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Molecular Templates' Presentations at the American Association of Cancer Research (AACR) Annual Meeting 2022 Highlight Potential of ETB Approach

Presentations from multiple pipeline programs feature clinical and preclinical data demonstrating the unique biology of Molecular Templates' technology

AUSTIN, Texas, April 12, 2022 (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), reviews highlights from the six poster presentations on its pipeline programs that were presented at the American Association of Cancer Research (AACR) Annual Meeting 2022, taking place April 8 - April 13, 2022 at the Ernest N. Morial Convention Center in New Orleans, LA. Copies of the posters presented at AACR can be found in the Investors section of Molecular Templates' website under Presentations.

"We believe that ETBs offer novel biology that have the potential to translate into unique clinical outcomes, even against well-explored targets," said Eric Poma, Ph.D., CEO and CSO of Molecular Templates. "We are seeing differentiated pharmacodynamic effects in patients in our Phase I study with MT-6402, our PD-L1 targeting agent, from both that agent's direct cell-kill effects and its antigen seeding ability. We believe we can leverage this unique biology across other targets such as CTLA-4, TROP-2, and TIGIT."

Poster Title: A Phase 1 Study of MT-6402, a novel Engineered Toxin Body (ETB) targeting PD-L1, in patients with PD-L1 expressing advanced solid tumors

Authors: David R. Spigel, MD; Eugene Ahn, MD, PhD; John D. Powderly, Herbert L. Duvivier, JD, MD; Drew Rasco, MD; Agnes Rethy, MD; Chris Moore, PhD; Amy Yuet, PhD; Angela Georgy, PharmD; Sandra R. Hankins; Swati Khanna, PhD; Joseph D. Dekker, MD; Brian A. Van Tine, MD
Abstract #: 7936

Poster highlights:

- Twelve patients with PD-L1+ relapsed/refractory disease have been treated to date across two dose cohorts: 16 mcg/kg (n=6) and 24 mcg/kg (n=6).
- Pharmacodynamic (PD) effects including monocyte and myeloid-derived suppressor

cell depletion and T cell activation have been observed in the majority of patients. The extent and timing of these PD effects appear dose-related with patients in the 24 mcg/kg cohort generally showing a more rapid and profound PD effect.

- One patient in the first cohort with non-small cell lung cancer (NSCLC) (osseous non-measurable disease only) that had progressed after prior checkpoint therapy (PD-1 and CTLA-4) showed qualitative reduction in tumor burden.

- One dose-limiting toxicity (DLT) was observed in a single patient (24 mcg/kg). The patient experienced dermatitis that resolved rapidly with systemic steroids. The patient was rechallenged without incident at 24 mcg/kg. No other DLTs have been reported.

Poster Title: Altering tumor immunophenotypes with PD-L1 engineered toxin bodies

Authors: Swati Khanna, Elizabeth M. Kapeel, Lauren R. Byrne, Elizabeth Saputra, Steven Rivera, Lindsey Aschenbach, Lilia A. Rabia, Garrett L. Cornelison, Rachael M. Orlandella, Brigitte Brieschke, Michaela Sousares, Jay Zhao, Garrett L. Robinson, Chris B. Moore, Joseph D. Dekker
Abstract #: 3543

Poster highlights

- Molecular Templates' Antigen Seeding Technology (AST) is a unique approach that allows for specific alteration of tumor immunophenotype to match pre-existing CD8+ T-cells in a patient. This approach is currently being tested clinically with MT-6402, a PD-L1 targeted ETB that delivers an HLA-A2 antigen derived from cytomegalovirus (CMV).

- Data are presented here demonstrating that MT-6402 can be altered to present antigens derived from CMV corresponding to other HLA genotypes, thereby broadening the potential patient population that could benefit from this approach.

Poster Title: A CTLA-4-targeted ETB for Treg depletion shows favorable preclinical efficacy and safety

Authors: Asis Sarkar, Rebecca Martin, Lauren R. Byrne, Kiheon Baek, James Pazar, Caleigh Howard, Swati Khanna, Lilia A. Rabia, Diana Adhikari, Michaela M. Sousares, Alvaro Aldana, Abdul G. Khan, Garrett L. Robinson, Jay Zhao, Chris B. Moore, Aimee Iberg
Abstract #: 3538

Poster highlights:

- CTLA-4-targeted ETBs are designed to preferentially deplete regulatory T cells (Tregs), via a direct cell kill mechanism of action that is independent of effector cells, in the tumor microenvironment (TME) to improve efficacy and reduce the toxicity associated with CTLA-4 targeted antibodies.

- In a transgenic mouse model expressing human CTLA-4 and bearing syngeneic subcutaneous tumors, CTLA-4 ETB treatment depleted Tregs in the TME.

- CTLA-4 ETB candidate was well tolerated in a non-human primate toxicology study.

- Overall, these preclinical data support the use of ETB technology to deplete immune suppressive regulatory T cells in the TME to allow immune reactivation to tumor.

Poster Title: Engineered Toxin Bodies (ETBs) targeting Trop2

Authors: Garrett L. Cornelison, Adam Bartos, Brigitte Brieschke, Jessica Momb, Ileana Pedraza, Elizabeth M. Kapeel, Rebecca Martin, Channing Pletka, Adrian Gonzalez, Joseph D. Dekker, Jay Zhao, John Majercak, Garrett L. Robinson.
Abstract: #326

Poster highlights:

- Trop2 targeted ETBs show in vitro target specific picomolar potency on Trop2 positive tumor cell lines.

- AST enabled Trop2 targeted ETBs to retain direct cell kill potency and alter the tumor immunophenotype to allow for antigen specific T-cell recognition.

- Final lead selection based on evaluation of additional targeting domains and AST antigens is underway.

Poster Title: Improving immunotoxin-based therapeutics for cancer with de-immunized Engineered Toxin Bodies

Authors: Rachael M. Orlandella, Elizabeth M. Kapeel, Swati Khanna, Brigitte Brieschke, Garrett L. Robinson, Joseph D. Dekker, and Chris B. Moore
Abstract #: 2579

Poster highlights:

- Molecular Templates has developed a de-immunized form of Shiga-like Toxin A (SLTA), incorporated into next-generation ETBs currently in clinical trials, that has demonstrated a lack of innate immune activation and capillary leak syndrome (CLS) in animal models and patients.

- Ex vivo assays using peripheral blood mononuclear cells (PBMCs) demonstrate that unmodified SLTA displays upregulation of CCL3, CCL4, TNFα and IL-6, indicating a similar, but not identical, pattern of cytokine release relative to the positive control, lipopolysaccharide (LPS), while the de-immunized SLTA did not activate cytokine or chemokine release.

- These data help confirm the observations in animal models and patients that indicate the de-immunized SLTA scaffold lacks the ability to trigger innate immunity seen with unmodified SLTA used in first generation ETBs.

Poster Title: C-KIT/CD117 targeted ETBs for cancer therapy and HSC transplant conditioning

Authors: Caleigh Howard, Shu Wiley, Wenzhao Dong, Andrea Mendiola, Veronica Partridge, Antonio Luz, Sara LeMar, Paul Amador, Amit Kumar Chaudhary, Joseph D. Dekker, Jay

Zhao, Ross Durland, Aimee Iberg
Abstract #: 335

Poster highlights:

- Molecular Templates has developed CD117 targeting ETBs that may have potential uses in myeloablation or in oncology.

- CD117 ETB drug conjugates with MMAF demonstrated increased cytotoxicity compared to stand-alone ETBs or inactive ETB drug conjugate controls and also highlighted the internalization augmenting capabilities of ETBs.

About Molecular Templates

Molecular Templates is a clinical-stage biopharmaceutical 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 "potential," "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 and ETB platform; 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; the expected participation and presentation at upcoming conferences; the expected timing for providing updates on MT-6402, MT-5111, and MT-0169, including any pre-clinical data; 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.

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