

MOLECULAR TEMPLATES

Corporate Presentation | 2021 Oppenheimer Healthcare Conference

(NASDAQ: MTEM)

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, TAK-169, and MT-6402, and our preclinical pipeline; our utilization of a next-generation ETB scaffold that has been designed to reduce or eliminate the propensity for innate immunity, including CLS, and to reduce the propensity for aggregation; our plans to enter the clinic with multiple candidates; our expected receipt of clinical data; our future cash needs; and statements relating to the outcome of our collaborations as they relate to our ETB platform; whether our collaborators will exercise their options and our receipt of future development, regulatory and sales milestones and royalty payments. 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 product candidate development; (3) risks relating to the commercialization, if any, of our proposed product 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.

MTEM: Developing Novel Therapeutics With a Unique Platform

Unique Biology and MOA

Engineered Toxin Bodies (ETBs) have the specificity of an antibody, can induce their own internalization, and are designed to act through a potent and unique mechanism of action(s): ribosomal destruction, antigen seeding

Global Partners

BMS: Multi-target collaboration (oncology)

Vertex: Multi-target collaboration (myeloablation)

Takeda: Multi-target collaboration (oncology)

Advancing Pipeline

POC with 1st-Gen ETB (CD20) demonstrated forced internalization, clinical activity. Two 2nd-gen ETBs (HER2, CD38) and one 3rd-gen ETB (PD-L1) in Phase 1 with improved activity, tolerability, and manufacturability over 1st-gen.

Future Opportunities

ETB platform provides continued pipeline opportunities via partnerships and internal development. Next-Gen ETBs in preclinical development against targets including CTLA-4, TROP-2, TIGIT, SLAMF-7

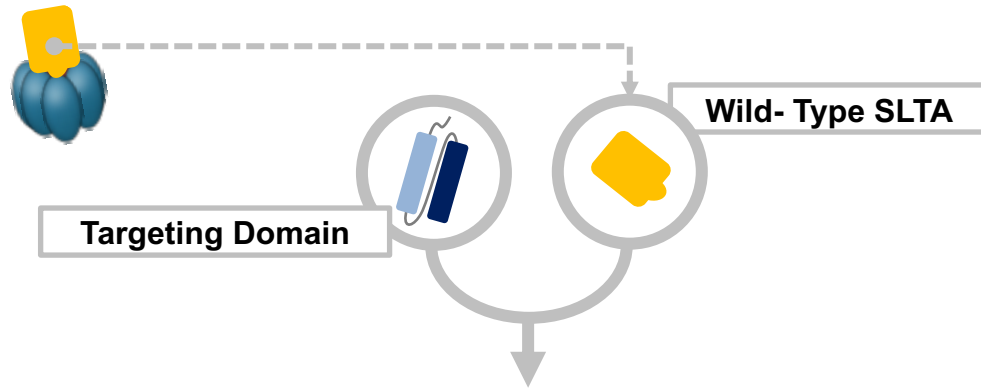
Known Targets for Early Signs of Tolerability and Response

ETBs against validated targets can provide evidence of tolerability and response as early as Phase 1

Strong Cash Position

Current cash funds operations into 2H23

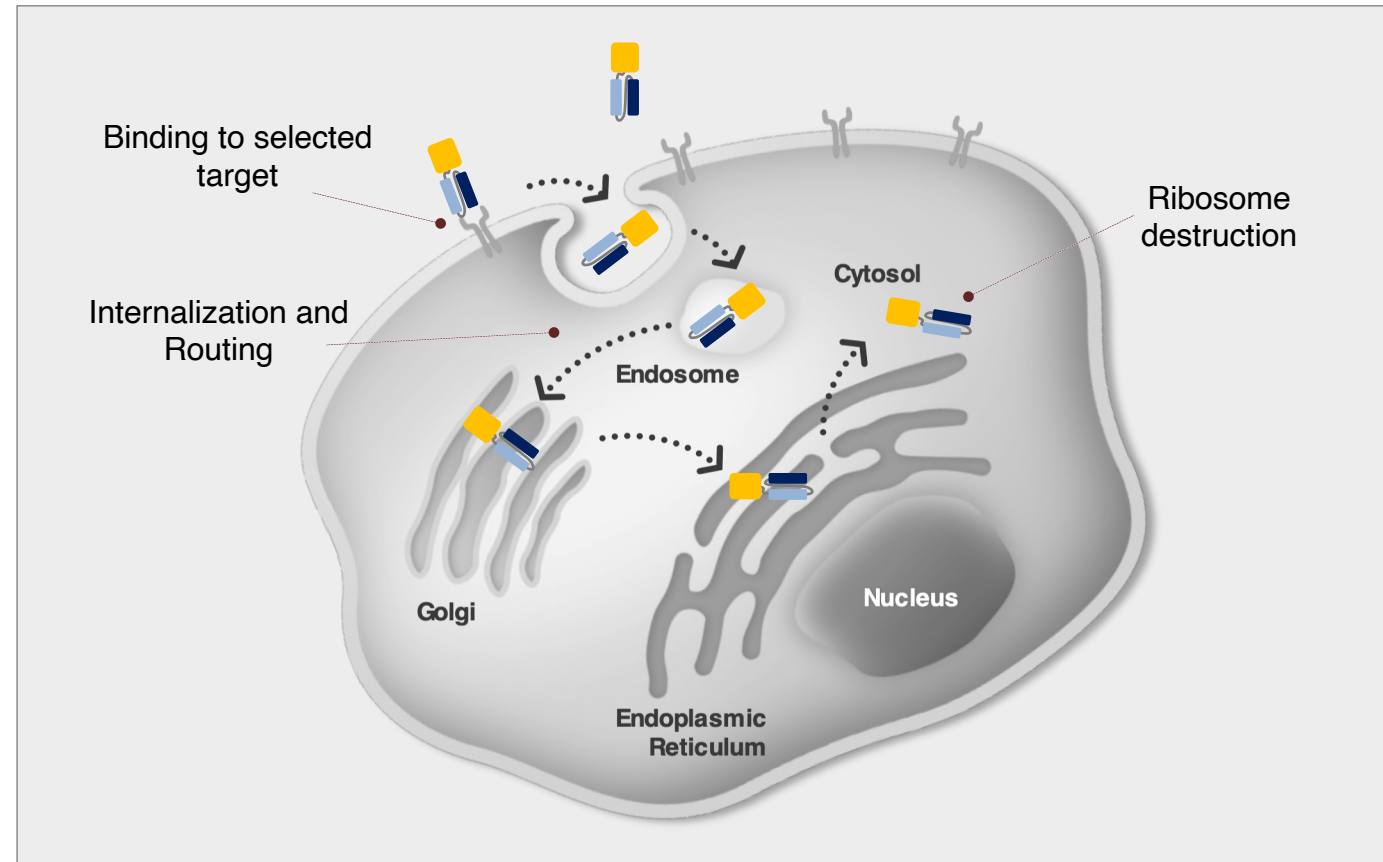
1st-Gen ETB: Targeted Biologics with Novel MOA



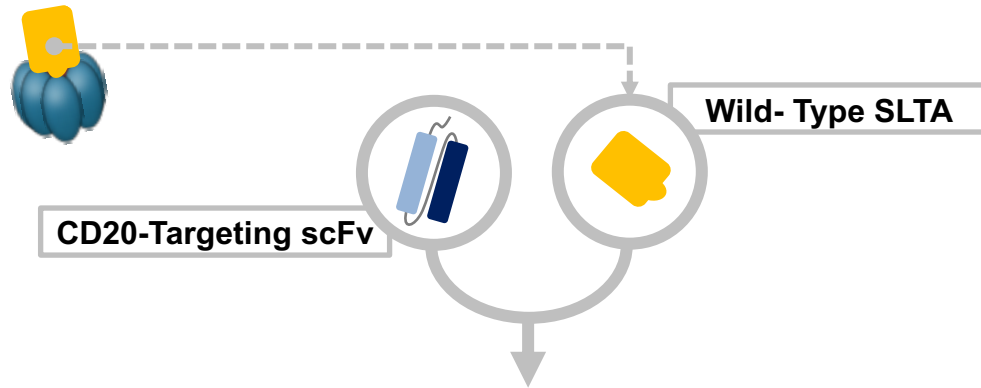
Engineered Toxin Bodies (ETBs)



- ETBs can be directed to any extracellular target
- ETBs retain the SLTA-mediated ability of:
 - Internalization (even against non-internalizing targets)
 - Routing to the cytosol
 - Enzymatic and irreversible destruction of ribosome



MT-3724: 1st-Gen POC Around Internalization and Single Agent Activity



Engineered Toxin Bodies (ETBs)



- Monotherapy activity with MT-3724 seen in heavily pre-treated DLBCL pts
- Manufacturing issues with molecule led to discontinuation
 - Gr 5 CLS in a patient receiving MT-3724 from highly aggregated lot of material
 - Inherent propensity for aggregation with 1st-gen ETBs



Patients evaluable for efficacy in phase I (n=25)

DLBCL or Mixed DLBCL/FL (n=19)

Low serum RTX levels (n=13)

2 Complete Responses (CR)

1 Complete Metabolic Response (CMR)

2 Partial Responses (PR)

3 Stable Disease (SD) (49%, 47% tumor reduction)

5 Progressive Disease (PD)

38% Objective Response Rate (ORR)^a

60% ORR at MTD: 2 CRs, 1 PR, 2 PD

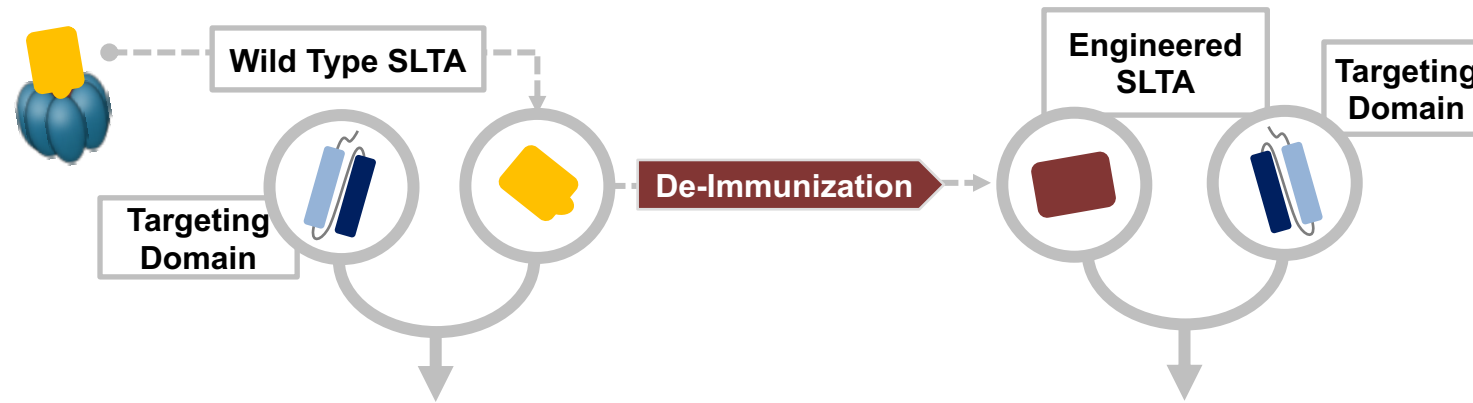
^a)Median number of prior therapies in responders was 3; responses seen in R-CHOP refractory pts. Includes 2 stable disease patients who had 49% and 47% tumor reductions



2nd-Generation ETBs

Increased Potency; Better Tolerability; Reduced Aggregation

2nd and 3rd Generation ETB Platforms Provide Improved Properties



	1 ST Generation ETB	2 nd Generation ETB
ETBs	MT-3724 (CD20)	MT-5111 (HER2), TAK-169 (CD38) in Ph I
Potency	Sub-nanomolar	Pico to sub-picomolar (reverse orientation)
SLTA Scaffold	Wild-type SLTA	DI SLTA; reduced innate immunity / CLS
Manufacturability	High propensity for aggregation: Free Cys, oxidation, and intermediate linker	Low propensity for aggregation: no free Cys or oxidation and short or long linker


















2nd-Gen ETBs Have Significantly Improved Potency, Safety, Developability

	1 st -Gen ETB (MT-3724)	2 nd -gen ETBs
Potency	Nanomolar	Pico to sub-picomolar • Improvements via ETB structure engineering
Toxin Scaffold	Wild-type SLTA	SLTA Engineered for reduced innate and adaptive immunogenicity
Therapeutic Index	<p>NHP Tox: HNSTD < 150 ug/kg^a</p> <div style="border: 1px solid purple; padding: 5px; text-align: center;"> <p>Therapeutic Index</p> <p>↕</p> <p>Nanomolar IC₅₀</p> </div>	<p>NHP Tox: HNSTD > 500 ug/kg^b</p> <div style="border: 1px solid purple; padding: 5px; text-align: center;"> <p>Therapeutic Index</p> <p>↕</p> <p>Pico to sub-picomolar IC₅₀</p> </div>
Manufacturing	Complex with high propensity for aggregation due to unpaired cysteine, oxidation step, and intermediate linker length	Simplified with low propensity for aggregation due to no unpaired cysteine, lack of oxidation step, and short or long linker forms

a) HNSTD due to innate immunity

b) For next-gen ETBs, HNSTD has been due to highest doses tested, not toxicity

Oncology Pipeline With Novel MOAs Driven by ETB Platform

Program	Ownership	Indication (Target)	Preclinical	Phase 1	Phase 2	Phase 3
TAK-169	 tem MOLECULAR TEMPLATES	Multiple Myeloma (CD38)				
MT-5111	 tem MOLECULAR TEMPLATES	Multiple – solid tumors (HER2)				
MT-6402	 tem MOLECULAR TEMPLATES	Multiple – solid tumors (PD-L1)				
CTLA-4	 tem MOLECULAR TEMPLATES	Multiple – solid tumors				
TROP-2	 tem MOLECULAR TEMPLATES	Triple-negative MBC, NSCLC				
TIGIT	 tem MOLECULAR TEMPLATES	Multiple – solid tumors				
SLAMF-7	 tem MOLECULAR TEMPLATES	Multiple myeloma				

 Completed  In-Progress

2nd-Generation ETBs

TAK-169 / CD38



CD38: A Key Target in Myeloma with Limited Available Modalities

Monoclonal Antibodies

- CD38 Mab activity in myeloma
- CD38 target persists after progression on CD38 Mab
- Mechanism of resistance to Mabs appears to be blocking effector function (eg, CD59 upregulation)

CAR-T / Bispecifics

- T-cell engagers have a proven role in multiple myeloma (BCMA)
- CD38 expressed on lymphocytes, NK cells, DCs, bone marrow progenitor cells, and plasma cells
- Promiscuous expression may drive T-cell activation / CRS

ADCs

- ADC are a proven modality in multiple myeloma (BCMA)
- Lack of internalization with CD38 has made CD38-ADC development challenging

TAK-169: A 2nd-Generation CD38-Targeted ETB

CD38 TARGETED

Single-chain variable fragment (scFv) with specificity to CD38. Binds in the presence of daratumumab



FORCED RECEPTOR INTERNALIZATION

Efficient internalization against CD38, a poorly-internalizing receptor



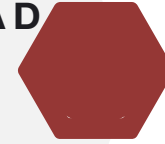
DEIMMUNIZED PAYLOAD

De-immunized SLTA payload for reduced innate and adaptive response. Reduced TLR4 interaction to minimize innate triggering (CLS)



NOVEL ENZYMATIC PAYLOAD

pM potency against CD38+ cells, including Dara-refractory primary MM cells

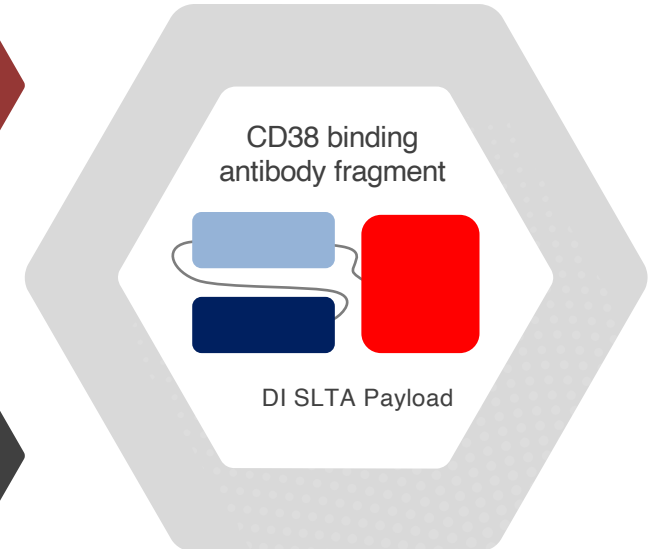


OTHER PROPERTIES

Fusion protein; no linker chemistry. Short serum half-life; irreversible intra-cellular effects



TAK-169: 2nd-Generation ETB



TAK-169 Update: MTEM to Assume Full Rights to Program

- **TAK-169 entered Ph I in 1Q20 as part of a co-development with Takeda in which Takeda had full control over clinical development**
- **On August 4, 2021, MTEM assumed full rights to TAK-169 from Takeda, including full control of TAK-169 clinical development**
 - Takeda communicated that its decision to turn over full rights of TAK-169, was the result of ongoing portfolio prioritization
 - MTEM's assumption of the full rights to TAK-169 is expected to result in cost savings in 2021
- **Study update**
 - Takeda enrolled four subjects since first patient was dosed in Feb 2020; 3 pts evaluable for efficacy with no responses seen
 - No CLS or life-threatening toxicities observed; MTD has not been reached and dose escalation is ongoing
 - One DLT (grade 2 myocarditis; high-sensitivity troponin elevation) seen in one pt
 - No EKG or echocardiographic abnormalities and no clinical symptoms were noted
 - A stable elevation lasting several days in high-sensitivity troponin was seen; no comparison to baseline was available
 - An independent radiologist and cardiologist reviewed the imaging in the case and concluded that there was weak to intermediate evidence of myocarditis; the patient had multiple pre-existing cardiac risk factors
 - No other cardiac adverse events were observed in any other subject
 - Pharmacokinetics have been in-line with predicted outcomes
 - NK cell depletion seen in all patients treated demonstrating pharmacodynamic activity at the 50 mcg/kg dose
- **Additional sites being opened and new patients enrolled with interim data read likely by year's end**

2nd-Generation ETBs

MT-5111 / HER2



MT-5111: A 2nd-Generation HER2-Targeted ETB

HER2 TARGETED

Single-chain variable fragment (scFv) with specificity to HER2. Binds a distinct epitope from trastuzumab/pertuzumab



SMALL SIZE FOR BETTER PENETRATION

55 kDa versus ~145 kDa for Mabs/ADCs



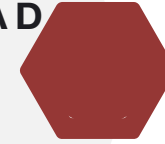
DEIMMUNIZED PAYLOAD

De-immunized SLTA payload for reduced innate and adaptive response. Reduced TLR4 interaction to minimize innate triggering (CLS)



NOVEL ENZYMATIC PAYLOAD

Primary mechanism of cell-kill - enzymatic ribosome destruction. pM potency against HER2+ cells

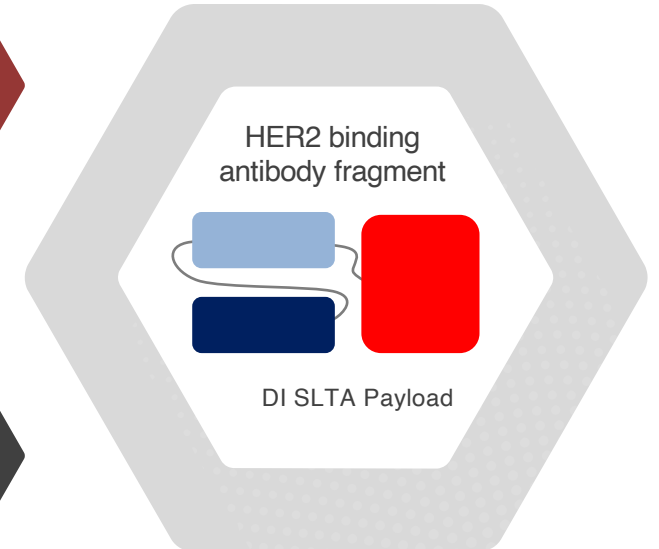


OTHER PROPERTIES

Fusion protein; no linker chemistry. Short serum half-life; irreversible intra-cellular effects



MT-5111: 2nd-Generation ETB



MT-5111 Update: Dosing and Patient Population

- **MT-5111 began dosing at 0.5 mcg/kg due to potential for cardiotox with HER2-targeting agents**
 - Starting dose for MT-5111 is 10- to 100-fold lower than the starting dose for our other ETBs
 - MT-3724 = 5 mcg/kg; MT-6402 = 16 mcg/kg; MT-0169 = 50 mcg/kg
 - Completed cohorts of 0.5, 1.0, 2.0, 3.0, 4.5, and 6.75 mcg/kg; no DLTs or CLS observed to date and dose escalation continues
- **Dose proportional increases seen in last cohorts**
 - Predictable increases in C_{max}; no unexpected C_{max} data observed
- **Internal modeling suggested required doses of 5 to 10 mcg/kg or higher for efficacy in MBC 2+ or 3+ pts**
 - MT-5111 currently dosing at 10 mcg/kg
 - No clear pharmacodynamic markers available for HER2-targeted agents
 - Most patients dosed to date have not been MBC 2+ or 3+ patients
- **MBC is tumor type most likely to show activity with a HER2 agent**
 - MBC expansion expected to initiate this year at 10 mcg/kg



3rd-Gen ETBs / Novel Approach to IO

MT-6402: PD-L1 targeting ETB with antigen seeding

MT-6402: A 3rd-Generation ETB Targeting PD-L1+ Tumor and TME Immune Cells

PD-L1 TARGETED

Single-chain variable fragment (scFv) with specificity to PD-L1. Binds PD-L1 on tumor and immune cells.



FORCED RECEPTOR INTERNALIZATION

Efficient internalization against PD-L1, a poorly-internalizing receptor.



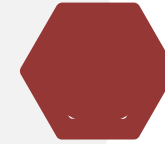
DEIMMUNIZED PAYLOAD

De-immunized SLTA payload for reduced innate and adaptive response. Reduced TLR4 interaction to minimize innate triggering (CLS)



NOVEL ENZYMATIC PAYLOAD

pM direct cell-kill potency against PD-L1+ tumor and immune cells. All other checkpoint agents rely on indirect cell kill of tumor cells and do not clear PD-L1 immune cells.

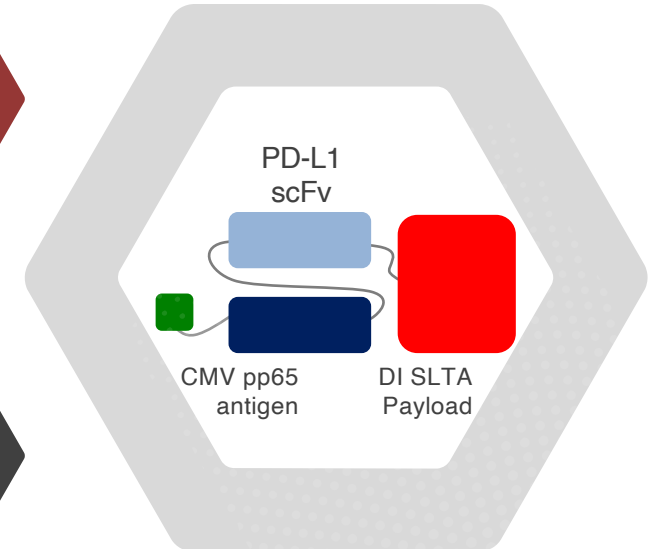


ANTIGEN SEEDING

MT-6402 induces expression of foreign class I pp65 antigen on surface of HLA-A2 tumor cells.



MT-6402: 3rd-Generation ETB



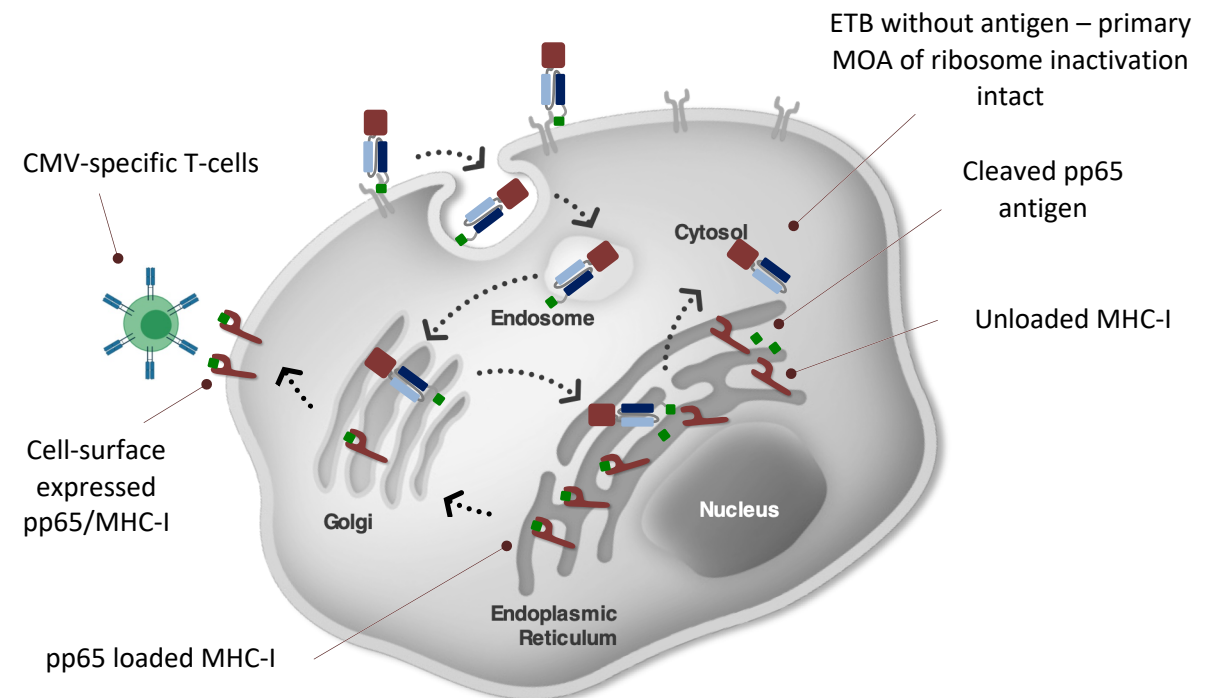
3rd-gen ETBs: Antigen Seeding Allows for Alteration of Tumor Immunophenotype

Fundamental alteration of immunophenotype on tumor with foreign viral antigens to redirect T-cell response

Engineered Toxin Bodies (ETBs) with AST



- ETBs localize to ER/cytosol to “seed” tumors with foreign non-self antigens
- Antigen cleaved intracellularly
- Presented on cell surface in context with MHC-I
- Delivery of pp65 CMV antigen
 - Mediate native CMV-specific T cell response to tumor
 - Large existing population infected with CMV
 - CMV-specific T-cells undergo “memory inflation” in response to persistent reactivation of CMV – less prone to exhaustion
 - Large reservoirs of CMV-specific T-cells with significant proportion specific to pp65 CMV epitope



MT-6402: Phase I Dose Escalation On-Going

- Open to patients with PD-L1+ tumor or PD-L1+ staining in TME; PD-L1 negative patients are excluded
 - Patients must have progressed on checkpoint therapy if indicated
- Dosing initiated on 7/9/21
 - Starting dose of 16 mcg/kg
 - Starting dose expected to have pharmacodynamic effects around primary mechanism of action and antigen seeding
- Interim data expected by year's end
 - First two cohorts of patients expected to be dosed by end of year

ETBs and IO: PD-L1 ETB in the Clinic; Potential New IO Targets in the Works

Potent effect on PD-L1+ tumor cells and immune cells

- ✓ Direct cell-kill on tumor cells through ribosomal destruction (MOA1) independent of tumor microenvironment
- ✓ *In vitro* and animal data suggest potent activity on PD-L1 immune cells and activation of immune system
- ✓ Novel alteration of cancer cell immunophenotype for pre-existing, synaptic T-cell recognition of tumor (MOA2)

Exploration of additional IO targets where ETB approach may provide substantial differentiation

- ✓ CTLA4 lead development work underway; Phase 1 start expected in 2022
- ✓ Potential safety and efficacy benefits around direct cell-kill of CTLA4+ T cells vs blocking
- ✓ Lead selection underway for ETB targeting TIGIT



Engineered Toxin Bodies

A Robust Pipeline with Clinical Data in 2021

ETB Technology Has Shown Unique Biology, PD, and Monotherapy Efficacy

- 1st-gen ETB showed forced internalization, pharmacodynamic effects, and monotherapy activity
 - Manufacturing issues around aggregation led to discontinuation
- 2nd-gen ETBs reduce potential for immunogenicity, increase potency, and enhance manufacturability
 - Scaffold changes made to solve aggregation issues
 - Higher dosing tolerated in NHPs due to de-immunization work; no signs of CLS in any patient treated with 2nd-gen ETB
 - Increased *in vitro* potency; notable PD effects observed in patients treated with TAK-169
- 3rd-gen ETB has all the advantages of 2nd-gen and antigen seeding
 - MT-6402 targets PD-L1+ tumor cells and PD-L1+ immune cells in the TME for destruction
 - MT-6402 can alter the immunophenotype and immunogenicity of HLA-A2+ tumor cells
 - Initiation of dosing at 16 mcg/kg is within predicted range of activity
- Strong balance sheet with cash into mid-2023
 - Open label studies with data reads beginning by year-end across all three clinical programs
 - Additional compounds being advanced into clinic; platform improvements underway