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Molecular Templates to Prioritize Next-Generation ETB Candidates

Molecular Templates to Assume Full Rights to TAK-169, Second Generation ETB Targeting CD38 for the Treatment of Multiple Myeloma

Development of First-Generation ETB MT-3724 Has Been Discontinued, Company to Focus on Development of Next-Generation ETB Product Candidates Including Clinical Stage MT-5111, TAK-169 and MT-6402

AUSTIN, Texas, April 05, 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 announced that, following discussion with its co-development partner Takeda, MTEM will assume full rights to TAK-169 including taking control of clinical development from Takeda. In addition, MTEM announced the decision to discontinue development of MT-3724, MTEM's only first-generation ETB. MTEM will focus on the clinical development of next-generation ETBs MT-5111, TAK-169, and MT-6402, as well as advancing next-generation preclinical ETB candidates against targets including CTLA-4, CD20, SLAMF-7 and CD45.

Takeda has communicated that its decision to turn over full rights of TAK-169, a second-generation ETB targeting CD38, was the result of Takeda's ongoing portfolio prioritization. MTEM believes that TAK-169 is a potent molecule with a novel mechanism of action in multiple myeloma. It has demonstrated a favorable safety and efficacy profile in in vivo models and potency against daratumumab refractory patient samples. TAK-169 is in an ongoing Phase 1 study with dose escalation planned through six dose cohorts, in which the first patient was dosed in February 2020. To date, Takeda has enrolled and treated four subjects in the Phase 1 study. There have been no life-threatening toxicities, and no signs of capillary leak syndrome (CLS). The maximum tolerated dose (MTD) has not been reached, patient screening continues, and dose escalation is ongoing. One dose limiting toxicity (grade 2 myocarditis) was assessed in one subject. A mild elevation in Troponin I was noted in this subject after the third dose of TAK-169. No EKG or echocardiographic abnormalities and no clinical symptoms were noted. A stable elevation in high-sensitivity troponin was seen although no comparison to baseline was available as baseline levels were not required per protocol at the time. An independent radiologist and cardiologist reviewed the imaging in the case and concluded that there was weak to intermediate evidence of myocarditis. The subject had multiple pre-existing cardiac risk factors. No other cardiac adverse events were observed in any other subject. Pharmacokinetic and pharmacodynamic data of this first cohort have been in-line with predicted outcomes. MTEM looks forward to accelerating the full enrollment and completion of this safety and dose-finding study. MTEM's manufacturing of TAK-169 has been qualified by Takeda and MTEM has sufficient TAK-169 drug supply to continue the Phase 1 study as planned. MTEM's assumption of the full rights to TAK-169 is

expected to result in cost savings in 2021 and MTEM's guidance of cash runway into 2H23 is unchanged. Upon transfer of the full TAK-169 rights to MTEM, per the terms of the collaboration agreement, MTEM will owe Takeda low-single digit royalties on future net sales of TAK-169. MTEM anticipates that the transition of TAK-169 development from Takeda to MTEM will be conducted over the next 90 days.

In conjunction with taking on full development of TAK-169, MTEM has decided to discontinue development of MT-3724 to focus its resources on the development of next-generation ETBs. As previously disclosed, MT-3724 was placed on partial clinical hold by the U.S. Food and Drug Administration (FDA) following a treatment-related fatality in one subject who experienced Grade 5 CLS in the Phase 2 MT-3724 monotherapy study. Markedly high pharmacokinetic assay readings were observed in this and other subjects treated with a specific lot of MT-3724 material. Apart from this one subject, no life-threatening CLS events have been observed in any subject treated with MT-3724 at any dose tested and no instances of CLS of Grade 2 or higher have been observed with monotherapy treatment at doses of 50 mcg/kg or lower from any other lot of MT-3724 material. The FDA placed MT-3724 on a full clinical hold in late March and requested additional information and the development of a new quantitative assay specific to MT-3724, which would take significant time and investment away from MTEM's priorities. At such time, MTEM had already discontinued dosing in all MT-3724 studies, as previously disclosed. Based on the foregoing, MTEM has now decided to discontinue development of MT-3724 to focus its resources on the development of next-generation ETBs.

There are no changes to the trials or plans for any other ETB product candidates, including MT-5111, TAK-169, and MT-6402, all of which utilize a next-generation ETB scaffold that has been designed to reduce or eliminate the propensity for innate immunity, including CLS. Furthermore, all MTEM ETBs other than MT-3724 are designed and manufactured to create a more homogeneous product that avoids the production of multiple species including protein aggregate species.

"We thank Takeda for co-discovering TAK-169 and all their efforts on developing the molecule. Takeda's decision to reprioritize its pipeline allows MTEM to assume full rights to this promising program and we plan to take immediate steps to accelerate new site activation and patient enrollment in the TAK-169 study to generate data this year. While we are disappointed to discontinue development of MT-3724 after demonstrating forced internalization and having seen promising single agent responses in heavily pretreated DLBCL patients, the program provided important clinical proof of concept for our ETB platform and sets the stage for success with our next-generation ETBs," said Eric Poma, Ph.D., Molecular Templates' Chief Executive and Scientific Officer. "Our next-generation ETBs including MT-5111, TAK-169, and MT-6402, all benefit from improvements over the first-generation ETB technology, including increased potency, a de-immunized Shiga-like Toxin A (SLT-A) scaffold, and simpler design and manufacturing resulting in a more homogeneous drug product. We look forward to making continued progress in 2021 with the Phase 1 studies of MT-5111, TAK-169, and MT-6402 and to advancing our earlier stage pipeline of next-generation ETBs against a variety of other targets."

About TAK-169

TAK-169 is an ETB consisting of a single chain variable fragment (scFv) with affinity for CD38, fused to the enzymatically active de-immunized SLT-A. TAK-169 is designed to bind

and kill CD38 expressing cells in a manner consistent with SLT-A mediated cellular cytotoxicity. TAK-169 has been specifically designed to avoid competition with and to overcome the primary mechanisms of tumor resistance to daratumumab, the first approved monoclonal antibody targeting CD38. In preclinical investigation TAK-169 has been shown to be active in the presence of daratumumab. As such, TAK-169 may have the potential to be combined with approved CD38 targeted therapies. TAK-169 mediated ribosomal inhibition and cell death take place intracellularly so changes in the tumor microenvironment, such as CD55/59 upregulation, which inhibit immune-mediated mechanisms such as antibody-dependent cell-mediated cytotoxicity (ADCC) or complement dependent cytotoxicity (CDC) are not expected to inhibit TAK-169 activity.

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 SLT-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, including the anticipated benefits of Molecular Templates' next-generation ETBs compared to its first-generation ETBs, such as MT-3724; statements relating to the development of MT-5111, TAK-169, and MT-6402; the expected budgetary impact of Molecular Templates' assumption of the full rights to TAK-169; the expected timing of submitting various IND applications 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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