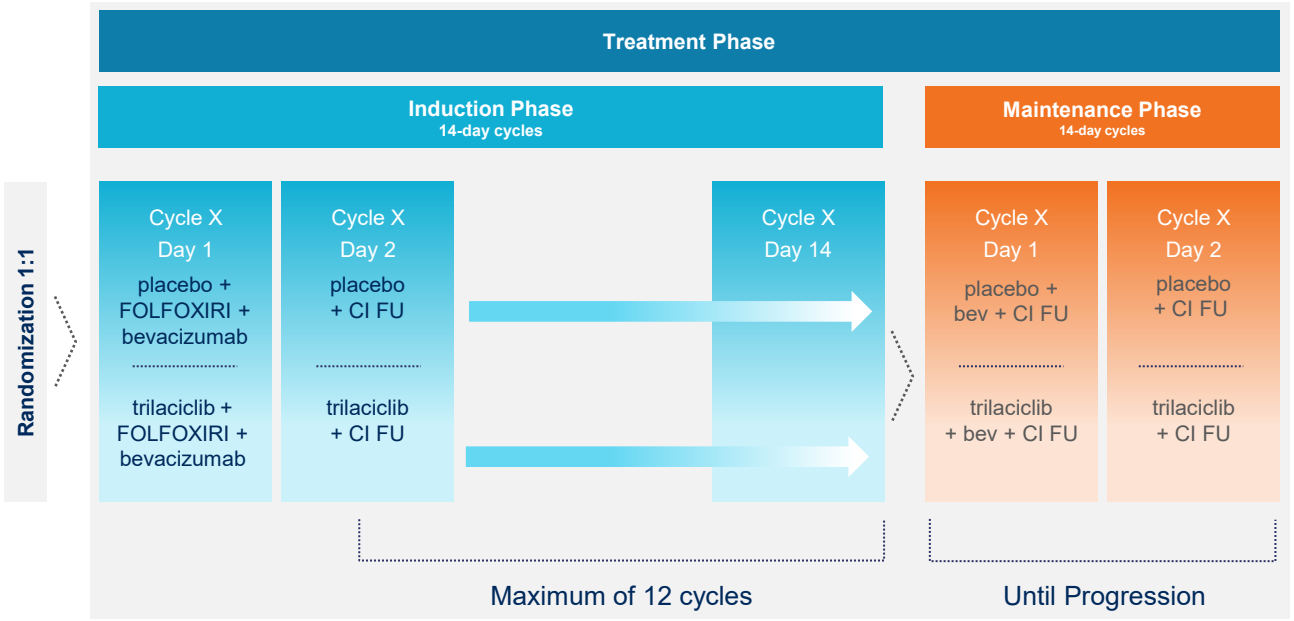
*1L TNBC and 2L TNBC cohorts being conducted under one study protocol.

The safety and efficacy of an investigational use of an approved product have not been established or approved by the FDA or other regulatory authorities.

Ongoing First-Line CRC Pivotal Trial: PRESERVE 1

FOLFOXIRI: most efficacious chemo regimen but highly myelosuppressive

Potential to significantly expand FOLFOXIRI usage supported by market research



PRIMARY ENDPOINT:
Myeloprotection

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

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Ongoing TNBC Pivotal Trial (1L / 2L Cohorts): PRESERVE 2

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

PRIMARY ENDPOINT:
Overall survival

SECONDARY ENDPOINTS:
PRO, myeloprotection measures, PFS/ORR

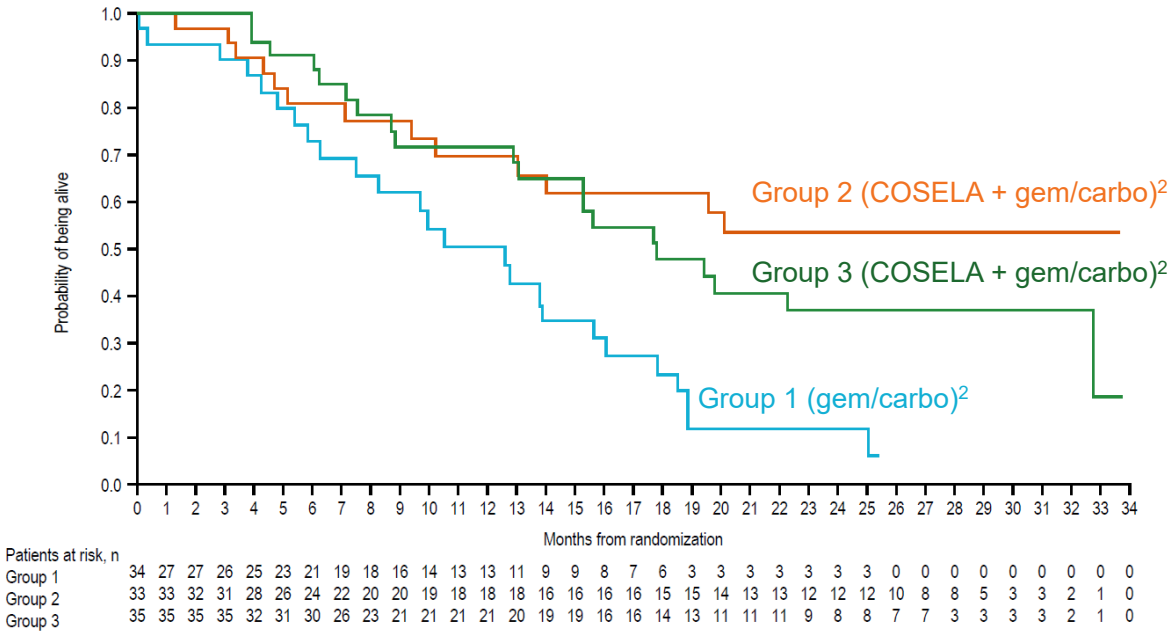
TARGET ENROLLMENT:
~170 1L and ~80 2L participants

Pivotal study evaluating trilaciclib in mTNBC (PD-L1 positive and negative patients) building upon robust OS benefit observed in prior Phase 2 study"

1. O'Shaughnessy et al., 2020 San Antonio Breast Cancer Symposium (SABCS), Poster #PD1-06

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 COSELA: COSELA administered on the day of chemotherapy (Group 2) or COSELA administered the day prior to and the day of chemotherapy (Group 3).

OS Improvement Observed, 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.
2. Patients randomized to receive gem/carbo chemotherapy only (Group 1) or gem/carbo plus one of two dosing schedules of COSELA: COSELA administered on the day of chemotherapy (Group 2) or COSELA administered the day prior to and the day of chemotherapy (Group 3).

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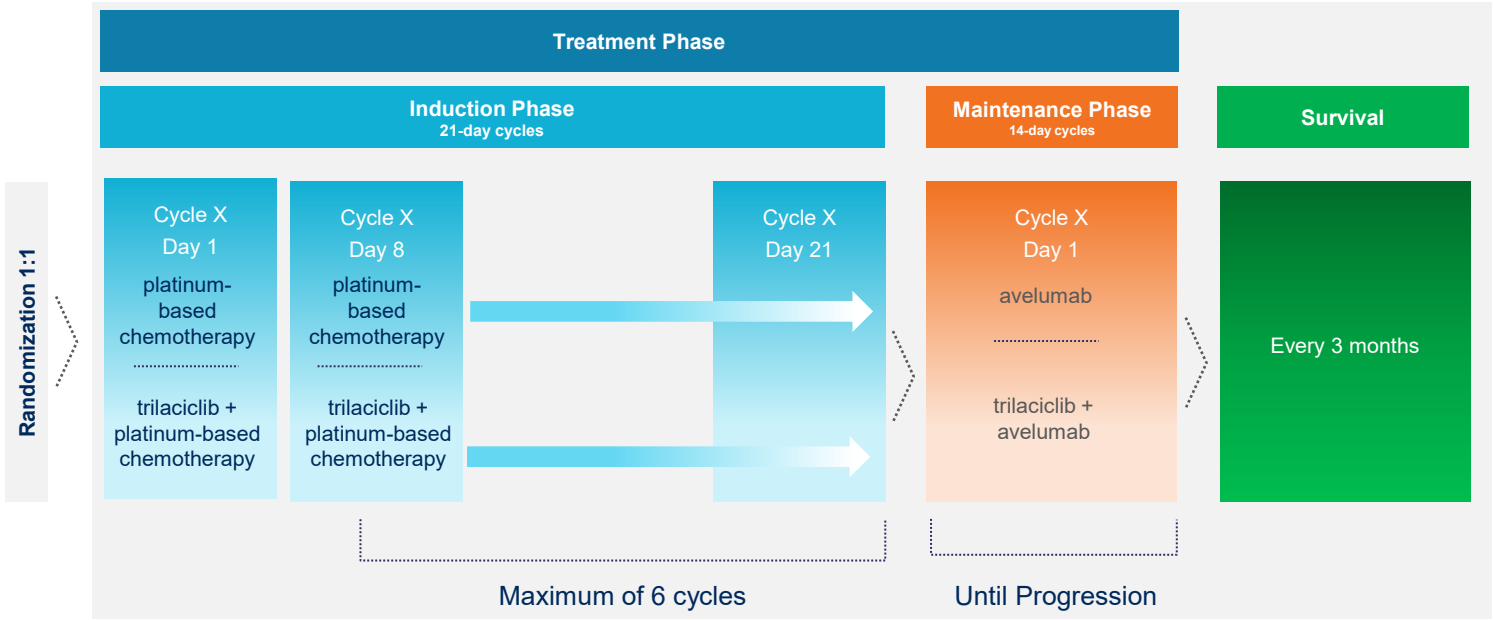
Ongoing Bladder (mUC) Study: PRESERVE 3

Building on strong rationale for trilaciclib + chemo + checkpoint inhibitor; data to date suggest potential for synergistic effect in known immunogenic tumor



PRIMARY ENDPOINT:
PFS

SECONDARY ENDPOINTS:
ORR, DCR, DOR, OS, myeloprotection measures

TARGET ENROLLMENT:
~90 participants

PATIENTS TREATED UNTIL PROGRESSION

Phase 2 study will provide meaningful data for trilaciclib in a known immunogenic setting; expected to help define future combination studies

G1 THERAPEUTICS

Two New Trilaciclib Phase 2 Trials in 2021

Antibody-Drug Conjugate Combo (ADC): 4Q21

Potential synergies for trilaciclib + ADC (sacitizumab-govitevcan hziy) combination

- Trilaciclib (in Phase 2 trial) and ADCs have both shown clinically meaningful and substantial improvements in overall survival
- Could act synergistically to improve patient outcome and reduce myelosuppressive side effects
- Antitumor efficacy and myeloprotective endpoints are being assessed in this trial.

Initial results of this study are expected in late 2022

Mechanism of Action (MOA): 4Q21

Designed to Further Investigate Immune-Based Antitumor MOA

- Evaluating changes in the tumor microenvironment post-dose
- Pathologic complete response endpoints will be evaluated in this trial
- Generating data to help identify additional tumor types and new treatment combinations to pursue in future studies

Initial results of this study are expected in late 2022

Important future expansion areas for trilaciclib with initial data expected in next 12 months

G1 THERAPEUTICS

Opportunity to Generate Meaningful Incremental Value from Out-Licensed Assets

Trilaciclib	Out-licensed	Greater China	Simcere	Up to $156M in milestones; double-digit royalties on annual net sales
Rintodestrant				Combination data presented at ASCO 2021; Currently evaluating partnering options
Lerociclib	Out-licensed	US EU, Japan	EQRx	Up to $290M in milestones; tiered royalties on annual net sales
		Asia PAC	GENOR BIOPHARMA	Up to $40M in milestones; tiered royalties on annual net sales
CDK2 Discovery Platform	Out-licensed		ARC THERAPEUTICS Connecting science and patients	

Potential Total Milestones of $486 Million; $475 Million Remaining as of June 30, 2021

G1 THERAPEUTICS

Rintodestrant Demonstrated a Favorable Oral SERD* Profile in Clinical Trials

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[1]:

- 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

Data from 40-patient Phase 1b combination arm with palbociclib presented at ASCO[2]:

- Patients had high degree of prior chemo in the advanced setting (48%); tend to respond less well to CDK4/6 inhibitors in combination with ETs
- Very well tolerated; no reported discontinuations due to TEAEs
- No ocular toxicity or bradycardia observed, both common with some other oral SERDs
- 60% CBR24 achieved in full analysis set
- 73% CBR24 in early relapse

* SERD = Selective Estrogen Receptor Degrader

Currently evaluating partnering options for rintodestrant

G1 THERAPEUTICS

[1]Aftimos *et al*., 2020 San Antonio Breast Cancer Symposium (SABCS), Poster #PS12-04
[2]Maglakelidze *et al*., American Society of Clinical Oncology (ASCO), Poster #1063

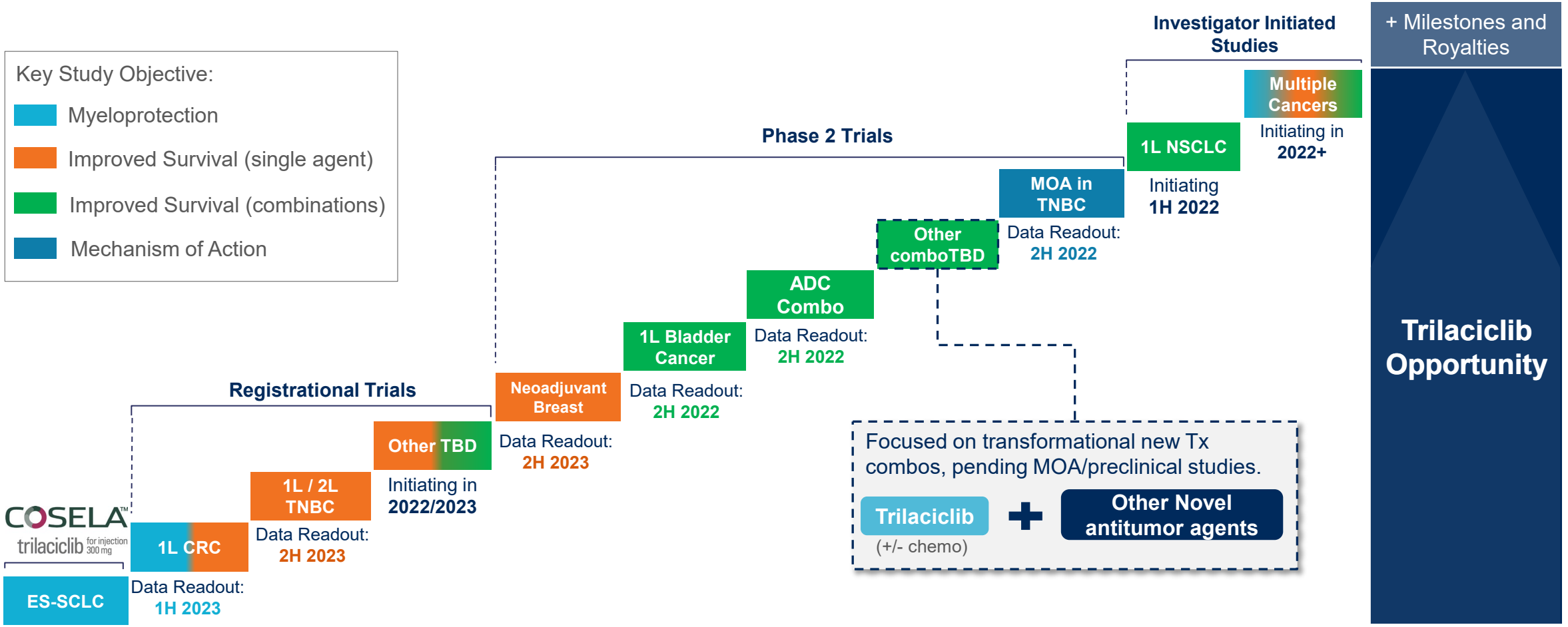
Continue to Efficiently Manage Capital

- **Cash runway into 2024**
  - Cash runway comprised of
    - $212M in cash and cash equivalents as of September 30, 2021
    - Incremental $45 million ($75 million in total) drawn down from amended and upsized $150 million debt facility; additional $25 million is currently available as of amendment closing
- **Potential future milestones (up to $475M) and royalties from licensing agreements**
- **Efficiently executing plan with lean organization**
  - Expect to leverage co-development opportunities with partner Simcere for potential cost and timing efficiencies

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

G1 THERAPEUTICS

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



Multiple data readouts to drive expansion and long-term growth