UNITED STATES
SECURITIES AND EXCHANGE COMMISSION
Washington, D.C. 20549

FORM 8-K

CURRENT REPORT
Pursuant to Section 13 or 15(d)
of the Securities Exchange Act of 1934

Date of Report (Date of earliest event reported): August 15, 2017

G1 THERAPEUTICS, INC.
(Exact name of registrant as specified in its charter)

Delaware	**001-38096**	**26-3648180**
(State or other jurisdiction of incorporation)	**(Commission File Number)**	**(IRS Employer Identification No.)**

79 T.W. Alexander Drive **4501 Research Commons, Suite 100** **Research Triangle Park, NC** **(Address of principal executive offices)**	**27709** **(zip code)**

Registrant's telephone number, including area code: (919) 213-9835

Check the appropriate box below if the Form 8-K filing is intended to simultaneously satisfy the filing obligation of the registrant under any of the following provisions:

☐ Written communications pursuant to Rule 425 under the Securities Act (17 CFR 230.425)

☐ Soliciting material pursuant to Rule 14a-12 under the Exchange Act (17 CFR 240.14a-12)

☐ Pre-commencement communications pursuant to Rule 14d-2(b) under the Exchange Act (17 CFR 240.14d-2(b))

☐ Pre-commencement communications pursuant to Rule 13e-4(c) under the Exchange Act (17 CFR 240.13e-4(c))

Indicate by check mark whether the registrant is an emerging growth company as defined in Rule 405 of the Securities Act of 1933 (17 CFR §230.405) or Rule 12b-2 of the Securities Exchange Act of 1934 (17 CFR §240.12b-2).

Emerging Growth Company ☒

If an emerging growth company, indicate by check mark if the registrant has elected not to use the extended transition period for complying with any new or revised financial accounting standards provided pursuant to Section 13(a) of the Exchange Act. ☒

Item 7.01 Regulation FD Disclosure.

The attached slides were presented by G1 Therapeutics, Inc. at the Wedbush PacGrow Healthcare Conference on August 15, 2017.

Item 9.01 Financial Statements and Exhibits.

(d) Exhibits

Exhibit No.	Description
99.1	Presentation for Wedbush PacGrow Healthcare Conference.

SIGNATURES

Pursuant to the requirements of the Securities Exchange Act of 1934, the Registrant has duly caused this report to be signed on its behalf by the undersigned thereunto duly authorized.

G1 THERAPEUTICS, INC.

By: /s/ Gregory J. Mossinghoff
Gregory J. Mossinghoff
Chief Business Officer

Date: August 17, 2017

EXHIBIT INDEX

Exhibit Number	Description
99.1	Presentation for Wedbush PacGrow Healthcare Conference.

Exhibit 99.1

Presentation for Wedbush PacGrow Healthcare Conference
August 15, 2017

Mark Velleca MD, PhD
Chief Executive Officer

79 T.W. Alexander Drive | 4501 Research Commons, Suite 100 | Research Triangle Park, NC 27709
919-213-9835 (P) | 919-741-5830 (F) | www.g1therapeutics.com

Forward-looking statements

This presentation and the accompanying oral commentary contain "forward-looking" statements within the meaning of the Private Securities Litigation Reform Act of 1995, known as the PSLRA, that are based on our beliefs and assumptions and on information available to us as of the date of this presentation. Forward-looking statements include information concerning our possible or assumed future results of operations, business strategies, development plans, regulatory activities, competitive position, potential growth opportunities, use of proceeds and the effects of competition. Forward-looking statements include all statements that are not historical facts and can be identified by terms such as "anticipate," "believe," "continue," "could," "estimate," "expect," "intend," "may," "might," "objective," "ongoing," "plan," "predict," "project," "potential," "should," "will," or "would," or the negative of these terms, or other comparable terminology intended to identify statements about the future.

We may not actually achieve the plans, intentions or expectations disclosed in our forward-looking statements. Forward-looking statements involve known and unknown risks, uncertainties, assumptions and other factors that may cause our actual results, performance or achievements to be materially different from any future results, performance or achievements expressed or implied by the forward-looking statements. Except as required by law, we assume no obligation to update these forward-looking statements publicly, or to update the reasons why actual results could differ materially from those anticipated in the forward-looking statements, even if new information becomes available in the future. The risks and uncertainties that we face are described in our most recent filings with the Securities and Exchange Commission.

G1 Therapeutics: clinical-stage oncology company

- Advancing the validated CDK4/6 inhibitor space
- Three wholly owned drug candidates addressing distinct multi-billion dollar markets
  - ✓ Trilaciclib is first-in-class with compelling clinical data; currently in four Phase 2 trials
  - ✓ G1T38 has best-in-class potential versus Ibrance and Kisqali
  - ✓ G1T48 (oral SERD) potentially first/best-in-class; on track for 4Q17 IND
- Multiple clinical read-outs and value inflection points in 2018

Experienced leadership, well financed

Management team

- Proven industry leaders with more than 75 years of oncology experience

Mark Velleca, MD, PhD - Chief Executive Officer

Raj Malik, MD - Chief Medical Officer

Greg Mossinghoff - Chief Business Officer

Terry Murdock - SVP, Development Operations

Jay Strum, PhD - Chief Scientific Officer

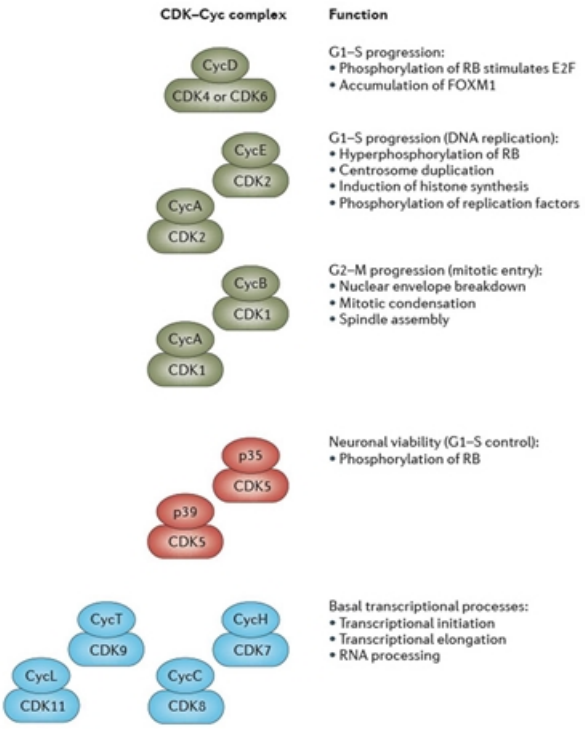
Board of Directors

Seth Rudnick, MD - board chairman
Glenn P. Muir - audit committee chair
Tyrell Rivers, PhD - MedImmune Ventures
Fred Eshelman, PharmD - Eshelman Ventures
Christy Shaffer, PhD - Hatteras Venture Partners
Mark Velleca, MD, PhD - CEO
Andrew Witty - former CEO, GSK

Investors

- ~ $96m in private financing
  - Cormorant
  - Franklin Templeton
  - Rock Springs Capital
  - RA Capital
- ~ $107m IPO - May 22, 2017
  - Nasdaq: GTHX

CDK4/6 is a validated and promising target

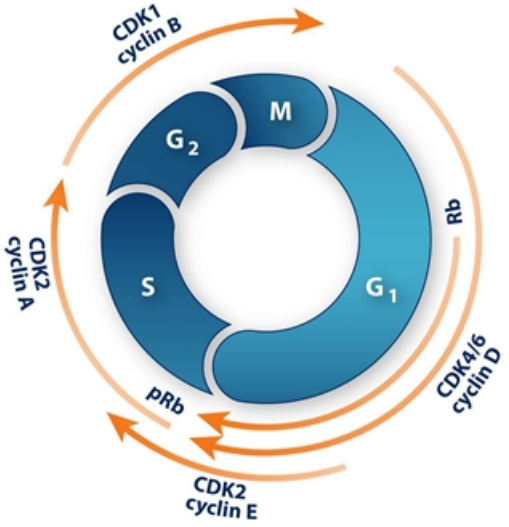


From: Nat Rev Drug Disc 2015;14:130-146

- Nobel Prize-winning science
- FDA accelerated approval of Pfizer's Ibrance for breast cancer in 2015
  - $2.1 billion revenue in 2016
  - $7 billion in estimated global peak sales
- Significant therapeutic and market potential in multiple other cancers
- G1 is the only biopharma with two clinical-stage CDK4/6 inhibitors:
  - trilaciclib
  - G1T38

G1 THERAPEUTICS

CDK4/6 typically required for cell cycle progression

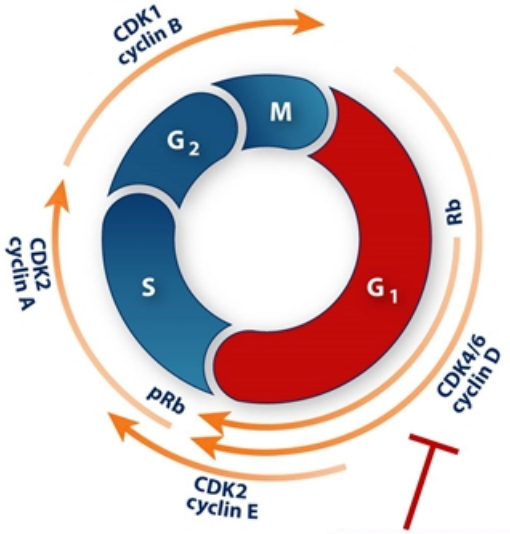


To grow and proliferate, all cells progress through four phases of the cell cycle

- G1 and G2 are gap or growth phases
- S phase: DNA synthesis
- M phase: cell division

G1 THERAPEUTICS

Selective CDK4/6 inhibition arrests cells in G1

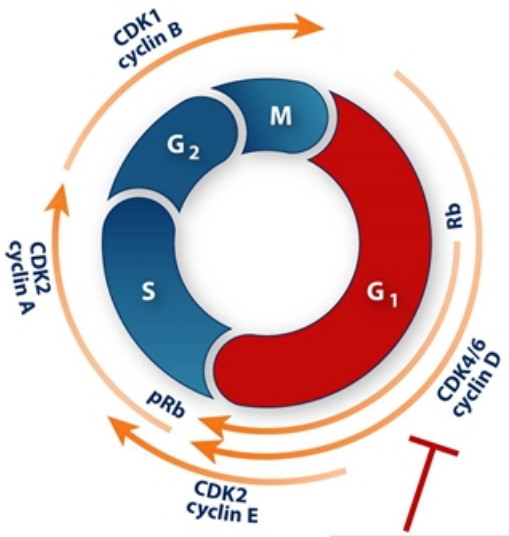


Selective CDK4/6 inhibition blocks Rb phosphorylation and progression from G1 to S phase: a cytostatic effect

G1 THERAPEUTICS

G1T38: arrests tumor cells in G1

Tumor cell



G1T38 blocks proliferation; potentiates tumor cell death when combined with other targeted therapy (e.g. SERD)

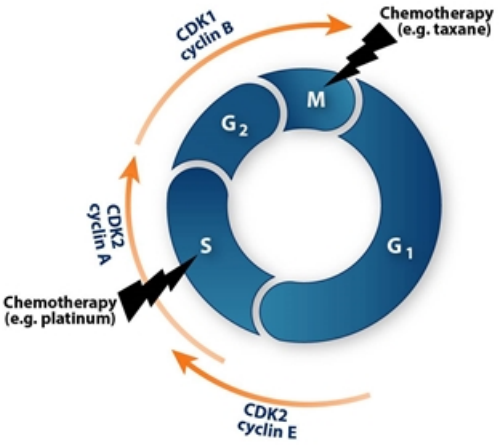
G1T38

- Highly selective CDK4/6 inhibitor with best-in-class potential
- Differentiated from Ibrance, Kisqali and abemaciclib
- Potential "backbone therapy" for multiple combination regimens in many CDK4/6-dependent tumors

G1 THERAPEUTICS

Many cancers do not require CDK4/6 to grow

CDK4/6-independent tumor cell

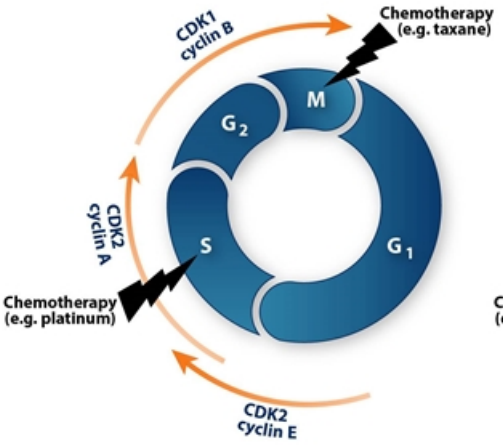


- CDK4/6-independent tumors can proliferate even in the presence of a CDK4/6 inhibitor
- Common CDK4/6-independent tumors include SCLC and TNBC
- Chemotherapy is typically used to treat these cancers
- Chemotherapy kills other cells such as hematopoietic stem and progenitor cells (HSPCs)

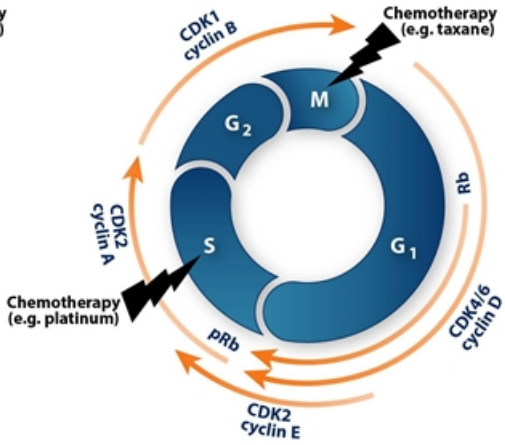
G1 THERAPEUTICS

Hematopoietic stem and progenitor cells (HSPCs) require CDK4/6

CDK4/6-independent tumor cell



HSPC

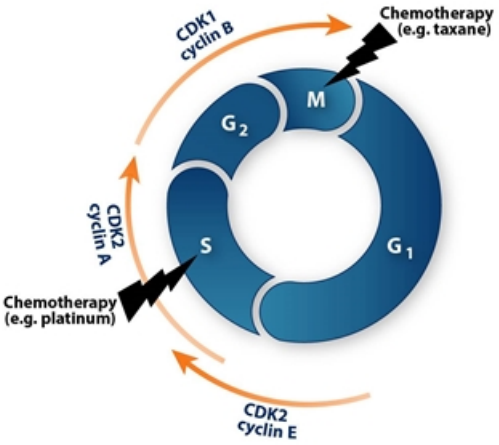


- HSPCs are the "reservoir" from which all blood and immune system cells are formed
- HSPCs are damaged by chemotherapy, causing myelosuppression and immunosuppression, limiting anti-tumor efficacy

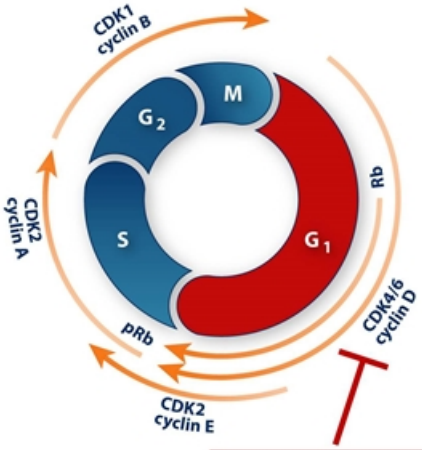
G1 THERAPEUTICS

Trilaciclib: transiently arrests HSPCs in G1

CDK4/6-independent tumor cell



HSPC



Trilaciclib transiently blocks progression through the cell cycle (G1 arrest), protecting HSPCs from damage by chemotherapy

Trilaciclib

- Short-acting IV therapy for patients with CDK4/6-independent tumors
- Preserves HSPCs from damage by chemo: myelopreservation
- Potential to improve tolerability/efficacy of chemotherapy, and chemo/checkpoint inhibitor combos
- First-in-class approach

G1 THERAPEUTICS

G1's CDK4/6 inhibitors: broad potential

Two distinct compounds rationally designed and optimized by G1, leveraging 10 years of expertise in CDK4/6 biology and chemistry

Drug	Tumor type	MOA	Dosing	Combination	Initial indications
Trilaciclib	CDK4/6-independent	Preserves HSPCs, enhances immune system function	IV, intermittent	Chemotherapy and/or checkpoint inhibitor	SCLC, TNBC
G1T38	CDK4/6-dependent	Stops tumor cell proliferation	Oral, daily	Growth-signaling inhibitors (e.g., SERD, EGFRi)	ER+, HER2- breast cancer, NSCLC

Each drug has potential to be backbone therapy for multiple combination regimens

G1 THERAPEUTICS

Key advantages of trilaciclib and G1T38

Trilaciclib: a first-in-class approach

- ✓ Rationally designed as a short-acting IV therapy given prior to chemo
- ✓ No known competitor (including PFE, NVS, LLY)
- ✓ PFE, NVS and LLY inhibitors do not have the PK profile required for this setting

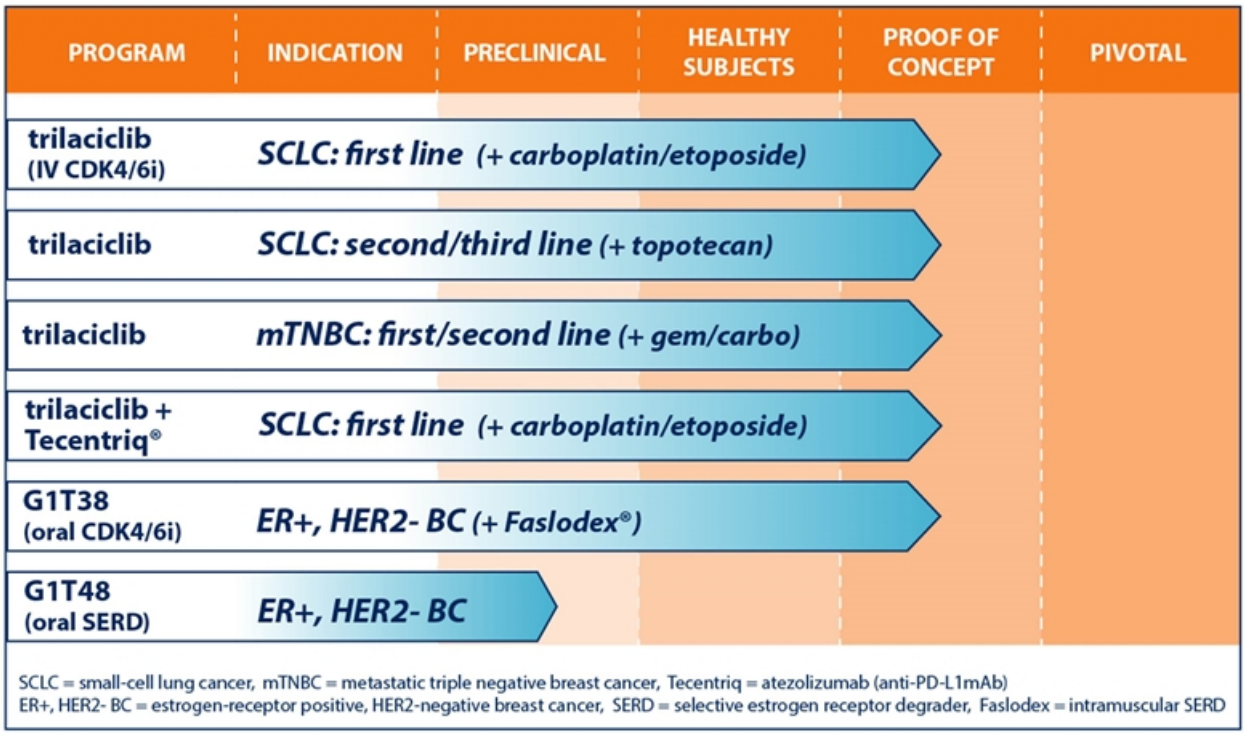
G1T38: overcoming competitors' liabilities, potentially best-in-class

Competition	**Ibrance - PFE** Long half-life leads to drug accumulation, neutropenia, and dosing holiday	**Kisqali - NVS** Neutropenia/dosing holiday, QT prolongation, DILI (additional monitoring)	**abemaciclib - LLY** High incidence of diarrhea due to insufficient selectivity (CDK2)
G1T38	Shorter half-life: potential for continuous daily dosing and less neutropenia	Clean hERG/QT, no DILI	High selectivity versus CDK2 and other kinases

G1 THERAPEUTICS

G1's development pipeline

- *G1 owns IP and worldwide commercial rights to all compounds*
- *13 issued composition-of-matter and methods-of-use patents*



G1 THERAPEUTICS

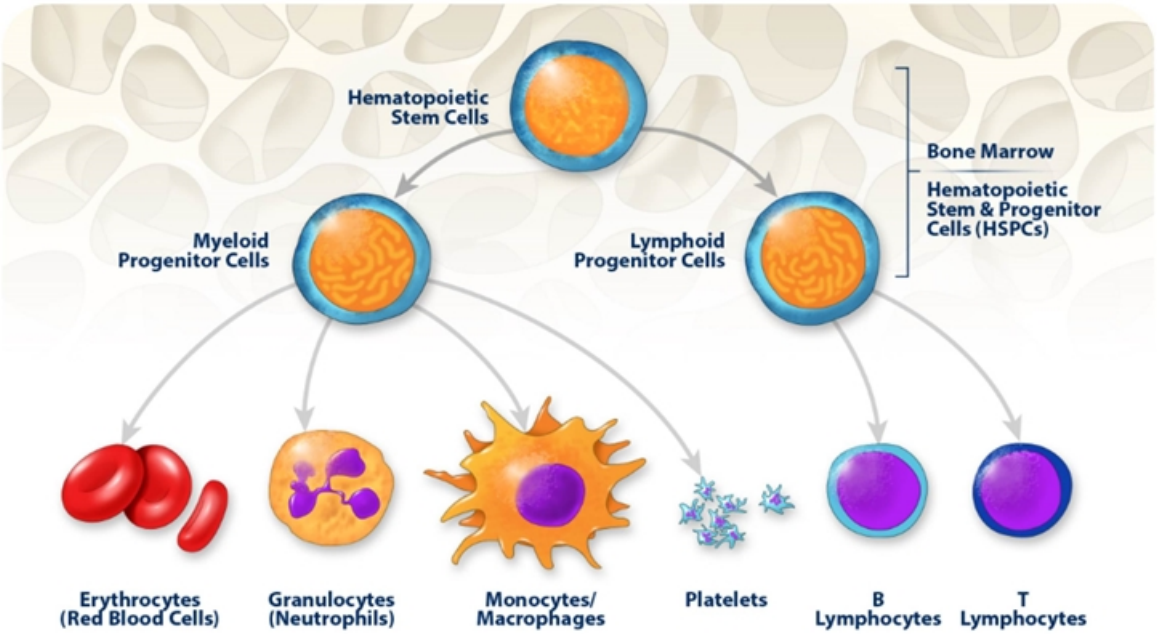
Key anticipated milestones through 2Q18

		3Q17	4Q17	1Q18	2Q18
Trilaciclib (iv CDK4/6i)	1st line-SCLC Phase 2a	enrollment completed (2Q17)		top-line randomized data	
	2nd/3rd-line SCLC Phase 2a				enrollment completed
	metastatic TNBC Phase 2				enrollment completed
	1st line-SCLC, Ph2 (+ Tecentriq)	enrollment continuing (through 2018)			
G1T38 (oral CDK4/6i)	ER+, HER2- BC Ph1b/2a (+ Faslodex)			Phase 1b enrollment completed; Phase 2a initiated	Phase 1b preliminary data
	EGFRm NSCLC Phase 1b/2 (+ Tagrisso)		IND filed	Phase 1b initiated	
G1T48 (oral SERD)	ER+, HER2- BC Phase 1/2a		IND filed		Phase 1 initiated

G1 THERAPEUTICS

TRILACICLIB DEVELOPMENT PROGRAM

Trilaciclib preserves HSPCs and enhances immune system function during chemotherapy



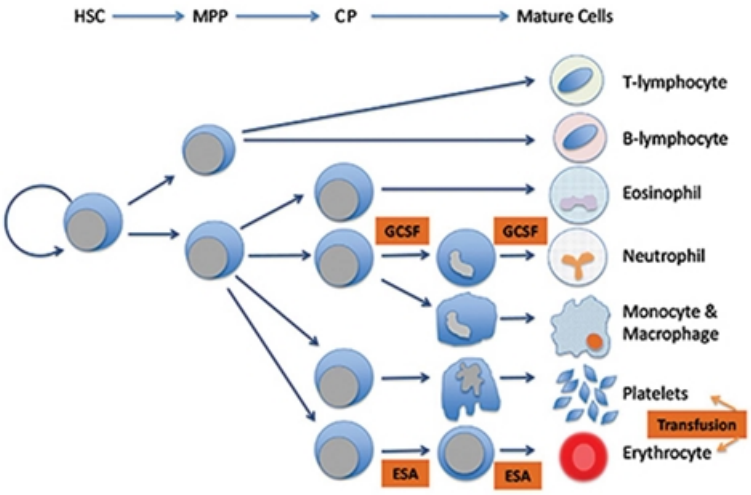
Opportunity to improve chemotherapy treatment outcomes and synergize with checkpoint combinations

G1 THERAPEUTICS

Trilaciclib addresses shortcomings of SOC

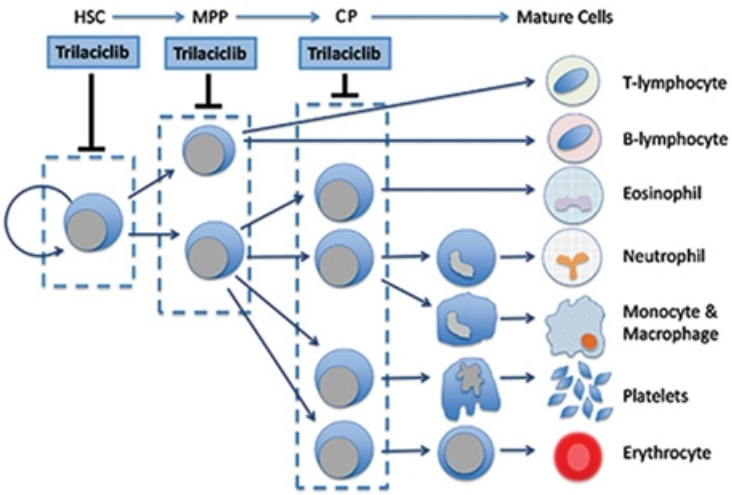
Current SOC: growth factors and transfusions

- lineage-specific support ***after*** damage by chemotherapy
- accelerates bone marrow exhaustion
- exacerbates myeloid skewing and chronic lymphopenia



Trilaciclib: preserves all blood lineages

- IV administration ***before*** chemo, prevents HSPC damage
- mitigates bone marrow exhaustion
- attenuates myeloid skewing, preserves lymphocytes



G1 THERAPEUTICS

Rationally designed product profile

- Reduce suppression of all hematopoietic lineages by protecting HSPCs from damage by chemotherapy (myelopreservation)
- Reduce clinically relevant consequences of myelosuppression - e.g. febrile neutropenia (FN) - and reduce overall cost of care from hospitalizations, growth factor support, transfusions
- Use with multiple chemotherapies in patients with CDK4/6-independent tumors: SCLC, TNBC, bladder, head and neck, others
- Dosing regimen fits with standard clinical practice
  - IV infusion of trilaciclib prior to chemotherapy
- Potential to increase anti-tumor activity and impact ORR/PFS/OS by:
  - enabling maintenance of planned chemotherapy dose and schedule
  - enhancing immune system function in context of chemo-mediated tumor cell death

G1 THERAPEUTICS

Trilaciclib value proposition - base case: myelopreservation-only, CDK4/6-independent

- ~ 1 million patients/year receive chemotherapy (US only)
- ~ 300,000 patients with CDK4/6-independent tumors eligible for trilaciclib
  - predominantly CDK4/6-independent: SCLC, TNBC, HPV^+ H&N, bladder, cervical, sarcomas
  - CDK4/6-independent subsets of: NSCLC, $HER2^+$ BC, uterus, esophagus, CRPC, CRC
- Worldwide market potential exceeds several billion dollars annually
  - assumes conservative patient capture rate and pricing
- Several upside case scenarios with compelling data in hand
  - efficacy enhancement
  - synergy with checkpoint inhibitor/chemo combos
  - use in CDK4/6-dependent tumors
- Potential to be "backbone therapy" for multiple chemo regimens and checkpoint/chemo combinations

Three ongoing POC trials in extensive-stage SCLC

Setting	Combination	Phase		Total # Patients	Primary Endpoints	Secondary Endpoints	Current Status
1st-line	carboplatin (AUC=5) and etoposide (100 mg/m^2)	1b: open label	2a: randomized (1:1), placebo-controlled	96 1b: 19 2a: 77	myelo-preservation: e.g. FN, transfusions	ORR, PFS, OS	2a enrollment completed; top-line data expected in 1Q18
2nd/3rd-line	topotecan (0.75 mg/m^2 and 1.5 mg/m^2)	1b: open label	2a: randomized (2:1), placebo-controlled	~ 120 1b: 32 2a: ~ 90	myelo-preservation: e.g. FN, transfusions	ORR, PFS, OS	2a enrollment completion anticipated 2Q18
1st-line	carboplatin/ etoposide/ Tecentriq	2: randomized (1:1), placebo-controlled		~ 100	OS	ORR, PFS, myelo-preservation	enrolling

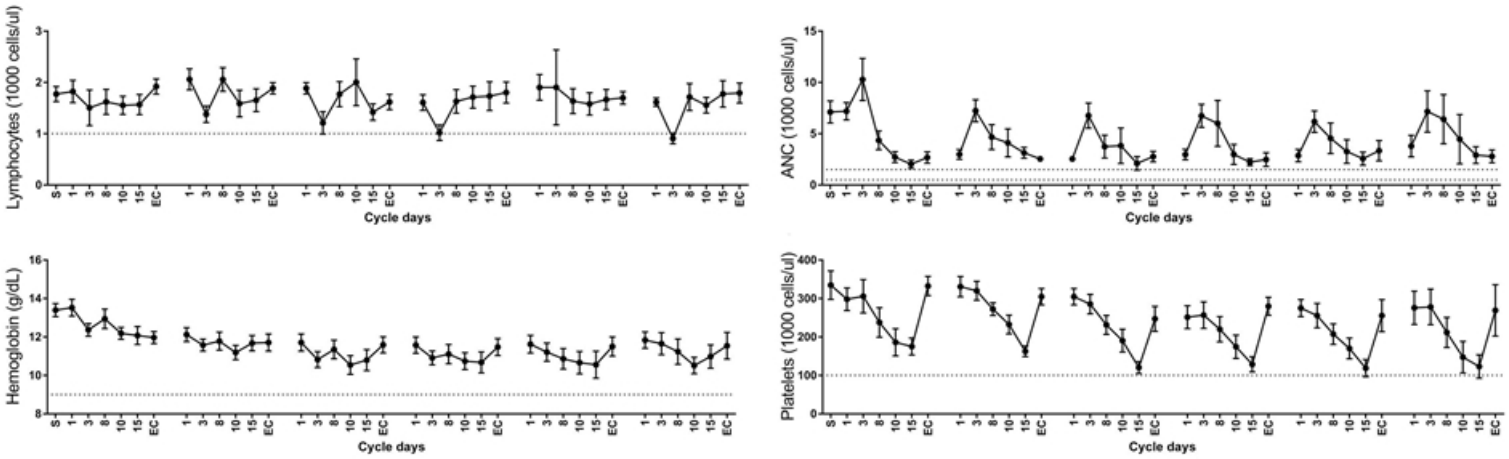
Compelling open-label data: no febrile neutropenia (FN) in 51 patients, >250 cycles chemo (historical FN rates ~ 30% with topotecan)

G1 THERAPEUTICS

1st-line SCLC Phase 1b/2a trial

- Trilaciclib + etoposide/carboplatin (EP) in patients with newly diagnosed extensive-stage SCLC (PS 0-2)
- Combination schedule in 21-day cycles
  - 30 min IV infusion of trilaciclib prior to EP on days 1-3
- Completed open-label Phase 1b trial
  - 19 patients enrolled, 17 evaluable for efficacy
  - data presented at ASCO 2017 (Rocha Lima et al)
- Randomized, double-blind, placebo-controlled Phase 2a trial ongoing
  - enrollment completed in 2Q17 (77 patients, 1:1 randomization)
  - top-line data expected in 1Q18

1st-line SCLC complete blood counts (CBCs): no clinically relevant myelotoxicity



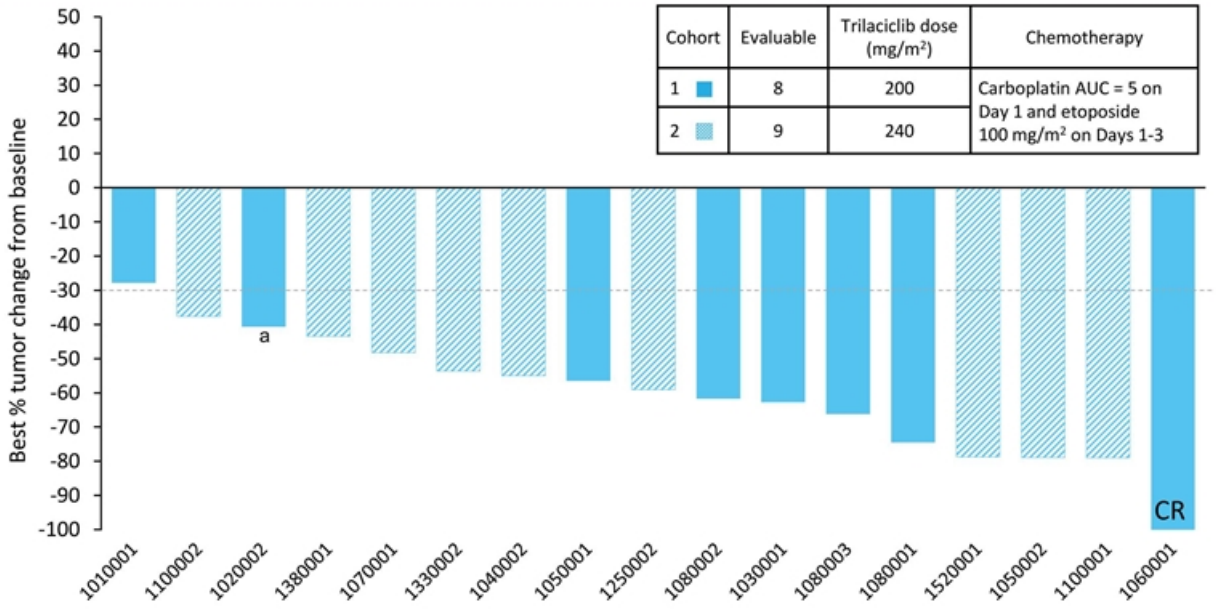
cohort 2 (n=9): Phase 2a dose of trilaciclib (240 mg/m^2)
S = baseline, EC = end cycle

Robust myelopreservation: mean CBCs above clinically relevant cytopenia thresholds for all blood lineages; no febrile neutropenia

G1 THERAPEUTICS

Data from Rocha Lima et al, ASCO 2017

1st-line SCLC: encouraging anti-tumor activity



Cohort	Evaluable	Trilaciclib dose (mg/m^2)	Chemotherapy
1	8	200	Carboplatin AUC = 5 on Day 1 and etoposide 100 mg/m^2 on Days 1-3
2	9	240	

Evaluable	CR	PR	SD	PD	ORR	CBR
17	1	14	1	1	88%	94%

Literature* etop/carb efficacy (n=387)

- 52% ORR (*only 1 CR*)
- 75% CBR

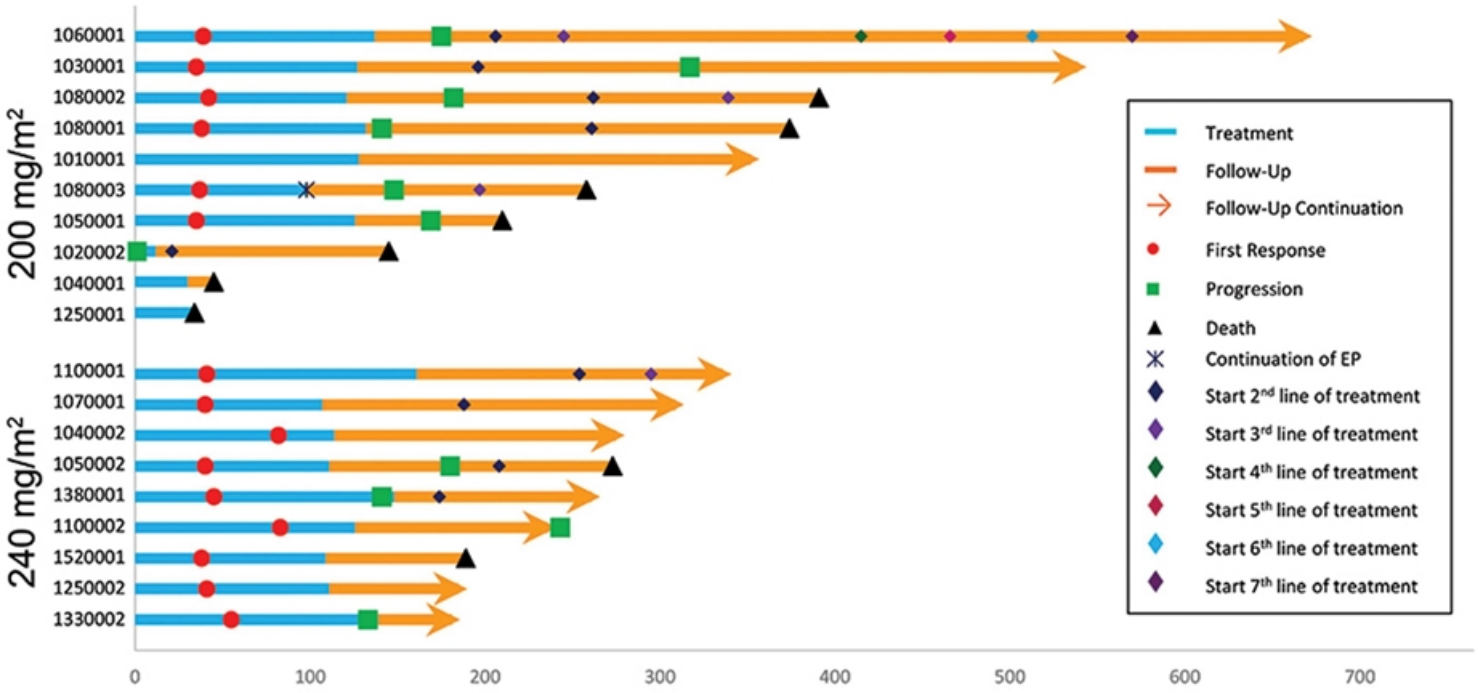
*Socinski et al, 2009

[a]Target lesion change consistent with PR at cycle 2; best response was PD due to occurrence of new lesions at cycle 2

G1 THERAPEUTICS

Data from Rocha Lima et al, ASCO 2017

1st-line SCLC: encouraging anti-tumor activity



G1 THERAPEUTICS

Data from Rocha Lima et al, ASCO 2017

SCLC 1b/2a trials: conclusions and plans

- Phase 1b data provides strong evidence of myelopreservation in both first-line and second/third line settings
- No febrile neutropenia: 51 open-label patients, >250 chemo cycles
- Better than historical overall response rates in first-line
- Both studies in randomized, placebo-controlled Phase 2a
- Top-line data from first-line study expected in 1Q18
- Potential to move rapidly into pivotal trials

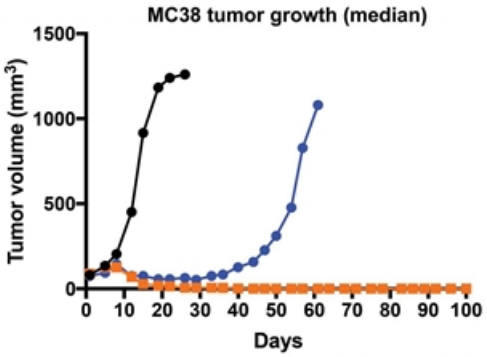
G1 THERAPEUTICS

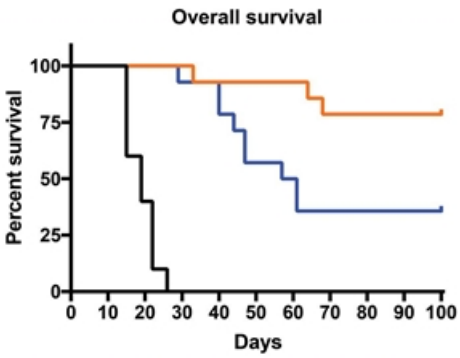
SCLC: trilaciclib/chemo/immune checkpoint inhibitor combination trial

- Trilaciclib: robust immune preservation when given with chemotherapy – preserves lymphocyte numbers/function
- Compelling preclinical data for combining trilaciclib/chemo with checkpoint inhibitor
- Non-exclusive collaboration with Genentech to evaluate trilaciclib/chemo/Tecentriq across multiple indications
- 2Q17: initiated a randomized placebo-controlled Phase 2 trial in 1st-line ES-SCLC (chemo/Tecentriq +/- trilaciclib)

Setting	Combination	Phase	Total # Patients	Primary Endpoints	Secondary Endpoints	Current Status
1st-line	carboplatin/ etoposide/ Tecentriq	2: randomized (1:1), placebo-controlled	~ 100	OS	ORR, PFS, myelo-preservation	enrolling

Trilaciclib enhances chemo/checkpoint efficacy in syngeneic CDK4/6-independent tumor model

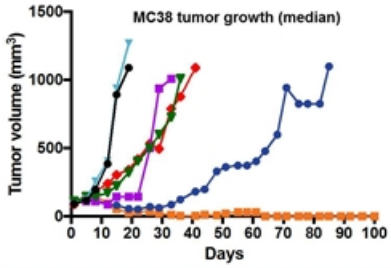




Legend	Combination treatment	ORR %	PR %	CR%	Med OS days
●	vehicle	0	0	0	19
●	oxaliplatin + anti-PD-L1	46	8	38	59
■	trilaciclib + oxaliplatin + anti-PD-L1	93	14	79	not reached

Trilaciclib: highly significant impact on:

- *ORR*
- *complete responses*
- *survival*



- vehicle
- trilaciclib
- oxaliplatin
- anti-PD-L1
- trilaciclib + oxaliplatin
- oxaliplatin + anti-PD-L1
- trilaciclib + oxaliplatin + anti-PD-L1

IP dosing regimen (for both experiments shown):
anti-PD-L1 100ug/animal D1,4,8,11; oxaliplatin 10mg/kg D1,8,15
trilaciclib 100mg/kg 30' before oxaliplatin

Repeat experiments demonstrate:

- reproducibility
- trilaciclib has no activity as monotherapy (expected with CDK4/6-independent tumor)
- similar effects with anti-PD-1 and other chemo regimens (data in 2017 AACR poster)

G1 THERAPEUTICS

Expansion to other indications: TNBC

- Significant unmet medical need in triple-negative breast cancer (TNBC)
- Gemcitabine/carboplatin ± trilaciclib in first/second-line metastatic TNBC
- ~ 90 patient, randomized, open-label Phase 2 trial initiated 1Q17
  - primary endpoints: myelopreservation (e.g. FN, transfusions)
  - secondary endpoints: ORR, PFS, OS
- Immunophenotyping to evaluate trilaciclib effects on T-cells
- Expect ~ 20% patients to have CDK4/6-dependent tumors
  - pathological confirmation of tumor CDK4/6 status, but enrolling "all comers"
  - will correlate response-rate with CDK4/6 status to determine applicability of approach in broader population (i.e. CDK4/6-dependent tumors)

G1T38 DEVELOPMENT PROGRAM

Strategic opportunities for G1T38: building combination oncology regimens

Significant scarcity value

- Only CDK4/6 inhibitor not owned by big pharma
- CDK4/6 inhibitors most effective when used in combination with other targeted therapies
- G1 owns both components of marketplace-validated combo (SERD + CDK4/6i)

Best-in-class potential

- Less neutropenia, potential for daily dosing without holiday
- No QT, DILI issues
- Better GI tolerability

Company	CDK4/6	Hormone Signaling	Kinase Growth Factors	Pathway Inhibitors	B-Cell Signaling
Novartis	✓	✓	✓	✓	
Pfizer	✓	✓	✓	✓	
Lilly	✓		✓	✓	
Roche		✓	✓	✓	✓
AstraZeneca		✓	✓	✓	✓
Bayer		✓	✓	✓	
Takeda		✓	✓	✓	
Amgen			✓		✓
Gilead			✓		✓
Sanofi		✓	✓	✓	
Abbvie					✓
Astellas		✓	✓	✓	
J&J		✓			✓
Bristol Myers		✓			
Celgene				✓	✓
Merck				✓	
G1	✓	✓			

G1 THERAPEUTICS

G1T38 differentiation: robust preclinical package and encouraging initial clinical data

- 2017 publications
  - *Molecular Cancer Research* (Stice et al, preclinical data in prostate cancer)
  - *Oncotarget* (Bisi et al, preclinical data in breast cancer and NSCLC)
- Extensive preclinical validation and differentiation
  - head-to-head studies with Ibrance (Bisi et al, 2017)
- Drug well-tolerated in 75 subject Phase 1a HNV trial
  - no DLTs or grade 3/4 AEs
  - differentiated PK profile (shorter t1/2, larger Vd than Ibrance and Kisqali)
- Encouraging early results in Phase 1b/2a breast cancer trial (in combination with Faslodex)
  - pharmacodynamic activity observed at first dose level
  - well-tolerated GI profile; no liver or CV AEs

G1 THERAPEUTICS

G1T38: backbone therapy for multiple combination regimens - potential development paths

Cancer	Indication/Line	G1T38 with:	Rationale
Breast	HR+/HER2- 1L	G1T48	Approval of palbociclib with fulvestrant; extension of mPFS from 4.6 to 9.5 months (PALOMA-3, Turner et al 2015, Cristofanilli et al 2016). G1T38 + G1T48 enhances efficacy and extends time to resistance in preclinical models (Wardell et al AACR 2017).
	HR-/HER2+ TDM1 failures ≥ 3L	trastuzumab + lapatinib	CDK4/6 inhibitors re-sensitize HER2+ cancers to HER2 blockade (Goel et al 2016, Malumbres 2016, Witkiewicz et al 2014). G1T38 + lapatinib/trastuzumab enhances efficacy and extends time to resistance in preclinical models.
NSCLC	EGFRm: 1L	EGFRi	CDK4/6 + EGFR inhibition overcomes resistance in preclinical models (Zhou et al 2016). G1T38 + EGFRi enhances efficacy and extends time to resistance in NSCLC EGFR^{T790M} murine model (Bisi et al 2017).
	EGFRm: EGFRi failures, 2L	osimertinib	
	ALKi failures, 2L	alectinib	ALK and CDK4/6 inhibition demonstrates synergy in preclinical models (Wood et al 2016).
	KRASm, ≥ 2L	MEKi	MEKi + CDK4/6i has significant anti-KRAS–mutant NSCLC activity (Tao et al 2016, LeBlanc et al 2016).
Prostate	CRPC 1L/2L	AR-blocker	Prostate tumor cells are highly dependent on cyclin D for cellular proliferation (Balk et al 2008). G1T38 demonstrates robust preclinical efficacy in CRPC models (Stice et al 2017).
Lymphoma	MCL, MZL, CLL, FL, DLBCL; 2L	BTKi	CDK4 activation drives BTKi resistance; CDK4/6i sensitizes MCL to ibrutinib (Chiron et al 2014). Positive clinical data in palbociclib/ibrutinib MCL study (Martin et al 2016).
Melanoma	BRAFm 1L	MEKi + RAFi	CDK4/6i enhances efficacy and extends time to resistance in preclinical models (Harris et al AACR 2017). MEKi + CDK4/6i are synergistic in BRAFm melanoma (Teh et al 2016).
RASm basket	CRC, pancreatic, cholangiocarcinoma	MEKi	CDK4/6 inhibitors enhance the efficacy of MEK inhibitors in KRASm tumors including CRC (Pek et al 2017, Ziemke et al 2015) and PDAC (Franco et al 2014, Franco et al 2016).
GIST	GIST; 3L after imatinib, sunitinib	regorafenib	GIST features CDKN2A loss/CCND1 amp (Yang et al 2008), which correlate with CDK4/6 inhibitor sensitivity. CDK4/6i is efficacious in imatinib resistant preclinical models (Eilers et al 2015).

G1T48 DEVELOPMENT PROGRAM

G1T48: oral SERD, strong strategic fit

- Ibrance approved only in combination with an anti-estrogen
  - first letrozole (aromatase inhibitor), then Faslodex (IM SERD)
- Multiple companies with oral SERDs in early development
- G1T48 provides a competitive advantage by controlling economics of a combination G1T38/48 regimen
  - stand-alone opportunity in early stage disease
- Compelling preclinical data package (2017 AACR poster)
  - more potent than Faslodex
- On track for IND filing in 4Q17

Key anticipated milestones through 2Q18

		3Q17	4Q17	1Q18	2Q18
Trilaciclib (iv CDK4/6i)	1st line-SCLC Phase 2a	enrollment completed (2Q17)		top-line randomized data	
	2nd/3rd-line SCLC Phase 2a				enrollment completed
	metastatic TNBC Phase 2				enrollment completed
	1st line-SCLC, Ph2 (+ Tecentriq)	enrollment continuing (through 2018)			
G1T38 (oral CDK4/6i)	ER+, HER2- BC Ph1b/2a (+ Faslodex)			Phase 1b enrollment completed; Phase 2a initiated	Phase 1b preliminary data
	EGFRm NSCLC Phase 1b/2 (+ Tagrisso)		IND filed	Phase 1b initiated	
G1T48 (oral SERD)	ER+, HER2- BC Phase 1/2a		IND filed		Phase 1 initiated

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APPENDIX: TRILACICLIB

Extensive preclinical and Phase 1 MOA data

- Preclinical validation of trilaciclib demonstrating:
  - transient and reversible G1 arrest of HSPCs
  - protection of HSPCs from damage by chemo (myelopreservation)
  - preservation of bone marrow and immune system function
  - improved complete blood cell count recovery after chemo
  - reduction of bone marrow exhaustion, superiority to GCSF
  - prevention of myeloid skewing and consequent lymphopenia
  - activation of effector T-cells in the tumor microenvironment
  - enhancement of chemotherapy and checkpoint inhibitor anti-tumor efficacy
- Robust pharmacodynamic effect in 45 subject Phase 1a HNV trial
  - transient G1 arrest of HSPCs
  - trilaciclib well-tolerated, no DLTs or SAEs
- Recent presentations and publications
  - meetings: AACR, ASCO, WCLC, EORTC/AACR/NCI
  - *Molecular Cancer Therapeutics* (Bisi et al, 2016)
  - *Science Translational Medicine* (He et al, 2017)

G1 THERAPEUTICS

Advantages of trilaciclib vs. GCSF

GCSF		Trilaciclib
Stimulates granulocyte-specific progenitors after damage by chemo		Protects HSPCs from damage by chemotherapy
Stimulates granulocyte production only		Preserves all hematopoietic lineages
Potential to reduce febrile neutropenia (if used prophylactically). No effect on other cytopenias		Reduce all cytopenias and transfusions (platelets, RBCs), GCSF usage, febrile neutropenia, bleeding, hospitalizations
No effect (other than on granulocyte production)		Enhances immune system function (effector T-cells) during chemotherapy
Exacerbates myeloid skewing		Prevents myeloid skewing and consequent lymphopenia
Accelerates bone marrow exhaustion		Prevents bone marrow exhaustion
Potential to increase secondary heme malignancies (MDS, AML)		Potential to reduce secondary heme malignancies (MDS, AML)
Injection-site irritation and bone pain		Convenient IV administration before chemo, fits standard clinical practice
Protein: high COGS		Small molecule: low COGS

G1 THERAPEUTICS

Myelopreservation via CDK4/6 inhibition: advantages of trilaciclib vs. Ibrance

- Short-acting pharmacology is key
  - goal is to rapidly arrest HSPCs in G1, with HSPCs re-entering the cell cycle after chemotherapy
  - T-cell stimulatory effect is seen with *transient* CDK4/6 inhibition
  - prolonged CDK4/6 inhibition is detrimental: blocks T-cell proliferation and causes myelosuppression
  - ideal PK profile: rapid Tmax, high Cmax, short t1/2
- Timing of CDK4/6 inhibition and chemotherapy is critical
  - trilaciclib's IV dosing provides exquisite control and fits standard clinical practice for chemo/checkpoints
  - trilaciclib Phase 1a bone marrow PD data demonstrate precise magnitude and duration of HSPC G1 arrest; IV PK/PD unknown for Ibrance
  - Ibrance has highly variable PK compared to trilaciclib; if HSPCs are not fully arrested or re-enter the cell cycle too soon, can lead to serious myelosuppression (seen in Ibrance/Taxol combo clinical trial)

✓ Trilaciclib is a short-acting IV drug with reproducible and well-understood human PK/PD and clinical experience in over 130 patients with three different chemotherapy regimens

× Ibrance is a long-acting oral drug with CYP3A contraindications that accumulates with repeat dosing and has unknown human IV PK/PD

G1 THERAPEUTICS

Trilaciclib has a very different human PK profile than Ibrance

Drug	Dose	Tmax (h)	Cmax (ng/ml)	t1/2 (h)*
trilaciclib	IV 192mg/m^2	0.47	1705	14.5
Ibrance	PO 125mg	7	52	25.9

* Trilaciclib terminal elimination phase contributes very little to AUC, effective t1/2 ~ 8hrs. Ibrance accumulates with repeat dosing; trilaciclib does not accumulate.

Trilaciclib data from He et al (*Science Translational Medicine*, 2017). Ibrance data from Flaherty et al (*CCR*, 2012).

Trilaciclib is more potent than Ibrance

Drug	IC_{50} (uM) CDK4	IC_{50} (uM) CDK6	IC_{50} (uM) CDK2-cyclin E	IC_{50} (uM) CDK2-cyclin A	CDK2-cyclinE/ CDK4 ratio	CDK2-cyclin A/ CDK4 ratio
trilaciclib	0.001	0.004	2.51	1.29	2510	1290
Ibrance	0.011	0.015	>10	>10	910	910

Trilaciclib data from Bisi et al (*MCT*, 2016). Ibrance data from Fry et al (*MCT*, 2004).

G1 THERAPEUTICS