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

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**FORM 8-K**

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

**Date of Report (Date of earliest event reported): November 8, 2017**

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

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**Delaware**  
(State or other jurisdiction  
of incorporation)

**001-38096**  
(Commission  
File Number)

**26-3648180**  
(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**

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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.

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**Item 5.02 Departure of Directors or Certain Officers; Election of Directors; Appointment of Certain Officers; Compensatory Arrangements of Certain Officers.**

On November 8, 2017, G1 Therapeutics, Inc. (the “Company”) announced the appointment of Barclay A. Phillips, 55, as Chief Financial Officer and Senior Vice President, Corporate Development. Mr. Phillips joins the Company from Novavax, Inc., a NASDAQ listed biotechnology company, where he served as Senior Vice President, Chief Financial Officer and Treasurer from June 2013 until October 2017, and where he led financial operations and was part of the executive team responsible for corporate strategy and mergers and acquisitions. Prior to his tenure with Novavax, Inc., Mr. Phillips was Senior Vice President and Chief Financial Officer at Micromet, Inc. from 2008 - 2012, where he was responsible for financial reporting, financial planning and analysis, and investor relations. Mr. Phillips earned his B.A. in Economics from the University of Colorado at Boulder.

The Company and Mr. Phillips have entered into an employment agreement, effective as of November 13, 2017 (the “Employment Agreement”). Pursuant to the Employment Agreement, Mr. Phillips will receive an initial annual base salary of \$370,000. Mr. Phillips is also eligible to receive an annual discretionary bonus award of up to 35% of his then-current base salary (“Discretionary Bonus”), as well as a performance-based bonus equal to \$120,000 (“Performance-Based Bonus”) with the Performance-Based Bonus to be determined using criteria specified in the Employment Agreement. The Discretionary Bonus award, if any, will be determined by the Company’s Board of Directors (the “Board”) or a committee thereof. The Company will also reimburse Mr. Phillips for relocation expenses up to \$100,000, subject to the terms set forth in the Employment Agreement.

In connection with his appointment, Mr. Phillips shall receive stock options to purchase 250,000 shares of the Company’s common stock, par value \$0.0001 per share (“Common Stock”), at an exercise price equal to the closing price of the Common Stock on the NASDAQ Global Select Market on November 13, 2017, in two awards: (i) an option to purchase 100,000 shares, which will be granted pursuant to and subject to the terms and conditions of the Company’s 2017 Equity Incentive Plan (the “2017 Plan Option”), and (ii) an option to purchase 150,000 shares, which will be granted outside the Company’s 2017 Equity Incentive Plan as an inducement material to Mr. Phillips’ joining the Company in accordance with NASDAQ Listing Rule 5635(c)(4) (the “Inducement Option” and together with the 2017 Plan Option, the “Stock Options”). The Stock Options will have a ten-year term and will vest as to 25% of the shares on the first anniversary of the commencement of Mr. Phillips’ employment with the Company and as to an additional 1/48th of the shares monthly thereafter, subject to Mr. Phillips’ continued service with the Company through the applicable vesting dates.

In the event of a change of control (as defined in the Employment Agreement) of the Company, 50% of any unvested portion of each of the 2017 Plan Option and the Inducement Option will vest immediately prior to, and subject to, the consummation of such change of control. In the event of a change of control of the Company in which Mr. Phillips’ employment is terminated by the Company without cause (as defined in the Employment Agreement) or Mr. Phillips resigns for good reason (as defined in the Employment Agreement) within 90 days of the change of control, the vesting of any remaining unvested portion of each of the 2017 Plan Option and the Inducement Option will accelerate. As a condition of employment, Mr. Phillips has entered into a Non-Competition and Non-Solicitation Agreement and a Confidentiality and Inventions Agreement with the Company. Mr. Phillips will also enter into an Indemnification Agreement with the Company relating to his employment.

Under the terms of the Employment Agreement, Mr. Phillips’ employment with the Company may be terminated at any time, with or without cause and without any prior notice, by either Mr. Phillips or the Company. If the Company terminates Mr. Phillips’ employment without cause or Mr. Phillips terminates his employment for good reason, he will be entitled to receive continuation of his then-current base salary for a period of twelve months (the “Severance Period”), which will be payable in periodic installments in accordance with the Company’s payroll practices and procedures beginning on the sixtieth (60<sup>th</sup>) day following Mr. Phillips’ termination.

A copy of the Employment Agreement is attached as an exhibit hereto.

There are no transactions to which the Company is a party and in which Mr. Phillips has a material interest that are required to be disclosed under Item 404(a) of Regulation S-K. Mr. Phillips has not previously held any positions with the Company and has no family relationship with any directors or executive officers of the Company.

The Company also announced that Gregory J. Mossinghoff, the Company's Chief Business Officer and current principal financial officer, will depart the Company in January 2018 to pursue an opportunity with an early stage therapeutics company.

**Item 7.01 Regulation FD Disclosure**

The Company is furnishing with this Current Report on Form 8-K a copy of its current corporate presentation slides. The information in these slides shall not be deemed "filed" for purposes of Section 18 of the Securities Exchange Act of 1934 (the "Exchange Act") or otherwise subject to the liabilities of that section, nor shall it be deemed incorporated by reference in any filing under the Securities Act of 1933, as amended, or the Exchange Act, except as expressly set forth by specific reference in such a filing.

**Item 9.01 Financial Statements and Exhibits.**

(d) Exhibits

<b>Exhibit No.</b>	<b>Description</b>
10.1	<a href="#"><u>Employment Agreement between the Company and Barclay A. Phillips, effective as of November 13, 2017.</u></a>
99.1	<a href="#"><u>Press Release dated November 8, 2017.</u></a>
99.2	<a href="#"><u>Corporate Presentation Slides.</u></a>

**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/ Mark A. Velleca, M.D., Ph.D.

Mark A. Velleca, M.D., Ph.D.

President and Chief Executive Officer

Date: November 13, 2017

**EMPLOYMENT AGREEMENT**

This EMPLOYMENT AGREEMENT (the “**Agreement**”), is made and entered into effective as of November 13, 2017 (the “**Effective Date**”), by and between G1 Therapeutics, Inc., a Delaware corporation (the “**Company**”), and Barclay Phillips (“**Employee**”).

1. **EMPLOYMENT; DUTIES.** The Company agrees to employ Employee as its Chief Financial Officer and Senior Vice President, Corporate Development, and Employee agrees to accept such employment upon the terms and conditions hereinafter set forth. Employee will perform such services for the Company as are customarily associated with such position and as may otherwise be assigned to Employee from time to time by the Company’s Chief Executive Officer or his designee. Employee will devote Employee’s full business time and attention to the business and affairs of the Company, and will perform Employee’s duties diligently and to the best of Employee’s ability, in compliance with the Company’s policies and procedures and the laws and regulations that apply to the Company’s business. Notwithstanding the foregoing, it will not be a violation of this Agreement for Employee to serve as a director of any company whose products do not compete with those of the Company and to serve as director, trustee, officer, or consultant to a charitable or non-profit entity; provided that: (a) such service does not adversely affect Employee’s compliance with his obligations under this Agreement, including but not limited to his devotion of full business time and attention to the business and affairs of the Company and his compliance with his Employee Non-Competition and Non-Solicitation Agreement and Employee Confidentiality and Inventions Agreement; and (b) Employee provides written notification of each such service to the Company.

Subject to any required approval, Employee will serve as Secretary of the Company’s Board of Directors during Employee’s employment hereunder. Employee’s service as Secretary of the Board will be without further compensation. Immediately upon termination of Employee’s employment with Company for any reason, Employee will resign any and all positions held by Employee whether as an officer of the Company or manager on the Board, or on the board of directors or managers of any subsidiary or affiliate of Company, or as a member of any committees thereof.

2. **TERM; TERMINATION.** Employee’s employment under this Agreement will commence as of the Effective Date and will continue until terminated by either party. Employee’s employment with the Company is at-will, and either party can terminate the employment relationship and/or this Agreement at any time, for any or no cause or reason, and with or without prior notice, subject to the applicable terms of Section 4. Upon termination of Employee’s employment by either party for any reason, Employee will resign Employee’s position(s), if any, as an officer or director of the Company, as a member of the Company’s Board of Directors (the “**Board**”) and any Board committees, as well as any other positions Employee may hold with or for the benefit of the Company and/or its affiliates.

3. **COMPENSATION.** As compensation for the services to be rendered by Employee under this Agreement, the Company will provide the following compensation and benefits during Employee’s employment hereunder.

(a) **BASE SALARY.** The Company will pay Employee a base salary (the “**Base Salary**”) at an annual rate of Three Hundred and Seventy Thousand Dollars (\$370,000), payable in equal installments in accordance with the Company’s customary payroll practices as in effect from time to time. The Base Salary may be reviewed from time to time by the Company and may be increased in the sole discretion of the Company. The Base Salary may also be decreased in connection with any Company-wide decrease in executive compensation.

(b) **PERFORMANCE-BASED BONUS.** The Company agrees to pay Employee a performance-based bonus (the “Performance-Based Bonus”) equal to \$120,000, with such Performance-Based Bonus to be paid on the second regularly scheduled payroll date in January 2018, provided that: (i) Employee must deliver a gap analysis of the financial practices and procedures of the Company prior to January 31, 2018, and (ii) Employee must be employed by the Company on the payment date in order to receive the Performance-Based Bonus.

(c) **ANNUAL BONUS.** Employee will be eligible to receive an annual calendar year bonus based upon Employee’s and the Company’s achievement of certain individual and Company goals that will be set for Employee by the Board or its designee (the “**Annual Bonus**”). The amount of the target Annual Bonus will be equal to thirty-five percent (35%) of Employee’s then-current Base Salary as of the date of the payment; provided that the actual amount of the Annual Bonus may be greater or less than such target amount. The Board or its designee will have the sole discretion to set the applicable individual and Company goals, to determine whether the goals have been met, and to determine the amount of the Annual Bonus. The Annual Bonus for any given year will be paid between January 1 and January 31 in the year immediately following the year in which the Annual Bonus, if any, is earned. Employee must be employed by the Company on December 31 of the bonus year in order to receive the Annual Bonus for that year.

(d) **STOCK OPTIONS.** Subject to approval by the Board or the Compensation Committee, effective on the Effective Date, Employee will be granted stock options to purchase an aggregate of 250,000 shares of the Company’s common stock (the “Common Stock”) at a per share exercise price equal to the closing sale price of the Common Stock on the Nasdaq Global Select Market on the date of grant, in two awards: (i) an option to purchase 100,000 shares, which will be granted pursuant to and subject to the terms and conditions of the Company’s 2017 Equity Incentive Plan (the “2017 Plan Option”), and (ii) an option to purchase 150,000 shares, which will be an inducement material to you joining the Company, pursuant to Rule 5635(c)(4) of the Nasdaq Listed Company Manual (the “Inducement Option” and together with the 2017 Plan Option, the “Options”) The 2017 Plan Option will be, to the maximum extent permissible, treated as an “incentive stock option” within the meaning of Section 422 of the Internal Revenue Code and the rules and regulations thereunder. The 2017 Plan Option will be further subject to the terms of a stock option agreement as approved by the Board setting forth the exercise price, vesting conditions and other restrictions, and the Inducement Option will be subject to all terms, vesting schedules and other provisions as set forth in a separate option agreement. One fourth (1/4th) of each of the 2017 Plan Option and the Inducement Option will vest on the first (1st) anniversary of the Effective Date, and one forty-eighth (1/48th) of each of the 2017 Plan Option and the Inducement Option will vest each month over the following thirty-six (36) months thereafter, so long as Employee remains employed by the Company through each such vesting date. Fifty percent (50%) of any unvested portion of the 2017 Plan Option and 50% of any unvested portion

of the Inducement Option will vest immediately prior to, and subject to, the consummation of a Change in Control (as defined below) and, subject to Employee's execution of the release of claims described in Section 4(b), any remaining unvested portion of the 2017 Plan Option and any remaining unvested portion of the Inducement Option will immediately vest if Employee's employment is terminated by the Company without Cause (as defined below) or Employee resigns with Good Reason (as defined below) within ninety (90) days following a Change in Control. A "Change in Control" means (i) the Company's merger or consolidation with or into another entity such that the stockholders of the Company prior to such transaction do not or are not expected to own a majority of the voting stock of the surviving entity, (ii) the sale or other disposition of all or substantially all of the assets of the Company, or (iii) the sale or other disposition of greater than fifty percent (50%) of the then-outstanding voting stock of the Company by the holders thereof to one or more persons or entities who are not then stockholders of the Company.

(e) VACATION. Employee will be eligible for paid vacation time off in accordance with, and subject to, the Company's policies and procedures in effect from time to time.

(e) BENEFITS. Employee will (subject to applicable eligibility requirements) receive such other benefits as are provided from time to time to other similarly-situated employees of the Company pursuant to the Company's policies and procedures as they may be instituted from time to time. All such benefits are subject to the provisions of their respective plan documents in accordance with their terms. Employee acknowledges and agrees that the Company has the unilateral right to amend, modify or terminate its employee benefit plans or policies to the maximum extent allowed by law.

(f) EXPENSE REIMBURSEMENT. The Company will reimburse Employee for all reasonable business expenses incurred by Employee in connection with the performance of Employee's duties hereunder, subject to Employee's compliance with the Company's reimbursement policies in effect from time to time. All reimbursements provided under this Agreement will be made or provided in accordance with the requirements of Section 409A of the Internal Revenue Code and the rules and regulations thereunder including, where applicable, the requirement that (i) any reimbursement is for expenses incurred during Employee's lifetime (or during a shorter period of time specified in this Agreement); (ii) the amount of expenses eligible for reimbursement during a calendar year may not affect the expenses eligible for reimbursement in any other calendar year; (iii) the reimbursement of an eligible expense will be made no later than the last day of the calendar year following the year in which the expense is incurred; and (iv) the right to reimbursement or in kind benefits is not subject to liquidation or exchange for another benefit.

(g) WITHHOLDINGS. The Company will withhold from any amounts payable under this Agreement, such federal, state and local taxes, as the Company reasonably determines are required to be withheld pursuant to applicable law.

(h) RELOCATION. To assist with relocation to North Carolina, the Company will reimburse Employee for reasonable expenses incurred in relocating Employee and Employee's family from Employee's existing residence to a new residence in the Raleigh/Durham area, up to a maximum of One Hundred Thousand Dollars (\$100,000) (the

“Relocation Assistance Payment”). The Relocation Assistance Payment will be distributed to Employee as follows: (i) Forty Thousand Dollars (\$40,000), which may be used to defray miscellaneous costs associated with the purchase of a residence in the Raleigh/Durham and travel and commuting costs to and from the area, will be paid on the second regularly scheduled payroll date in January 2018, provided that Employee must be employed by the Company on the payment date in order to receive such payment; and (ii) Sixty Thousand Dollars (\$60,000) will be held in reserve for the transport, by an approved carrier, of Employee’s normal household goods and other items deemed qualifying deductible expenses under the Internal Revenue Code and corresponding guidelines in effect as of the Effective Date, also provided that Employee must be employed by the Company on the payment date in order to receive any such payment. Within thirty (30) days after incurring any covered expense, Employee will provide such documentation as may be reasonably requested by the Company to substantiate expenses to be reimbursed. In exchange for the Company covering relocation expenses, should Employee leave the Company for any reason other than death, disability or termination without Cause within twelve (12) months of the Effective Date, Employee will be responsible for repayment of one hundred percent (100%) of the Relocation Assistance Payment. All such repayment will be due in full within thirty (30) days of Employee’s separation from the Company.

#### 4. EFFECT OF TERMINATION.

(a) GENERALLY. When Employee’s employment with the Company is terminated for any reason, Employee, or Employee’s estate, as; the case may be, will be entitled to receive the compensation and benefits earned through the effective date of termination, along with reimbursement for any approved business expenses that Employee has timely submitted for reimbursement in accordance with the Company’s expense reimbursement policy or practice.

(b) SEPARATION BENEFITS UPON CERTAIN TERMINATIONS. If the Company terminates Employee’s employment without Cause (as defined below), or if Employee resigns Employee’s employment for Good Reason (as defined below), then conditioned upon Employee executing a Release (as defined below) following such termination, Employee will be entitled to receive the following payments (the “Separation Benefits”): (i) an amount equal to payment of Employee’s then-current Base Salary for a period of twelve (12) months.

The Separation Benefits are conditioned upon Employee executing a release of claims in a form satisfactory to the Company (the “**Release**”) within the time specified therein, which Release is not revoked within any time period allowed for revocation under applicable law.

The Separation Benefits will be payable to Employee over time in accordance with the Company’s payroll practices and procedures, beginning on the sixtieth (60th) day following the termination of Employee’s employment with the Company, provided that the Company, in its sole discretion, may begin the payments earlier. For avoidance of doubt, the termination of Employee’s employment as a result of Employee’s death or disability (meaning the inability of Employee, due to the condition of Employee’s physical, mental or emotional health, effectively to perform the essential functions of Employee’s job with or without reasonable accommodation for a continuous period of more than 90 days or for 90 days in any period of 180 consecutive days, as determined by the Board in its sole discretion in consultation with a physician retained by the Company) will not constitute a termination without Cause triggering the rights described in this Section 4(b).

(c) **CAUSE.** For purposes of this Agreement, “Cause” means: (i) Employee’s fraud, embezzlement or misappropriation with respect to the Company; (ii) Employee’s material breach of fiduciary duties to the Company; (iii) Employee’s willful or negligent misconduct; (iv) Employee’s material breach of this Agreement; (v) Employee’s willful failure or refusal to perform Employee’s material duties under this Agreement or failure to follow any specific lawful instructions of the Company; (vi) Employee’s conviction or plea of nolo contendere in respect of a felony or of a misdemeanor involving moral turpitude; (vii) Employee’s alcohol or substance abuse which has a material adverse effect on Employee’s ability to perform Employee’s duties under this Agreement; or (viii) Employee’s engagement in a form of discrimination or harassment prohibited by law (including, without limitation, discrimination or harassment based on race, color, religion, sex, national origin, age or disability). In the event that the Company concludes that Employee has engaged in acts constituting in Cause as defined in clause (iii), (iv), (v), or (vi) above, prior to terminating this Agreement for Cause the Company will provide Employee with at least fifteen (15) days’ advance written notice of the specific circumstances constituting such Cause, and an opportunity to correct such circumstances.

(d) **GOOD REASON.** In order for Employee to resign for Good Reason, Employee must provide written notice to the Company of the existence of the Good Reason condition within thirty (30) days of the initial existence of such Good Reason condition. Upon receipt of such notice, the Company will have thirty (30) days during which it may remedy the Good Reason condition and not be required to provide for the benefits described in Section 4(b) above as a result of such proposed resignation if successfully remedied. If the Good Reason condition is not remedied within such thirty (30) day period, Employee may resign based on the Good Reason condition specified in the notice effective no later than thirty (30) days following the expiration of the thirty (30) day cure period. For purposes of this Agreement, “**Good Reason**” means the occurrence of any of the following events without Employee’s consent: (i) a material reduction of Employee’s Base Salary not generally applicable to other executive-level employees of the Company, (ii) a material diminution of Employee’s authority, duties, or responsibilities, (iii) a relocation of Employee’s primary workplace to a location that is more than fifty (50) miles from the location of Employee’s primary workplace as of the date hereof, or (iv) the Company’s material breach of this Agreement.

(e) **APPLICATION OF INTERNAL REVENUE CODE SECTION 409A.** Notwithstanding anything to the contrary set forth herein, any payments and benefits provided under this Section 4 that constitute “deferred compensation” within the meaning of Section 409A of the Internal Revenue Code and the regulations and other guidance thereunder and any state law of similar effect (collectively “Section 409A”) will not commence in connection with Employee’s termination of employment unless and until Employee has also incurred a “**Separation From Service**” (as such term is defined in Treasury Regulation Section 1.409A-1 (h) (a “Separation From Service”), unless the Company reasonably determines that such amounts may be provided to Employee without causing Employee to incur an additional tax under Section 409A. The parties intend that each installment of the Separation Benefits payments provided for in this Agreement is a separate “payment” for purposes of Treasury Regulation Section 1.409A”

2(b)(2)(i). For the avoidance of doubt, the parties intend that payments of the Separation Benefits set forth in this Agreement satisfy, to the greatest extent possible, the exemptions from the application of Section 409A provided under Treasury Regulation Sections 1.409A-1(b)(4), 1.409A-1 (b)(5) and 1.409A-1 (b)(9) .. However, if the Company determines that the Separation Benefits constitute “deferred compensation” under Section 409A and Employee is, on the termination of service, a “specified employee” of the Company or any successor entity thereto, as such term is defined in Section 409A, then, solely to the extent necessary to avoid the incurrence of the adverse personal tax consequences under Section 409A, the timing of the Separation Benefits payments will be delayed until the earlier to occur of: (i) the date that is six months and one day after Employee’s Separation From Service, or (ii) the date of Employee’s death (such applicable date, the “**Specified Employee Initial Payment Date**”), the Company (or the successor entity thereto, as applicable) will (A) pay to Employee a lump sum amount equal to the sum of the Separation Benefits payments that Employee would otherwise have received through the Specified Employee Initial Payment Date if the commencement of the payment of the Separation Benefits had not been so delayed pursuant to this Section and (B) commence paying the balance of the Separation Benefits in accordance with the applicable payment schedules set forth in this Agreement.

(f) **NO FURTHER OBLIGATIONS.** Except as expressly provided above or as otherwise required by law, the Company will have no obligations to Employee in the event of the termination of this Agreement for any reason.

5. **EMPLOYEE REPRESENTATIONS.** Employee represents and warrants that Employee is not obligated or restricted under any agreement (including any non-competition or confidentiality agreement), judgment, decree, order or other restraint of any kind that could impair Employee’s ability to perform the duties and obligations required of Employee hereunder. Employee further agrees that Employee will not divulge to the Company any confidential information and/or trade secrets belonging to others, including Employee’s former employers, nor will the Company seek to elicit from Employee such information. Consistent with the foregoing, Employee will not provide to the Company, and the Company will not request, any documents or copies of documents containing such information.

6. **NOTICES.** Any notice required to be given hereunder will be sufficient if in writing and hand delivered or sent by mail, return receipt requested, postage prepaid, in the case of Employee, to Employee’s address shown on the Company’s records, and in the case of the Company, to 79 T.W. Alexander Drive, 4401 Research Commons, Suite 105, Research Triangle Park, NC 27709, or to such other addresses as either party will specify to the other.

7. **AMENDMENT; WAIVER.** No amendment of any provision of this Agreement will be valid unless the amendment is in writing and signed by the Company and Employee. No waiver of any provision of this Agreement will be valid unless the waiver is in writing and signed by the waiving party. The failure of a party at any time to require performance of any provision of this Agreement will not affect such party’s rights at a later time to enforce such provision. No waiver by a party of any breach of this Agreement will be deemed to extend to any other breach hereunder or affect in any way any rights arising by virtue of any other breach.

8. **GOVERNING LAW: VENUE.** This Agreement will be governed by and construed in accordance with the laws of the State of North Carolina, without regard to that body of law known as choice of law. The parties agree that any litigation arising out of or related to this Agreement or Employee's employment by the Company will be brought exclusively in any state or federal court in Durham County, North Carolina. Each party (i) consents to the personal jurisdiction of said courts, (ii) waives any venue or inconvenient forum defense to any proceeding maintained in such courts, and (iii) agrees not to bring any proceeding arising out of or relating to this Agreement or Employee's employment by the Company in any other court.

9. **BENEFIT.** This Agreement will be binding upon and will inure to the benefit of each of the parties hereto, and to their respective heirs, representatives, successors and permitted assigns. Employee may not assign any of Employee's rights or delegate any of Employee's duties under this Agreement.

10. **ENTIRE AGREEMENT: OTHER AGREEMENTS.** This Agreement contains the entire agreement and understanding by and between the Company and Employee with respect to the subject matter hereof, and any representations, promises, agreements or understandings, written or oral, not herein contained will be of no force or effect; provided that Employee is also subject to the terms and conditions of (i) that certain Employee Non-Competition and Non-Solicitation Agreement by and between Employee and the Company, and (ii) that certain Employee Confidentiality and Inventions Agreement by and between Employee and the Company, each of which remains in full force and effect.

11. **CAPTIONS: RULE OF CONSTRUCTION.** The captions in this Agreement are for convenience only and in no way define, bind or describe the scope or intent of this Agreement. The terms and provisions of this Agreement will not be construed against the drafter or drafters hereof. All parties hereto agree that the language of this Agreement will be construed as a whole according to its fair meaning and not strictly for or against any of the parties hereto.

12. **COUNTERPARTS.** This Agreement may be executed in one or more counterparts, each of which will be deemed an original but all of which together will constitute one and the same agreement. Facsimile or PDF reproductions of original signatures will be deemed binding for the purpose of the execution of this Agreement.

13. **SEVERABILITY.** Each provision of this Agreement is severable from every other provision of this Agreement. Any provision of this Agreement that is determined by any court of competent jurisdiction to be invalid or unenforceable will not affect the validity or enforceability of any other provision. Any provision of this Agreement held invalid or unenforceable only in part or degree will remain in full force and effect to the extent not held invalid or unenforceable.

14. **SURVIVAL.** The terms of Sections 4 through 14 will survive the termination or expiration of this Agreement for any reason.

*[Signature Page Follows.]*

IN WITNESS WHEREOF, the parties have executed this Agreement effective as of the Effective Date.

**G1 THERAPEUTICS, INC.**

By: /s/ Mark Velleca

Name: Mark Velleca

Title: CEO

**EMPLOYEE:**

/s/ Barclay Phillips

Barclay Phillips



## G1 Therapeutics Makes Key Executive Appointments

*Barclay Phillips appointed Chief Financial Officer and Senior Vice President, Corporate Development*

*Chandra Lovejoy named Vice President, Global Regulatory Affairs*

**RESEARCH TRIANGLE PARK, N.C., November 8, 2017** – G1 Therapeutics, Inc. (NASDAQ: GTHX), a clinical-stage oncology company, today announced the appointments of Barclay (Buck) Phillips as Chief Financial Officer and Senior Vice President, Corporate Development, and Chandra Lovejoy as Vice President, Global Regulatory Affairs.

“We are pleased to welcome Buck and Chandra to the G1 team. Buck has strong cross-functional expertise having led financial strategy and reporting for two publicly traded biotechnology companies, as well as a deep understanding of the equity capital markets from his time as an investor. Buck’s leadership and experience in public financings and corporate development will help catalyze G1’s next phase of growth,” said Mark Velleca, MD, PhD, Chief Executive Officer of G1 Therapeutics. “In addition, we look forward to leveraging Chandra’s expertise in global regulatory strategy and clinical trial design as we advance our therapies toward multiple data readouts in 2018, and expand our pipeline through additional studies.”

Mr. Phillips brings to G1 more than 25 years of capital markets, financial strategy and business development experience in life sciences and venture capital. In his most recent role, Mr. Phillips served as Senior Vice President, Chief Financial Officer and Treasurer of Novavax, where he led financial operations and was part of the executive team responsible for corporate strategy and mergers and acquisitions. While at Novavax, Mr. Phillips managed operating expense growth from \$50 million to more than \$270 million per year, and successfully raised more than \$800 million in multiple equity and debt financings. Prior to Novavax, Mr. Phillips was Senior Vice President and Chief Financial Officer at Micromet, which was acquired by Amgen in 2012 for \$1.2 billion. Earlier in his career, Mr. Phillips served as Managing Director at Vector Fund Management, and Biotechnology Analyst and Director of Venture Investments at Invesco Funds Group. Mr. Phillips has a Bachelor of Arts in economics from the University of Colorado at Boulder.

Ms. Lovejoy has nearly two decades of experience in global drug development, specializing in oncology. Most recently, she led global regulatory strategy as Senior Vice President, Global Regulatory Affairs and Head of Quality at Sierra Oncology. Earlier in her career, Ms. Lovejoy held roles of increasing responsibility at Endocyte, including Global Vice President of Regulatory Affairs, and at Genentech, where she served as regulatory lead on the AVASTIN® team. Ms. Lovejoy has led cross-functional team activities from IND applications, implementation and conduct of global clinical trials, successful negotiations with FDA and EMA regarding complex pivotal trials, to the submission and review of marketing applications. Ms. Lovejoy has a Master of Science in Regulatory Affairs from San Diego State University, and a Bachelor of Science in Organizational Behavior from the University of San Francisco.

In addition, G1 announced that Chief Business Officer Greg Mossinghoff will depart the Company in January of 2018 to pursue an opportunity with an early stage therapeutics company.

“Greg has played a key role in building G1 from the ground up,” added Dr. Velleca. “I would like to thank Greg for his many contributions to G1 and wish him continued success.”



## **About G1 Therapeutics**

G1 Therapeutics, Inc., is a clinical-stage biopharmaceutical company focused on the discovery and development of novel therapeutics for the treatment of cancer. G1's two clinical assets, trilaciclib and G1T38, are CDK4/6 inhibitors, a validated and promising class of targets for anti-cancer therapeutics. Trilaciclib and G1T38 have broad therapeutic potential in many forms of cancer and may serve as the backbone of multiple combination regimens. In addition, G1 is advancing G1T48, a potential first/best-in-class oral selective estrogen receptor degrader, or SERD, which is targeted for the treatment of ER+ breast cancer.

G1 is based in Research Triangle Park, N.C. For additional information about G1, please visit [www.g1therapeutics.com](http://www.g1therapeutics.com).

## **Forward-Looking Statements**

*This press release 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 news release include, but are not limited to, the therapeutic potential of trilaciclib, G1T38 and G1T48, and the timing for data readouts regarding G1 Therapeutics' product candidates, and are based on G1 Therapeutics' expectations and assumptions as of the date of this press release. Each of these forward-looking statements involves risks and uncertainties. Factors that may cause G1 Therapeutics' actual results to differ from those expressed or implied in the forward-looking statements in this press release are discussed in G1 Therapeutics' filings with the U.S. Securities and Exchange Commission, including the "Risk Factors" sections contained therein and include, but are not limited to, the inherent uncertainties associated with developing new products or technologies and operating as a development-stage company; G1's ability to complete clinical trials for, obtain approvals for, and commercialize any of its product candidates; G1's ability to recruit and enroll patients in our studies; competition in the industry in which we operate; and market conditions. Except as required by law, G1 Therapeutics assumes no obligation to update any forward-looking statements contained herein to reflect any change in expectations, even as new information becomes available.*

###

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November 2017

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# 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, Kisqali and Verzenio
  - ✓ **G1T48 (oral SERD)** has first/best-in-class potential; on track for 4Q17 IND
- Multiple clinical data readouts, **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

Terry Murdock - SVP Development Operations

Buck Phillips - CFO, SVP Corporate Development

Jay Strum, PhD - Chief Scientific Officer



## Board of Directors

Seth Rudnick, MD - board chairman

Fred Eshelman, PharmD - Eshelman Ventures

Glenn P. Muir - audit committee chair

Tyrell Rivers, PhD - MedImmune Ventures

Christy Shaffer, PhD - Hatteras Venture Partners

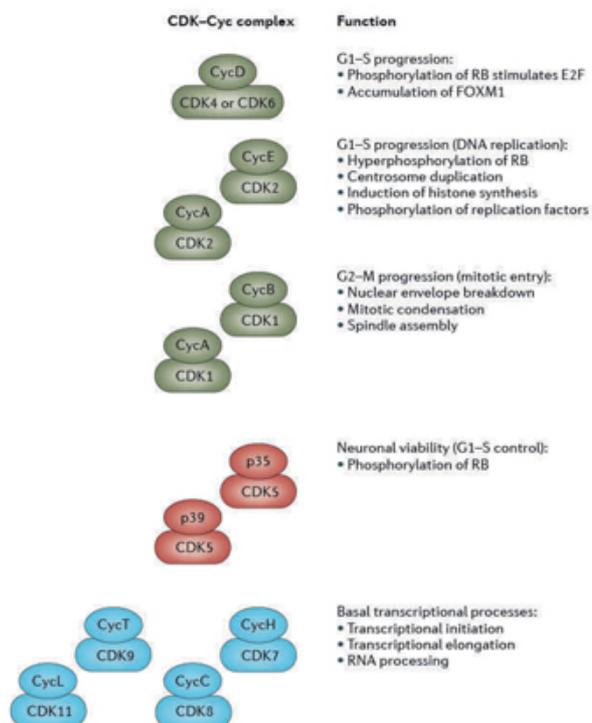
Mark Velleca, MD, PhD - CEO

Andrew Witty - former CEO of GSK

## Investors

- ~ \$96m private (4Q13, 1Q15, 2Q16)
  - Cormorant
  - Franklin Templeton
  - RA Capital
  - Rock Springs Capital
  - Tavistock
- ~ \$107m IPO - May 22, 2017
  - Nasdaq: GTHX

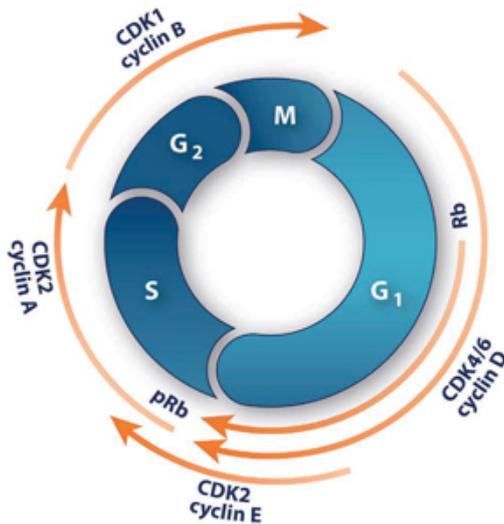
# CDK4/6 is a validated and promising target



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

- Nobel Prize-winning science
- FDA approval of Ibrance in 2015, Kisqali and Verzenio in 2017
- ~ \$11 billion estimated global peak sales in breast cancer alone
- Significant therapeutic and market potential in multiple other cancers
- G1 is the only biopharma with two clinical-stage CDK4/6 inhibitors:
  - trilaciclib
  - G1T38

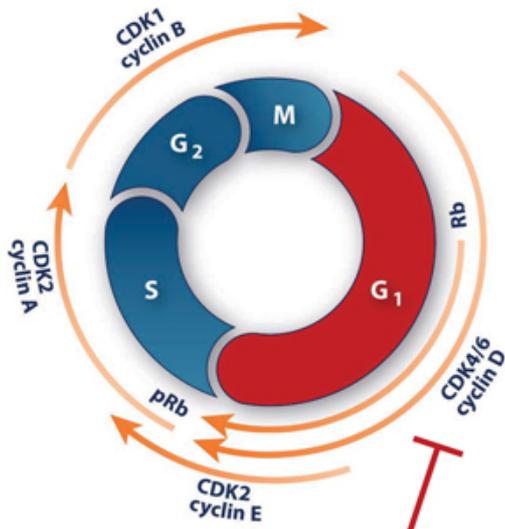
# CDK4/6 typically required for cell cycle progression



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

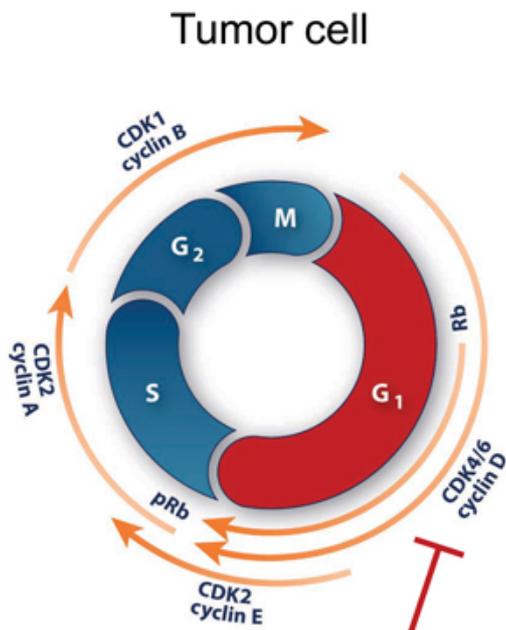
- G<sub>1</sub> and G<sub>2</sub> are gap or growth phases
- S phase: DNA synthesis
- M phase: cell division

# Selective CDK4/6 inhibition arrests cells in G1



Selective CDK4/6 inhibition blocks Rb phosphorylation and progression from G<sub>1</sub> to S phase: a cytostatic effect

# G1T38: arrests tumor cells in G1



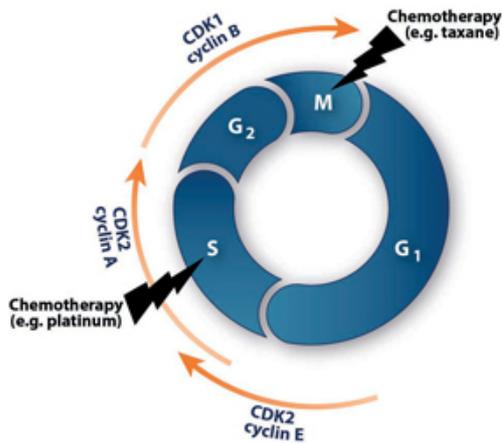
G1T38 blocks proliferation; potentiates tumor cell death when combined with other targeted therapy (e.g. SERD)

## G1T38

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

# Many cancers do not require CDK4/6 to grow

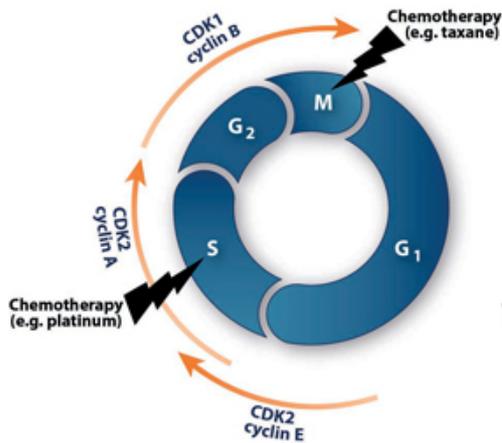
## CDK4/6-independent tumor cell



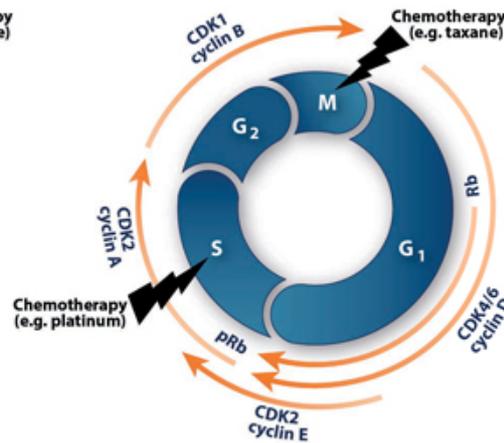
- CDK4/6-independent tumors can proliferate even in the presence of a CDK4/6 inhibitor
- Common CDK4/6-independent tumors include SCLC and TNBC
- Chemotherapy is typically used to treat these cancers
- Chemotherapy kills other cells, such as hematopoietic stem and progenitor cells (HSPCs)

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

CDK4/6-independent tumor cell



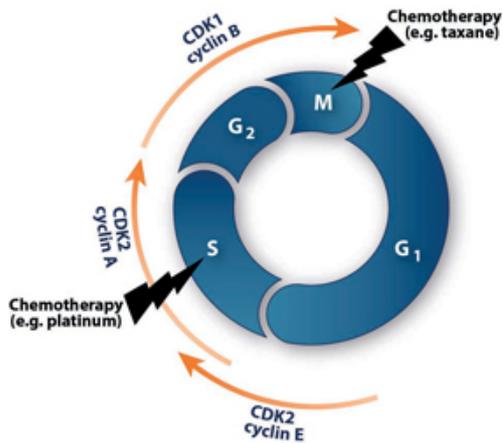
HSPC



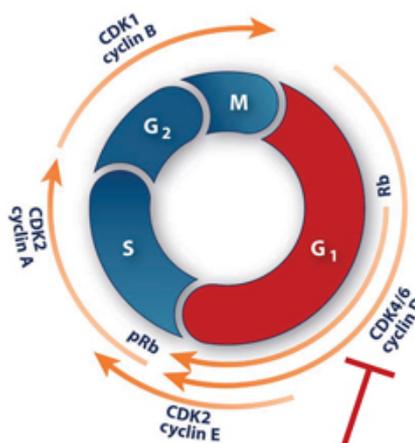
- HSPCs are the “reservoir” from which all blood and immune system cells are formed
- HSPCs are damaged by chemotherapy, causing myelosuppression and immunosuppression, limiting anti-tumor efficacy

# Trilaciclib: transiently arrests HSPCs in G1

## CDK4/6-independent tumor cell



## HSPC



## 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'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 can be backbone therapy for multiple combination regimens*
- ✓ *G1 owns IP and worldwide commercial rights to all compounds*
- ✓ *15 issued composition-of-matter and methods-of-use patents*

# 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: best-in-class potential by overcoming competitors' liabilities*

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

# G1's development pipeline

		Preclinical	Phase 1	Phase 2	Phase 3
<b>Trilaciclib</b> (iv CDK4/6i)	1 <sup>st</sup> -line SCLC (+ carbo/etop)	█	█	█	
	2 <sup>nd</sup> /3 <sup>rd</sup> -line SCLC (+ topotecan)	█	█	█	
	metastatic TNBC (+ gem/carbo)	█	█	█	
	1 <sup>st</sup> -line SCLC (+ Tecentriq/ carbo/etop)	█	█	█	
<b>G1T38</b> (oral CDK4/6i)	ER <sup>+</sup> , HER2- BC (+ Faslodex)	█	█		
	EGFRm NSCLC (+ Tagrisso)	█			
<b>G1T48</b> (oral SERD)	ER <sup>+</sup> , HER2- BC (monotherapy)	█			

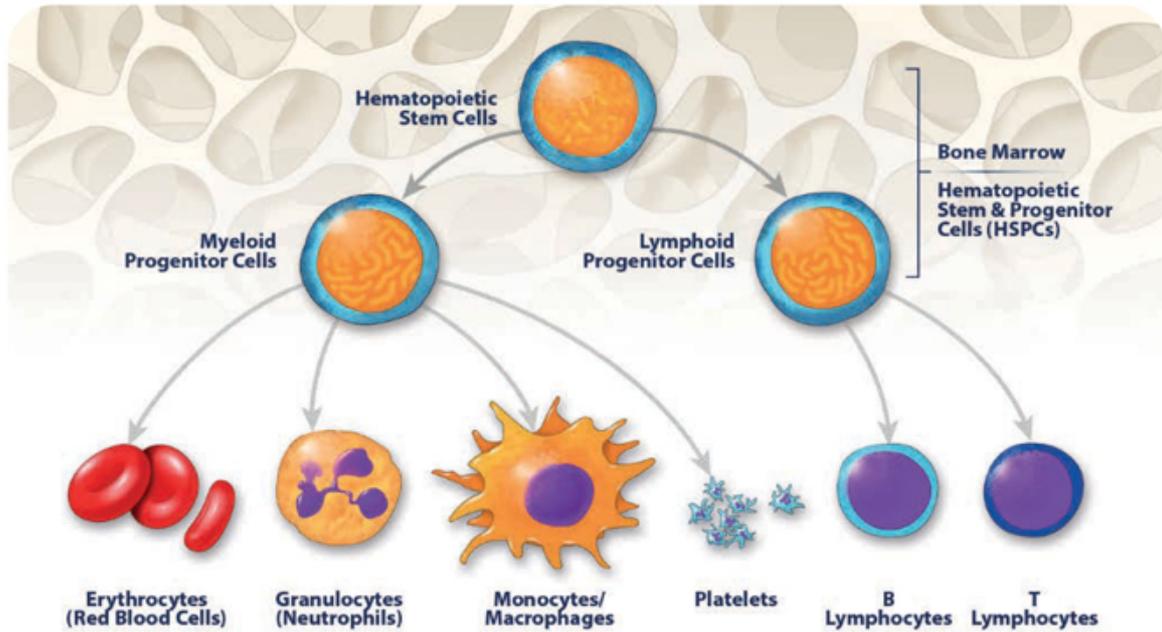
# Key anticipated milestones through 2018

		4Q17	1Q18	2Q18	2H18
Trilaciclib (iv CDK4/6i)	1 <sup>st</sup> -line SCLC (+ carbo/etop) Phase 2a	enrollment completed (2Q17)	top-line randomized data		present randomized data at medical meeting
	2 <sup>nd</sup> /3 <sup>rd</sup> -line SCLC (+ topotecan) Phase 2a			complete enrollment	top-line randomized data
	metastatic TNBC (+ gem/carbo) Phase 2			complete enrollment	present preliminary data at medical meeting
	1 <sup>st</sup> -line SCLC (+ Tecentriq/ carbo/etop) Phase 2				complete enrollment
G1T38 (oral CDK4/6i)	ER <sup>+</sup> , HER2- BC (+ Faslodex) Phase 1b/2a			present Phase 1b preliminary data at medical meeting	Phase 2a complete enrollment
	EGFRm NSCLC (+ Tagrisso) Phase 1b/2	IND filed	initiate Phase 1b		
G1T48 (oral SERD)	ER <sup>+</sup> , HER2- BC (monotherapy) Phase 1/2a	file IND		initiate Phase 1	

# TRILACICLIB DEVELOPMENT PROGRAM



# Trilaciclib preserves HSPCs and enhances immune system function during chemotherapy

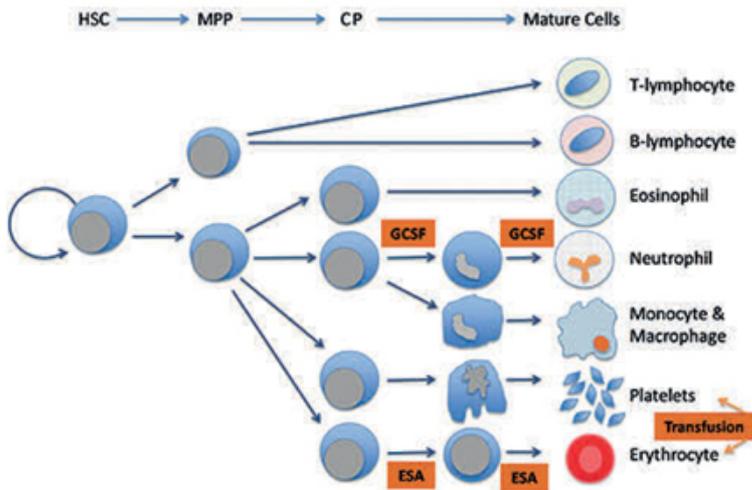


Opportunity to improve chemotherapy treatment outcomes and synergize with checkpoint combinations

# Trilaciclib addresses shortcomings of SOC

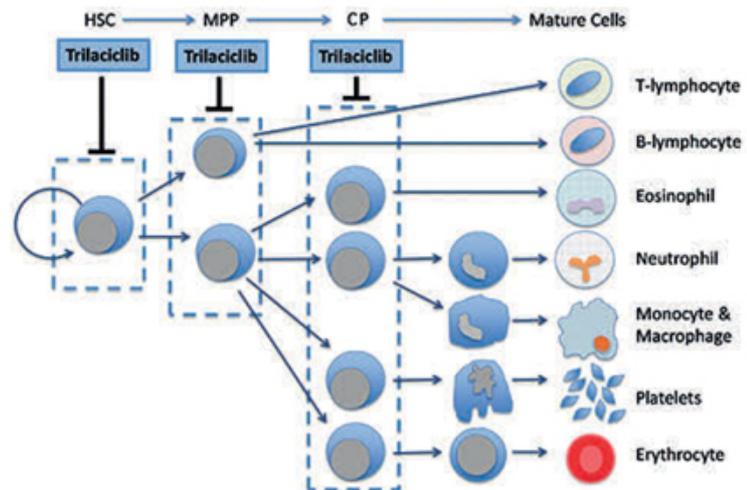
## Current SOC: growth factors and transfusions

- 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



# 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

# 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

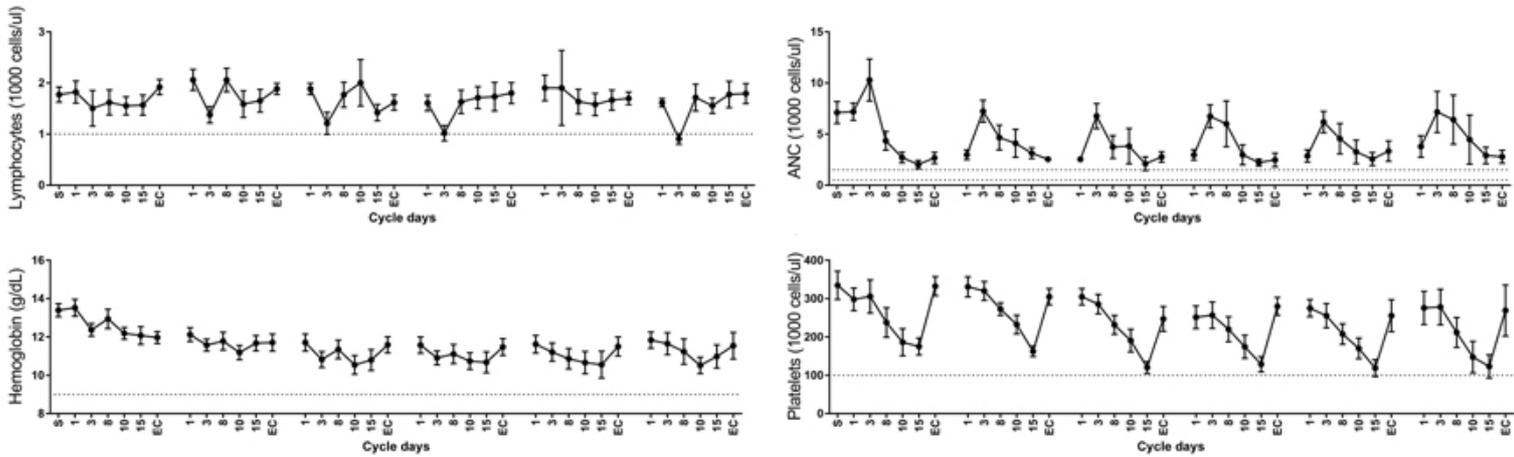
Setting	Combination	Phase		Total # Patients	Primary Endpoints	Secondary Endpoints	Current Status
1 <sup>st</sup> -line	carboplatin (AUC=5) and etoposide (100 mg/m <sup>2</sup> )	1b: open label	2a: randomized (1:1), placebo-controlled	96 1b: 19 2a: 77	myelo-preservation: e.g. FN, transfusions	ORR, PFS,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

# 1<sup>st</sup>-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

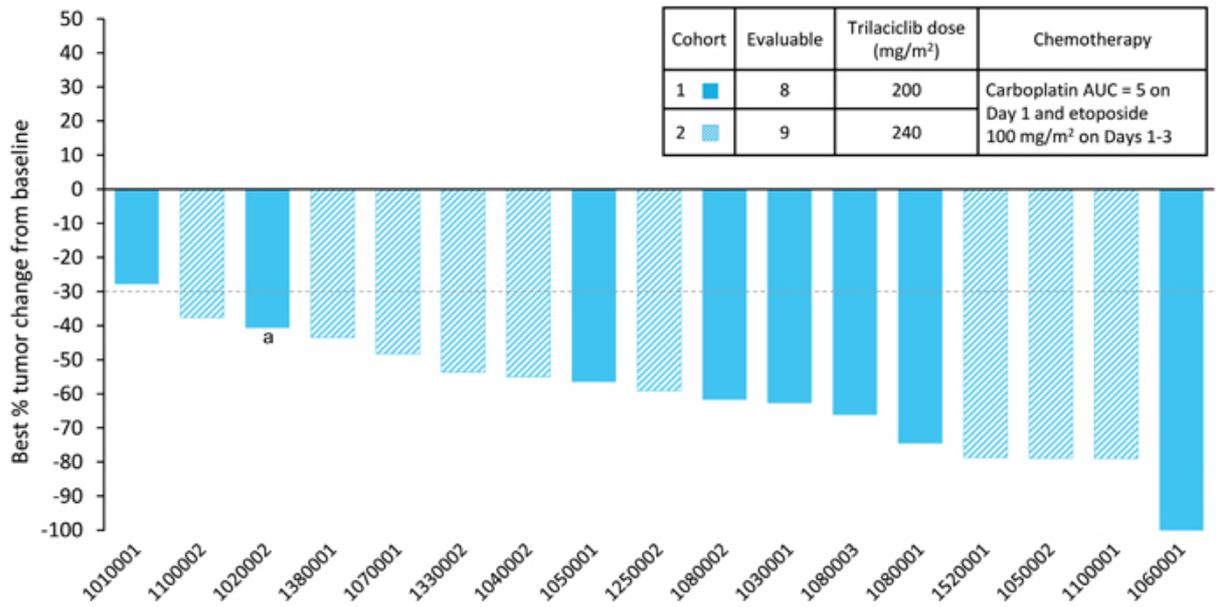
# 1<sup>st</sup>-line SCLC complete blood counts (CBCs): no clinically relevant myelotoxicity



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

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

# 1<sup>st</sup>-line SCLC: encouraging anti-tumor activity



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

Literature\* etop/carb efficacy (n=387)

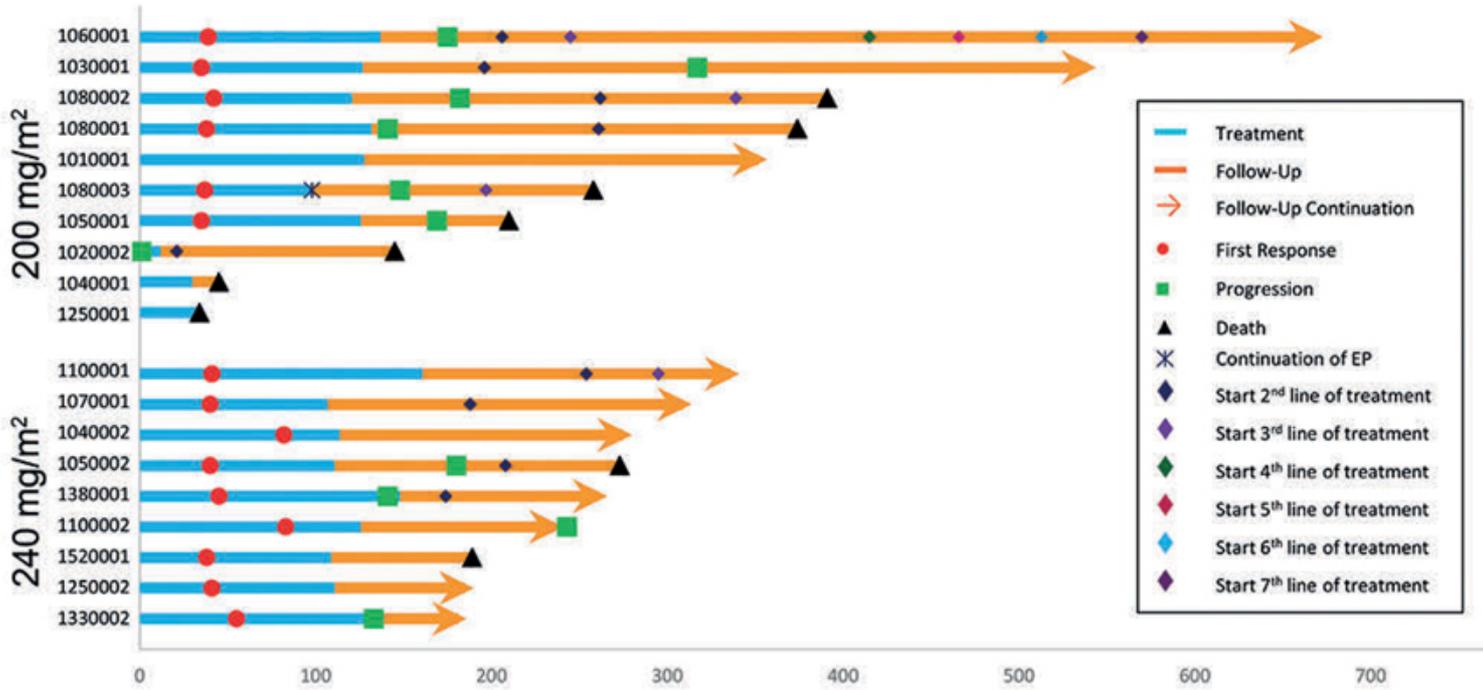
- 52% ORR (*only 1 CR*)

- 75% CBR

\*Socinski et al, 2009

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

# 1<sup>st</sup>-line SCLC: encouraging anti-tumor activity



# SCLC 1b/2a trials: conclusions and plans

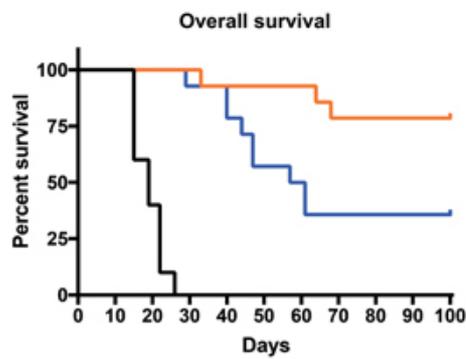
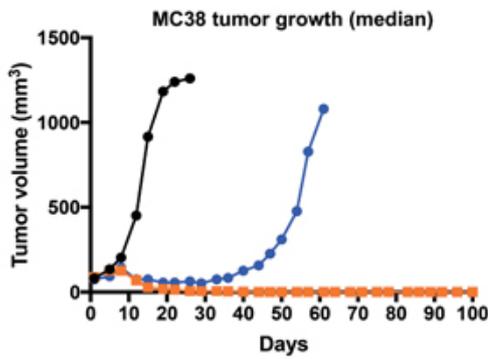
- Phase 1b data provides strong evidence of myelopreservation in both first-line and second/third line settings
- No febrile neutropenia: 51 open-label patients, >250 chemo cycles
- Improved overall response vs. historical rates in first-line
- Both studies in randomized, placebo-controlled Phase 2a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

# SCLC: trilaciclib/chemo/immune checkpoint inhibitor combination trial

- Trilaciclib: robust immune preservation when given with chemotherapy, preserves lymphocyte numbers/function
  - Roberts et al., 2017 EORTC-NCI-AACR
- Compelling preclinical efficacy when trilaciclib/chemo is combined with checkpoint inhibitor
  - Sorrentino et al., 2017 AACR; Deng et al., 2017 *Cancer Discovery*
- Non-exclusive collaboration with Genentech to evaluate trilaciclib/chemo/Tecentriq across multiple indications
- 2Q17: initiated a randomized placebo-controlled Phase 2 trial in 1<sup>st</sup>-line ES-SCLC (chemo/Tecentriq +/- trilaciclib)

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

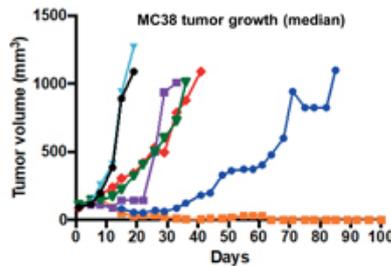
# Trilaciclib enhances chemo/checkpoint efficacy in syngeneic CDK4/6-independent tumor model



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 has a 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 (Sorrentino et al., 2017 AACR)

# Expansion to other indications: TNBC

- Significant unmet medical need in triple-negative breast cancer (TNBC)
- Gemcitabine/carboplatin  $\pm$  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, VTE 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	✓	✓			

# 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 *Oncotarget*)
- Drug well-tolerated in 75 subject Phase 1a single-dose HNV trial
  - no DLTs or grade 3/4 AEs; no QT, DILI, VTE concerns
  - differentiated PK profile: shorter t<sub>1/2</sub>, larger V<sub>d</sub> than Ibrance, Kisqali
- Encouraging early results in Phase 1b/2a breast cancer trial (in combination with Faslodex) with continuous dosing of G1T38
  - pharmacodynamic activity observed at first dose level
  - well-tolerated GI profile; no liver or CV AEs
  - plan to present preliminary Phase 1b data in 2Q18

# 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 $\geq$ 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 <sup>T790M</sup> 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, $\geq$ 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 (Wardell et al., 2017 AACR)
  - more potent than Faslodex
- On track for IND filing in December 2017

# Key anticipated milestones through 2018

		4Q17	1Q18	2Q18	2H18
<b>Trilaciclib</b> (iv CDK4/6i)	1 <sup>st</sup> -line SCLC (+ carbo/etop) Phase 2a	enrollment completed (2Q17)	top-line randomized data		present randomized data at medical meeting
	2 <sup>nd</sup> /3 <sup>rd</sup> -line SCLC (+ topotecan) Phase 2a			complete enrollment	top-line randomized data
	metastatic TNBC (+ gem/carbo) Phase 2			complete enrollment	present preliminary data at medical meeting
	1 <sup>st</sup> -line SCLC (+ Tecentriq/ carbo/etop) Phase 2				complete enrollment
<b>G1T38</b> (oral CDK4/6i)	ER <sup>+</sup> , HER2- BC (+ Faslodex) Phase 1b/2a			present Phase 1b preliminary data at medical meeting	Phase 2a complete enrollment
	EGFRm NSCLC (+ Tagrisso) Phase 1b/2	IND filed	initiate Phase 1b		
<b>G1T48</b> (oral SERD)	ER <sup>+</sup> , HER2- BC (monotherapy) Phase 1/2a	file IND		initiate Phase 1	

# 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, Kisqali, and Verzenio
  - ✓ **G1T48 (oral SERD)** potentially first/best-in-class; on track for 4Q17 IND
- Multiple clinical read-outs and **value inflection points in 2018**

# 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)
  - *Cancer Discovery* (Deng et al., 2017)
  - *Science Translational Medicine* (He et al., 2017)

# 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

# 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 more than 160 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

# Trilaciclib has a very different human PK profile than Ibrance

Drug	Dose	Tmax (h)	Cmax (ng/ml)	t1/2 (h)*
trilaciclib	IV 192mg/m <sup>2</sup>	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 <sub>50</sub> (uM) CDK4	IC <sub>50</sub> (uM) CDK6	IC <sub>50</sub> (uM) CDK2-cyclin E	IC <sub>50</sub> (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).