



G1 THERAPEUTICS, INC. 2018 ANNUAL REPORT

LETTER FROM THE CEO

Dear Fellow Shareholders:

Over the course of 2018 and early 2019, we have made significant advancements across all three of our clinical-stage drug development programs, trilaciclib, lerociclib, and G1T48, positioning G1 with an exciting opportunity to improve the lives of people living with cancer.

Recently, we took an important step toward making trilaciclib available to patients who may benefit from this first-in-class myelopreservation agent. In April, we announced that based on written feedback from our end-of-Phase 2 meeting with the U.S. Food and Drug Administration (FDA) and discussions with European regulatory authorities, we plan to submit marketing applications in the U.S. and Europe for trilaciclib for myelopreservation in small cell lung cancer (SCLC). Our team is working on these submissions now; the next step is a pre-New Drug Application (NDA) meeting with the FDA, which we anticipate will be scheduled later this year. We plan to file an NDA in 2020 and submit a Marketing Authorization Application (MAA) to the European Medicines Agency (EMA) subsequent to an NDA filing.

Since the start of 2018, we achieved important milestones across seven separate clinical trial programs that will support our trilaciclib regulatory filings, demonstrated proof-of-concept for lerociclib, and positioned us to present the first clinical data for G1T48 later this year. In addition, we have strengthened our leadership team and financial position. Highlights from 2018 and early 2019 included:

- **Reported positive multi-lineage myelopreservation data from three randomized, double-blind, placebo-controlled Phase 2 clinical trials of trilaciclib in small cell lung cancer (SCLC):** Our NDA and MAA submissions will be based on currently available data from three randomized, double-blind, placebo-controlled SCLC clinical trials, as well as safety data collected across all completed and ongoing clinical trials. In 2018, we reported positive findings from our Phase 2 trial of trilaciclib in combination with chemotherapy in first-line SCLC in March 2018, and presented additional data at the European Society for Medical Oncology (ESMO) 2018 Congress. In the fourth quarter of 2018, we reported positive preliminary data from Phase 2 trials in first-line SCLC in combination with chemotherapy/Tecentriq[®] (atezolizumab) and second/third-line SCLC in combination with chemotherapy. In all three trials, patients receiving trilaciclib showed statistically significant improvements in duration and occurrence of severe neutropenia (primary endpoints) and clinically meaningful reductions in G-CSF administrations and red blood cell transfusions. Treatment was well tolerated and the safety profile of trilaciclib was consistent across the three trials.

- **Presented preliminary improved progression-free survival data from randomized Phase 2 clinical trial of trilaciclib in combination with chemotherapy in patients with metastatic triple-negative breast cancer (mTNBC):** In December 2018, we presented data from our Phase 2 trial of trilaciclib in patients with mTNBC at the 2018 San Antonio Breast Cancer Symposium. There was an improvement in preliminary median progression-free survival (PFS) in patients receiving trilaciclib compared to the control arm, and patients on trilaciclib received more chemotherapy cycles than those in the control arm. The safety profile of trilaciclib was consistent with previously reported trials; no trilaciclib-related serious adverse events were reported. The company expects to present updated PFS data in 4Q19.
- **Reported encouraging preliminary lerociclib Phase 1b clinical trial results in estrogen receptor-positive, HER2-negative (ER+, HER2-) breast cancer in combination with Faslodex® (fulvestrant):** We presented Phase 1b data at the 2018 American Society of Clinical Oncology (ASCO) Annual Meeting that provided the rationale for initiating our ongoing dose expansion Phase 2a trial. We are exploring the potential for lerociclib to be dosed with less monitoring for neutropenia, which would be a significant differentiating feature from other CDK4/6 inhibitors.
- **Initiated a Phase 1b/2 clinical trial assessing lerociclib in combination with Tagrisso® (osimertinib) in EGFR-mutant non-small cell lung cancer (NSCLC):** This is the first trial of lerociclib outside of breast cancer. Based on its clinical and safety profile, we believe there is opportunity to develop lerociclib as a treatment for multiple tumor types.
- **Initiated the first clinical trial of our selective estrogen receptor degrader (SERD), G1T48, in women with ER+ breast cancer:** Preliminary results from this trial are expected later this year. With its differentiated chemistry and high potency, we believe that G1T48 could be best-in-class and benefit ER+ breast cancer patients.
- **Added key senior leadership:** We hired talented individuals to lead our commercial, legal and biostatistics teams, and expanded the development, commercial and technical operations experience of our Board of Directors with the addition of Garry Nicholson, Cynthia Schwalm and Willie Deese.
- **Executed two successful financings:** By raising capital in March and September, we are in a solid financial position that will enable us to advance our three clinical-stage assets.

These achievements have positioned us to realize multiple value inflection points in 2019/2020, including:

- Anticipate filing a NDA for trilaciclib for myelopreservation in SCLC in 2020, with a subsequent MAA filing in Europe.
- Initiate additional clinical trials to evaluate trilaciclib in multiple tumor types and chemotherapy regimens beginning in 2020, pending feedback from regulatory authorities.
- Report additional data from all four randomized Phase 2 trilaciclib clinical trials in 2019.
- Present preliminary proof-of-concept data from the Phase 1 clinical trial of G1T48 in ER+ breast cancer in 2H19.
- Present preliminary dose-escalation data from the Phase 1b clinical trial of lerociclib/Tagrisso in NSCLC in 3Q19.
- Present additional data from the Phase 1b clinical trial of lerociclib/Faslodex in ER+, HER2-breast cancer in 4Q19.

On behalf of the entire G1 team and Board of Directors, thank you for supporting our mission to discover, develop and deliver innovative therapies that improve the lives of those affected by cancer. I look forward to providing you with clinical and regulatory updates in the coming months that have the potential to make a meaningful impact on oncology practice and our company's value.

A handwritten signature in black ink, appearing to read "Mark Velleca". The signature is fluid and cursive, with a long horizontal stroke at the end.

Mark Velleca, M.D., Ph.D.
Chief Executive Officer