UNITED STATES
SECURITIES AND EXCHANGE COMMISSION
Washington, D.C. 20549

FORM 8-K

CURRENT REPORT
Pursuant to Section 13 or 15(d)
of the Securities Exchange Act of 1934

Date of Report (Date of earliest event reported): March 8, 2022

Molecular Templates, Inc.
(Exact name of registrant as specified in its charter)

Delaware	**001-32979**	**94-3409596**
(State or other jurisdiction of incorporation)	**(Commission File Number)**	**(IRS Employer Identification No.)**

9301 Amberglen Blvd, Suite 100
Austin, TX 78729
(Address of principal executive offices and zip code)

Registrant's telephone number, including area code: (512) 869-1555

(Former name or former address, if changed since last report)

Check the appropriate box below if the Form 8-K filing is intended to simultaneously satisfy the filing obligations of the registrant under any of the following provisions:

☐ Written communications pursuant to Rule 425 under the Securities Act (17 CFR 230.425)

☐ Soliciting material pursuant to Rule 14a-12 under the Exchange Act (17 CFR 240.14a-12)

☐ Pre-commencement communications pursuant to Rule 14d-2(b) under the Exchange Act (17 CFR 240.14d-2(b))

☐ Pre-commencement communications pursuant to Rule 13e-4(c) under the Exchange Act (17 CFR 240.13e-4(c))

Securities registered pursuant to Section 12(b) of the Act:

Title of each class	Trading Symbol(s)	Name of each exchange on which registered
Common Stock, $0.001 par value	**MTEM**	**The Nasdaq Global Select Market**

Indicate by check mark whether the registrant is an emerging growth company as defined in Rule 405 of the Securities Act of 1933 (§230.405 of this chapter) or Rule 12b-2 of the Securities Exchange Act of 1934 (§240.12b-2 of this chapter).

Emerging growth company ☐

If an emerging growth company, indicate by check mark if the registrant has elected not to use the extended transition period for complying with any new or revised financial accounting standards provided pursuant to Section 13(a) of the Exchange Act. ☐

Item 7.01 Regulation FD Disclosure.

Attached hereto as Exhibit 99.1 and incorporated by reference herein is the March 8, 2022 Cowen Health Care Conference presentation of Molecular Templates, Inc.

The information set forth under this "Item 7.01. Regulation FD Disclosure," including Exhibit 99.1 attached hereto, shall not be deemed "filed" for any purpose, and shall not be deemed incorporated by reference into any filing under the Securities Act of 1933, as amended, or the Securities Exchange Act of 1934, as amended, regardless of any general incorporation language in any such filing, except as shall be expressly set forth by specific reference in such filing.

Item 9.01 Financial Statements and Exhibits.

(d) Exhibits

Exhibit 99.1	Cowen Health Care Conference Presentation, dated March 8, 2022.
Exhibit 104	Cover Page Interactive Data File (embedded within the Inline XBRL document)

SIGNATURES

Pursuant to the requirements of the Securities Exchange Act of 1934, the registrant has duly caused this report to be signed on its behalf by the undersigned hereunto duly authorized.

Molecular Templates, Inc.

Date: March 8, 2022

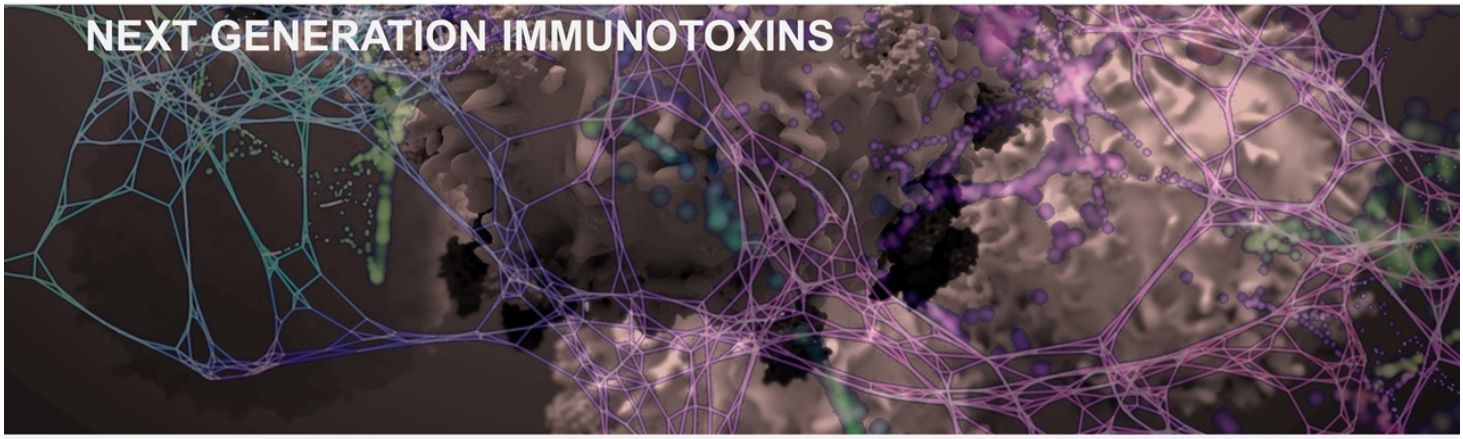
By: /s/ Eric E. Poma, Ph.D.
Name: Eric E. Poma, Ph.D.
Title: Chief Executive Officer

Exhibit 99.1

MOLECULAR TEMPLATES

MOLECULAR TEMPLATES

NEXT GENERATION IMMUNOTOXINS



Cowen Presentation

Forward-Looking Statements

Except for statements of historical fact, the statements in this presentation are forward-looking statements, including, but not limited to, statements regarding the future development of our proprietary Engineered Toxin Body (ETB) technology; statements relating to the development of MT-5111, MT-0169, and MT-6402, and our preclinical pipeline; statements regarding the safety or potential efficacy of our drug or biologic candidates, including the anticipated benefits of our next-generation ETBs; our belief that our proprietary ETB technology provides for a differentiated mechanism of action that may address some of the limitations associated with currently available cancer therapeutics; statements regarding expected demand and opportunities for certain targets; expected program milestones; the timing, progress and results of pre-clinical studies and clinical trials for our drug or biologic candidates or any future candidates; the timing or likelihood of regulatory filings, including expected timing for submission and approval of various IND applications; the expected participated and presentation at upcoming conferences; our expected receipt of clinical data; the expected timing for data updates on our pipeline; our future cash needs; the length of time for which our cash resources are expected to be sufficient; and statements relating to the outcome of our collaborations as they relate to our ETB platform. These statements constitute "forward-looking statements" within the meaning of Section 27A of the Securities Act and Section 21E of the Securities Exchange Act and are usually identified by the use of words such as "anticipates," "believes," "estimates," "expects," "intends," "may," "plans," "projects," "seeks," "should," "will," and variations of such words or similar expressions. These forward-looking statements reflect our current views about our plans, intentions, expectations, strategies and prospects, which are based on the information currently available to us and on assumptions we have made. Although we believe that our plans, intentions, expectations, strategies and prospects as reflected in or suggested by those forward-looking statements are reasonable, we can give no assurance that the plans, intentions, expectations or strategies will be attained or achieved. Furthermore, actual results may differ materially from those described in the forward-looking statements and will be affected by a variety of risks and factors that are beyond our control. These statements involve risks and uncertainties that can cause actual results to differ materially from those in such forward-looking statements. Important factors that may cause actual results to differ materially from the results discussed in the forward-looking statements include risks and uncertainties, including (1) our failure to secure and maintain relationships with collaborators; (2) risks relating to clinical trials and other uncertainties of drug or biologic candidate development; (3) risks relating to the commercialization, if any, of our proposed drug or biologic candidates (such as marketing, regulatory, product liability, supply, competition, and other risks); (4) dependence on the efforts of third parties including our strategic partners; (5) dependence on intellectual property; and (6) risks from global pandemics including COVID-19. Further information regarding these and other risks is included under the heading "Risk Factors" in our filings with the Securities and Exchange Commission available from the SEC's website (www.sec.gov). Existing and prospective investors are cautioned not to place undue reliance on these forward-looking statements, which speak only as of the date hereof. These forward looking statements reflect management's current views and we do not undertake to update any of these forward-looking statements to reflect a change in events or circumstances that occur after the date of this presentation except as required by law.

Developing Novel Oncology Therapies with Differentiated Technology Platform

Unique MOA and I/O approach

- Unique biological MOA of: (i) forced cellular internalization once bound to target and (ii) potent direct cell kill via enzymatic ribosome destruction
- Delivery of viral antigens to redirect resident T-cell response to tumor (Antigen Seeding)
- Emerging data supporting innovative immuno-oncology approach to directly modify immunosuppressive tumor microenvironment

Robust Preclinical Pipeline and Key Partnerships

- TROP-2, TIGIT, SLAMF-7
- Collaboration with pharma partner to discover and develop products containing ETBs directed to multiple targets

Key 2022 Program Milestones

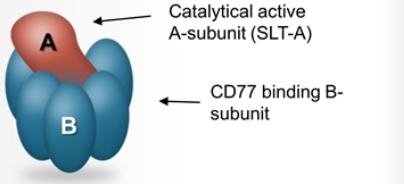
- MT-6402 novel I/O MOA Phase 1 data
- MT-5111 initial Phase 1 breast cancer expansion
- MT-0169 initial Phase 1 myeloma data
- CTLA-4 program IND filing

Strong Balance Sheet

- 3Q21 cash balance of $175M to fund operations into 4Q23

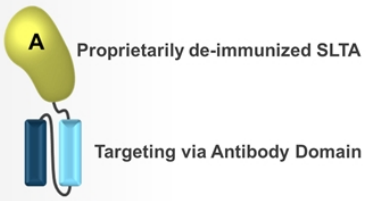
The Engineered Toxin Body (ETB) Platform: *Targeted Biologics with Novel MOAs*

Wild-type Shiga-Like Toxin (SLT) Biology

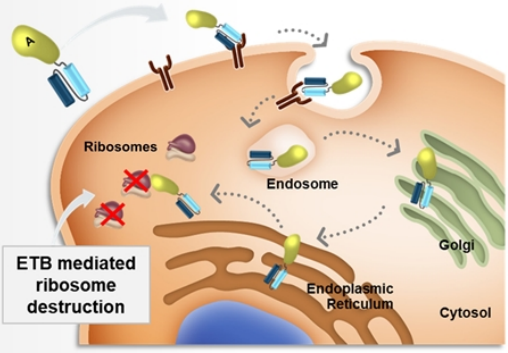


- Binds CD77 (non-internalizing GSL) and mediates its own internalization
- A-subunit mediates translocation to cytosol an enzymatically destroys ribosome

Engineered Toxin Body (ETB) Platform



ETBs Retain Intrinsic Biology of SLT-A Subunit



- ETBs specifically bind target and induce their own internalization through SLT-A payload
- Endosomal escape and routing to cytosol
- Potent enzymatic destruction of ribosomes

MOLECULAR TEMPLATES

I/O APPROACH: MT-6402

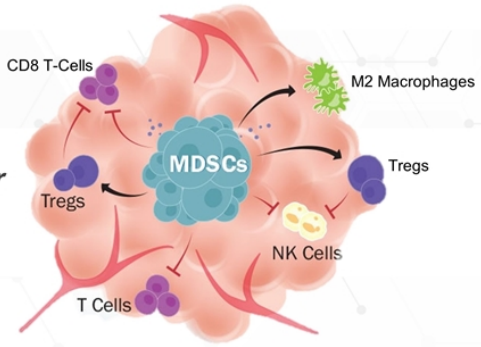
DIRECT PD-L1 TARGETED CELL-KILL AND ANTIGEN SEEDING

Immune phenotype may determine sensitivity to PD-L1 checkpoint therapies

High frequency of peripheral MDSCs correlate to low likelihood of response to checkpoint therapies[1]

- Myeloid derived suppressive cells (MDSCs) express PD-L1 and promote an immunosuppressive tumor microenvironment
- Frequency of peripheral PD-L1+ monocytes predicts responses to CTLA-4 and PD-1 inhibitors

FDA approved PD-L1 checkpoint antibodies do not alter immune subtypes or cytokines



1. Weber R; Front Immunol. 2018; 9: 1310; Image from RnD Systems

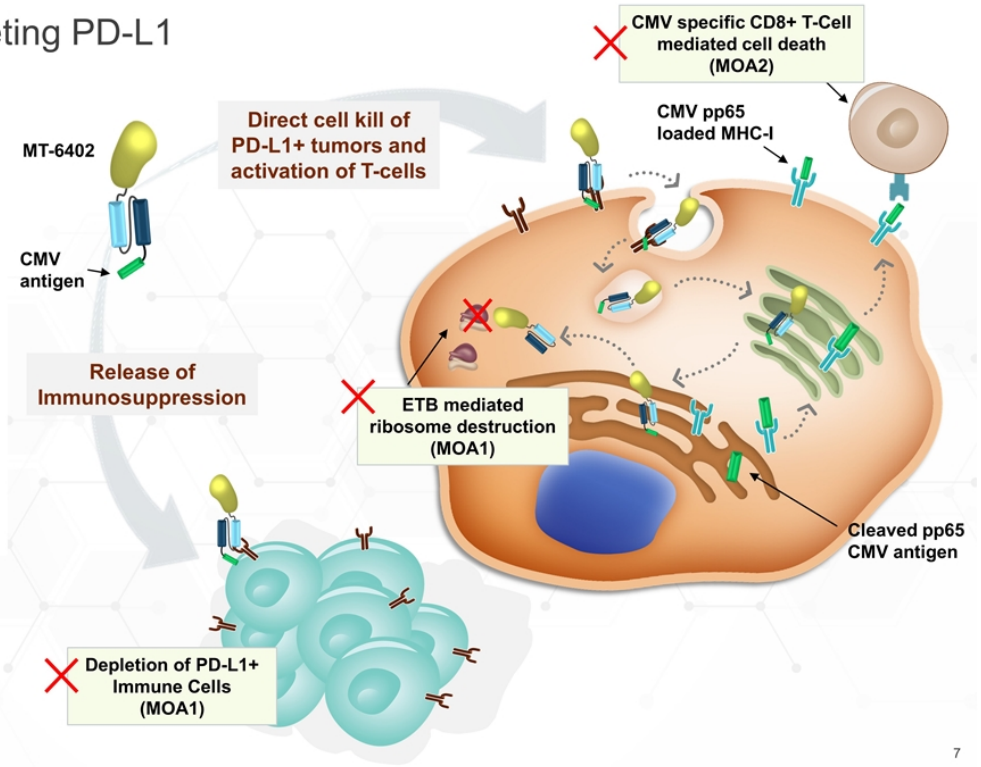
MT-6402: Dual MOA targeting PD-L1

Destroys PD-L1 Expressing Cells – MOA1

- Potent direct cell-kill (pM) against PD-L1+ tumor cells
- Potent direct cell-kill (pM) against PD-L1+ immune cells to activate the immune system

Antigen Seeding Technology (AST) – MOA2

- Delivers pp65 CMV antigen for cell surface expression in context with MHC-I
- Mediates native CMV-specific T-cell response to tumor
- For CMV infected, large reservoirs of CMV-specific T-cells

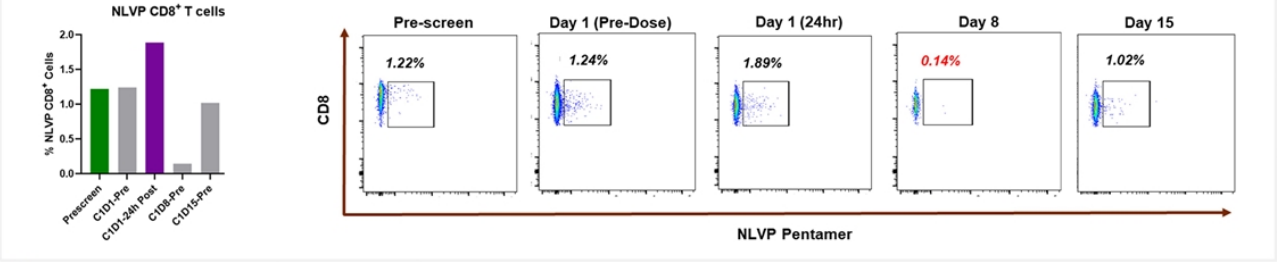


MT-6402 Ongoing Phase 1: Unique PD Effects With Signs of Clinical Benefit

- **No DLTs observed in 16 mcg/kg cohort; dose escalation on-going at 24 mcg/kg**
  - No safety concerns noted to date
  - NSCLC pt with non-measurable bone disease saw resolution of 3 out of 4 lesions and reduction in uptake with remaining lesion
  - Data update expected at AACR 2022
- **Peripheral monocyte numbers and frequencies greatly reduced in majority of patients upon treatment**
  - Correlates with CCL2 increase (cytokine that directs monocyte movement to tissues)
- **Cells associated with immunosuppression and tumor non-response are lost in the periphery**
  - Monocytic myeloid derived suppressor cells (MDSCs) and Tregs are reduced in the periphery
  - NK cells and CD8+ T cells are increased in the periphery
  - General CD8+ T cells increase and coincident increase in cytokines like IL-2
- **CMV specific CD8 T cells are mobilized in Antigen Seeding Technology (AST) engaged subjects (HLA:A2, CMV+)**

MT-6402: Early Signals of Antigen Seeding MOA in Phase 1

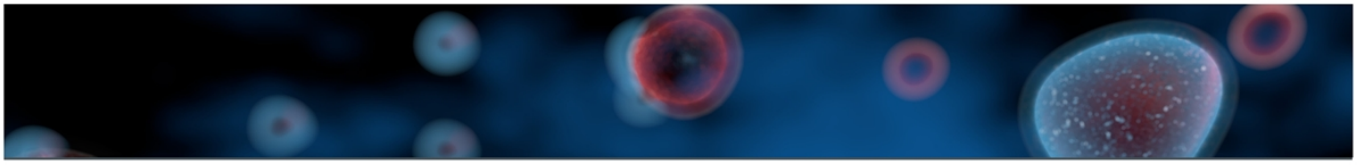
- **Subject 001 – HLA-A2 CMV+ patient (i.e., antigen-seeing eligible patient)**
  - NSCLC chemotherapy-ineligible patient whose disease had progressed following treatment with a combination of checkpoint inhibitors (ipilimumab and nivolumab); patient has non-measurable bone disease
  - On-going monocyte depletion of >95% observed beginning in cycle 2 and on-going at 6+ months of dosing
- **CMV specific CD8 T-cells increased post dose 1 and marked decrease observed by day 8**
  - Initial increase of ~ 50% in CMV antigen-specific T-cells after dosing with MT-6402
  - 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)
  - Reconstitution of CMV-specific T-cells at Day 15 is consistent with the temporal patterns of an antigenic T cell proliferative event
- **Multiple sites of bone disease resolved (3 of 4) on bone scan with only one remaining site which showed decreased uptake**



MOLECULAR TEMPLATES

ANTI-CTLA-4 ETB

DIFFERENTIATED I/O APPROACH TARGETING CTLA-4

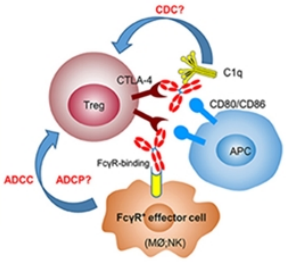


CTLA-4 targeting ETB IND filing expected in 2H22

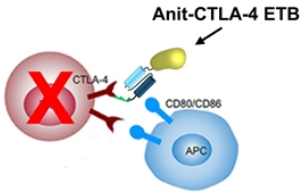
Need to clear CTLA-4+ Tregs from TME to allow for immune surveillance of tumor

- Tregs in the TME express high levels of CTL-4 and can drive immunosuppressive tumor microenvironment
- CTLA-4 targeting ETB has a potent mechanism of CTLA-4 targeted cell-kill that may not be subject to immunosuppression
- ETB approach is designed to avoid CD8 T-cell activation to prevent autoimmune toxicity

Existing antibody therapies to CTLA-4 may not mediate efficient cell kill given general immunosuppression in the TME



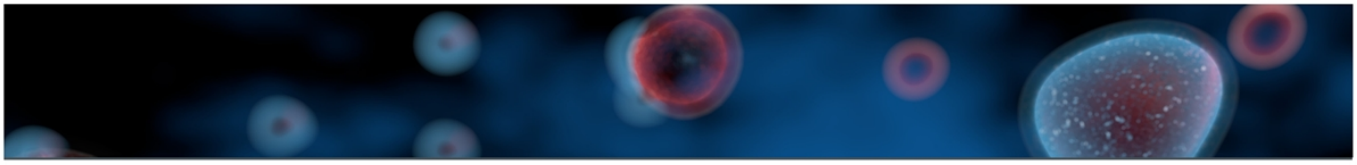
Mab mediated clearance dependent on effector cell function which is inhibited by TME



ETB CTLA-4 targeted cell-kill not dependent on effector cell or TME

MT-5111

ANTI-HER2 ETB



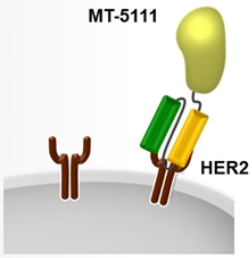
HER2 Remains a Key Target for Breast Cancer

- Recent advances confirm responsiveness of breast cancer to new MOAs targeting HER2
- Despite high response rates and longer durations of response, recent ADCs are not cures and unmet need for metastatic patients will remain

Demand for new mechanisms of action targeting HER2 persists

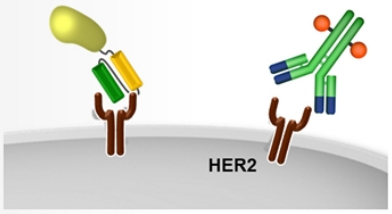
MT-5111: Anti-HER2 ETB with Differentiated Binding and MOA profile

MT-5111 Profile



- Binds HER2 at a distinct epitope from trastuzumab and pertuzumab
- De-immunized Shiga-Like Toxin (SLT-A) Payload
- Reduced TLR4 interaction to minimize innate triggering (CLS)
- Potent direct cell kill (pM) against HER2 expressing cancer cells

MT-5111 Differentiation vs ADC

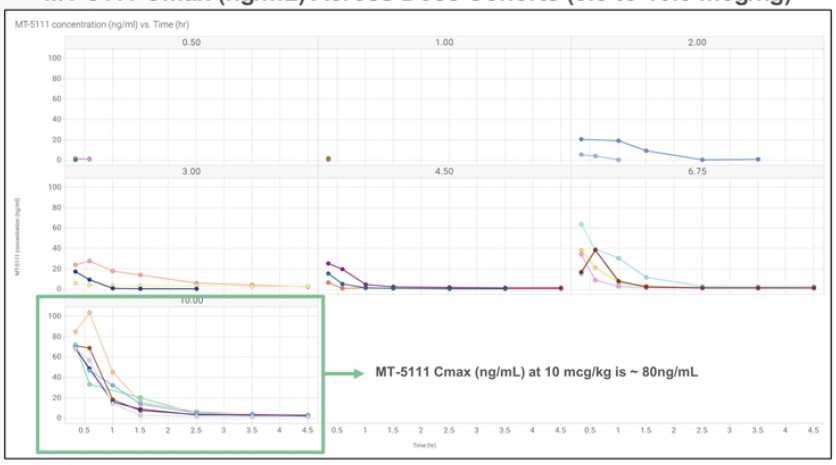


- Potent MOA of direct cell kill that does not appear subject to resistance mechanism to Mabs or ADC chemo payloads
- Distinct HER epitope binding allows for combination potential with Mabs and ADCs
- Smaller size (monomer – 55kDa) may allow for improved tumor penetration
- No conjugation chemistry involved to improve manufacturability

MT-5111: Dose Levels at 10 mcg/kg or Higher Likely Needed for Activity

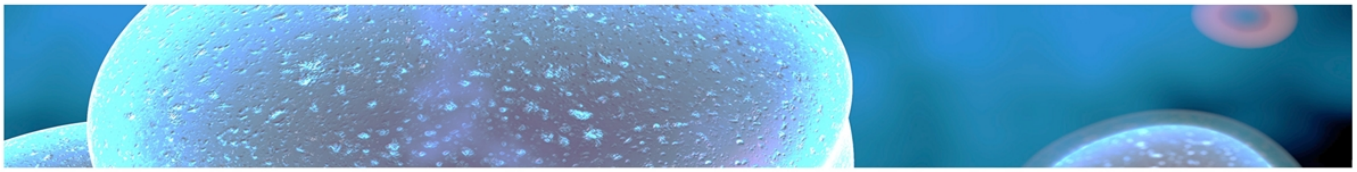
- **27 patients dosed with no DLTs or CLS observed to date - dose escalation continues**
- **Dose level at 13 mcg/kg and breast cancer dose expansion cohort (10 mcg/kg) currently enrolling with >20 sites open**

MT-5111 Cmax (ng/mL) Across Dose Cohorts (0.5 to 10.0 mcg/kg)



MT-0169

ANTI-CD38 ETB



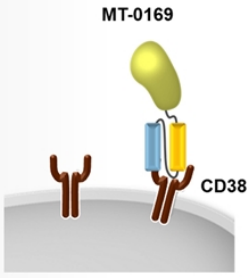
CD38 Remains a Key Target in Myeloma with Limited Available Modalities

- Mabs are currently the only validated modality targeting CD38
- Lack of CD38 internalization prohibits ADC development and promiscuity of target may deter CAR-T and bispecifics
- BCMA for myeloma has been more tenable target for multiple modalities
- More modalities trying to establish dominant position with BCMA than CD38

Opportunity for novel modes of action targeting CD38

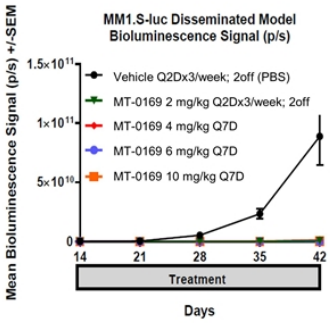
MT-0169: New Modality Targeting CD38

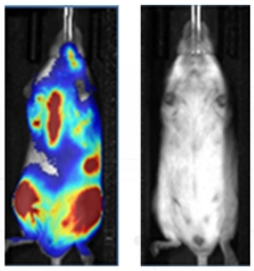
MT-0169 Profile



- Binds CD38 with high specificity and potency retained even in presence of daratumumab (overlapping epitope)
- De-immunized Shiga-Like Toxin (SLT-A) Payload
- Reduced TLR4 interaction to minimize innate triggering (CLS)
- Potent direct cell kill against CD38 expressing cancer cells (sub pM – most potent ETB created to date)

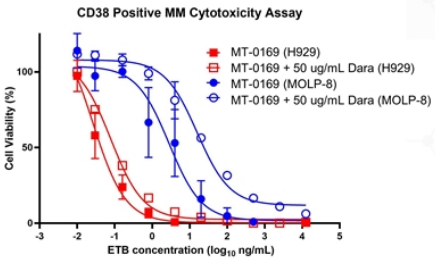
Potent Antitumor Activity in Various Xenograft Models[1]

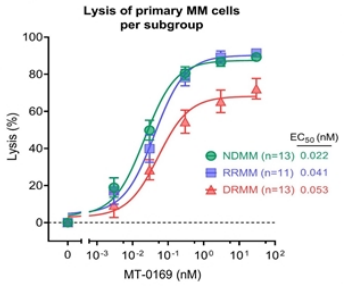




Activity in Presence of Dara and in Dara Refractory Primary MM Cells[1]

1. 2019 AACR Abstract 2384





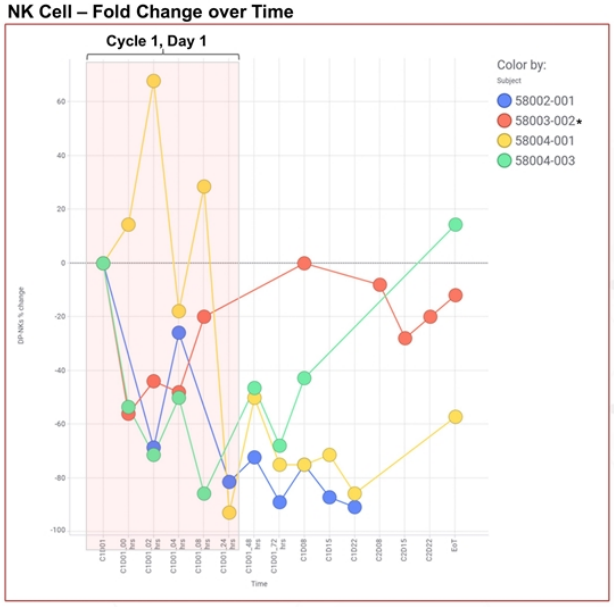
MT-0169: PD Activity Observed in Phase 1 and Safety Signals

- **Five pts treated to date with two pts with cardiac AEs that meet criteria for DLT**
  - Evaluation of both AEs triggered by asymptomatic elevations in high-sensitivity troponin
  - The first DLT was an asymptomatic, rapidly reversible episode of myocarditis that did not require treatment
  - The second DLT was an asymptomatic, nonischemic cardiomyopathy that also resolved within 1-2 months
  - Similar clinically relevant cardiac AEs not seen with any other ETB at any dose in clinic

- **DLTs may be due to MT-0169 activity against low CD38-expression in cardiac endothelium**
  - Starting dose of 50 mcg/kg is highest starting dose for any ETB
  - Rapidity and depth of CD38+ NK cell depletion in humans was unanticipated by NHP data
    - Lack of NK cells can drive eosinophilic infiltration in experimental model of myocarditis
  - Cardiotox not seen with CD38 Mabs likely due to low CD38 MFI and limited ability for effector function (ADCC, CDC) in tissue

- **The patient with cardiomyopathy had evidence of symptomatic benefit (reduction in myeloma bone pain)**
  - Anti-tumor effects can take longer than PD effects due to proliferative nature of malignancy

NK Cell – Fold Change over Time



**Patient 58003-002 had low CD38 expression on NK cells*

Corporate Summary

- **Clinical data milestones expected across three ETB programs in 2022**
  - MT-6402 demonstrating early signs of clinical benefit and pharmacodynamic activity
  - MT-5111 drug exposure levels now in therapeutic range
  - MT-0169 shows potent pharmacodynamic activity; moving forward with dose reduction
- **Potential for initiation of combination studies across programs by early 2023**
- **New IND for CTLA4 ETB (differentiated I/O approach to CTLA-4) at YE22**
  - Expect one new ETB IND each year
- **Ongoing pharma partnership**
- **Cash runway to end of 2023**

Advancing Wholly Owned Clinical Pipeline with Novel MOAs

ETB PROGRAM	TARGET	MOA	INDICATION
MT-6402	PD-L1	• Direct cell kill • Antigen Seeding (CMV antigen)	Solid Tumors
MT-5111	HER2	Direct cell-kill	Breast Cancer
MT-0169	CD38	Direct cell-kill	Multiple Myeloma
ETB Candidate	CTLA-4	Direct cell-kill	Solid Tumors
ETB Candidate	TIGIT	Direct cell-kill	Solid Tumors
ETB Candidate	TROP-2	• Direct cell kill • Antigen Seeding (CMV antigen)	Solid Tumors
ETB Candidate	SLAMF-7	Direct cell-kill	Multiple Myeloma

- **Relevant data updates on pipeline expected throughout 2022**
- **Data presentations expected at AACR (Apr), ASCO (Jun), SITC (Nov), SABC (Dec), and ASH (Dec)**