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TSX: TRIL

TRILLIUM THERAPEUTICS PROVIDES DATA UPDATE, ANNOUNCES PHASE 1B/2 PROGRAM PRIORITIES ACROSS HEMATOLOGIC MALIGNANCIES AND SOLID TUMORS, AND REPORTS GOVERNANCE CHANGES

- *TTI-622 monotherapy shows 33% objective response rate (ORR) in relapsed/refractory (R/R) lymphomas at 0.8-18 mg/kg doses, including 3 new responses (1 Complete Response (CR) + 2 Partial Responses (PRs)) since last data disclosure;*
- *TTI-621 monotherapy shows 18-29% ORR in R/R T- and B-cell lymphomas at 0.2-2.0 mg/kg doses, including 3 new responses (1 CR + 2 PRs) in cutaneous T-cell lymphoma (CTCL) since last data disclosure;*
- *TTI-622 and TTI-621 have been well tolerated at doses up to 18 mg/kg and 2.0 mg/kg weekly, respectively; neither drug candidate reached a maximum tolerated dose (MTD) level;*
- *Phase 1b/2 program across seven hematologic and solid tumor indications has been initiated, with studies across nine patient settings to start over approximately the next twelve months;*
- *Scott Myers joins the Board of Directors; Robert Kirkman and Tom Reynolds retire from the Board of Directors; Tom Reynolds to focus on SAB and senior advisor roles.*

CAMBRIDGE, MA, April 28, 2021 – Trillium Therapeutics Inc. (NASDAQ/TSX: TRIL), a clinical stage immuno-oncology company developing innovative therapies for the treatment of cancer, today provided a data update, announced Phase 1b/2 program priorities across seven hematologic and solid tumor indications, and reported governance changes with its Board of Directors.

"We have reached a critical milestone in Trillium's evolution," said Jan Skvarka, Trillium's President and CEO. "We have built a robust foundation for advancing into a Phase 1b/2 program – a foundation of two highly differentiated CD47 assets with monotherapy proof-of-concept across several lymphoma indications. Our new data further solidify our position in the CD47 field as having potentially class-leading single agent activity with both TTI-622 and 621, as well as potentially best-in-class tolerability with TTI-622. Furthermore, we are particularly excited to observe substantial anti-tumor activity in the skin of our CTCL patients, which suggests that TTI-622 and 621 have the ability to exit blood circulation and penetrate skin tumors, thus underscoring the potential of both drug candidates to treat solid tumors. Finally, new translational data suggest that natural killer cell engagement plays a key role in what we believe is TTI-621's mechanism of action, thus further differentiating TTI-621 in the CD47 field."

"We are now rapidly advancing into a Phase 1b/2 program, with multiple shots on goal – two drug candidates, seven target indications, multiple drug combinations – in patients with hematologic malignancies and solid tumors," added Ingmar Bruns, Chief Medical Officer. "Over the next twelve months, we expect to initiate studies across nine patient settings. The pipeline represents a portfolio of different risk-reward opportunities, multiple potentially accelerated regulatory paths to market, and a total addressable US patient population of over 30,000 patients in our entry settings. In parallel, we are continuing to evaluate less frequent dosing regimens than our current weekly dosing. This is supported by pharmacokinetic data, and, in the case of TTI-622, clinical experience with two CR patients who are on every three- and four-week dosing schedules."

"On a more personal note, as we are announcing governance changes, we would like to thank Bob Kirkman for his invaluable contributions over his eight-year tenure with Trillium as a Board member, including periods when he held Chair and Executive Chair roles," said Dr. Skvarka. "Bob has played a pivotal role in transitioning the CEO leadership in 2019, and positioning the company for our subsequent transformation program in 2020. Trillium would not be where it is today without Bob's leadership, hands-on contributions and personal sacrifices. We will sorely miss Bob, and wish him all the best as he scales down his professional commitments."

TTI-622 Study Update

As of the data cutoff date of April 12, 2021, a total of 42 patients have been enrolled in the ongoing open-label Phase 1 dose escalation study of TTI-622 in patients with R/R lymphoma (NCT03530683). Patients received weekly intravenous doses between 0.05 and 18 mg/kg. All dose levels were very well-tolerated and an MTD was not reached. Adverse events (AEs) were predominantly Grade 1-2; related AEs ≥Grade 3 were neutropenia (9%), thrombocytopenia (5%) and anemia (2%). Pharmacokinetic data demonstrated dose-proportional increases in drug exposure between 8 and 18 mg/kg, and support evaluating less frequent dosing. Objective responses were achieved in 9 of 27 (33%) heavily pre-treated response-evaluable patients at dose levels ≥0.8 mg/kg, and included 2 CRs and 7 PRs. Three responses (1 CR and 2 PRs) at 12 and 18 mg/kg were obtained since the last data disclosure at the American Society of Hematology (ASH) 2020 Annual Meeting. All responses occurred within the first eight weeks of treatment across multiple lymphoma indications. One CR patient (0.8 mg/kg dose level) has been on study for more than 22 months and was transitioned to monthly dosing. The second CR patient (18 mg/kg) achieved a response after receiving only two doses with a 4-week dosing interval and is being maintained on every three weeks (Q3W) dosing. The study is continuing, with 3 more patients at 18 mg/kg pending response assessments as of the April 12, 2021 cutoff date.

TTI-621 Study Update

We have provided a further update on the safety data and anti-tumor activity observed in the ongoing open-label Phase 1 dose escalation study of intravenous TTI-621 in patients with R/R hematologic malignancies (NCT02663518). The study consists of four parts: (a) "Parts 1-3" in hematologic malignancies, with dosing up to 0.5 mg/kg weekly, now complete; and (b) "Part 4" in CTCL, with dosing at 0.5 mg/kg weekly and higher, currently ongoing. As of the data cutoff date of April 12, 2021, TTI-621 was well-tolerated and an MTD in Part 4 was not reached. Across Parts 1-4, the most common treatment-related AEs ≥Grade 3 were thrombocytopenia (22%), which was transient and not dose-limiting, anemia (8%), neutropenia (6%), and infusion-related reactions (4%), which occurred mostly at the first dose and were effectively managed by prophylactic treatment. Monotherapy activity was observed in CTCL (19% ORR, n=62), peripheral T-cell lymphoma (18% ORR, n=22) and diffuse large B-cell lymphoma (DLBCL) (29% ORR, n=7).

Three responses (1 CR and 2 PRs) in CTCL patients treated at 1.4 and 2.0 mg/kg were obtained since the last data disclosure at ASH 2020. Emerging translational data from patient samples suggest that NK cell activation plays a key role in the anti-tumor activity of TTI-621, in addition to inhibition of the "don't eat me" signal and delivery of a pro-phagocytic signal. This highly differentiated proposed mode of action, together with encouraging monotherapy activity and good tolerability, prompt continued and focused further investigation of TTI-621. The study is continuing, with 3 more patients at 2.0 mg/kg pending response assessments as of the April 12, 2021 cutoff date.

Phase 1b/2 Program

Based on the strong and differentiated foundation that Trillium has built, including potentially class-leading monotherapy activity, the Company is initiating Phase 1b/2 programs with both TTI-622 and TTI-621. These programs will initially cover seven indications (four hematological cancers, three solid tumors), and study TTI-622 and TTI-621 primarily in combination with other anti-cancer agents.

Specifically, TTI-622 will be evaluated in the following settings and combination regimens:

- R/R multiple myeloma, in a combination with carfilzomib + dexamethasone;
- First line p53 mutant acute myeloid leukemia (AML), in a combination with azacitidine;
- First line elderly or unfit p53 wild type AML patients, in a combination with azacitidine and venetoclax;
- R/R DLBCL, in a combination with anti-PD-1, in an investigator-sponsored trial at Mayo Clinic;
- Platinum-resistant ovarian cancer, in a combination with chemotherapy; and
- A second solid tumor combination study to be announced later this year.

These studies will be initiated with 8 mg/kg weekly dosing, or potentially less frequent dosing regimens at higher doses.

The Phase 1b/2 program for TTI-622 has now been initiated with the dosing of a first multiple myeloma patient with TTI-622 in a combination with carfilzomib + dexamethasone. Both AML cohorts are open for enrollment, and we expect the first patients to be dosed this quarter.

TTI-621 will be evaluated in the following settings and combination regimens:

- Second line peripheral T-cell lymphoma (PTCL), as a TTI-621 monotherapy;
- R/R DLBCL, in a combination with anti-PD-1, in an investigator-sponsored trial at Mayo Clinic; and
- First line leiomyosarcoma, a subtype of soft tissue sarcoma, in a combination with doxorubicin.

Initial Phase 1b/2 studies will be initiated at two dose levels (0.2 mg/kg and up to 2.0 mg/kg weekly); different levels may be chosen based on overlapping toxicities with combination agents.

In addition, bi-weekly (Q2W) and Q3W dosing schedules will be evaluated for each molecule in the ongoing monotherapy dose escalation studies.

Governance Update

Effective April 28, 2021, Scott Myers is joining the Board of Directors. Scott is an accomplished executive who brings to the Board nearly three decades of pharmaceutical and medical device industry experience. Previously, he served as CEO of AMAG Pharmaceuticals, Rainier Therapeutics, Cascadian Therapeutics, and Aerocrine AB. He currently serves on the Boards of Directors of Selecta Biosciences and Harpoon Therapeutics. We are very excited that Scott has agreed to join the Board, and look forward to benefitting from his extensive executive experience and track record of building successful biotechnology companies.

Robert Kirkman elected to retire from the Board of Directors, effective April 28, 2021. Robert has served as a director since December 2013, the Chair of the Board since March 2019, and acted as the Executive Chair from April 2019 to March 2020.

As previously announced, Tom Reynolds joined our scientific advisory board (SAB) in November 2020. Due to the resulting loss of his independent status as a Board member, Tom is now (effective April 28, 2021) retiring from the Board to focus on the SAB role, as well as to serve as a senior advisor to assist with initiation of our extensive Phase 1b/2 program and a scale-up of the clinical development organization.

Upcoming Milestones and Guidance

In 2021, Trillium expects two data updates:

- TTI-622 data update from the ongoing dose escalation study in R/R lymphomas at a medical conference in 4Q 2021; and
- TTI-621 data update from the ongoing dose escalation study in R/R CTCL at a medical conference in 4Q 2021.

Over approximately the next twelve months, the Company plans to initiate studies in the following indications and patient settings:

- TTI-622 + azacitidine combination in p53 mutant AML patients in 2Q 2021 (enrollment open);
- TTI-622 + azacitidine + venetoclax combination in elderly or unfit p53 wild type AML patients in 2Q 2021 (enrollment open);
- TTI-622 + chemotherapy combination in platinum-resistant ovarian cancer patients in 2H 2021;
- TTI-622 combination study in a to-be-announced solid tumor indication in 1H 2022;
- TTI-622 + anti-PD-1 and TTI-621 + anti-PD-1 in DLBCL patients in 4Q 2021 to 1H 2022 (investigator-sponsored trial);
- TTI-621 monotherapy study in PTCL in 3Q 2021; and
- TTI-621 + doxorubicin combination in leiomyosarcoma in 3Q 2021.

As all of the above studies are open-label trials, the Company expects a robust flow of new data updates and multiple catalysts in 2022, in addition to the above mentioned updates from the continuing dose escalation studies in the fourth quarter of 2021.

As of March 31, 2021, Trillium had $276 million in cash, cash equivalents, and marketable securities, sufficient to fund operations and the above outlined clinical development priorities into 2023.

R&D Day Presentation and Webcast

The archived webcast from Trilium's R&D Day can be found at https://event.on24.com/wcc/r/3129711/BFCFD551CEEF86B1D97BBE20BF99A46C and will be available on Trillium's website for 30 days. The R&D Day presentation can be found on our website at www.trilliumtherapeutics.com.

About Trillium Therapeutics

Trillium is an immuno-oncology company developing innovative therapies for the treatment of cancer. The company's two clinical programs, TTI-622 and TTI-621, target CD47, a "don't eat me" signal that cancer cells frequently use to evade the immune system.

For more information visit: www.trilliumtherapeutics.com

Caution Regarding Forward-Looking Information

This press release contains forward-looking statements within the meaning of the Private Securities Litigation Reform Act of 1995 and applicable United States federal securities laws and forward-looking information within the meaning of Canadian securities laws (collectively, "forward-looking statements"). The use of words such as "may," "will," "could", "should," "expects," "intends," "plans," "anticipates," "believes," "estimates," "predicts," "projects," "seeks," "endeavor," "potential," "continue" or the negative of such words or other similar expressions can be used to identify forward-looking statements. Forward-looking statements in this press release include, but are not limited to, express or implied statements regarding the therapeutic potential and monotherapy activity of our programs, our clinical development plans and our expectations with respect to the timing of clinical development milestones, including with respect to initiating Phase 1b/2 studies in hematological and solid tumor malignancies, the expected timing of the release of further data on Trillium's TTI-622 and TTI-621 studies, and our expected cash runway. With respect to the forward-looking statements contained in this press release, Trillium has made numerous assumptions regarding, among other things: the impact of the COVID-19 pandemic on its operations, the effectiveness and timeliness of preclinical and clinical trials; and the completeness, accuracy and usefulness of the data. While Trillium considers these assumptions to be reasonable, these assumptions are inherently subject to significant scientific, business, economic, competitive, market and social uncertainties and contingencies. Additionally, there are known and unknown risk factors that could cause Trillium's actual results, performance or achievements to be materially different from any future results, performance or achievements expressed or implied by the forward-looking statements contained in this press release. A discussion of risks and uncertainties facing Trillium appears in Trillium's Annual Report on Form 10-K for the year ended December 31, 2020, with the U.S. Securities Exchange Commission, each as updated by Trillium's continuous disclosure filings, which are available at www.sedar.com and at www.sec.gov. All forward-looking statements herein are qualified in their entirety by this cautionary statement, and Trillium disclaims any obligation to revise or update any such forward-looking statements or to publicly announce the result of any revisions to any of the forward-looking statements contained herein to reflect future results, events or developments, except as required by law.

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