November 30, 2021

Molecular Templates Provides Corporate Update and Outlines 2022 Milestones

Unique PD-L1-mediated immune changes and early signs of anti-tumor activity with MT-6402

Continued dose-finding with MT-5111 and MT-0169

Pipeline advancing with IND planned for CTLA-4 program in 2H22

MTEM to Present at Evercore ISI 4th Annual HealthCONx on December 2nd, 2021

AUSTIN, Texas, Nov. 30, 2021 (GLOBE NEWSWIRE) -- Molecular Templates, Inc.(Nasdaq: MTEM, “Molecular Templates,” or “MTEM” or “the Company”), a clinical-stage biopharmaceutical company focused on the discovery and development of proprietary targeted biologic therapeutics, engineered toxin bodies (ETBs), provided a corporate update and outlined expected 2022 milestones.

“2021 was a year of growth for MTEM as we advanced our multiple pipeline programs,” said Eric Poma, Ph.D., Chief Executive and Chief Scientific Officer of Molecular Templates. “As we end the year and move into 2022, we look forward to generating further clinical data that builds on the unique biology we are seeing from three ongoing studies with MT-6402, MT-5111, and MT-0169. We expect to file an IND in 2H22 for our CTLA-4 program and will continue to advance our earlier stage pipeline with ETBs in preclinical development targeting TIGIT, TROP-2, and SLAMF7.”

2021 Accomplishments, Status Updates, and Expected 2022 Milestones

MT-6402 (PD-L1 ETB with Antigen Seeding)

MT-6402 is the first of the Company’s 3rd-generation ETBs to enter the clinic. It targets PD-L1 and incorporates the Company’s antigen seeding technology. MT-6402 was designed to directly destroy PD-L1+ tumor cells and alter the immunosuppressive tumor microenvironment through direct cell-kill of PD-L1+ immune cells. In addition, antigen seeding allows MT-6402 to induce the presentation of an MHC class I CMV antigen on tumor cells for pre-existing CD8 T-cell recognition and destruction in HLA-A2+ CMV+ patients. A Phase I study in relapsed/refractory patients with PD-L1-expressing tumors and/or immune cells in the tumor microenvironment was initiated in 2H21 at a starting dose of 16 mcg/kg. Highlights from the on-going Phase I study include:

- 4 patients have been treated (2 NSCLC, 1 melanoma, 1 ovarian) with no dose limiting toxicities (DLTs) to date
    - 1 patient with stable disease (SD) at 5+ months with reduction in non-measurable bone metastasis

    - 3 patients with progressive disease
- Target-mediated, HLA type-independent pharmacodynamic effects after MT-6402 treatment observed in majority of patients including peripheral CD14+ monocyte depletion
    - One patient had monocyte depletion of >95% that was achieved in cycle 2 and is maintained and on-going at 5+ months of treatment, demonstrating potential for sustained effect with repeat dosing
    - One patient had monocyte depletion of 90% that was achieved in cycle 2 and sustained through two cycles of therapy before the patient discontinued the study for disease progression at the end of cycle 2
    - One patient had monocyte depletion of ~21% but discontinued at the end of cycle 1 for disease progression
    - One patient had no evidence of monocyte depletion but discontinued after 10 days on therapy for disease progression and did not complete cycle 1
    - Similar depletion was not observed in non-PD-L1-expressing cells (i.e., NK cells, B-cells, etc) nor was monocyte depletion noted in patients treated with other ETBs (MT-3724, MT-0169, or MT-5111)
- Significant increases in key cytokines including IL- 2 and activated CD8+ T-cell markers including CD69 noted in patients
- Comparable immune subset and/or cytokine changes not seen with approved PD-L1 agents
- One HLA-A2 CMV+ patient (i.e., antigen-seeding eligible patient) has been treated to date
    - Patient is a NSCLC chemotherapy-ineligible patient whose disease had progressed following treatment with a combination of checkpoint inhibitors (ipilimumab and nivolumab); patient has non-measurable bone disease
    - On-going monocyte depletion of >95% observed at 5+ months of dosing
    - Initial increase of ~ 50% in CMV antigen-specific T-cells after dosing with MT-6402 with subsequent near-complete extravasation of CMV antigen-specific T-cells from the periphery despite a general increase in total peripheral CD8+ effector T-cells (effect not seen in non-HLA-A2 CMV-negative patients)
    - Multiple sites of bone disease had resolved on bone scan with only one remaining site which showed decreased uptake
- Dose escalation continues as planned
- In November, MT-6402 was granted Fast Track Designation for the treatment of patients with advanced NSCLC expressing PD-L1

“We are excited to see pharmacodynamic effects with MT-6402 this early in dose escalation in the Phase I study. No approved checkpoint agent has shown an ability to alter immune subset composition or induce cytokine changes in a PD-L1-targeted fashion,” said Roger Waltzman, MD, Chief Medical Officer of Molecular Templates. “We believe that the actual clearance of PD-L1+ immune cells and not merely the steric inhibition of PD-L1 on immune cells may work to more potently alleviate tumor-mediated immunosuppression by removing immunosuppressive myeloid cells acting as a barrier to immunotherapy. Additionally, we are seeing early evidence supporting our unique antigen seeding approach to alter tumor immunophenotype. We are excited to see this unique biology potentially driving patient benefit and believe these data support both monotherapy treatment in relapsed/refractory patients as well as future combination studies in earlier lines of therapy with PD-1 antibodies or other therapies.”

MT-5111 (HER2 ETB)

MT-5111 is the Company's 2nd-generation ETB targeting HER2. It is designed to avoid competition with and to overcome the primary mechanisms of tumor resistance to current therapies that target HER2. MT-5111 destroys HER2-positive tumor cells through a novel mechanism of action (enzymatic ribosomal destruction), targeting HER2 via a distinct epitope from trastuzumab and pertuzumab, and improving tumor penetration with a smaller size compared to HER2 antibodies (55 kDa vs 146 kDa). Dose escalation is on-going in the Phase I study with dose levels now at drug concentrations that are predicted to be active in metastatic breast cancer. Dose escalation will continue in solid tumor HER2-positive patients, and an expansion cohort in patients with metastatic breast cancer was initiated in 4Q21. Highlights from the on-going Phase I include:

- 27 patients have been treated to date with MT-5111 across 7 dose escalation cohorts ranging from 0.5 mcg/kg to 10 mcg/kg without any DLT's
- MT-5111 has been well-tolerated with no significant immuno- or cardiotoxicity observed
- The expansion cohort for patients with metastatic breast cancer is open for enrollment
    - Dosing in the cohort is at 10 mcg/kg with the potential for dose-escalation
    - Dose levels of 10 mcg/kg or higher are expected to be required to achieve drug concentration levels that could drive efficacy in breast cancer

"We believe we are now at dose levels in the Phase I study that should be in the therapeutic range for MT-5111, and, with the opening of the breast cancer cohort, we are assessing the activity in the patient population we believe is most likely to respond," said Dr. Roger Waltzman. "We believe the tolerability to date supports further dose escalation."

MT-0169

MT-0169 is the Company's 2nd-generation ETB targeting the CD38 receptor, found on the surface of multiple myeloma and non-Hodgkin lymphoma (NHL) cells. MT-0169 was designed to destroy CD38+ tumor cells through induced internalization of CD38 and cell destruction through a novel mechanism of action (enzymatic ribosomal destruction). MT-0169 is the most potent ETB developed to date and the study initiated with the highest starting dose for any ETB. Relevant pharmacodynamic data from patients treated in the first dose cohort show NK cell depletion consistent with maximal levels achieved with CD38 antibody therapy. MTEM assumed full rights to MT-0169 in August 2021 and is opening new sites for the Phase I study. As part of a protocol amendment, CD38+ NHL patients will be dosed in addition to myeloma patients. Highlights from the on-going phase I include:

- 5 multiple myeloma patients have been treated to date
- No serious adverse events (SAEs) have been observed. Two cardiac adverse events were observed that meet criteria for DLT. Both evaluations were triggered by asymptomatic elevations in high-sensitivity troponin values. As previously disclosed, the first DLT was an asymptomatic, rapidly reversible episode of myocarditis that did not require treatment. The second DLT occurred recently and is an asymptomatic, nonischemic cardiomyopathy. We believe both DLTs may be due to activity against low CD38-expressing cells in the cardiac endothelium. We have not seen evidence of any clinically relevant cardiac adverse event such as myocarditis or cardiomyopathy in any

other ETB program (MT-3724, MT-5111, MT-6402) at any dose.
- Clearance of CD38+ NK cells noted in all patients with maximal levels of depletion occurring within 24 hours and consistent with maximal depletion seen with CD38 antibodies
    - Rapidity and depth of CD38+ NK cell-kill is substantially higher in humans than what was seen in non-human primate studies
- One patient has shown symptomatic benefit with a reduction in myeloma-induced bone pain
- A revised protocol will be submitted to explore dose reduction with MT-0169 to reduce the risk of toxicity caused by the destruction of low CD38-expressing cells and enable patients to continue MT-0169 therapy for a duration that may drive tumor benefit

“MT-0169 has shown potent and rapid pharmacodynamic activity against CD38+ NK cells with early signs of clinical benefit,” said Dr. Roger Waltzman. “The pharmacodynamic activity of NK cell-kill at 50 mcg/kg exceeded what was expected based on the non-human primate data and is consistent with maximal achievable levels. In general, we have observed that MT-3724, MT-6402, and MT-0169 have all shown substantially more pharmacodynamic activity in patients compared to what was seen in NHPs at equivalent or higher doses. We will be exploring lower doses in the proposed revised protocol and expect to report additional data in 2022.”

Preclinical Pipeline

MTEM continues to advance its pipeline with its CTLA-4 and TIGIT ETBs representing novel approaches to key immune-oncology targets and its TROP2 and SLAMF7 ETBs applying unique biology to validated targets. MTEM also continues to expand the capabilities of the ETB technology.

- IND filing of CTLA-4 program expected in 2H22
- Lead selection for TIGIT, TROP-2 with antigen seeding, and SLAMF-7 is ongoing
- Additional target selection and scaffold improvements expected in 2022

“We continue to move forward with programs against new targets using the unique biology of ETBs, and we continue to advance the biology of the ETB scaffold,” continued Dr. Poma. “We believe MT-6402 and our CTLA-4 and TIGIT programs represent a new way of altering the immune environment in patients with cancer through targeting and destroying myeloid-derived suppressor cells and regulatory T cells (Tregs). Additionally, we believe that new mechanisms of action against validated targets like TROP-2 and SLAMF-7 are needed in these diseases with high unmet medical need.”

Key Milestones for 2022

“We believe that 2022 will be another exciting year for the Company with potentially transformational data across our three ongoing clinical programs, an IND filing expected for our CTLA-4 ETB and continued preclinical development,” concluded Dr. Poma. “We have substantial cash reserves into 4Q23 to drive development of a broad range of compounds at MTEM.”

- Continued data read-outs on all three clinical programs
- IND filing for ETB targeting CTLA-4

- Advancement of ETBs targeting TROP2, TIGIT, SLAMF-7
- The Company has cash runway into 4Q23

Participation in Evercore ISI 4th Annual HealthCONx

The Company will participate in a fireside chat and hold 1-on-1 investor meetings at the Evercore ISI 4th Annual HealthCONx, to take place November 30 – December 2, 2021.

Presentation details can be found below:

Presenter:	Dr. Eric Poma, Chief Executive Officer and Chief Scientific Officer
Date:	Thursday, December 2, 2021
Time:	3:30-3:50 PM Eastern Time in Track 3
Webcast:	https://wsw.com/webcast/evercore21/mtem/2366778

The webcast will be archived on the "News & Media" page of MTEM's corporate website under Events.

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, including the anticipated benefits of Molecular Templates' next-generation ETBs; statements relating to the development and evaluation of MT-5111, MT-0169, and MT-6402; the expected timing of submitting various IND applications and conducting studies and generating data; Molecular Templates' receipt of future development, regulatory and sales milestones and royalty payments; the expected participation and presentation at upcoming conferences; the length of time for which Molecular Templates' cash resources are expected to be sufficient; 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; Molecular Templates' ability to timely enroll patients in its clinical trials; 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.

Contacts:
Sean McLennan
Interim Chief Financial Officer
sean.mclennan@mtem.com
512-334-6664

Joyce Allaire
LifeSci Advisors, LLC
jallaire@lifesciadvisors.com

Source: Molecular Templates, Inc.