April 12, 2021

Molecular Templates Announces Poster Presentations on its Engineered Toxin Bodies at the American Association of Cancer Research (AACR) Virtual Annual Meeting I

Posters will feature data on MT-5111 (targeting HER2), MT-6402 (targeting PD-L1) and a novel CTLA-4-targeted ETB

AUSTIN, Texas, April 12, 2021 (GLOBE NEWSWIRE) -- Molecular Templates, Inc. (Nasdaq: MTEM, “Molecular Templates,” or “MTEM”), a clinical-stage biopharmaceutical company focused on the discovery and development of proprietary targeted biologic therapeutics, engineered toxin bodies (ETBs), today reported that three posters featuring data on its pipeline programs and technology platform will be presented at the AACR Virtual Annual Meeting I, taking place April 10-15, 2021.

Title:	**Phase 1 Study of the Novel Immunotoxin MT-5111 in Patients with HER2+ Tumors**
Authors:	Zev A. Wainberg, MD; Monica M. Mita, MD; Minal A. Barve, MD; Erika P. Hamilton, MD; Andrew J. Brenner, MD, PhD; Frances Valdes, MD; Daniel Ahn, DO; Joleen Hubbard, MD; Jason Starr, DO; Christine Burnett, PhD; Joshua Pelham; Eric T. Williams, PhD; Aimee Iberg, PhD; Thomas Strack, MD; Andrés Machado Sandri, MD; Brian A. Van Tine, MD, PhD
Abstract #	CT130

This poster summarizes results from a data cut in December 2020 for an ongoing Phase 1, first in human, open-label, dose escalation and expansion study of MT-5111 in subjects with HER2+ solid tumors. MT-5111 has a novel mechanism of action that may not be subject to resistance mechanisms that exist for current HER2 therapies, binds a distinct epitope on HER2 that allows for potential combination with trastuzumab-based therapies, and, at 55kDa, is significantly smaller than other HER2 antibody or ADC therapies. As of the data cut in December 2020, 16 study subjects had been treated in the 3+3 cohort escalation. The cancer types included biliary tract (n=6), breast (n=6), pancreatic (n=2), gastric (n=1), and colon (n=1). Results to date show that MT-5111 has been well tolerated at escalated doses up to Cohort 5 (4.5 µg/kg), which allowed for the progression to Cohort 6 (6.75 µg/kg). There have not been any dose limiting toxicities nor any signs of cardiotoxicity to date, and the MTD has not been reached. Pharmacokinetic data for the first 5 cohorts matched simulations based on non-human primate studies. Exposures at 4.5 µg/kg have reached

approximately 5x the IC 50 of HER2-expressing cell lines.

Three patients experienced stable disease as best response per RECIST 1.1 criteria (1 pancreatic at 4.5 µg//kg, 1 breast at 2 µg//kg, 1 biliary tract at 2 µg/kg). As previously reported, one subject with metastatic breast cancer in cohort 2 (1 µg/kg) remained on treatment for 10 cycles with stable disease; although she had unmeasurable disease by RECIST criteria, she had three sub-centimeter hepatic lesions that disappeared at the end of cycle 8 before she discontinued for clinical progression/symptomatic deterioration at cycle 10. This subject had received three prior HER2 targeting regimens which initially included pertuzumab plus trastuzumab followed by trastuzumab and TDM1 as monotherapies. Dose escalation continues and no dose limiting toxicities have been observed to date at 6.75 µg/kg (Cohort 6).

The HER2+ breast cancer expansion cohort is planned to be initiated in 2Q21 at a dose of 10 µg/kg (anticipated to be a therapeutic dose level), pending adequate safety from the 10 µg/kg dose escalation cohort. Dose escalation in all HER2+ tumor types will continue (including potential cohorts beyond 10 µg/kg) to determine the recommended Phase 2 dose while the breast cancer expansion cohort collects efficacy and safety data. As doses higher than 10 µg/kg are considered to be tolerable in the dose escalation cohort, the dose will be increased in the breast cancer cohort accordingly.

Title: **Preclinical Characterization of a Novel CTLA-4-Targeted ETB for Direct Treg Depletion**

Authors: Khanna, Caleigh Howard, Lilia A. Rabia, Alvaro Aldana, Jay Zhao, Asis Sarkar, Eric Williams, Banmeet Anand, Betty Chang, Chris Moore, Hilario J. Ramos, Aimee Iberg -- Molecular Templates Inc., Austin, TX.

Abstract # 1627

Current CTLA-4 antibodies have shown efficacy in oncology but have been limited by toxicity issues and an inability to clear regulatory T cells (Tregs) from the tumor microenvironment (TME). CTLA-4-targeted ETBs are designed to preferentially deplete Tregs in the TME to improve efficacy and reduce the toxicity associated with CTLA-4 targeted antibodies. This study explored the preclinical characterization of a lead candidate CTLA-4-targeted ETB. CTLA-4-ETB-A directly binds and specifically kills CTLA-4 positive cells *in vitro* and induces apoptosis of *ex-vivo* expanded Tregs. CTLA-4-ETB-A is designed to bind CTLA-4 in a manner unique from classic blocking antibodies and is not expected to have sustained blocking ability in vivo due to the relatively short half-life of an ETB compared to a neutralizing monoclonal antibody. The authors predict this will allow for focused Treg depletion in the TME based on target expression levels, while sparing autoreactive T cell activation in the periphery to reduce or eliminate the toxicity seen with CTLA-4 antibodies. In a transgenic mouse model expressing human CTLA-4 and bearing syngeneic subcutaneous tumors, CTLA-4 expression was highest on the Treg cells within the tumor microenvironment compared to other T cell populations and compartments. In this model, it was demonstrated that ETB treatment depletes Tregs in the TME, supporting the overall hypothesis. Peripheral CD4+ T cell proliferation was observed in response to ETB treatment. Initial tox assessment was performed in a non-human primate (NHP) model. ETB candidate A was well tolerated up to 450 µg/kg. An increase in proliferating CD4+ and CD8+ central memory T cells was observed and is a potential pharmacodynamic effect.

Title: **Engineered Toxin Bodies Targeting PD-L1 to Alter Tumor Immunophenotypes and Delivery Broad Antigenic Diversity and Patient Coverage**

Authors: Swati Khanna, Elizabeth Saputra, Wenzhao Dong, Lindsey Aschenbach, Lilia A. Rabia, Garrett L. Cornelison, Michaela Sousares, Jay Zhao, Lee Robinson, Betty Chang, Hilario J. Ramos, Joseph D. Dekker
Molecular Templates Inc., Austin, TX

Abstract 1628
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MT-6402 is an ETB designed to deliver a unique and dual mechanisms of action approach for directly targeting tumors that express PD-L1 on the tumor and/or the TME. Unlike current checkpoint inhibitors which only bind PD-L1 and sterically block interactions with PD-1, MT-6402 directly destroys PD-L1+ tumor and TME immune cells. MT-6402 has dual mechanisms of action that include the enzymatic destruction of ribosomes and the delivery of a viral class I antigen derived from CMV (pp65) into the targeted tumor, referred to as Antigen Seeding Technology (AST), for presentation on the target tumor cell surface to alter the tumor immunophenotype and induce a CMV specific T-cell response. MT-6402's antigen seeding CMV pp65 payload covers the largest MHC haplotype in the US. Delivery of foreign antigens that are restricted to additional MHC haplotypes could broaden the patient population that could benefit from AST. ETBs based on MT-6402 that deliver additional antigens retain expected potency and target binding, while also activating donor CTLs with matched haplotypes. ETBs delivering antigens to a broader population are under investigation for in vivo safety, efficacy and function. The MT-6402 IND filing has been accepted by the FDA with the Phase 1 first-in-human study expected to begin dosing in 2Q21.

About Molecular Templates

Molecular Templates is a clinical-stage company focused on the discovery and development of targeted biologic therapeutics. Our proprietary drug platform technology, known as engineered toxin bodies, or ETBs, leverages the resident biology of a genetically engineered form of Shiga-like Toxin A subunit to create novel therapies with potent and differentiated mechanisms of action for cancer and other serious diseases.

Forward-Looking Statements

This press release contains forward-looking statements for purposes of the Private Securities Litigation Reform Act of 1995 (the "Act"). Molecular Templates disclaims any intent or obligation to update these forward-looking statements, and claims the protection of the Act's Safe Harbor for forward-looking statements. All statements, other than statements of historical facts, included in this press release regarding strategy, future operations, future financial position, future revenue, projected expenses, prospects, plans and objectives of management are forward-looking statements. In addition, when or if used in this press release, the words "may," "could," "should," "anticipate," "believe," "estimate," "expect," "intend," "plan," "predict" and similar expressions and their variants, as they relate to Molecular Templates may identify forward-looking statements. Examples of such statements include, but are not limited to, statements regarding the safety or potential efficacy of Molecular Templates' drug or biologic candidates; statements relating to the development of

MT-5111, MT-6402 and CTLA-4; the expected timing of submitting various IND applications, initiating and completing enrollment of cohorts, initiating and conducting studies and generating data; the expected participation and presentation at upcoming conferences; the anticipated effects of the COVID-19 pandemic on Molecular Templates' ongoing clinical studies, manufacturing and preclinical development; and Molecular Templates' belief that its proprietary biologic drug platform technology, or ETBs, provides for a differentiated mechanism of action that may address some of the limitations associated with currently available cancer therapeutics.

Forward-looking statements are not guarantees of future performance and involve risks and uncertainties. Actual events or results may differ materially from those discussed in the forward-looking statements as a result of various factors including, but not limited to, the uncertainties inherent in the preclinical and clinical development process; whether Molecular Templates' cash resources will be sufficient to fund its continuing operations for the periods and/or trials anticipated; the ability of Molecular Templates' to protect its intellectual property rights; risks from global pandemics including COVID-19; and legislative, regulatory, political and economic developments, as well as those risks identified under the heading "Risk Factors" in Molecular Templates' filings with the SEC. There can be no assurance that any of Molecular Templates' drug or biologic candidates will be successfully developed, manufactured or commercialized, that final results of clinical trials will be supportive of regulatory approvals required to market products, or that any of the forward-looking information provided herein will be proven accurate. Any forward-looking statements contained in this press release speak only as of the date hereof, and Molecular Templates specifically disclaims any obligation to update any forward-looking statement, whether because of new information, future events or otherwise.

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