May 2, 2022

Dear Stockholders of Tempest,

In advance of Tempest's first annual meeting of stockholders as a public company and in my inaugural letter to stockholders, I am pleased to report that the company significantly advanced on multiple fronts in 2021. In addition to emerging from a competitive merger process as a public company, the team advanced two clinical programs (including one into a global, randomized study with F. Hoffmann La Roche (Roche)), expanded the pipeline to include a fourth novel program, and welcomed three new Directors to the Board who bring extensive clinical development and business expertise.

Looking forward, we believe 2022 could be a transformative year for Tempest. We are planning to present our first clinical data at the 2022 American Society of Clinical Oncology (ASCO) Annual Meeting in June, and are proud that ASCO selected our TPST-1120 Phase 1 abstract for a podium presentation. We believe this is the beginning of a series of potential catalysts for the next 12 to 18 months, including additional data from TPST-1120 in the randomized study and the first monotherapy and combination therapy data from our second clinical program, TPST-1495. In addition, we plan to continue to develop our two preclinical programs, which we believe collectively provides a diversified portfolio of novel small molecule oncology programs designed to both leverage the immune system and target tumors directly, with the potential to treat a wide range of tumors.

Clinical Progress

TPST-1120 is our first clinical program and is an oral small molecule therapy that targets PPARα, a transcription factor that regulates fatty acid oxidation (FAO), a pathway used by diverse cancers to support their growth and to avoid the immune system. By inhibiting PPARα, TPST-1120 is designed to inhibit tumor proliferation and angiogenesis and stimulate anti-cancer immunity, and if approved, it will be first-in-class.

We have nearly completed the TPST-1120 Phase 1 dose and schedule optimization study in advanced patients: the monotherapy arm is complete and the combination arm is fully enrolled. We have observed both stable disease as a monotherapy and promising objective responses in combination with nivolumab, including in subjects previously refractory to anti-PD-1 therapy, and we are looking forward to presenting these data at ASCO. In addition, we announced a collaboration with Roche in March 2021 that accelerated the development of TPST-1120 into a first-line randomized global Phase 1b/2 study in patients with hepatocellular carcinoma (HCC). Roche is running the study, which will compare TPST-1120 in combination with the standard-of-care regimen of atezolizumab and bevacizumab, compared to the standard of care alone. We are excited about this study for multiple reasons. HCC is a high expressor of PPARα and we also expect to see a significant number of patients with a mutation in the β-catenin gene, which is known to confer a greater reliance on the metabolic pathway that TPST-1120 inhibits. In addition, there are independent mechanistic rationales to combine TPST-1120 with each of atezolizumab and bevacizumab separately, so we look forward to the potential of the triplet for HCC patients. We announced that the first patient was enrolled in Fall 2021, and expect to have initial data by the end of 2022 or early next year.

Our second clinical program, TPST-1495, is also an oral small molecule therapy and like TPST-1120 is designed to target tumor cells directly and activate development of tumor-targeted immunity. We opened the Phase 1 dose and schedule optimization study during the height of the pandemic, and the clinical team did a great job keeping it moving forward, with the opening of an additional combination arm of the study in the Fall of 2021.

TPST-1495 is designed to directly inhibit the cancer-promoting EP2 and EP4 prostaglandin (PGE2) receptors from signaling in the cancer cells to inhibit both tumor growth and immune suppression, while sparing very similar receptors known as EP1 and EP3 and allowing them to signal. We believe this is important because while PGE2 signaling through EP2 and EP4 has been observed to stimulate tumor proliferation, enhance angiogenesis and suppress immune function in the tumor microenvironment, EP1 and EP3 signaling are required for a functional anti-cancer immune response. In addition, recent data show that PGE2 production and expression of the EP2 and EP4 receptors can be increased in patients undergoing treatment with immune checkpoint inhibitors, leading these patients to become refractory to this therapy. This is known as adaptive immune resistance, and supports the clinical rationale to evaluate TPST-1495 in combination with immune checkpoint inhibitors. TPST-1495 is in ongoing monotherapy and combination therapy dose and schedule optimization studies in patients with advanced solid tumors, with the potential to expand in indications known to be prostaglandin-driven, including colorectal cancer (CRC) and in a tumor indication-agnostic, biomarker-selected cohort. Although we are aware of several clinical programs targeting only EP4, we further believe this is necessary but insufficient given the nature of the combined expression of both EP2 and EP4 receptors in multiple tumors. If approved, TPST-1495 would also be first-in-class.

Pipeline Progress

In addition to our two clinical programs, Tempest is advancing two novel preclinical programs that continue the theme in our portfolio of agents designed to have a dual mechanism of action that target tumor cells directly and leverage the human immune system, and to be orally available.

The first program is designed to modulate an important target in cancer where earlier methods have been met with limited success to date, and we believe Tempest's TREX-1 program may be the solution. STING, which stands for Stimulator of Interferon Genes, is a critical innate immune sensor for the development of anti-tumor immunity that malignant cells can inactivate. However, we believe that selective activation of the STING pathway may be achieved through targeted inhibition of TREX-1, a cytosolic DNA exonuclease overexpressed in tumor cells that modulates STING signaling. In vitro and in vivo studies have shown that Tempest's compounds enhance the activation of the STING pathway in DNA-stimulated human and mouse cells. Furthermore, preclinical results in several tumor models have shown synergies of its TREX-1 compounds with low doses of doxorubicin, demonstrating significant therapeutic anti-tumor efficacy and survival.

Finally, in September 2021, we announced the in-license of a fourth program via an exclusive license with the University of California at Berkeley for intellectual property covering a drug target that was discovered in the laboratory of Russell Vance, Ph.D., professor of molecular and cell biology at U.C. Berkeley and a Howard Hughes Medical Institute investigator. Dr. Vance also joined our advisory board. The target is a component of a newly defined pathway that controls the production of a cytokine that tumors can evolve to block to promote metastasis and avoid immune recognition. To our knowledge,

Tempest is the only company with an active program designed to hit this target, and we have elected to keep the target confidential for the time being.

Building a Better Organization

2021 also saw significant progress in the expansion of Tempest's industry talent and access to the capital markets. In June, we emerged as a public company from a competitive merger process and completed a simultaneous financing. At the same time, Geoff Nichol, M.B., Ch.B., M.B.A., joined our Board. Geoff has nearly 30 years' experience in drug development, and recently retired from the role of Chief Medical Officer at BioMarin. Shortly thereafter, Christine Pellizzari, JD, and Ronit Simantov, M.D., joined our Board in July and August, respectively. Christine is currently the Chief Legal Officer at Science 37, after a long tenure with Insmed where she was Chief Legal Officer. Ronit is the Chief Medical Officer at Gamida Cell, which she joined after serving as the head of oncology global medical affairs at Pfizer. Geoff, Christine and Ronit bring extensive clinical development, capital markets, transactional, and legal experience to the team, and we are thrilled to have them on the Board.

Looking forward in 2022

We are looking forward to a potentially transformative 2022. Notwithstanding emerging as a public company in a challenging biotech market, the Tempest team continued to advance the programs in a timely manner and expand the portfolio with a new, novel program. We believe the strong fundamentals of this diversified portfolio, managed by an experienced team and Board, sets Tempest up for success. We look forward to our first clinical data release at ASCO, and to keeping you appraised of the company's progress throughout 2022.

Sincerely,

Stephen R. Brady
Chief Executive Officer