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Molecular Templates, Inc. Provides Update on MT-5111 Phase 1 Study

Phase 1 Study Dose Escalation Ongoing in All HER2 Positive Tumor Types
HER2 Positive Breast Cancer Expansion Cohort Planned to be Initiated in 1H21
Expansion Cohorts in Additional Tumors Types to Begin When MTD or Recommended Phase 2 Dose is Reached

AUSTIN, Texas, Dec. 21, 2020 (GLOBE NEWSWIRE) -- Molecular Templates, Inc. (Nasdaq: MTEM, "Molecular Templates," "MTEM" or "the Company"), a clinical-stage biopharmaceutical company focused on the discovery and development of proprietary targeted biologic therapeutics, engineered toxin bodies (ETBs), today provided an update on the Phase 1 study for MT5111, MTEM's HER2 targeted ETB.

To date, 16 study subjects have been treated in the dose escalation portion of this study. Five cohorts (0.5, 1.0, 2.0, 3.0, and 4.5 µg/kg/week) have been successfully completed and the sixth cohort (6.75 µg/kg) has been initiated. Pharmacokinetic (PK) data confirm the predicted human PK based on non-human primate studies. PK modeling has suggested that doses equal to or greater than 5.0 µg/kg are likely needed for efficacy.

Study subjects dosed to date had tumor types including metastatic breast cancer (n=6; two at 0.5 µg/kg, one at 1 µg/kg, one at 2 µg/kg, and two at 3 µg/kg), metastatic biliary tract carcinoma (n=6; two at 0.5 µg/kg, one at 1 µg/kg, two at 2 µg/kg, and one at 4.5 µg/kg), metastatic pancreatic cancer (n=2, both at 4.5 µg/kg), and one each of metastatic colon adenocarcinoma (3 µg/kg) and metastatic gastroesophageal junction adenocarcinoma (1 µg/kg). These study subjects had a median of four prior lines of therapy and a median of two prior HER2-targeting regimens; subjects with breast cancer received a median of six prior lines of therapy, four of which contained HER2-targeting agents.

MT5111 appears to be well tolerated with no dose limiting toxicities (DLTs) observed in any cohort. In particular, no signs of cardiotoxicity have been observed to date, while monitoring the subjects' EKGs, troponin values and pro-BNP with each treatment, and serial echocardiograms with every other cycle. The most commonly reported adverse events (AEs) that may be causally related among the four dosing cohorts and for which source-verified data were available were: fatigue (n=3), AST increased (n=2) at 0.5 µg/kg and 1 µg/kg, and chills (n=2). These most commonly reported AEs were all of grade 1 or 2 severity. No cases of capillary leak syndrome (any grade) were observed.

Fifteen of the 16 subjects have discontinued for disease progression. One study 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 disease progression (new breast lesion) at cycle 10. This subject had

received three prior HER-2 targeting regimens which initially included pertuzumab plus trastuzumab followed by trastuzumab and T-DM1 as monotherapies. One subject with metastatic pancreatic cancer in cohort 5 (4.5 µg/kg/dose) remains on study in cycle 2.

Cohort 6 (6.75 µg/kg) is now open for enrollment with cohort 7 (10 µg/kg) expected to open in 1Q21. The HER2positive breast cancer expansion cohort is planned to be initiated in 1H21 at a dose of 10 µg/kg (anticipated to be a therapeutic dose level), pending adequate safety. Dose escalation will continue to determine the Recommended Phase 2 Dose while the breast cancer expansion cohort collects efficacy and safety data.

“We are encouraged by the safety profile of MT-5111 to date in these heavily pretreated study subjects. Based on preclinical data, we believe that the study has reached clinically active dose levels, said Eric Poma, Ph.D., Molecular Templates’ Chief Executive and Chief Scientific Officer. “Given that HER2 positive breast cancer patients have generally had the highest response rates to other HER2-targeted therapies, we look forward to generating data from both the HER2-positive breast cancer cohort as well as the broader HER2-positive cohort enrolling all tumor types. We expect to provide an update on results from the subject currently on treatment as well as higher dose cohorts from the dose escalation portion of the Phase 1 study in 1H21.”

About MT-5111

MT5111 is an ETB consisting of a single chain variable fragment (scFv) with affinity for HER2, fused to the enzymatically active de-immunized Shiga-like toxin-A subunit (SLTA). In preclinical studies MT5111 specifically binds and kills HER2 expressing cells in a manner consistent with SLTA mediated cellular cytotoxicity. MT5111 has been specifically designed to avoid competition with and to overcome the primary mechanisms of tumor resistance to current HER2 targeted therapies. To accomplish this, first, MT5111 binds a HER2 domain that is distinct from the trastuzumab and pertuzumab binding sites, which results in MT5111 HER2-mediated binding and cell kill even in the presence of these monoclonal antibodies. As such, MT5111 may have the potential to be combined with other HER2 targeted therapies. Second, SLTA is a large molecule protein and is not a substrate of drug efflux transporters such as MDR1 which has been demonstrated to be one of the primary mechanisms of resistance to the antibody drug conjugate, TDM1. Third, MT5111 mediated ribosomal inhibition and cell death take place intracellularly so changes in the tumor microenvironment that inhibit immune-mediated mechanisms such as antibody-dependent cell-mediated cytotoxicity (ADCC) are not expected to inhibit MT5111 activity. Finally, mutations to the HER2 kinase domain that can induce constitutive downstream signaling to drive tumor proliferation are not expected to interfere with MT5111 activity, given that its mechanism of action is not dependent upon kinase domain binding and MT5111 works directly on ribosomes to mediate ribosomal inhibition and cell death. Based on these mechanisms of action, MT5111 represents a novel HER2 targeted therapy which could provide benefit in patients with HER2-positive cancers and potentially overcome mechanisms of tumor resistance to existing HER2-targeted therapies.

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 the Company's drug or biologic candidates, statements relating to the development of MT5111; our utilization of a next-generation ETB scaffold that has been designed to reduce or eliminate the propensity for innate immunity, including CLS; the expected timing of submitting various IND applications, initiating and completing enrollment of cohorts and conducting studies; and the Company's 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 risks associated with the uncertainties inherent in the preclinical and clinical development process; whether the Company's cash resources will be sufficient to fund its continuing operations for the periods and/or trials anticipated; the ability of the Company to protect its intellectual property rights; risks from global pandemics including COVID19; and legislative, regulatory, political and economic developments, as well as those risks identified under the heading "Risk Factors" in the Company's filings with the SEC. Any forward-looking statements contained in this press release speak only as of the date hereof, and the Company specifically disclaims any obligation to update any forward-looking statement, whether because of new information, future events or otherwise.

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