Innovations in Oncology:
The Science of Trilaciclib

September 15, 2022

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 expectations for COSELA® to impact survival, COSELA's ability to impact the future of standard of care, COSLEA's dual benefits efficacy, and COSELA's preclinical data may not be indicative of results in clinical trials. Each of these forward-looking statements involves risks and uncertainties. Factors that may cause our actual results to differ from those expressed or implied in the forward-looking statements in this presentation are discussed in our filings with the U.S. Securities and Exchange Commission, including the "Risk Factors" sections contained therein and include, but are not limited to, our ability to continue to commercialize COSELA (trilaciclib); our ability to complete clinical trials for, obtain approvals for and commercialize additional indications of COSELA; our 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 commercial-stage company; and market conditions. Except as required by law, we assume no obligation to update any forward-looking statements contained herein to reflect any change in expectations, even as new information becomes available.

Agenda

Welcome and Agenda
Will Roberts, Vice President, Investor Relations
& Corporate Communications

Introduction to G1 Therapeutics
Jack Bailey, Chief Executive Officer

Trilaciclib: From Premise to Promise
Raj Malik, M.D., Chief Medical Officer

Trilaciclib (transient CDK4/6/i) as Immunomodulatory Therapy for Cancer
Shom Goel, B Med Sci, MBBS, FRACP, Ph.D.,
Peter MacCallum Cancer Centre, The University of Melbourne

The Synergistic Potential of Trilaciclib
John Yi, Ph.D., Sr. Director, Translational Medicine

Clinical Development: Expanding the Trilaciclib Opportunity
Symantha Melemed, Ph.D., Vice President, Clinical Development

Moderated Discussion: The Colorectal Cancer Treatment Landscape
Richard Goldberg, M.D., Professor Emeritus and former Director, West Virginia University Cancer Institute (WVUCI)
Moderator: Norm Nagl, Ph.D., Vice President, Medical Affairs

Trilaciclib Market Opportunity and Future Focus
Mark Avagliano, Chief Business Officer

Concluding Remarks and Transition to Q&A
Jack Bailey, Chief Executive Officer

Q&A with G1 Leadership

G1 THERAPEUTICS

Introduction to G1 Therapeutics

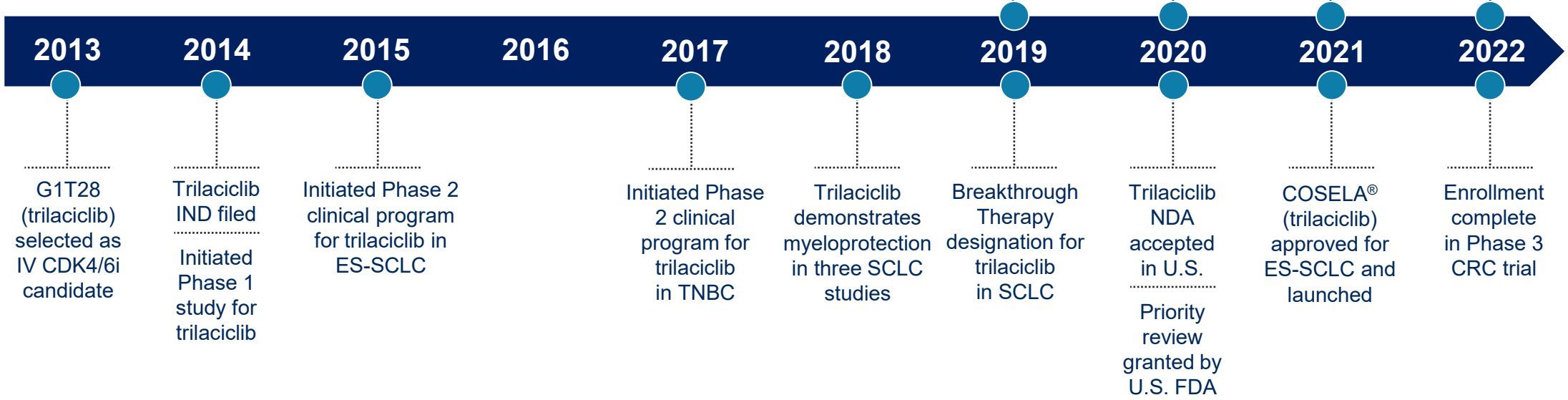
Jack Bailey, Chief Executive Officer

G1 and Trilaciclib

Leading Research into Cell Cycle Modulation since 2008

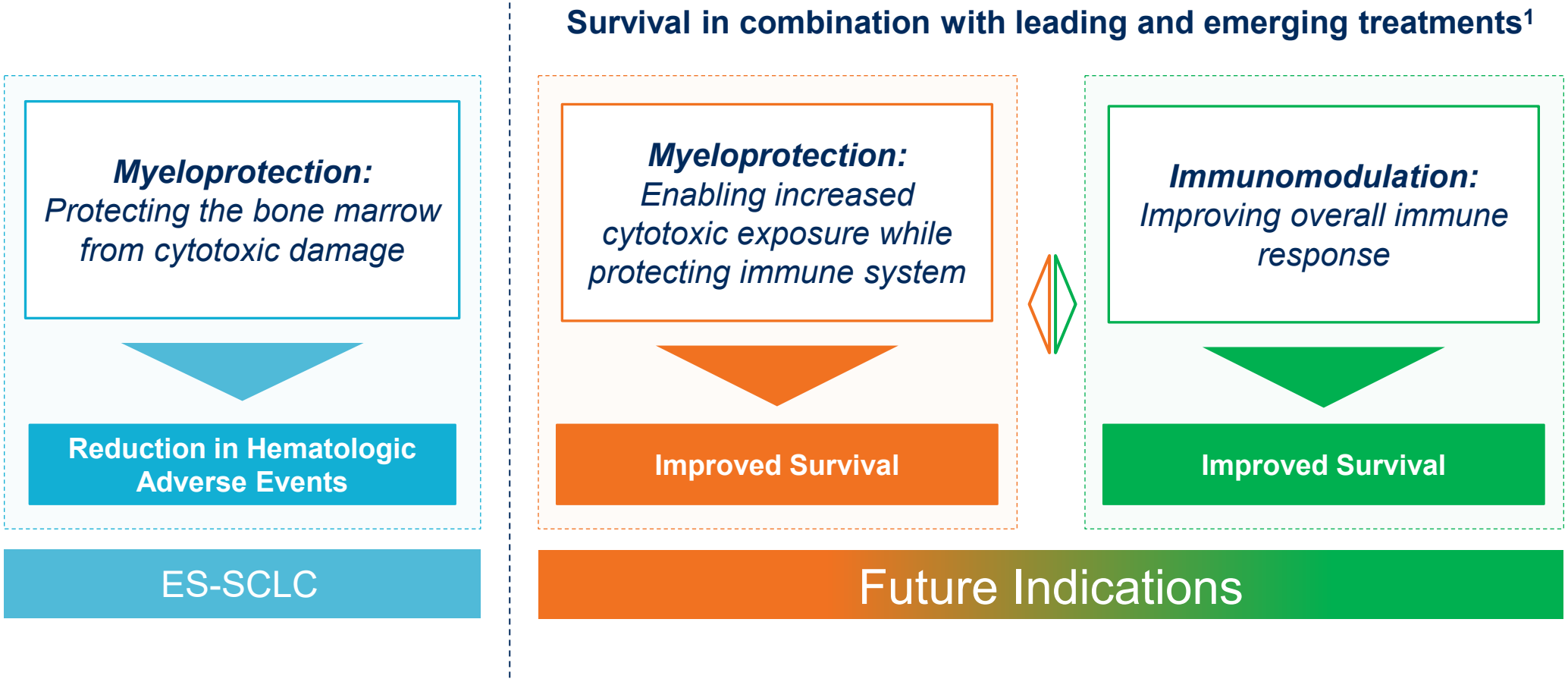
2008-2012

G1 founded by Ned Sharpless & Kwok-Kin Wong: Modulate the cell-cycle to protect the bone marrow from damage by chemotherapy



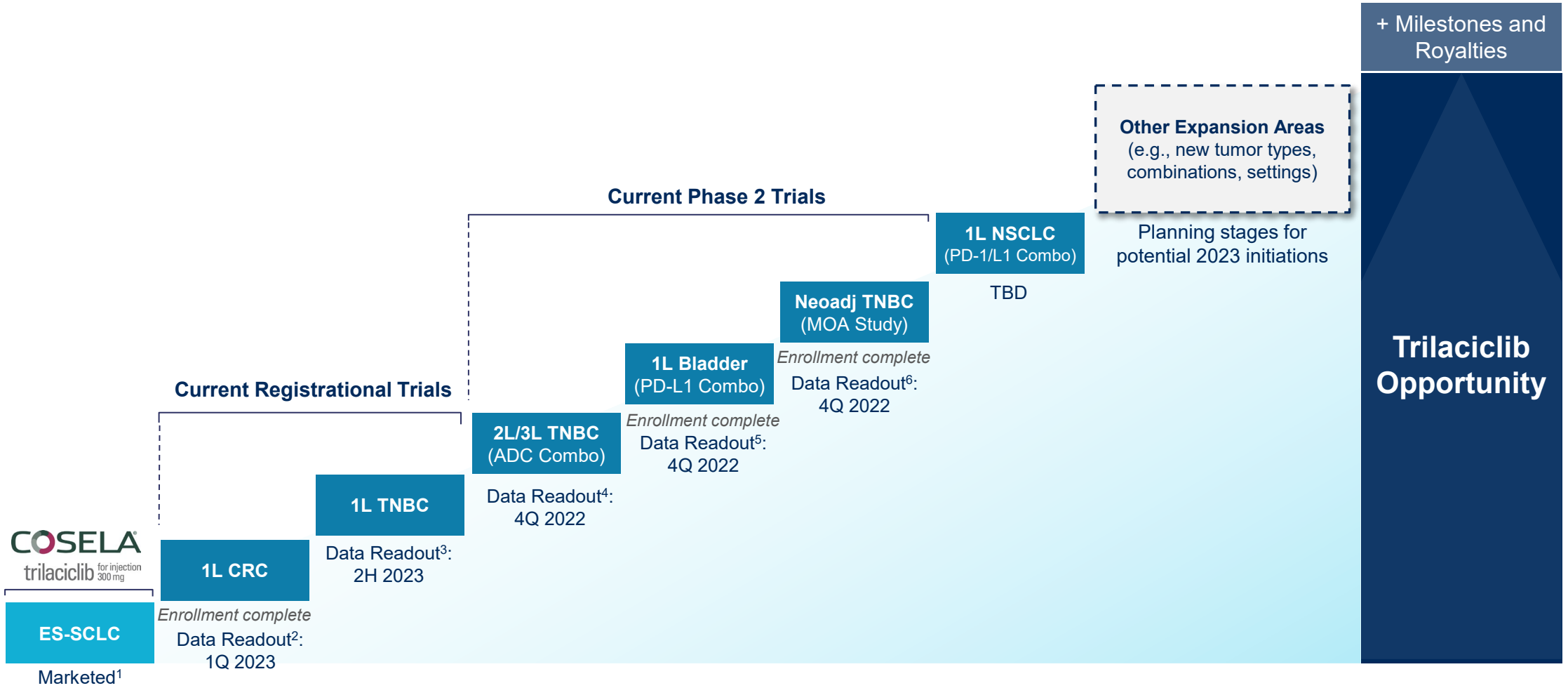
G1 THERAPEUTICS

Currently Pursuing Trilaciclib Across Key Growth Platforms



[1] *Clinical evaluation underway; 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.*

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



1. COSELA is marketed in the U.S. by G1 and conditionally approved in Greater China to be marketed by our partner, Simcere
2. 1L CRC data readout in 1Q 2023 expected to include results for myeloprotection and Objective Response Rate (ORR) endpoints
3. 1L TNBC data readout in 2H 2023 expected to include interim results for Overall Survival (OS); interim OS analysis to be conducted by its DMC in 2H 2023
4. 2L / 3L TNBC (in combination with an ADC) initial data in 4Q 2022 expected to include ORR and myeloprotection endpoints
5. 1L Bladder Cancer (in combination with an anti-PD-L1) initial data in 4Q 2022 expected to include ORR and myeloprotection endpoints
6. MOA in Neoadjuvant TNBC +/- PD-1 inhibitor (investigator discretion); data readout in 4Q 2022 to include results for immune endpoints; data readout in 1H 2023 to include pCR

Takeaways for Today

- Trilaciclib's unique effects attributable to transient, potent, and selective CDK4/6 inhibition and directly targeting the host
- Trilaciclib enhances multiple immunological processes within the cancer immunity cycle
- Potential for improved survival via improved immune response (immunomodulation) and increased cytotoxic exposure while protecting immune system (myeloprotection)
- New preclinical data show consistent synergistic potential
- Meaningful data read-outs starting in the next three months and continuing through 2023
- Trilaciclib represents a pipeline-in-a-molecule opportunity with significant expansion opportunities in future standard of care

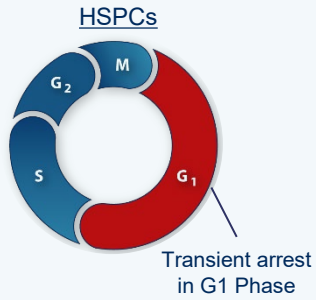
G1 THERAPEUTICS

Trilaciclib: From Premise to Promise

Raj Malik, M.D., Chief Medical Officer

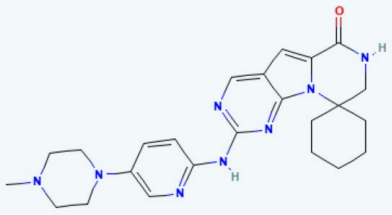
Evolution of G1 and Exciting Road Ahead

Original Premise



To protect HSPCs from damage caused by chemo through transient G1 arrest

Unique Product



Rationally designed and optimized a unique IV transient CDK4/6 inhibitor

Initial Indication

Demonstrated robust myeloprotection across three Phase 2 ES-SCLC studies

Robust OS in TNBC

OS hazard ratios in Ph2:

0.31 – 0.40

Robust survival effects in Ph2 study consistent with immune-modulation

Dual Benefits

Potential to improve overall survival through:

1. Increased cytotoxic exposure
2. Enhanced anti-tumor immunity

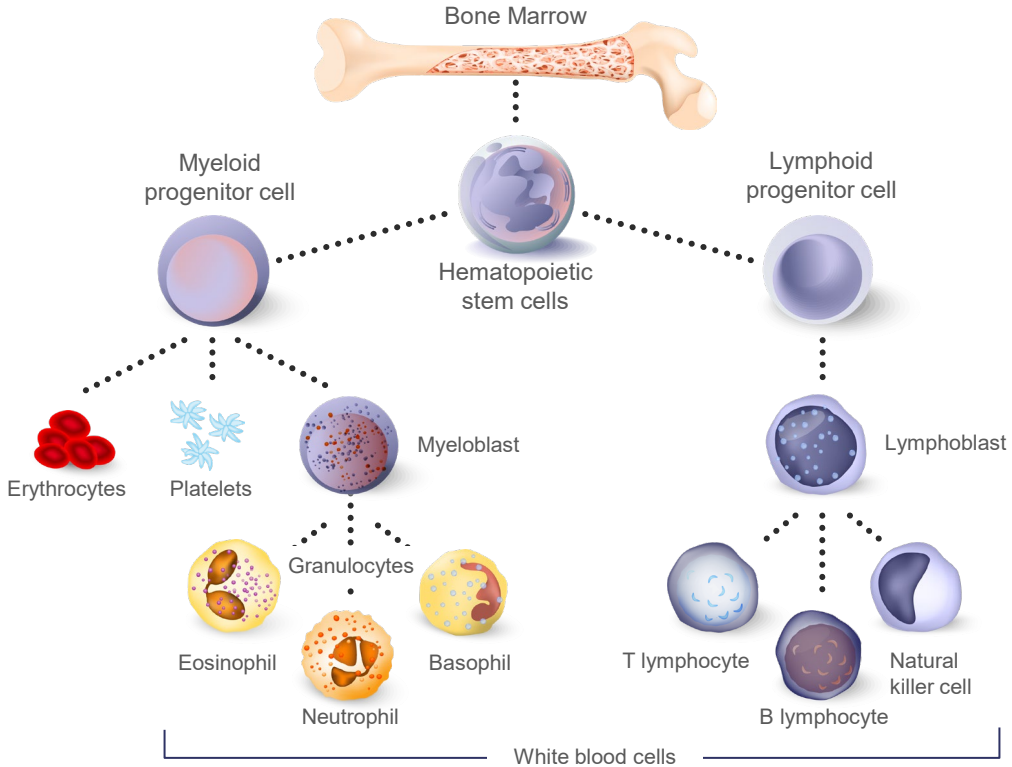
Aggressively investigating dual benefit impact across multiple tumor types

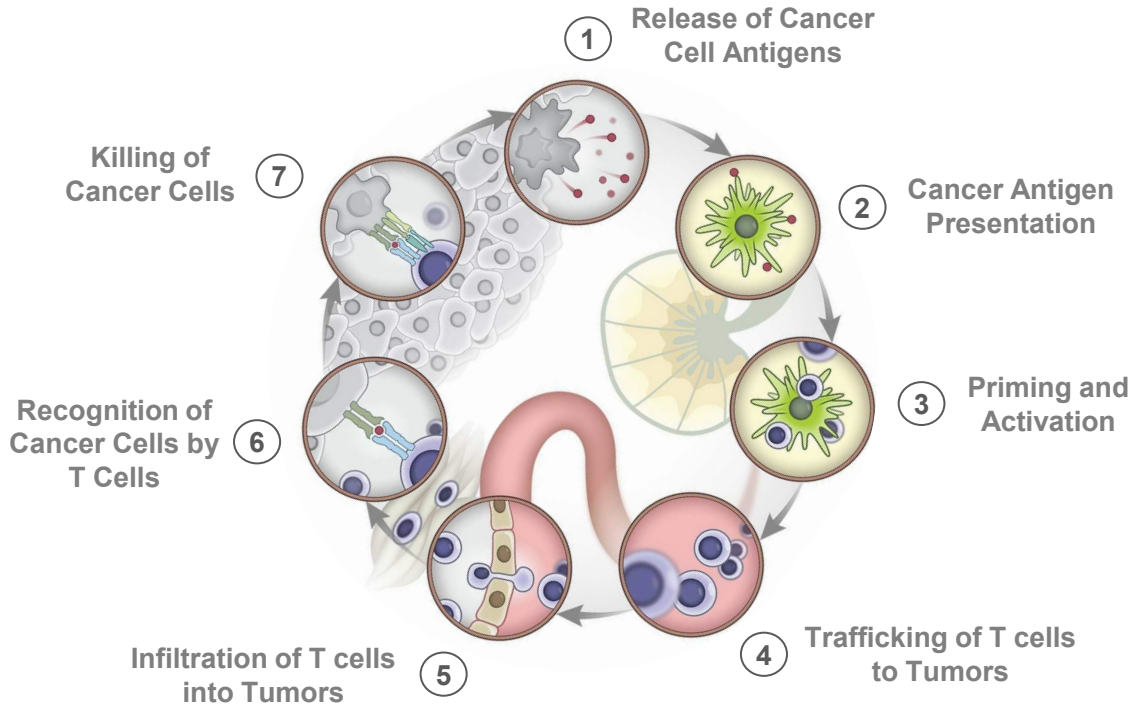
Multiple clinical studies ongoing to demonstrate the dual benefits of trilaciclib and the potential to improve overall survival

G1 THERAPEUTICS

Effects of Trilaciclib Directly Target the “Host”

Patient Bone Marrow and Tumor Immune Microenvironment





Trilaciclib’s robust effects on bone marrow and immune system function occur through the distinct properties of trilaciclib

Hematopoietic tree adapted from ‘Hematopoietic Tree, Plasma Cell’, National Cancer Institute Visuals Online: https://visualsonline.cancer.gov/details.cfm?imageid=7177

Host Effects Driven by Transient CDK4/6 Inhibition

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

Ability to improve the immune response when administered in treatment combination[4-11]

Reduces Hematologic Adverse Events

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

Improves patients' quality of life

Decreases rescue interventions, hospitalizations, associated costs

Protects immune system function from damage by cytotoxic therapy

Enables patients to tolerate greater exposure to cytotoxic therapy

Improves Anti-Tumor Immune Response

- ↑ MHC-I & II
- ↑ IL-2 / IFNγ secretion
- ↑ Th1 cytokines
- ↓ Treg / MDSCs
- ↑ Memory T cells

Enhances T cell activation

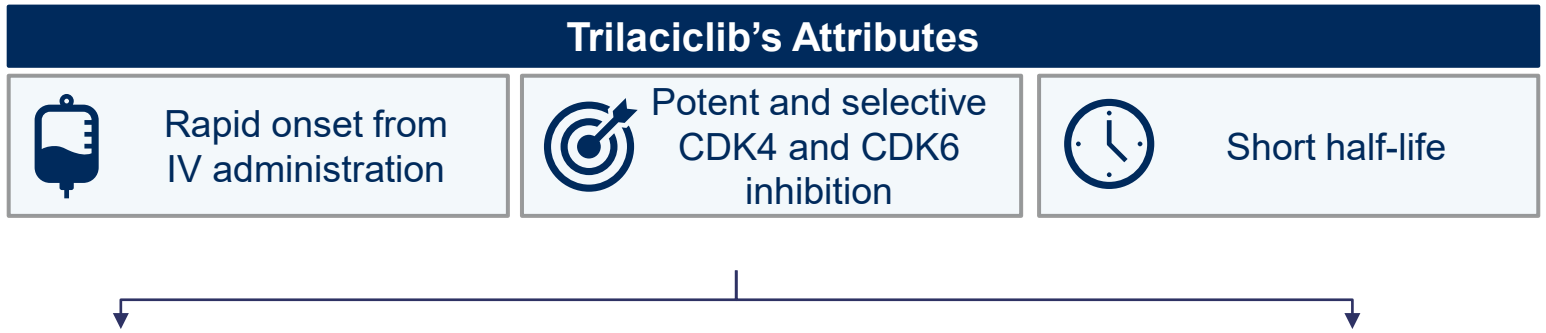
Favorably alters the tumor microenvironment

Improves long-term immune surveillance

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. 10: Lai A, et al. Journal for ImmunoTherapy of Cancer 2020;8:e000847. doi:10.1136/jitc-2020-000847. 11. Lelliott EJ, et al. CDK4/6 Inhibition Promotes Antitumor Immunity through the Induction of T-cell Memory. Cancer Discov. 2021 Oct;11(10):2582-2601. DOI: 10.1158/2159-8290.CD-20-1554.

G1 THERAPEUTICS

Unique Attributes of Trilaciclib



Controlled administration and clean G1 arrest reduces hematologic AEs caused by chemotherapy and may increase ability to receive longer treatment durations

Transient CDK4/6 inhibition modulates multiple immune functions while also allowing beneficial T cell proliferation which may improve patients' anti-tumor immune response

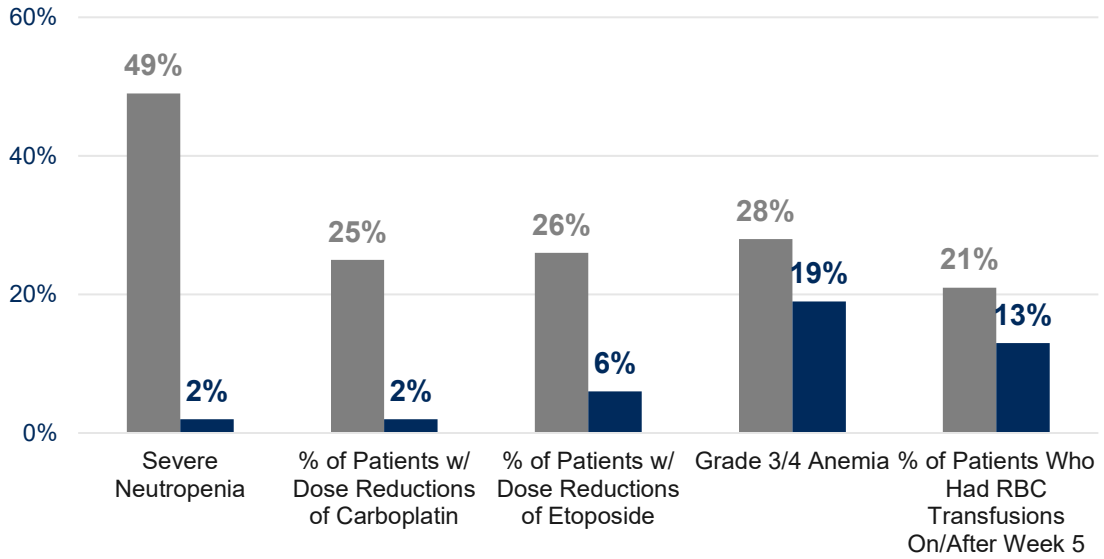
The profile of trilaciclib drives robust patient benefits of myeloprotection and/or potential to increase anti-tumor immunity

G1 THERAPEUTICS

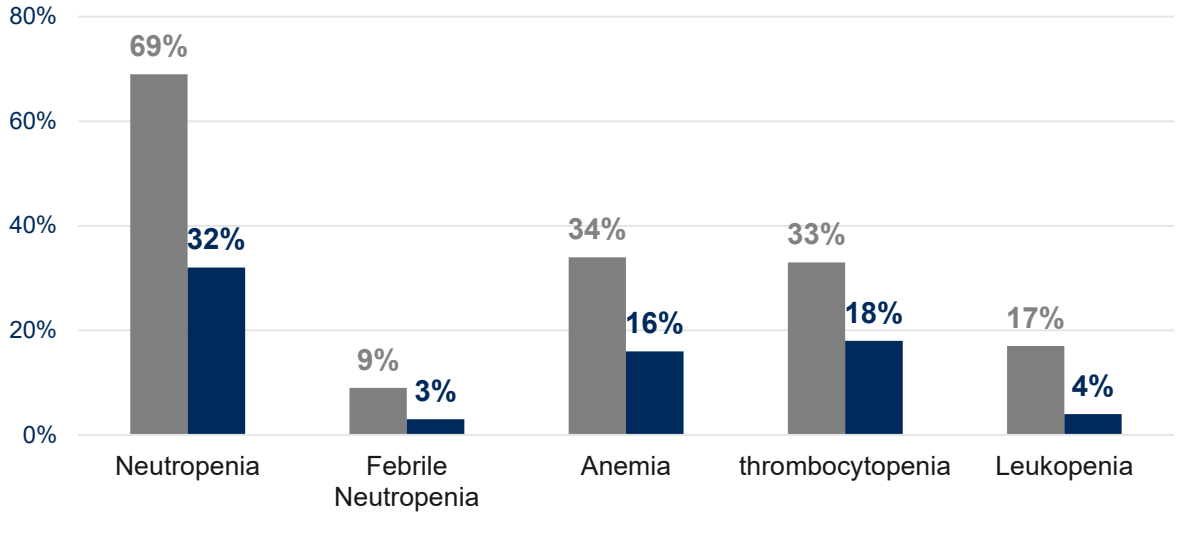
Meaningful Reduction in Adverse Events in ES-SCLC

Phase 2: Randomized Studies

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



Reduced Grade 3/4 Hematological Adverse Reactions Occurring in Patients Treated with trilaciclib and Placebo[2]



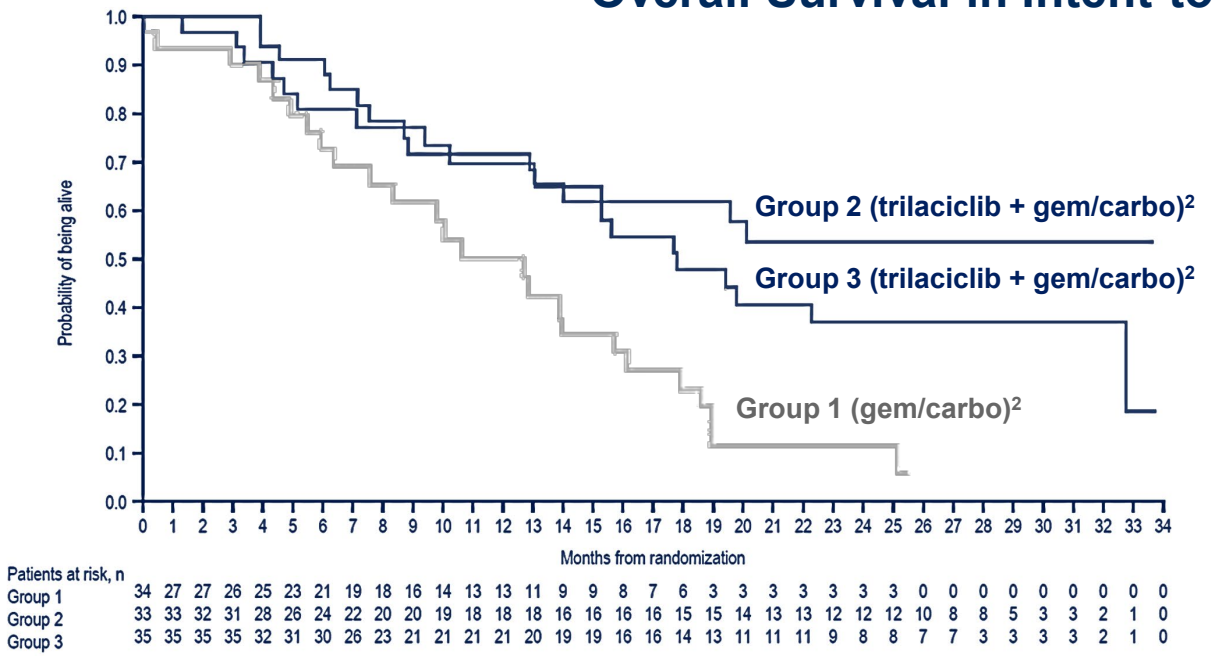
Trilaciclib demonstrated reductions in multiple myelosuppressive consequences and hematologic adverse events across multiple randomized SCLC studies

1. [1]COSELA™ (trilaciclib) label, 10003 Rev. 2/2021 US-2100006
2. Weiss et al., 2020 American Society of Clinical Oncology (ASCO), Abstract #384

Observed Robust OS Improvement in mTNBC Study

Phase 2: Combination with Chemotherapy

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

OS continued to improve over time and at greater rate than PFS for trilaciclib, consistent with a robust immunomodulatory effect

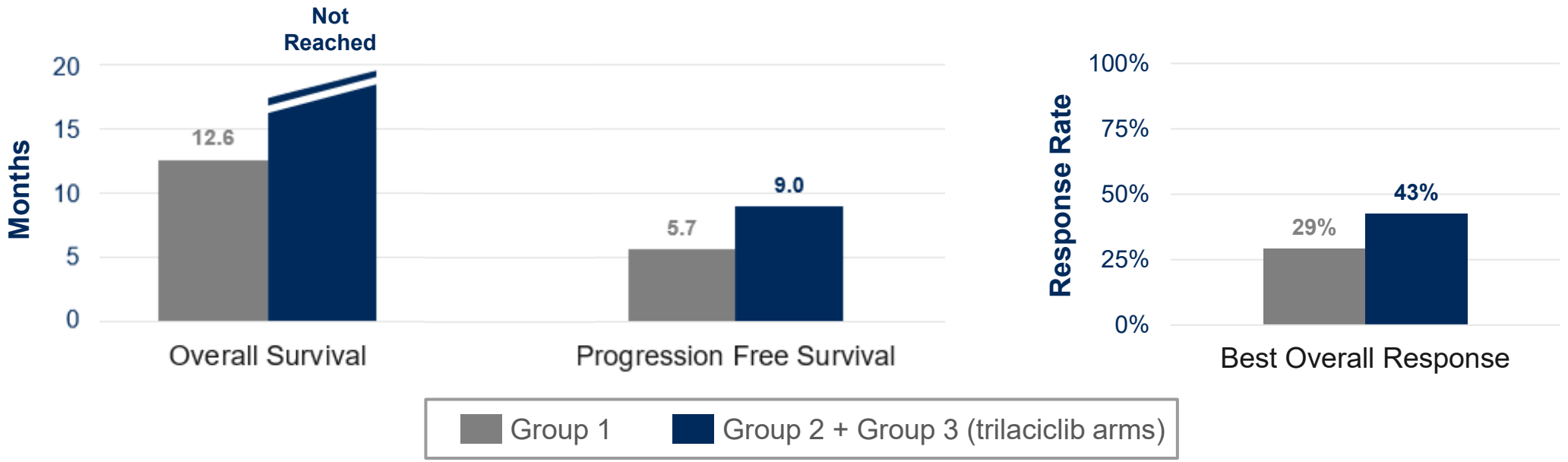
1. O'Shaughnessy et al., 2020 San Antonio Breast Cancer Symposium (SABCS), Poster #PD1-06. Note: primary endpoints relating to reduction in severe neutropenia not achieved in this study.
2. Patients randomized to receive gem/carbo chemotherapy only (Group 1) or gem/carbo plus one of two dosing schedules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

Overall Survival Most Significant Effect in mTNBC Study

Phase 2: Combination with Chemotherapy

Greatest Effect ⟵ ⟶ ***Least Effect***

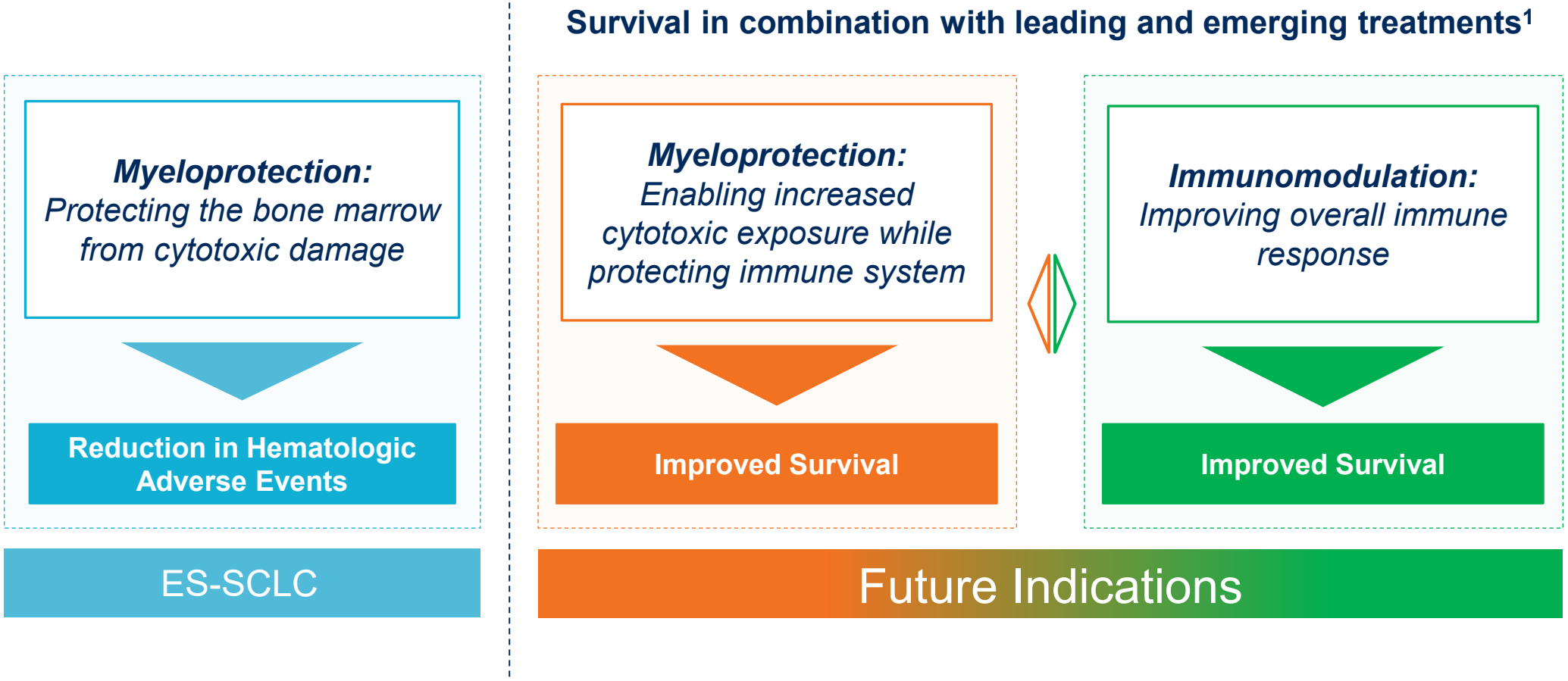
P-Values	0.001	0.108	0.235



Trilaciclib demonstrated the most robust effect on OS, consistent with its observed immunomodulatory effects

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).

Currently Pursuing Trilaciclib Across Key Growth Platforms



[1] Clinical evaluation underway; 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.

Trilaciclib's Effects Depend on Treatment Setting and Tumor Type

	Evidence for myeloprotection with cytotoxic / payload	Extended cycles of therapy	Known immunogenic tumor	Combination with immunotherapy
1L Colorectal Cancer (Phase 3: +FOLFOXIRI)	✓	✓		
2L / 3L TNBC (Phase 2: +Sacituzumab)	✓	✓	✓	
1L TNBC (Phase 3: +Gem/Carbo)		✓	✓	
1L Bladder Cancer (Phase 2: +Gem/Platinum and avelumab maintenance)		✓	✓	✓
Neoadjuvant TNBC (Phase 2: ACT +/- PD-(L)1i)		✓	✓	✓
ES-SCLC (Marketed)	✓	Myeloprotection benefits; no increase in OS demonstrated		*

Myeloprotection: Protecting the bone marrow from cytotoxic damage

Myeloprotection: Enabling increased cytotoxic exposure while protecting immune system

Immunomodulation: Improving overall immune response

* One of the three ES-SCLC trials included atezolizumab in the treatment regimen; however, trilaciclib was not dosed with atezolizumab for maintenance portion of study.

Key Takeaways: From Premise to Promise

- Trilaciclib's unique effects are directly targeted on the host
- Robust effects attributable to unique transient, potent, and selective CDK4/6 inhibition
- Protection of patient's bone marrow leads to multilineage myeloprotection benefits
- Improved immune system function and myeloprotection anticipated to lead to anti-tumor efficacy
- In ongoing trials, most robust anti-tumor efficacy effect expected on survival, with least impact on response rate
- Meaningful data read-outs starting in the next three months

G1 THERAPEUTICS

Trilaciclib as immunomodulatory therapy for cancer

Shom Goel B Med Sci, MBBS, FRACP, PhD

Peter MacCallum Cancer Centre

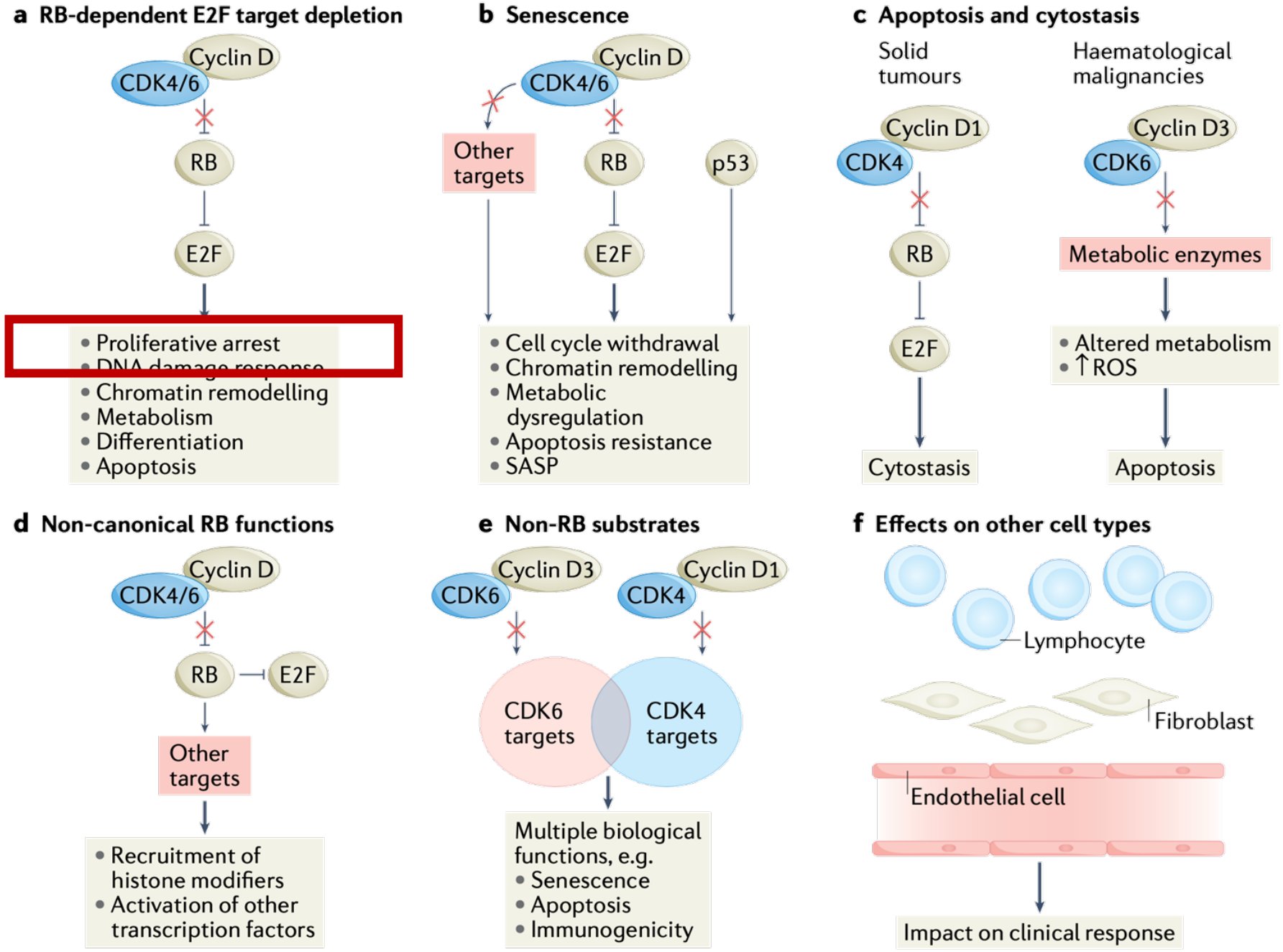
The University of Melbourne

Sustained proliferation: a hallmark of cancer

Certain cancer cells are heavily dependent on **CDKs 4 and 6** for proliferation and/or survival

3 agents approved as therapy for luminal breast cancer

CDK4/6 inhibition: Beyond cell cycle arrest



Goel et al
Nature Reviews Cancer
2022

LETTER

doi:10.1038/nature23465

CDK4/6 inhibition triggers anti-tumour immunity

Shom Goel[1,2]*, Molly J. DeCristo[3,4]*, April C. Watt[1], Haley BrinJones[1], Jaclyn Sceneay[3,4], Ben B. Li[1], Naveed Khan[1], Jessalyn M. Ubellacker[3,4], Shaozhen Xie[1], Otto Metzger-Filho[2], Jeremy Hoog[5], Matthew J. Ellis[6], Cynthia X. Ma[5], Susanne Ramm[7,8], Ian E. Krop[2], Eric P. Winer[2], Thomas M. Roberts[1], Hye-Jung Kim[9,10]§, Sandra S. McAllister[3,4,11,12]§ & Jean J. Zhao[1,12,13]§

CDK4/6 inhibitor-induced anti-tumor immunity
- Clues from the past -

TCR Antigen–Induced Cell Death Occurs from a Late G1 Phase Cell Cycle Check Point

Natalie A. Lissy,* Linda F. Van Dyk,*
Michelle Becker-Hapak, Adita Vocero-Akbani,
Jason H. Mendler, and Steven F. Dowdy†
Howard Hughes Medical Institute
and Division of Molecular Oncology
Departments of Pathology and Medicine
Washington University School of Medicine
St. Louis, Missouri 63110

Immunity 1998

A common E2F-1 and p73 pathway mediates cell death induced by TCR activation

Natalie A. Lissy*, Penny K. Davis*, Meredith Irwin†, William G. Kaelin† & Steven F. Dowdy*

Nature 2000

Regulation of T Cell Differentiation and Alloimmunity by the Cyclin-Dependent Kinase Inhibitor p18ink4c

Emily A. Rowell[1], Liqing Wang[2], Neelanjana Chunder[2], Wayne W. Hancock[1,2], Andrew D. Wells[1,2]*

PLOS One 2014

CDK4/6 inhibitor-induced anti-tumor immunity - Confirmation of mechanism -

Tumor cell antigen presentation
- Goel *Nature* 2017
- Schaer *Cell Rep* 2018
- Stopfer *Nat Comm* 2020
- Knudsen *Gut* 2020
- Charles *Oncoimmunology* 2021
- Watt *Nature Cancer* 2021
- Wu *J Trans Med* 2022

Tumor cell chemokine secretion
- Ruscetti *Science* 2018
- Uzhachenko *Cell Rep* 2021

Suppression of Treg proliferation
- Goel *Nature* 2017
- Lai *JITC* 2020
- Whittle *Clin Cancer Res* 2020
- Uzhachenko *Cell Rep* 2021

Generation of immune memory
- Goel *Nature* 2017
- Lelliott *Cancer Discovery* 2021
- Heckler *Cancer Discovery* 2021

Effector T cell activation
- Deng *Cancer Discovery* 2018

Combination with checkpoint inhibitors
- Goel *Nature* 2017
- Zhang *Nature* 2018
- Schaer *Cell Rep* 2018
- Jerby-Arnon *Cell* 2018
- Deng *Cancer Discovery* 2018
- Knudsen *Gut* 2020
- Lai *JITC* 2020
- Uzhachenko *Cell Rep* 2021

Trilaciclib: uniquely poised to exploit the immunomodulatory properties of CDK4/6 inhibitors

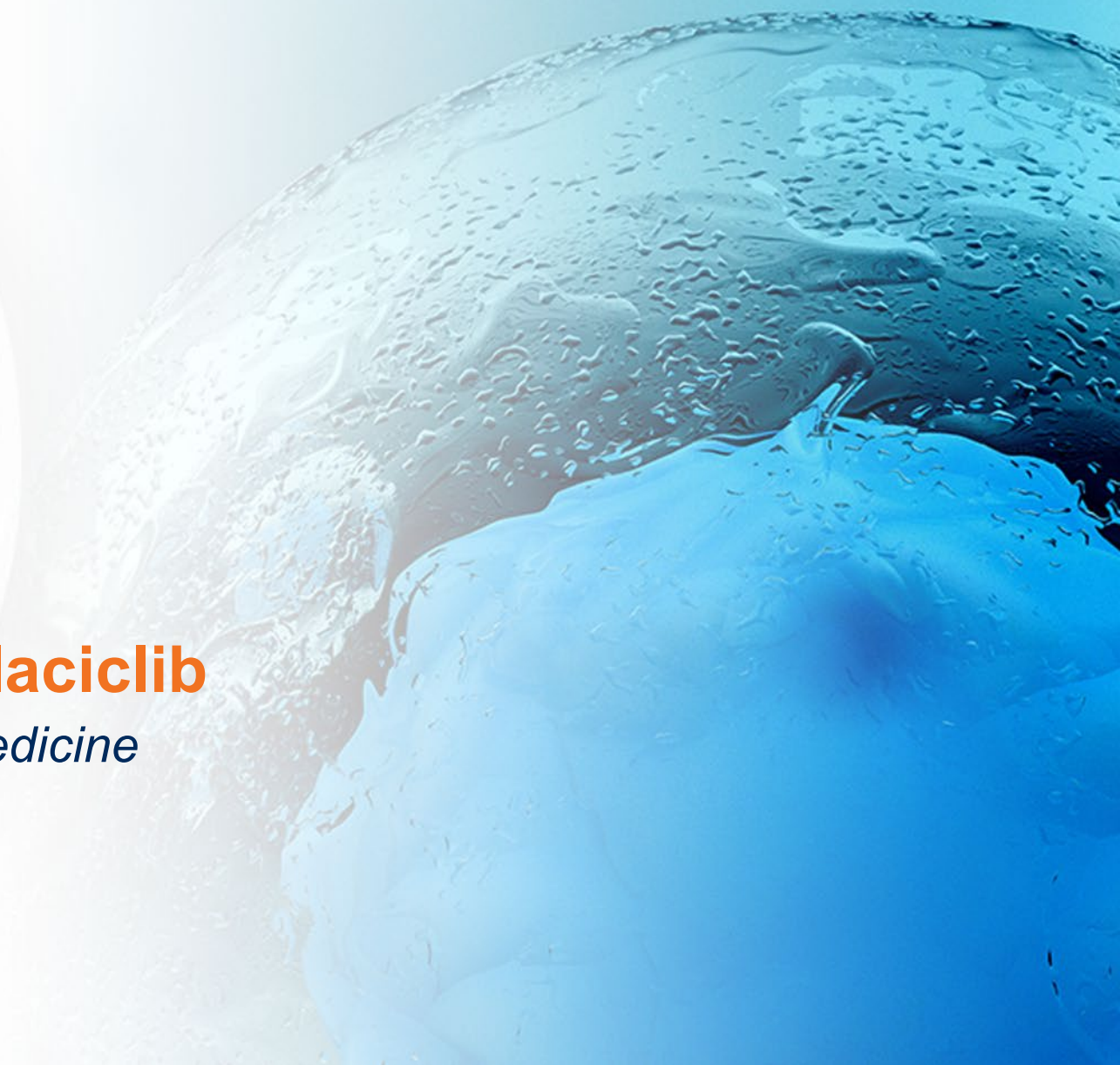
Intravenous administration enables potentiation of anti-tumor immunity:

- Precision with intermittent dosing
- Temporal control of T cell transcriptome
- Balancing T cell function and number
- Easy integration with existing standards of care

Potential for combination with chemotherapy, immunotherapy, or both across a wide range of cancer types

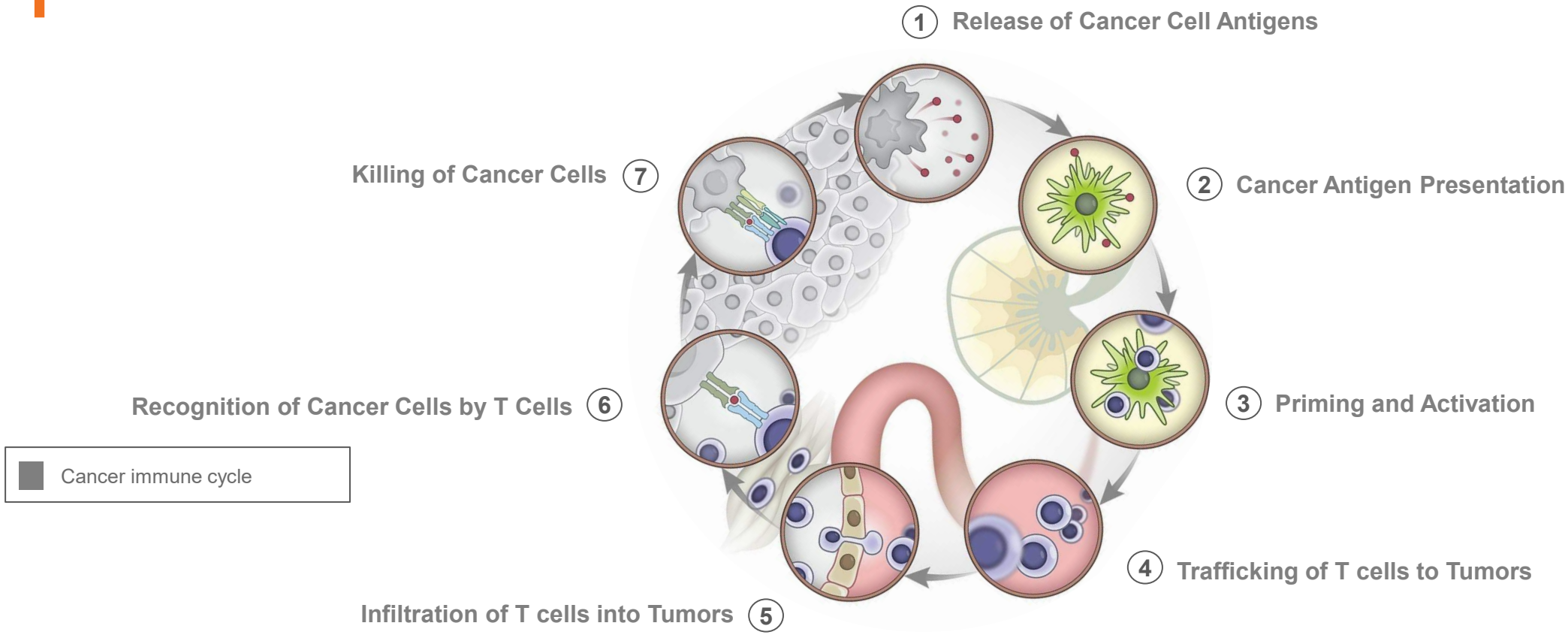
The Synergistic Potential of Trilaciclib

John Yi, Ph.D., Sr. Director, Translational Medicine



Potential to Enhance the Cancer Immunity Cycle

Ideal for Combination Use



Cancer immunity cycle graphic adapted from Chen & Mellman. Oncology Meets Immunology: The Cancer-Immunity Cycle. Immunity. 2013;39(1):1-10. doi:10.1016/j.immune.2013.07.012.

1. Goel S, DeCristo MJ, et al. CDK4/6 inhibition triggers anti-tumour immunity. Nature. 2017.
2. Deng J, Wang ES, Jenkins RW, et al. CDK4/6 inhibition augments antitumor immunity by enhancing T-cell activation. Cancer Discov. 2018;8(2):216-233. doi:10.1158/2159-8290.CD-17-0915.
3. Uzhachenko R, et al. Metabolic modulation by CDK4/6 inhibitor promotes chemokine-mediated recruitment of T cells into mammary tumors. Cell Rep. 2021;35(1):108944/j.celrep.2021.108944.
4. Lai AY, et al. CDK4/6 inhibition enhances antitumor efficacy of chemotherapy and immune checkpoint inhibitor combinations in preclinical models and enhances T-cell activation in patients with SCLC receiving chemotherapy. Journal for ImmunoTherapy of Cancer. 2020; 8:e000847. doi:10.1136/ jitc-2020-000847.
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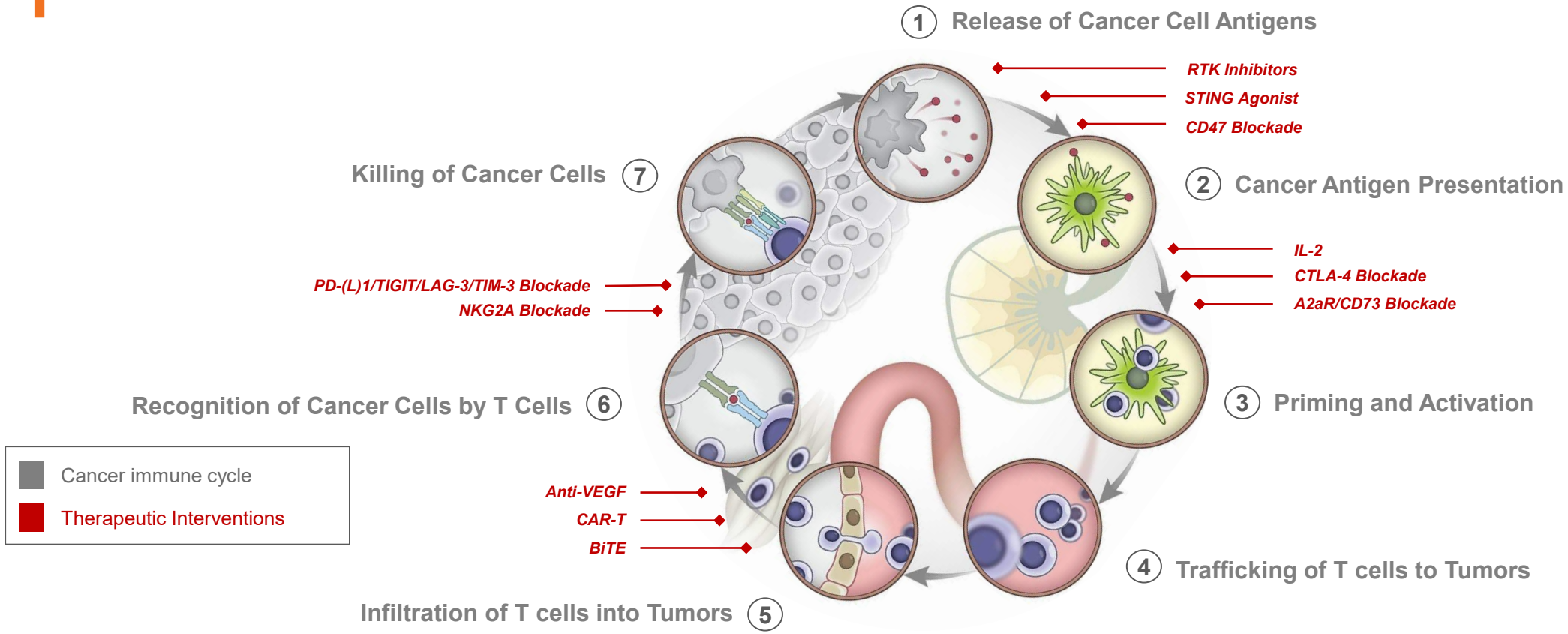

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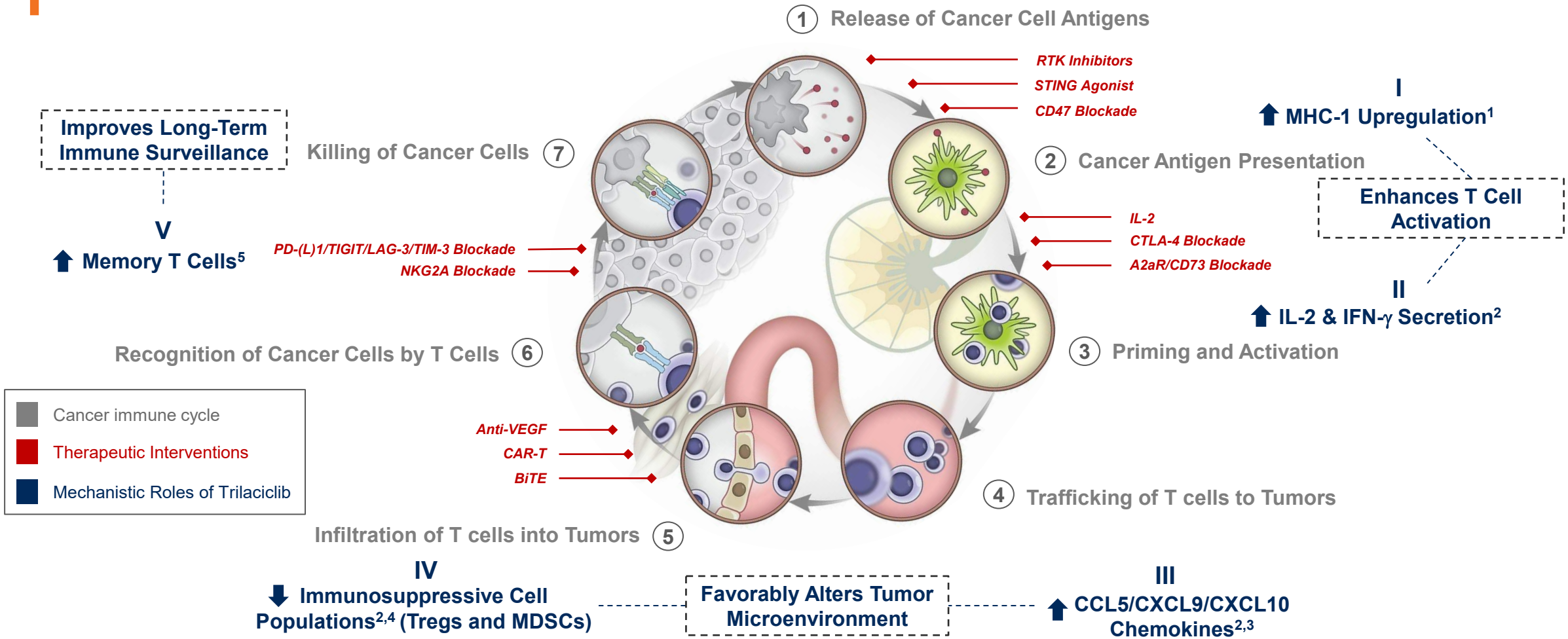

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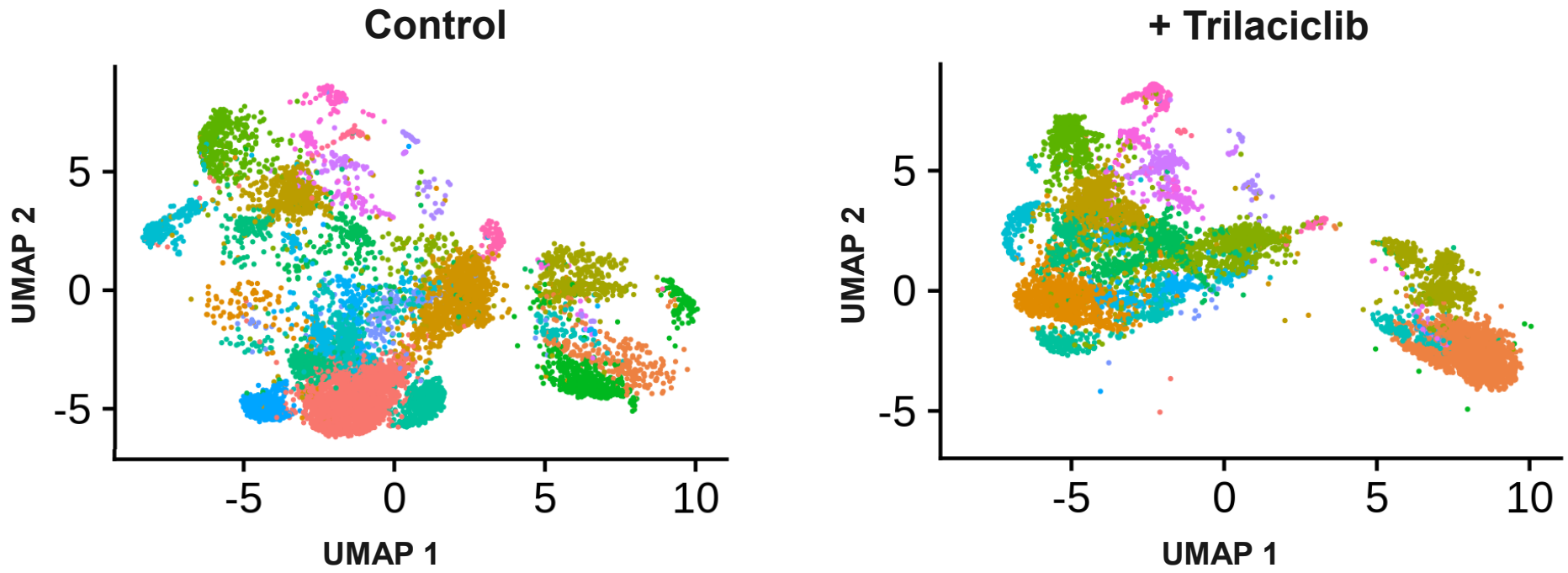
5. Lelliott EJ, et al. CDK4/6 Inhibition Promotes Antitumor Immunity through the Induction of T-cell Memory. Cancer Discov. 2021 Oct;11(10):2582-2601. DOI: 10.1158/2159-8290.CD-20-1554; and Heckler M, Ali LR, et al. Inhibition of CDK4/6 promotes CD8 T-cell memory formation. Cancer Discov. 2021 Oct;11(10):2564-2582. doi: 10.1158/2159-8290.CD-20-1540

Gene Expression Changes Within Tumor Infiltrating T Cells



Note: In a MMTV-rtTA/tetO-HER2 model of breast cancer, mice were treated with a single dose of trilaciclib. Single cell RNA-Seq performed on sorted tumor-derived CD3+ T cells 24 hours after treatment.

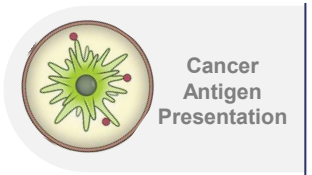
Gene expression changes with trilaciclib potentiates the broad immune modulating effect

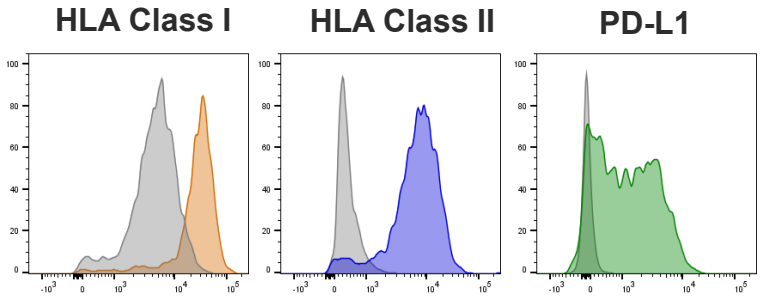
G1 THERAPEUTICS

* Work conducted in collaboration with Dr. Shom Goel (Peter MacCallum Institute)

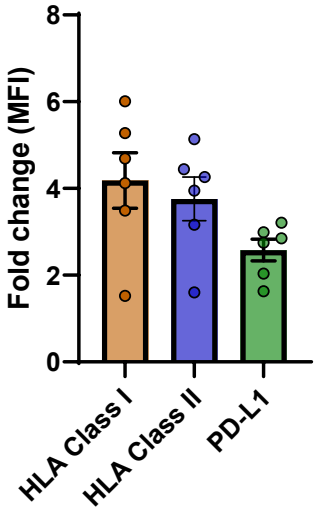
Enhanced Potential for Antigen Presentation and T Cell Activation

Upregulation of MHC and PD-L1
(on MCF-7 Cell Line)



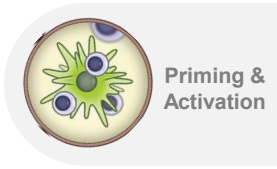


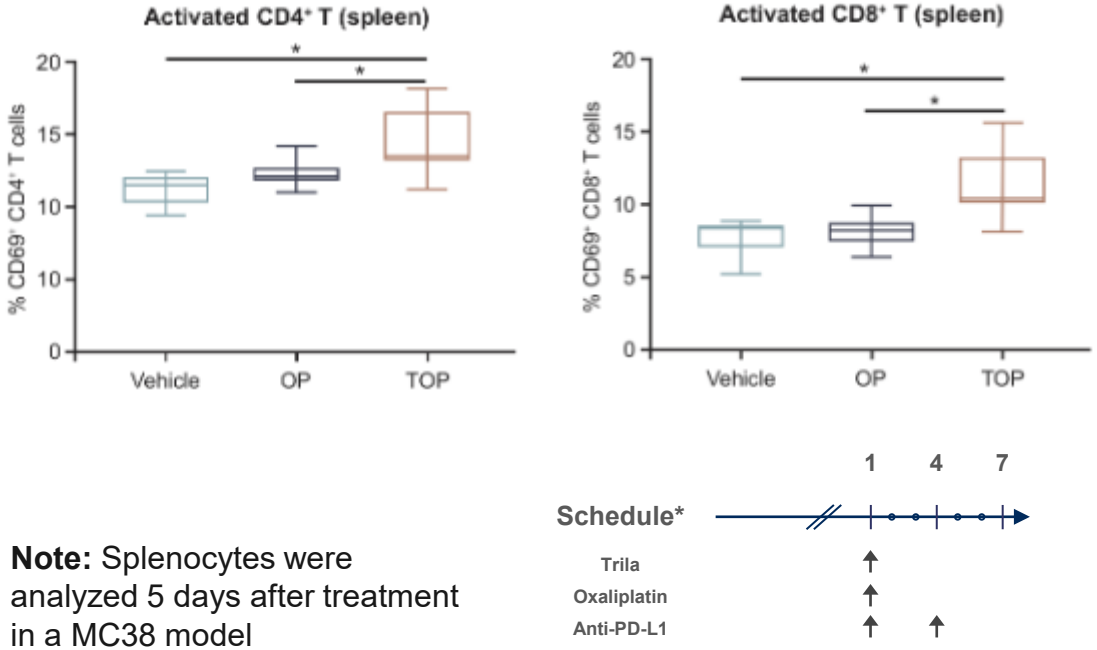
Trilaciclib vs Control



Note: MCF-7 breast cancer cell line were cultured with supernatant from stimulated PBMCs (+/- trilaciclib; 100nM).

Enhanced T Cell Activation[1]
(trilaciclib + oxaliplatin + anti-PD-L1)



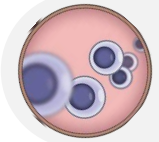


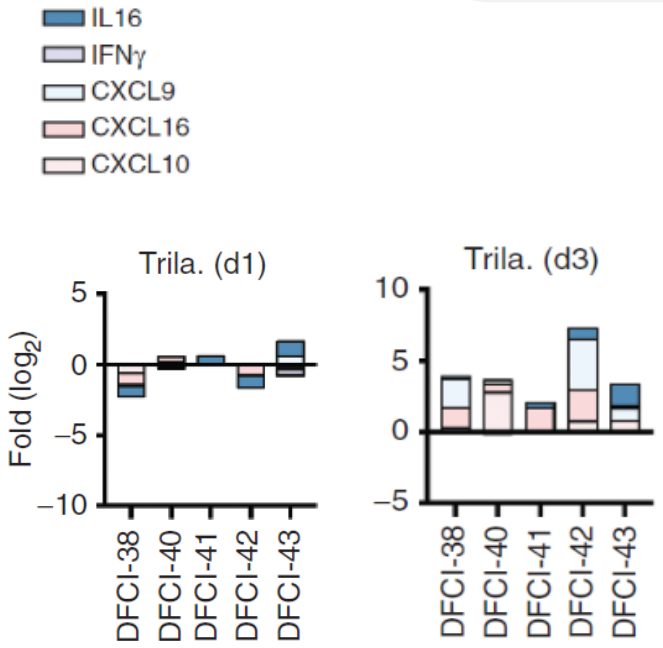
Note: Splenocytes were analyzed 5 days after treatment in a MC38 model

1. Lai AY, Sorrentino JA, Dragnev KH, et al. Journal for ImmunoTherapy of Cancer 2020; 8:e000847. doi:10.1136/jitc-2020-000847.

Favorable Alteration of the Tumor Microenvironment

Increased Chemokines & Cytokines[1]

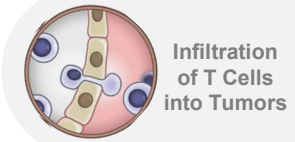


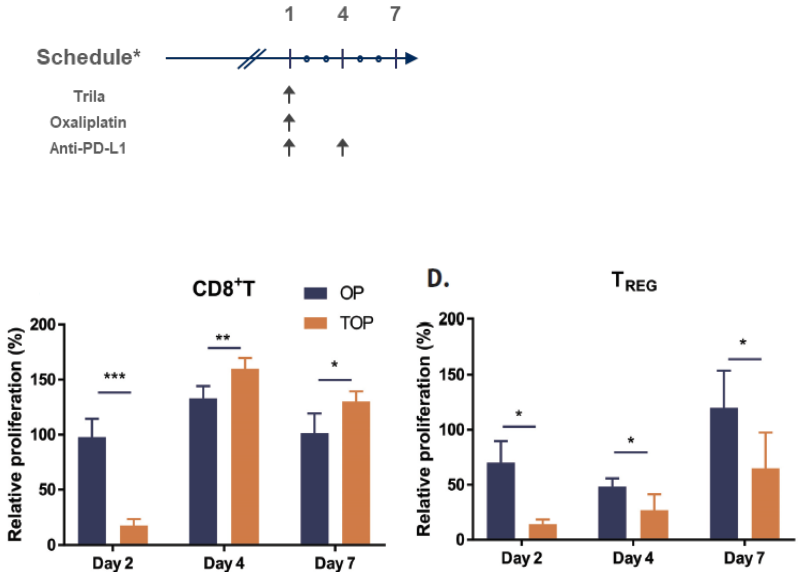


Note: Multiplex immunoassay performed on patient-derived organoid cultures

Prolonged Arrest of Treg Proliferation[2]

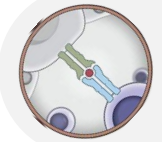
(trilaciclib + oxaliplatin + anti-PD-L1)

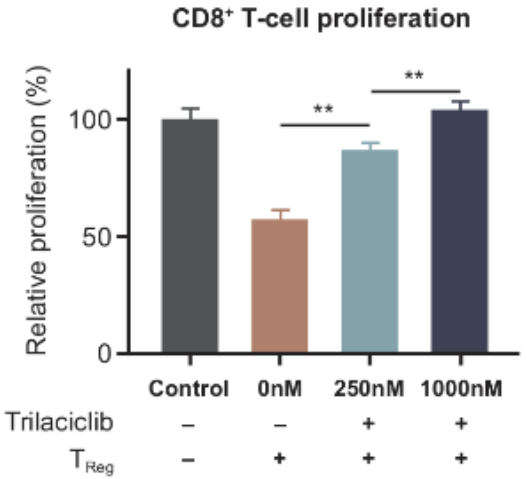




Note: Relative proliferation is defined as the proportion of EdU+ cells in vehicle-treated samples

Suppression of Treg Function [1]





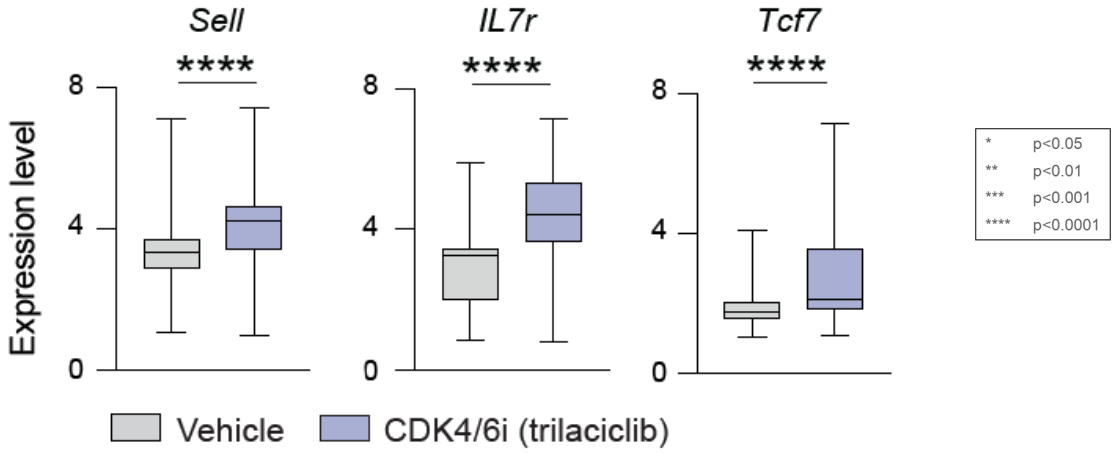
Note: Tregs were pretreated with trilaciclib prior to Treg suppression assay.

1. Deng J, Wang ES, Jenkins RW, et al. CDK4/6 inhibition augments antitumor immunity by enhancing T-cell activation. Cancer Discov. 2018;8(2):216-233. doi:10.1158/2159-8290.CD-17-0915.
2. Lai AY, et al. CDK4/6 inhibition enhances antitumor efficacy of chemotherapy and immune checkpoint inhibitor combinations in preclinical models and enhances T-cell activation in patients with SCLC receiving chemotherapy. Journal for ImmunoTherapy of Cancer. 2020; 8:e000847. doi:10.1136/ jitc-2020-000847.

Improvement of Long-Term Immune Surveillance

Expression of Memory-Associated Genes[1]

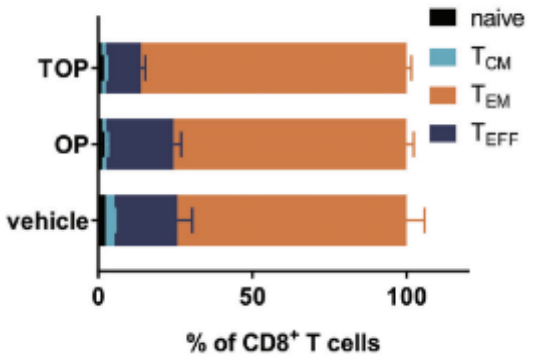
Recognition of Cancer Cells by T Cells



Note: Expression of Memory-associated genes at day 7 following trilaciclib treatment.

Preferential Differentiation into Memory CD8 T Cells[2]

Recognition of Cancer Cells by T Cells



Comparison of frequency of intra-tumor T cell subsets between OP and TOP groups

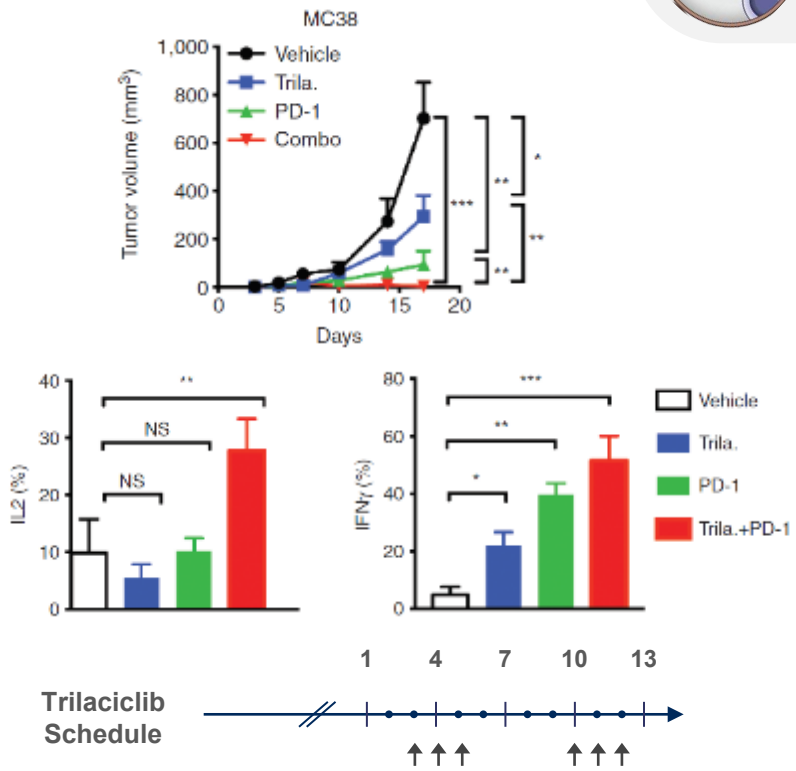
T cell subset	OP (Mean % ±SEM)	TOP (Mean % ±SEM)	P-value
Naïve CD8+	1.2 ± 0.5	1 ± 0.4	0.81
CD8+ T_{EFF}	21.8 ± 2.5	11.3 ± 1.4	*0.01
CD8+ T_{EM}	75.6 ± 2.3	86.2 ± 1.6	*0.01
CD8+ T_{CM}	1.5 ± 0.6	1.5 ± 0.4	0.97

Note: CD8+ T cells were divided into four subsets using CD62L and CD44 markers: naïve T cells (CD62L+CD44-), effector (TEFF,CD62L+CD44-), central memory (TCM, CD62L+ CD44+), and effector memory (TEM, CD62L-CD44+).

1. Lelliott EJ, et al. CDK4/6 Inhibition Promotes Antitumor Immunity through the Induction of T-cell Memory. Cancer Discov. 2021 Oct;11(10):2582-2601. DOI: 10.1158/2159-8290.CD-20-1554; and Heckler M, Ali LR, et al. Inhibition of CDK4/6 promotes CD8 T-cell memory formation. Cancer Discov. 2021 Oct;11(10):2564-2582. doi: 10.1158/2159-8290.CD-20-1540
2. Lai AY, et al. 2018 AACR Annual Meeting, Abstract #1752

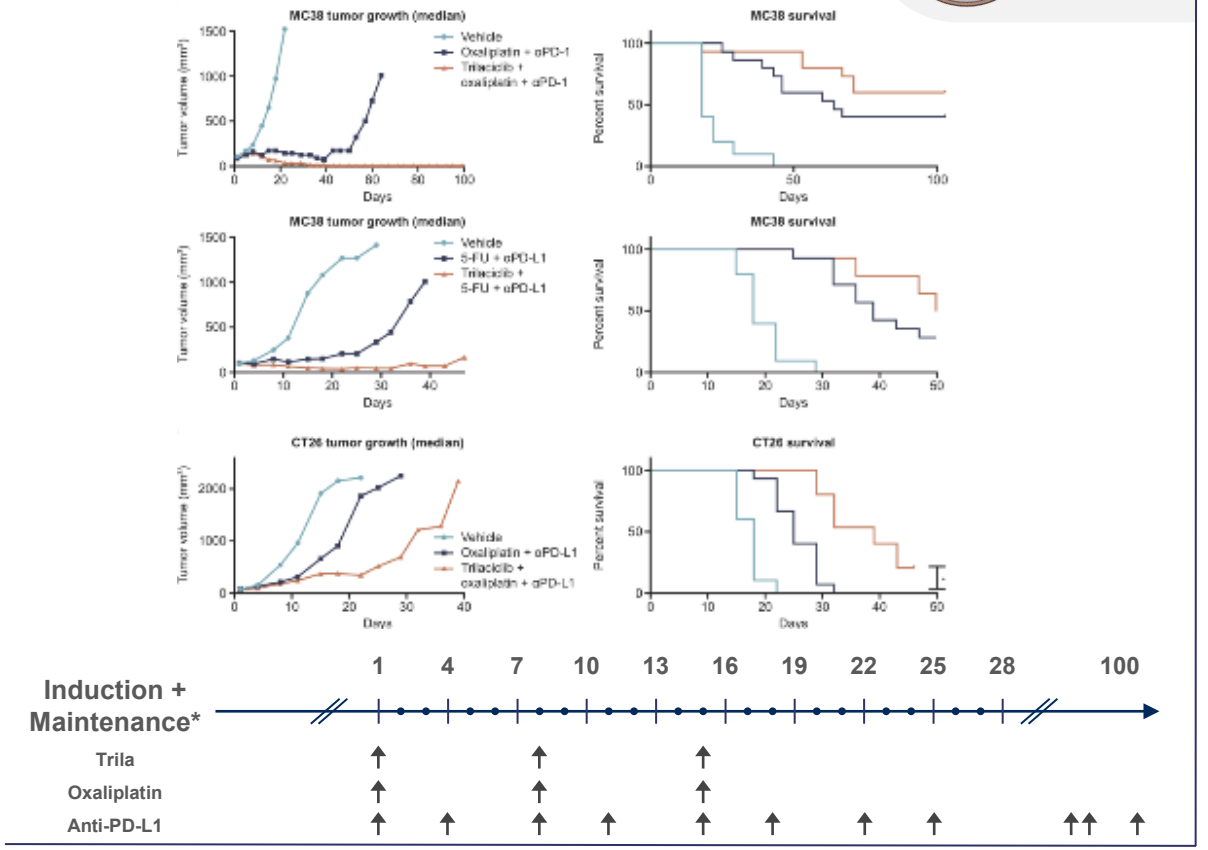
Synergistic Anti-Tumor Activity with PD-(L)1 Inhibitors and Chemotherapy

Trilaciclib Combined with a PD-1 inhibitor[1]



Note: Cytokines were evaluated on Day 17

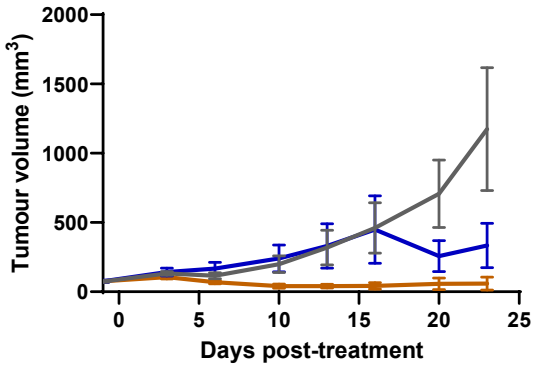
Trilaciclib Combined with a PD-(L)1 + Chemo[1]

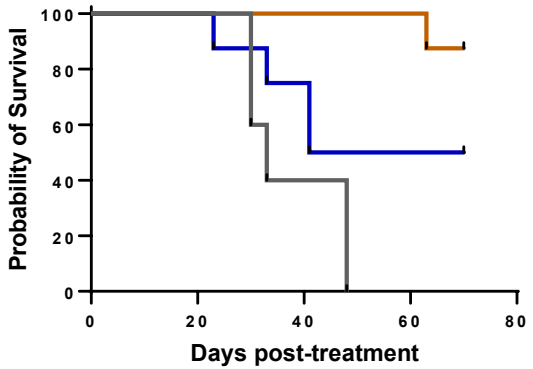


1. Deng J, Wang ES, Jenkins RW, et al. CDK4/6 Inhibition Augments Antitumor Immunity by Enhancing T-cell Activation. Cancer Discov. 2018;8(2):216- 33. **2**. Lai AY, Sorrentino JA, Dragnev KH, et al. Journal for ImmunoTherapy of Cancer 2020; 8:e000847. doi:10.1136/jitc-2020-000847.

Efficacy of Combination Therapy with Inhibitory Receptors

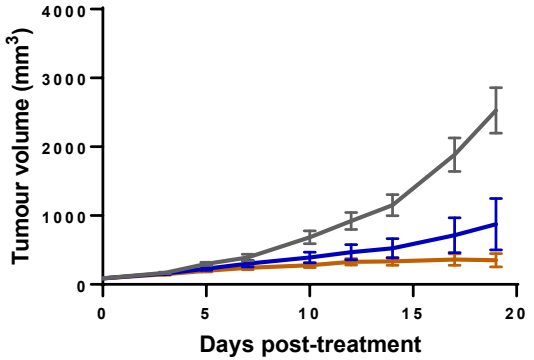
Trilaciclib + Dual Checkpoint Blockade (CT26 Model)

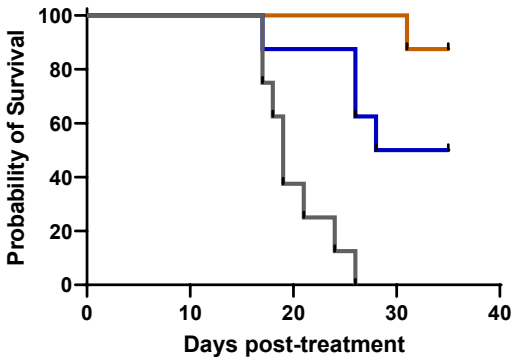




qwk vehicle
biwk α-PD-1 + biwk α-LAG3
qwk trilaciclib + α-PD-1 + α-LAG3

Trilaciclib + Checkpoint and Adenosine Pathway Blockade (CT26 Model)





qwk vehicle
biwk α-PD-1 + biwk α-CD73
qwk trilaciclib + biwk α-PD-1 + biwk α-CD73

Trilaciclib supports therapies inhibiting both checkpoint and adenosine pathways

G1 THERAPEUTICS

Key Takeaways: The Synergistic Potential of Trilaciclib

- Trilaciclib has the potential to enhance multiple immunological processes within the cancer immunity cycle[1]
  - Enhances T cell activation
  - Favorably alters the tumor microenvironment
  - Improves long-term immune surveillance
- Trilaciclib provides synergistic benefit in combination with checkpoint and adenosine pathway inhibition
  - Added survival benefit when combined with PD-1 and LAG3 or CD73 inhibitors
- Ongoing Phase 2 TNBC MOA study will confirm and expand trilaciclib's benefit in additional combination therapy opportunities

G1 THERAPEUTICS

Clinical Development: Expanding the Trilaciclib Opportunity

Symantha Melemed, Ph.D., Vice President, Clinical Development

Trilaciclib's Effects Depend on Treatment Setting and Tumor Type

	Evidence for myeloprotection with cytotoxic / payload	Extended cycles of therapy	Known immunogenic tumor	Combination with immunotherapy
1L Colorectal Cancer (Phase 3: +FOLFOXIRI)	✓	✓		
2L / 3L TNBC (Phase 2: +Sacituzumab)	✓	✓	✓	
1L TNBC (Phase 3: +Gem/Carbo)		✓	✓	
1L Bladder Cancer (Phase 2: +Gem/Platinum and avelumab maintenance)		✓	✓	✓
Neoadjuvant TNBC (Phase 2: ACT +/- PD-(L)1i)		✓	✓	✓
ES-SCLC (Marketed)	✓	Myeloprotection benefits; no increase in OS demonstrated		*

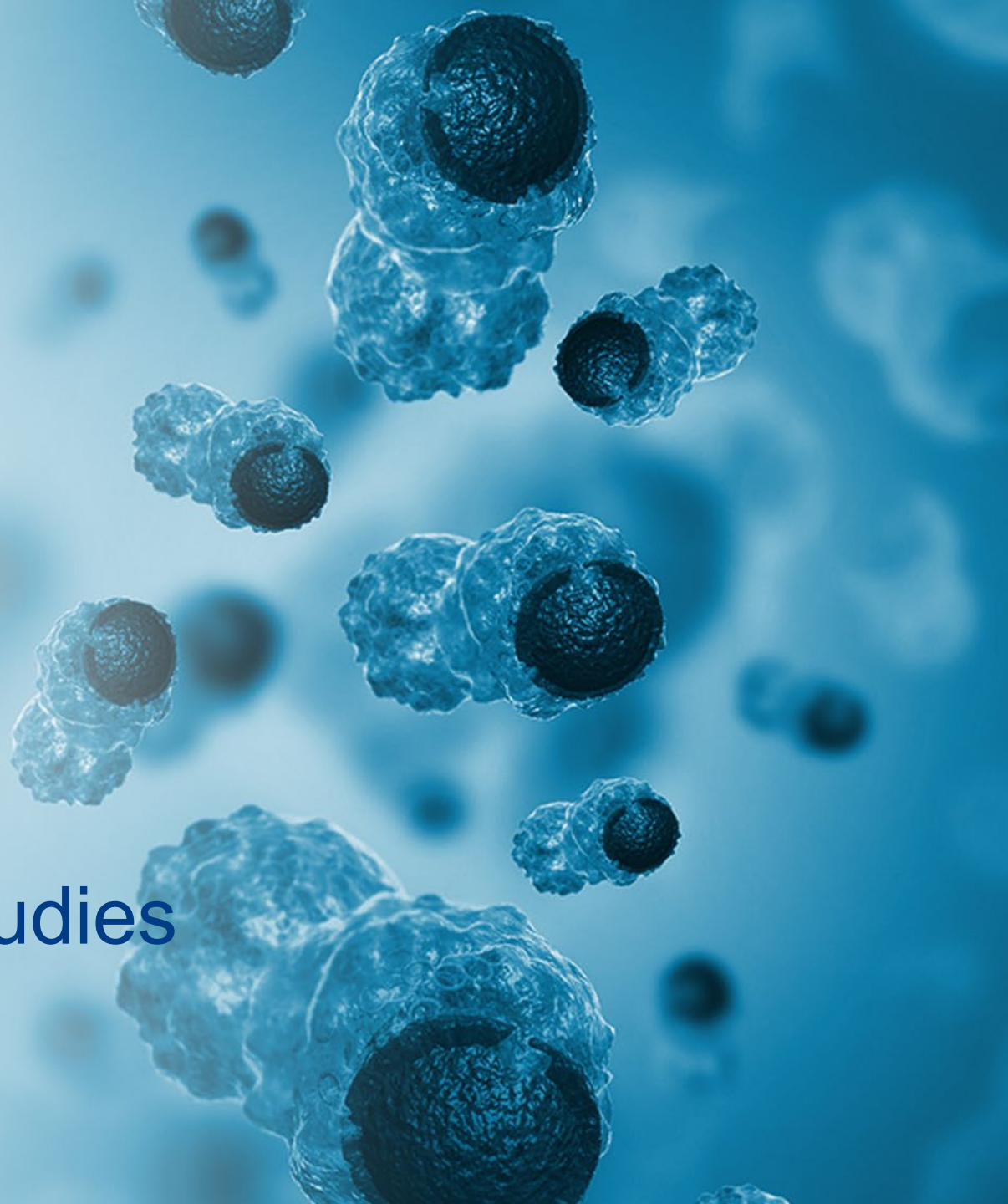
Myeloprotection: Protecting the bone marrow from cytotoxic damage

Myeloprotection: Enabling increased cytotoxic exposure while protecting immune system

Immunomodulation: Improving overall immune response

* One of the three ES-SCLC trials included atezolizumab in the treatment regimen; however, trilaciclib was not dosed with atezolizumab for maintenance portion of study.

Ongoing Pivotal Phase 3 Studies



First-Line CRC Benchmark Data (from a meta-analysis[1])

Foundational Data for PRESERVE 1: Triplet Efficacious but Highly Myelosuppressive

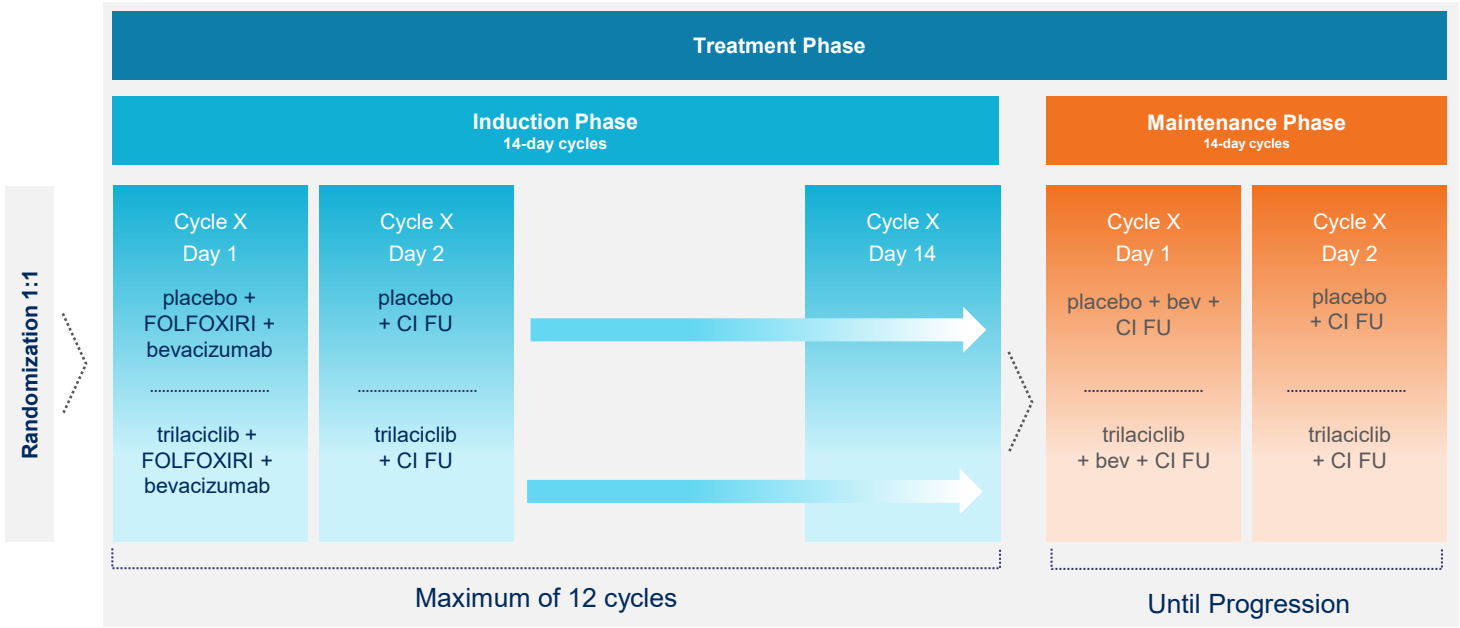
	FOLFOXIRI + bevacizumab (N = 846)	Doublet + bevacizumab (N = 851)	P Value
Efficacy Data:			
ORR	64.5%	53.6%	<.001
Median PFS	12.2	9.9	<.001
Median OS	28.9	24.5	<.001
***Most Common Adverse Events**:* *(Grade 3 - 4 AEs occurring > 5%)*			
Neutropenia[2]	45.8%	21.5%	<.001
Diarrhea	17.8%	8.4%	<.001
Arterial Hypertension	7.8%	7.8%	.938
Febrile Neutropenia	6.3%	3.7%	.019
Nausea	5.5%	3.0%	.016
Venous Thromboembolism	5.5%	5.7%	.892
Mucositis	5.1%	2.9%	.024

1. Cremolini C, et al. Individual Patient Data Meta-Analysis of FOLFOXIRI Plus Bevacizumab Versus Doublets Plus Bevacizumab as Initial Therapy of Unresectable Metastatic Colorectal Cancer. J Clin Oncol 2020;38:3314 -3324
2. Note: Grade 4 neutropenia ~19% for FOLFOXIRI + bevacizumab and ~7% for doublet + bevacizumab based on TRIBE2 results (Cremolini, et al. Upfront FOLFOXIRI plus bevacizumab and reintroduction after progression versus mFOLFOX6 plus bevacizumab followed by FOLFIRI plus bevacizumab in the treatment of patients with metastatic colorectal cancer (TRIBE2): a multicentre, open-label, phase 3, randomised, controlled trial. Lancet Oncol 2020; 21: 497–507.

Ongoing P3 First-Line CRC Pivotal Trial: PRESERVE 1

Myeloprotection & Extended Cycles

FOLFOXIRI: most efficacious chemo regimen but highly myelosuppressive
Potential to significantly expand FOLFOXIRI usage supported by market research



PRIMARY ENDPOINT:
Myeloprotection
SN during Induction & DSN Cycles 1-4
Powering unchanged

SECONDARY ENDPOINTS:
PFS/OS, PRO

ENROLLMENT COMPLETED:
326 participants

STATISTICS:
Myelo + PRO: $\alpha = 0.04$
PFS/OS: $\alpha = 0.01$

Initial results in 1Q 2023

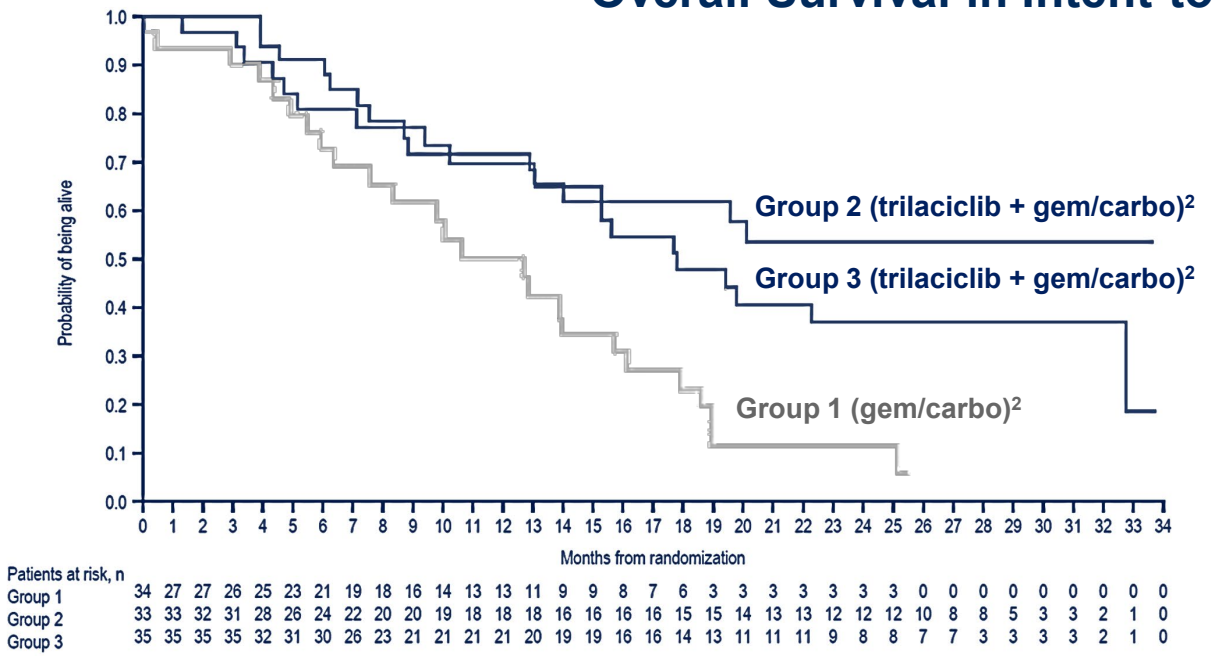
Strong support from preclinical models for the benefits of trilaciclib in combination with 5-FU-based chemo regimens

G1 THERAPEUTICS

Observed Robust OS Improvement in mTNBC

Completed Phase 2: Foundational Data for PRESERVE 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

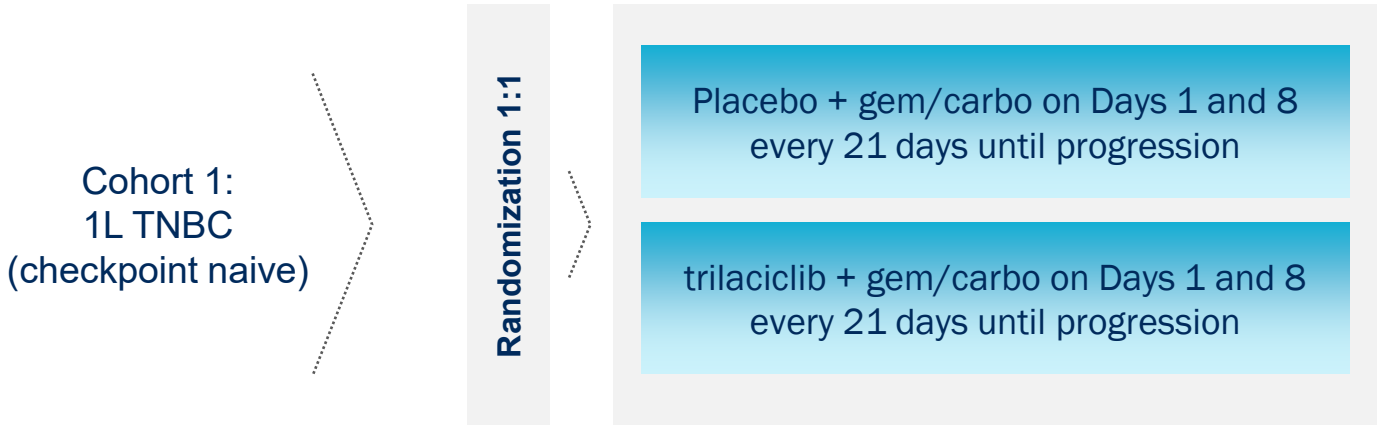
Fast Track Designation granted as a result of these data (July 2021)

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).

Ongoing First-Line TNBC P3 Pivotal Trial: PRESERVE 2

Extended Cycles & Immunogenic Tumor

Initial positive evidence of efficacy across subsets and line of treatment in Phase 2 trial[1]
Evaluating 1L patients (PD-L1 positive and negative patients)



PRIMARY ENDPOINT:
Overall Survival

SECONDARY ENDPOINTS:
PRO, myeloprotection measures, PFS/ORR

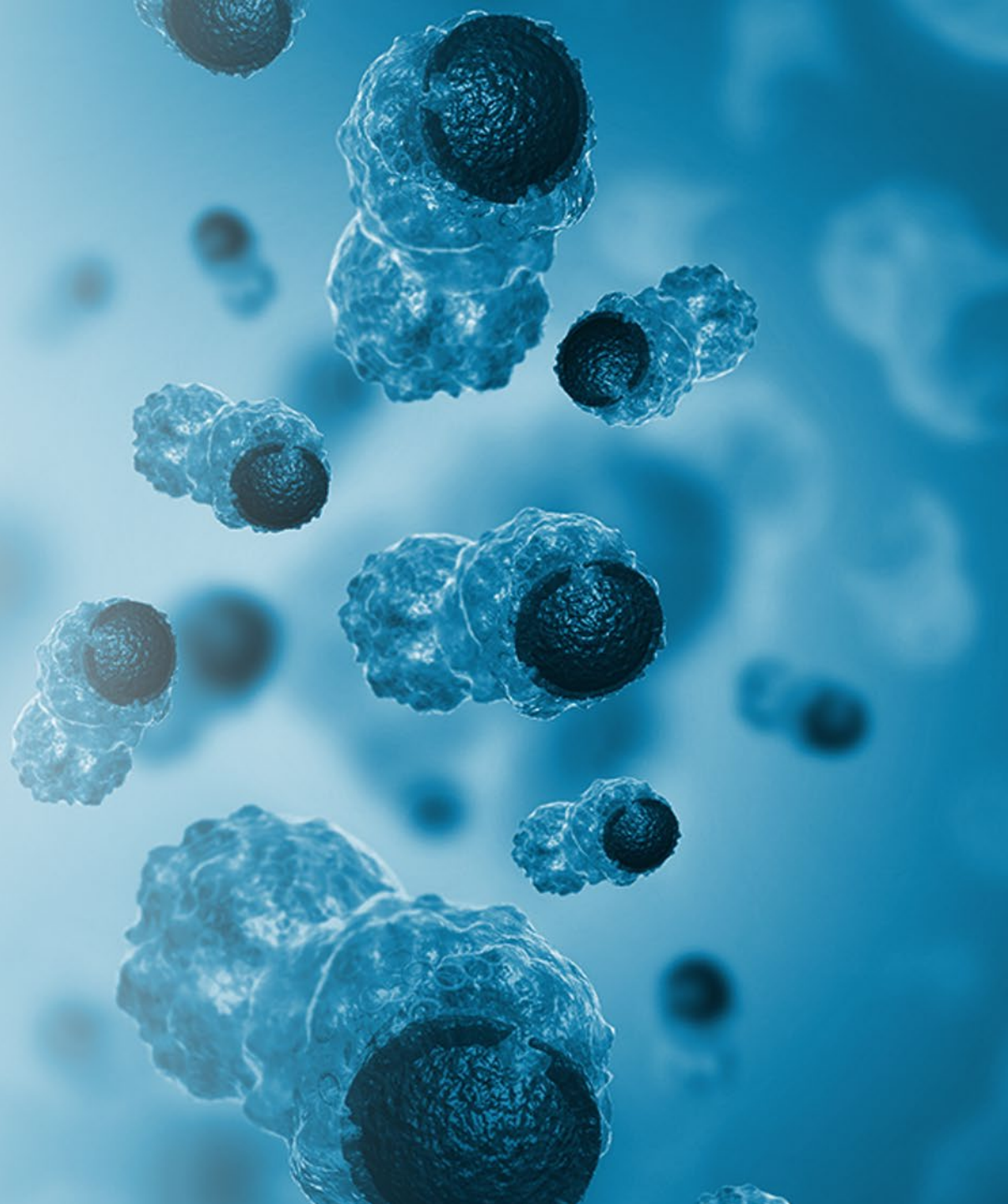
TARGET ENROLLMENT:
~180 1L participants

Interim OS analysis at 70% of events in 2H 2023

Pivotal study evaluating trilaciclib in mTNBC 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

Ongoing Phase 2 Studies



Three Near-Term Phase 2 Proof of Concept Readouts

Proof of Concept Study	Key Goals of Study Related to Trilaciclib
2L / 3L TNBC (Phase 2)	1. Evaluate **myeloprotection benefits with an ADC** (sacituzumab govitecan in this study) 2. Determine whether increased cytotoxic exposure and potential synergy **increases PFS / OS**
1L Bladder Cancer (Phase 2)	1. Demonstrate ability to **increase survival across additional tumors** (i.e., beyond mTNBC) 2. Evaluate if **synergistic benefits with a CPI** observed preclinically is translatable to humans
Neoadjuvant TNBC (Phase 2)	1. Clinically **confirm mechanistic effects** that appear to be driving increased immunomodulation 2. Evaluate if there is an anti-tumor efficacy **signal in early stage** TNBC patients

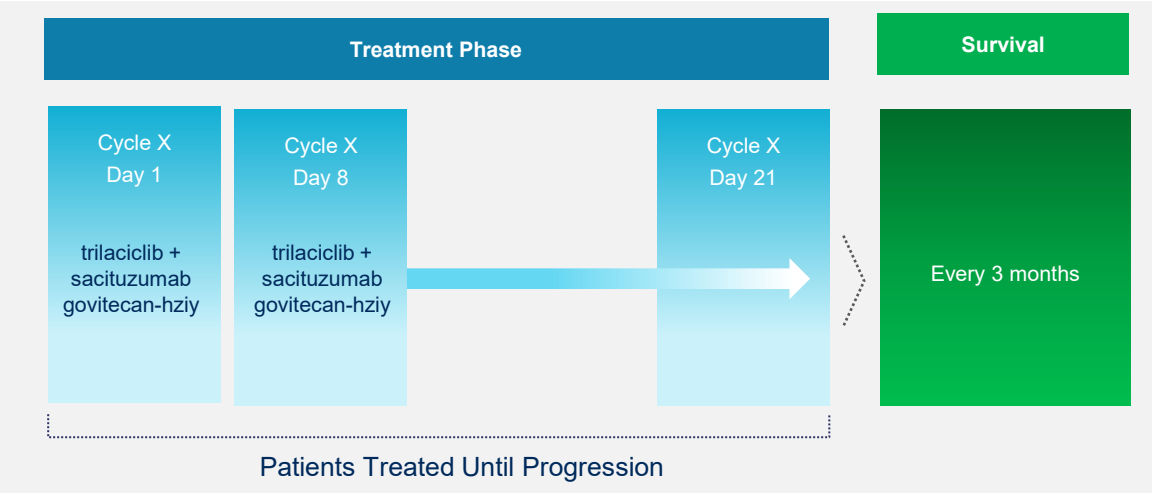
G1 THERAPEUTICS

Phase 2 ADC Combination Study: 2L/3L Metastatic TNBC

Myeloprotection, Extended Cycles & Immunogenic Tumor

Evaluate synergistic combo potential of trilaciclib and sacitizumab govitecan-hziy, each of which have individually demonstrated clinically meaningful OS improvements in TNBC

Single Arm:
2L/3L TNBC



PRIMARY ENDPOINT:
PFS

SECONDARY ENDPOINTS:
ORR, CBR, OS, myeloprotection measures

TARGET ENROLLMENT:
~40 participants

PATIENTS TREATED UNTIL PROGRESSION

Initial results in 4Q 2022

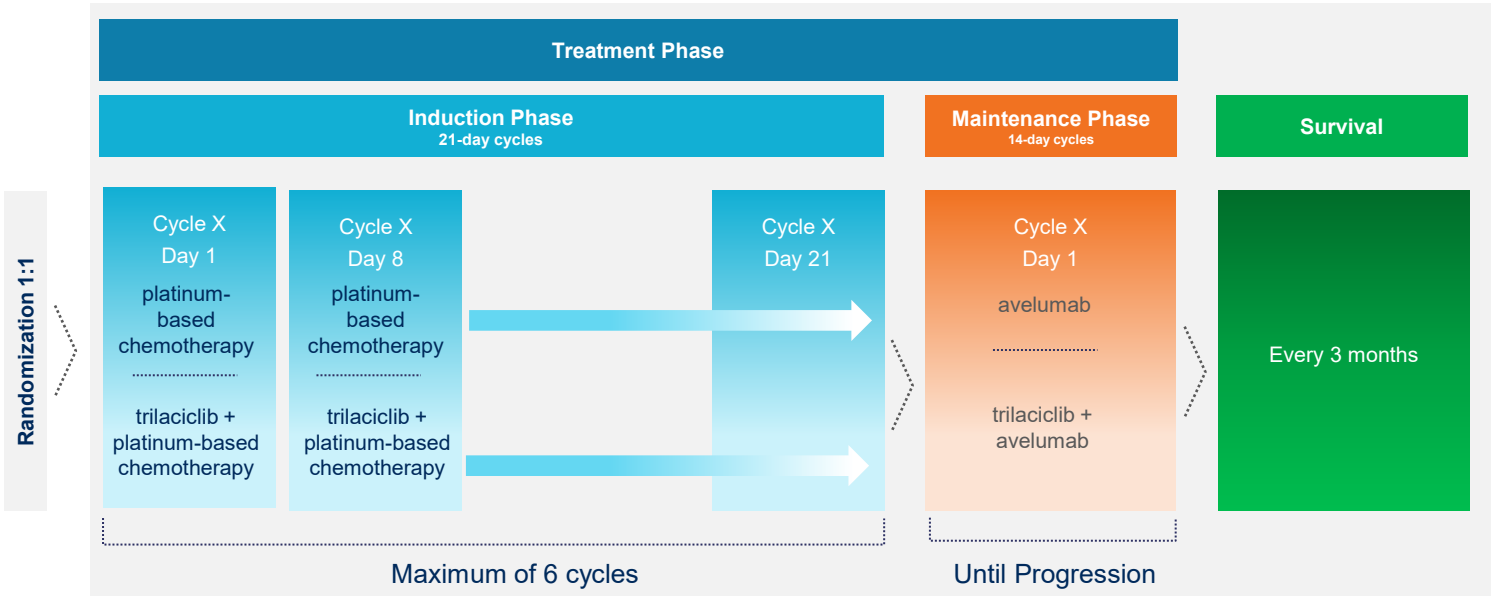
Strong belief in clinical rationale underlying this combo; data generated will be instructive in evaluating future ADC combo possibilities

G1 THERAPEUTICS

Phase 2 Bladder (mUC) Study: PRESERVE 3

Extended Cycles, Immunogenic Tumor & Combination with Immunotherapy

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

ENROLLMENT COMPLETED:
92 participants

PATIENTS TREATED UNTIL PROGRESSION

Initial results in 4Q 2022

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

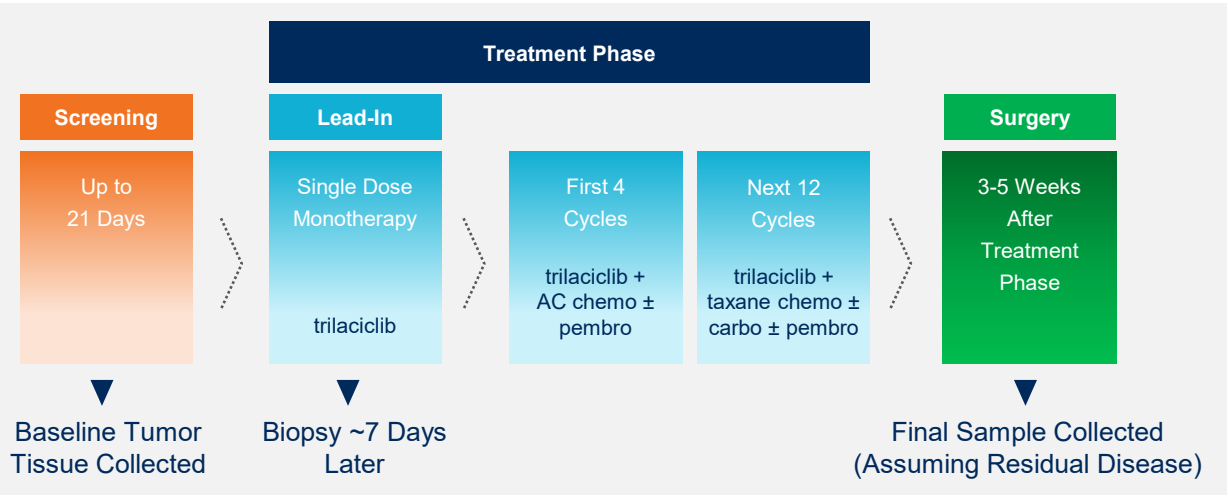
G1 THERAPEUTICS

Phase 2 Neoadjuvant TNBC: Mechanism of Action (MOA) Study

Extended Cycles, Immunogenic Tumor & Combination with Immunotherapy

Confirm immune-based properties of trilaciclib and its potential role in increasing the anti-tumor efficacy of chemotherapy with and without a checkpoint inhibitor

Single Arm:
Early-stage TNBC



PRIMARY ENDPOINT:
Immune-based MOA

SECONDARY ENDPOINTS:
pCR, immune response and profiling measures

ENROLLMENT COMPLETED:
24 patients

Initial results in 4Q 2022

Data generated from MOA study will inform design of future additional pivotal studies across multiple tumor types and treatment combinations

G1 THERAPEUTICS

Key Takeaways: Expanding the Trilaciclib Opportunity

- Robust portfolio of ongoing Phase 2 and Phase 3 studies
- Phase 3 label expansion opportunities in CRC and TNBC

  Initial results available in 2023 ➡ Registration

- Phase 2 trials providing proof of concept for trilaciclib in multiple treatment combinations with drug classes expected to be foundational in future standards of care

  Initial results available in 2022 ➡ Pivotal Studies

G1 THERAPEUTICS

Moderated Discussion: The Colorectal Cancer Treatment Landscape

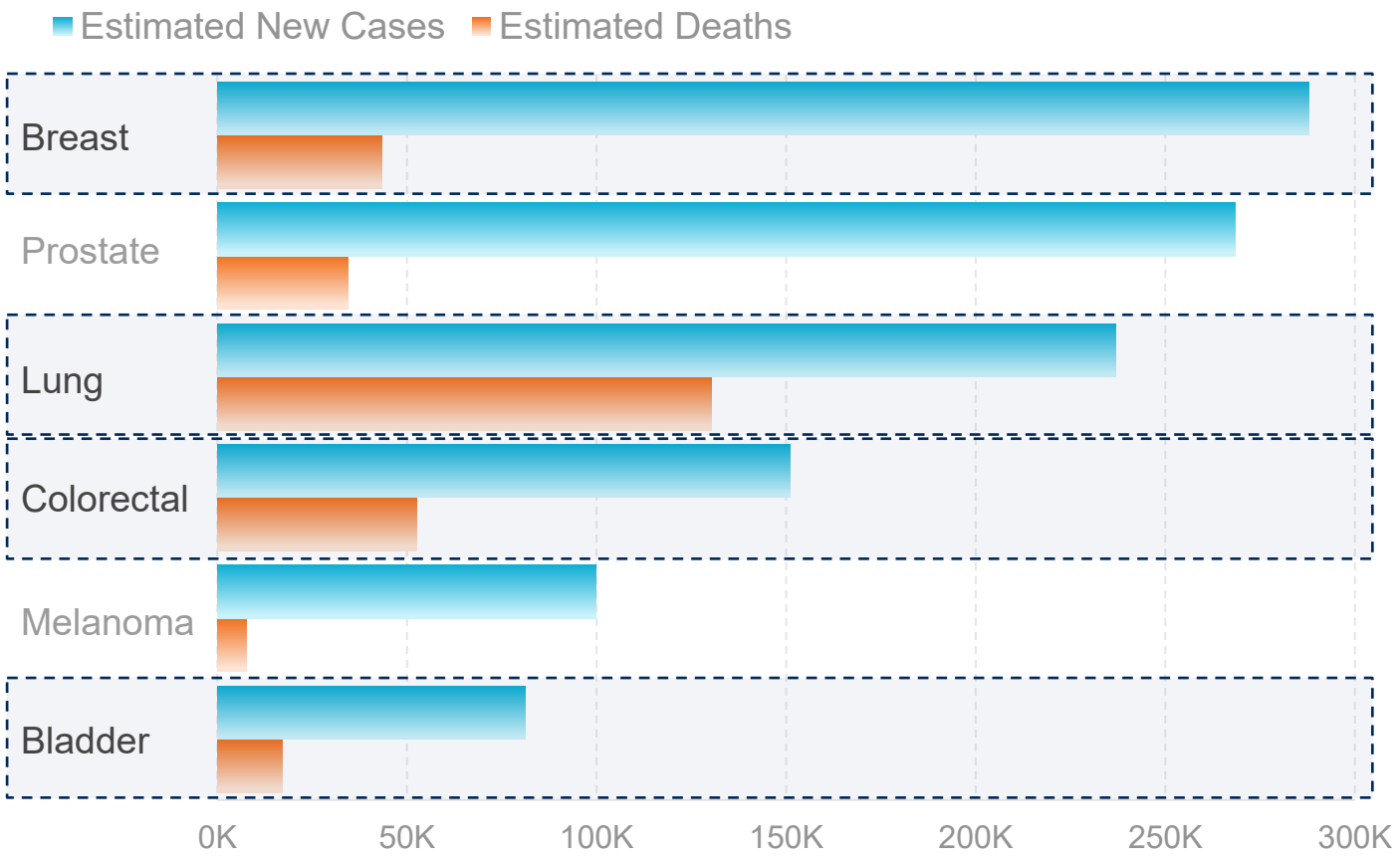
Richard Goldberg, M.D., Professor Emeritus and former Director, West Virginia University Cancer Institute (WVUCI)
Moderator: Norm Nagl, Ph.D., Vice President, Medical Affairs

Trilaciclib Market Opportunity and Future Focus

Mark Avagliano, Chief Business Officer

Currently Focused on Common Tumor Types

U.S. Annual Incidence and Deaths[1]



G1 Development and Commercialization

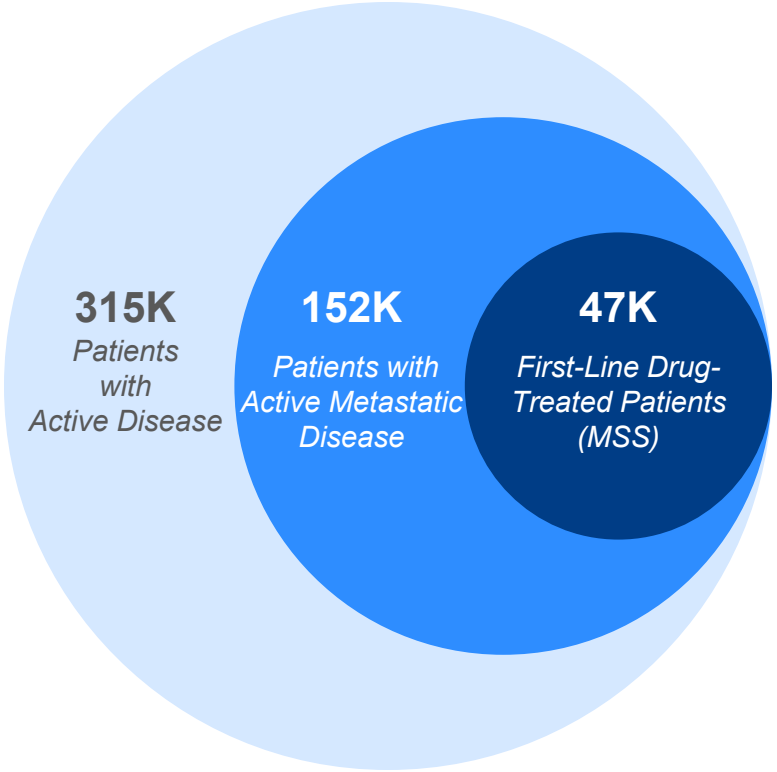
POC	Pivotal	Marketed
☑ 2L/3L TNBC ☑ Neo(adj) TNBC	☑ 1L TNBC	
☑ 1L NSCLC		COSELA™ trilaciclib for injection 300 mg ES-SCLC
	☑ 1L CRC	
☑ 1L Bladder		

☑ Ongoing ☑ Planned

1. Estimated new cases and deaths from National Cancer Institute for 2022 for the six most common tumor types (ranked by annual incidence).

1L CRC: Meaningful Near-Term Potential Opportunity

U.S. CRC Patient Population (2021)[1]



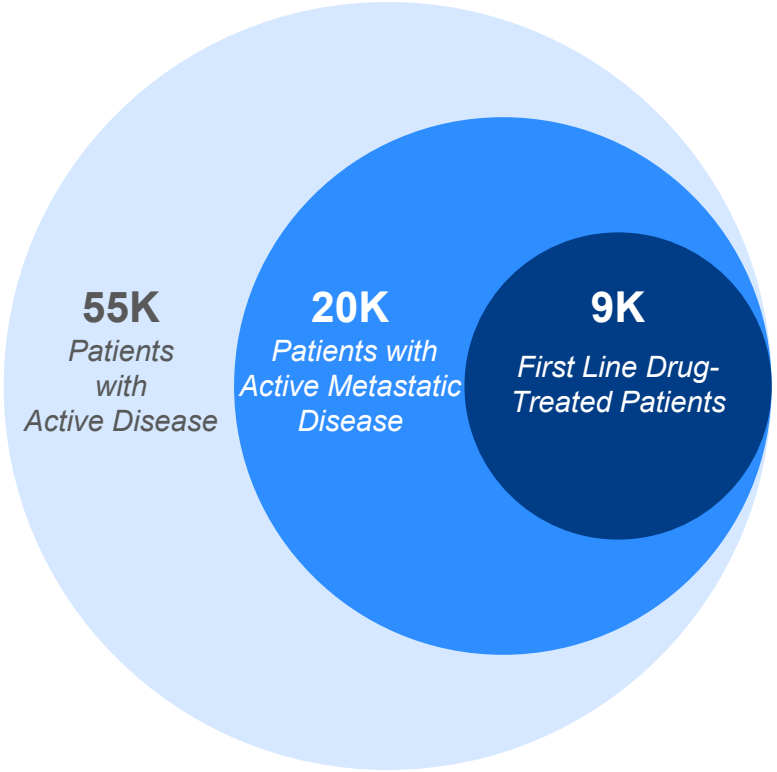
- **Chemotherapy remains primary backbone for mCRC**
  - Majority of patients have microsatellite stable (MSS) tumors
  - ~47k annual first-line drug-treated MSS CRC patients in the U.S
- **FOLFOXIRI only used in ~10% to ~20% of U.S. patients**
  - Most efficacious regimen but currently limited due to toxicities
  - Typically reserved for younger healthier patients with larger tumors
- **Significant potential to expand FOLFOXIRI usage**
  - Meaningfully reduced myelosuppression addresses critical hurdle
  - Patients receive 4 vials of trilaciclib for each 2-week cycle

Meaningfully reducing the myelosuppression associated with FOLFOXIRI expected to enable broader use across 1L MSS CRC patients

1. Estimates from secondary data, and internal analysis and primary research

1L TNBC: Important Area of High Unmet Need

U.S. TNBC Patient Population (2021)[1]



- **TNBC tumors are aggressive and difficult to treat**
  - Categorized by lack of HR expression and HER2 gene amplification
  - Trilaciclib demonstrated robust survival benefit with chemo in Ph2
- **Chemo +/- targeted therapy remains first-line TNBC SoC**
  - ~9k annual first-line drug treated TNBC patients in the U.S.
  - Targeted therapies only demonstrated benefit in subpopulations
- **Trilaciclib demonstrated broad benefit in Phase 2**
  - Benefit observed across PD-(L)1+ and PD-(L)1- subpopulations
  - Patients receive 4 vials of trilaciclib for each 3-week cycle

Meaningfully increasing overall survival broadly across 1L TNBC subpopulations addresses a high unmet need area (particularly without increasing toxicity)

1. Estimates from secondary data, and internal analysis and primary research

Three Near-Term Phase 2 Proof of Concept Readouts

Proof of Concept Study	Key Goals of Study Related to Trilaciclib
2L / 3L TNBC (Phase 2)	1. Evaluate **myeloprotection benefits with an ADC** (sacituzumab govitecan in this study) 2. Determine whether increased cytotoxic exposure and potential synergy **increases PFS / OS**
1L Bladder Cancer (Phase 2)	1. Demonstrate ability to **increase survival across additional tumors** (i.e., beyond mTNBC) 2. Evaluate if **synergistic benefits with a CPI** observed preclinically is translatable to humans
Neoadjuvant TNBC (Phase 2)	1. Clinically **confirm mechanistic effects** that appear to be driving increased immunomodulation 2. Evaluate if there is an anti-tumor efficacy **signal in early stage** TNBC patients

These data will be important to confirm ability for trilaciclib to add meaningful benefit to patients in strategically important treatment settings

G1 THERAPEUTICS

Potentially Ideal Treatment Settings for Future Studies

1 Myeloprotection: Enabling increased cytotoxic exposure while protecting immune system

- **ADCs** (in areas ADC monotherapy may become SoC)
- **ADC Combinations** (in areas ADC combinations may become SoC)
- **Other Highly Myelotoxic Regimens** (e.g., FOLFIRINOX)

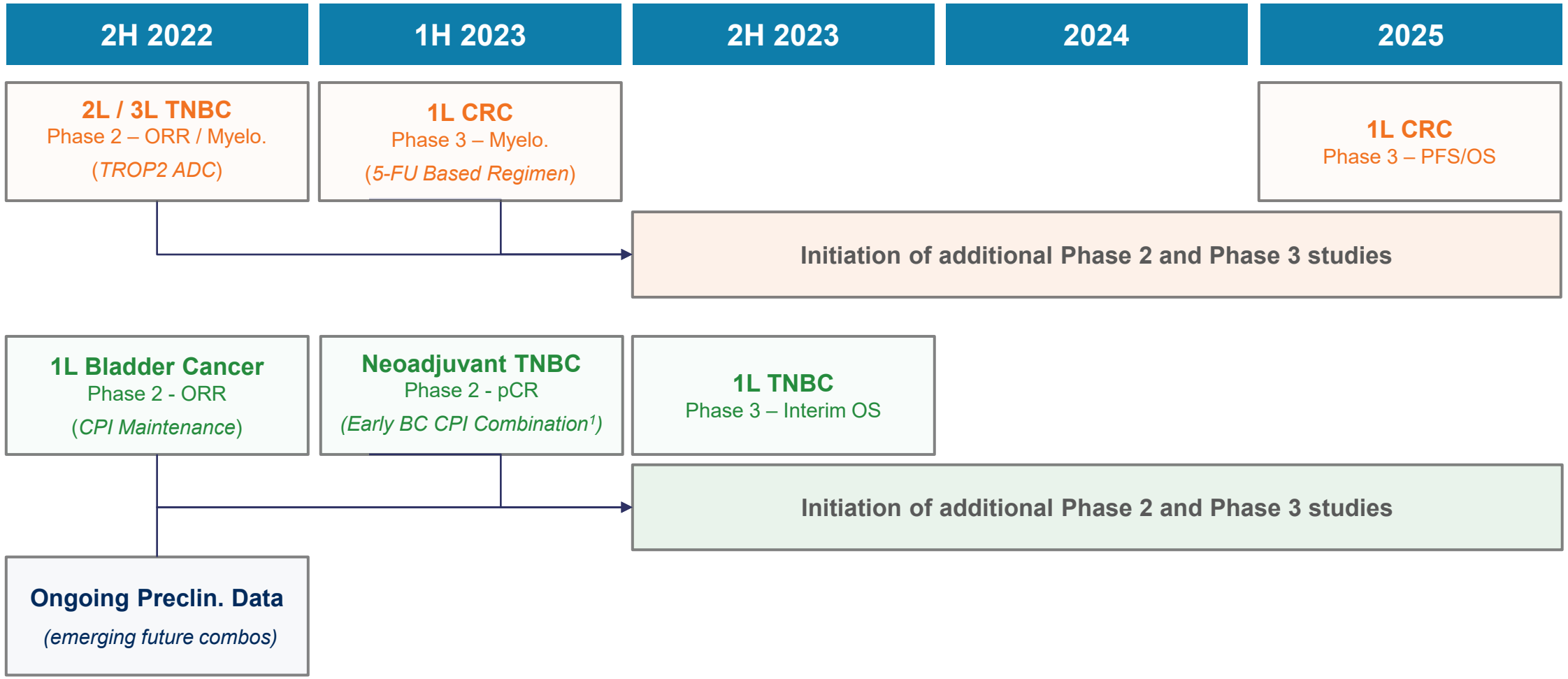
2 Immunomodulation: Improving overall immune response

- **CPI + Chemo/ADC** (in immunogenic tumors)
- **CPI Maintenance** (metastatic or adjuvant uses)
- **Future CPI Combos** (e.g., PD-(L)1i + anti-LAG3; PD-(L)1i + anti-CD73)

Focused on ideal treatment settings where trilaciclib has unique ability to further improve survival in combination with important leading and emerging treatments

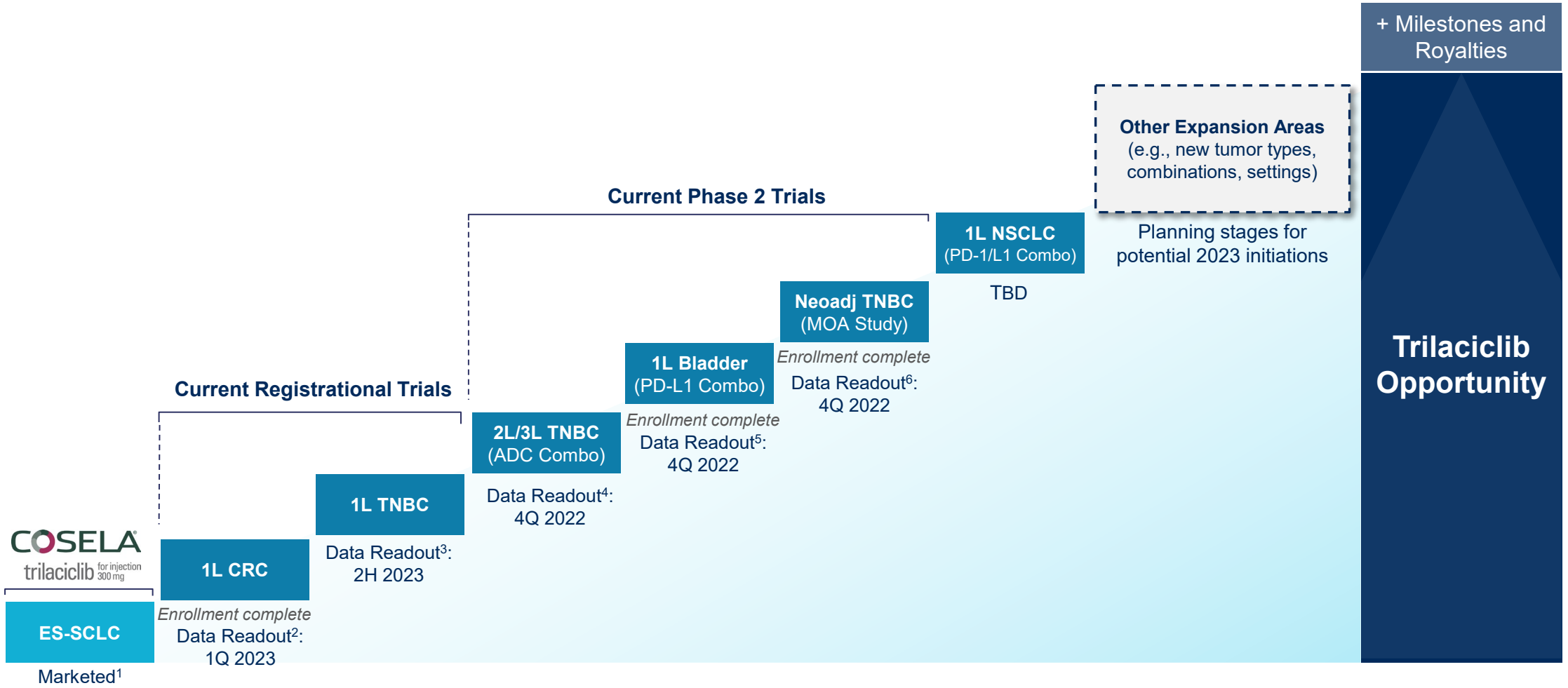
G1 THERAPEUTICS

Near-Term Data to Guide Future Development Decisions



1. Investigator discretion on whether to use CPI in study.

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



1. COSELA is marketed in the U.S. by G1 and conditionally approved in Greater China to be marketed by our partner, Simcere
2. 1L CRC data readout in 1Q 2023 expected to include results for myeloprotection and Objective Response Rate (ORR) endpoints
3. 1L TNBC data readout in 2H 2023 expected to include interim results for Overall Survival (OS); interim OS analysis to be conducted by its DMC in 2H 2023
4. 2L / 3L TNBC (in combination with an ADC) initial data in 4Q 2022 expected to include ORR and myeloprotection endpoints
5. 1L Bladder Cancer (in combination with an anti-PD-L1) initial data in 4Q 2022 expected to include ORR and myeloprotection endpoints
6. MOA in Neoadjuvant TNBC +/- PD-1 inhibitor (investigator discretion); data readout in 4Q 2022 to include results for immune endpoints; data readout in 1H 2023 to include pCR

Concluding Remarks and Transition to Q&A

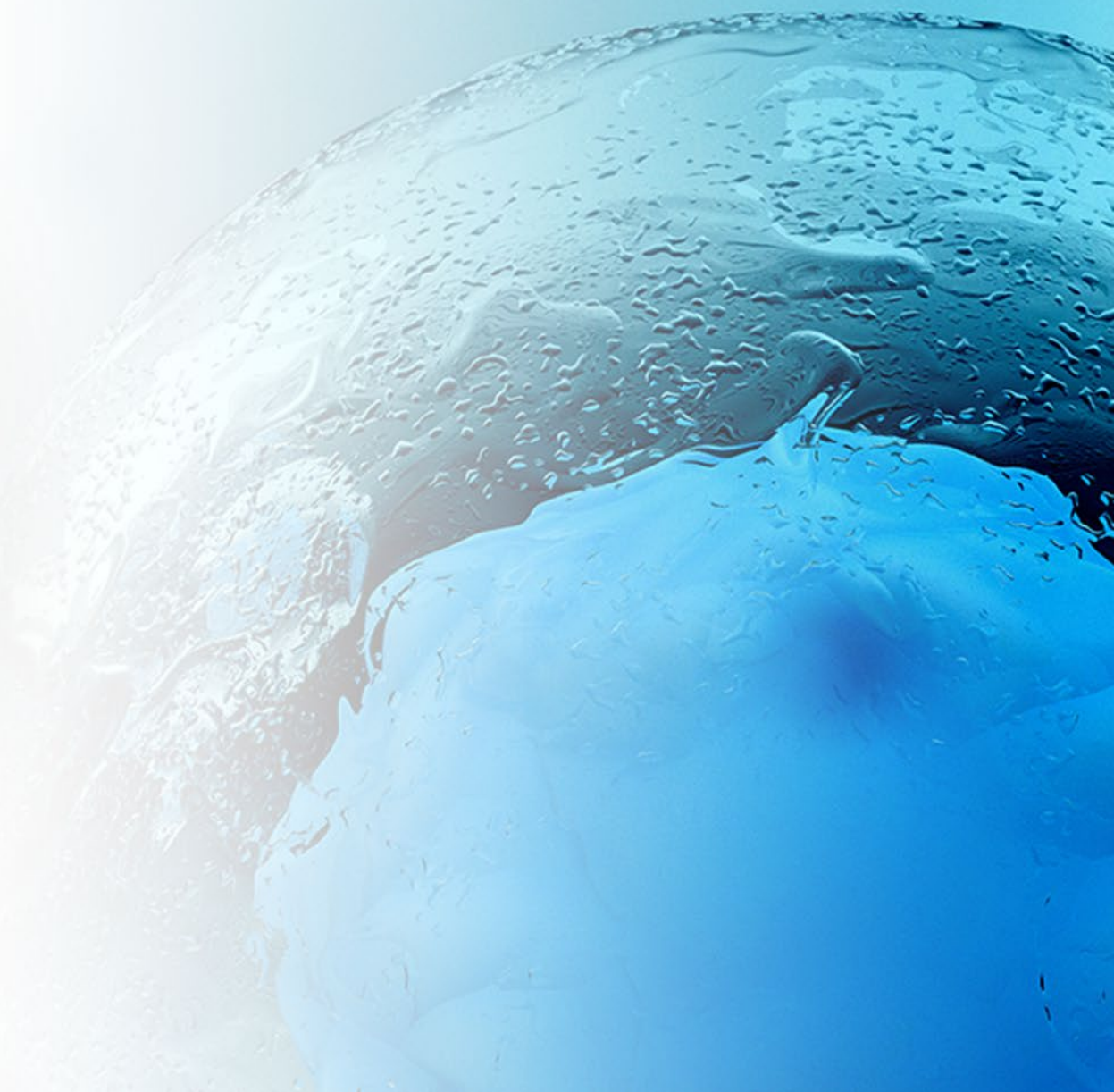
Jack Bailey, Chief Executive Officer

Highlights from Today's Event

- Trilaciclib's unique effects attributable to transient, potent, and selective CDK4/6 inhibition and directly targeting the host
- Trilaciclib enhances multiple immunological processes within the cancer immunity cycle
- Potential for improved survival via improved immune response (immunomodulation) and increased cytotoxic exposure while protecting immune system (myeloprotection)
- New preclinical data show consistent synergistic potential
- Meaningful data read-outs starting in the next three months and continuing through 2023
- Trilaciclib represents a pipeline-in-a-molecule opportunity with significant expansion opportunities in future standard of care

G1 THERAPEUTICS

Q&A with G1 Leadership



Innovations in Oncology:
The Science of Trilaciclib

September 15, 2022