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 potential lifting of the partial clinical hold on our MT-3724 clinical trials; statements relating to the development of the MT-3724, MT-5111, TAK-169, and MT-6402; our utilization of a next-generation ETB scaffold that has been designed to reduce or eliminate the propensity for innate immunity, including CLS; our plans to enter the clinic with multiple candidates; our expected receipt of clinical data; and our future cash needs. 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) our ability to successfully resolve the partial clinical hold with regard to MT-3724; (4) risks relating to the commercialization, if any, of our proposed product candidates (such as marketing, regulatory, product liability, supply, competition, and other risks); (5) dependence on the efforts of third parties including our strategic partners; (6) dependence on intellectual property; and (7) 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 MOA**
Engineered Toxin Bodies (ETBs) have the specificity of an antibody, can induce their own internalization, and act through a potent and unique mechanism of action: ribosomal destruction.

**Advancing Pipeline**
MT-3724 has shown single agent responses in advanced DLBCL. ETBs targeting CD38 and HER2 in Phase 1. PD-L1 ETB Phase 1 expected to start dosing 1H21.

**Known Targets for Early Signs of Safety & Efficacy**
ETBs against validated targets can provide evidence of safety and response as early as Phase 1.

**Global Partners**
**Takeda**: CD38 co-development, multi-target collaboration, equity investment. **Vertex**: Multi-target collaboration around myeloablation, equity investment.

**Future Opportunities**
ETB platform provides continued pipeline opportunities via partnerships and internal development. ETBs in preclinical development against targets including CTLA-4, SLAMF-7, CD45.

**Strong Cash Position**
Current cash funds operations into 2H22 without additional business development.
ETBs: Novel Mechanisms of Action in Oncology

ETBs use an antibody domain for targeting genetically fused to a de-immunized SLTA

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

Iterative improvements made to ETB scaffold

- Clinical validation of forced internalization, safety, and efficacy with 1st-Gen ETB (MT-3724)
- 2nd-Gen ETBs have been engineered to have:
  - Increased potency
  - Decreased adaptive immunity
  - Decreased innate immunity via reduced TLR4 affinity
- 3rd-Gen ETBs have all the properties of the 2nd-Gen and can specifically alter the immunophenotype of tumor cells via antigen seeding technology (AST)
# The Evolution of Immunotoxins: From Ontak to ETBs

<table>
<thead>
<tr>
<th>Cytokine-targeted</th>
<th>scFv-targeted</th>
<th>Next-Gen ETBs</th>
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<tbody>
<tr>
<td>Approved agents: Ontak and Elzonris</td>
<td>Approved agents: Lumoxiti</td>
<td><strong>Genetically engineered SLTA</strong></td>
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<tr>
<td>High levels of CLS from cytokine ligand and bacterial protein</td>
<td>Reduced levels of CLS from bacterial protein</td>
<td><strong>TAK-169, MT-5111, MT-6402</strong></td>
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<tr>
<td>Development of ADAs</td>
<td>Development of ADAs</td>
<td>Low/no CLS due to genetic engineering of SLTA</td>
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<tr>
<td>Good efficacy in heavily pre-treated patients</td>
<td>Good efficacy in heavily pre-treated patients</td>
<td>Limited ADAs due to de-immunization</td>
</tr>
<tr>
<td>Target must internalize</td>
<td><strong>Target must internalize</strong></td>
<td>Increased potency with less frequent dosing</td>
</tr>
</tbody>
</table>

## Cytokine-targeted
- Unmodified Diphtheria toxin
- Cytokine ligand

## scFv-targeted
- Unmodified Pseudomonas toxin
- scFv ligand

## Next-Gen ETBs
- Genetically engineered SLTA
- **TAK-169, MT-5111, MT-6402**

- Low/no CLS due to genetic engineering of SLTA
- Limited ADAs due to de-immunization
- Increased potency with less frequent dosing

**Forced target internalization (SLTA)**
MT-3724

1st-Gen ETB Targeting CD20 for Lymphomas
MT-3724: 1\textsuperscript{st}-Gen CD20-Targeted ETB

**CD20 Targeted**
Single-chain variable fragment (scFv) with specificity to CD20

**Forced Target Internalization**
Efficient internalization against CD20, a non-internalizing receptor

**Wild-Type Payload**
Wild-type Shiga-like toxin A-subunit payload. Retains TLR4 interaction

**Other Properties**
Fusion protein; no linker chemistry. Short serum half-life; irreversible intra-cellular effects. MOA believed to be reliant on $C_{max}$ not AUC

**Novel Enzymatic Payload**
Primary mechanism of cell-kill is enzymatic ribosome destruction

MT-3724
1\textsuperscript{st}-Gen ETB

- CD20 binding scFv
- WT SLTA Payload
MT-3724: Activity Demonstrated in DLBCL

Phase 1/1b study conducted in heavily pretreated B-cell lymphoma patients
  • Median age of 65
  • Median of 4 prior NHL therapies; median of 2 prior anti-CD20 Mabs

Deep and prolonged dose-dependent B-cell depletion observed

Favorable tolerability profile
  • Maximum tolerated dose (MTD) established at 50 µg/kg
    - Dose cohorts of 5, 10, 20, 50, 75, and 100 µg/kg evaluated
  • Dose-limiting toxicities (DLTs) were non-life threatening grade 2/3 events including grade 2 capillary leak syndrome (CLS) which resolved upon cessation of dosing; CLS did not recur upon re-challenge at lower doses

High serum levels of Rituxan® (RTX) inhibits MT-3724 activity
  • 0/6 response rate
  • Patients screened out for high RTX in ongoing studies

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
### MT-3724: Ongoing Clinical Development Pending Removal of Clinical Hold

<table>
<thead>
<tr>
<th>Development Strategy</th>
<th>Indication</th>
<th>Description</th>
</tr>
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</table>
| MT-3724 Monotherapy        | R-R DLBCL 3L+               | Patients ≥ 2 prior lines of Tx  
Negative serum RTX  
Independent DSMB and central efficacy review  
Will enroll up to 100 patients; registrational intent as monotherapy |
| MT-3724 + Lenalidomide     | R-R DLBCL 2L+               | 2L/3L DLBCL patients (chemo-exhausted/ineligible)  
Preliminary evidence of efficacy in early stages of dose-escalation                                |
| MT-3724 + Gemcitabine and Oxaliplatin | R-R DLBCL 2L+ | 2L/3L DLBCL patients (transplant ineligible, chemo-eligible)  
Preliminary evidence of efficacy in early stages of dose-escalation |
MT-3724: Update on Partial Clinical Hold

- One subject death occurred on 20-Oct-2020 in the MT-3724 monotherapy study due to grade 5 capillary leak syndrome (CLS)
  - Subject was a seventh line DLBCL patient (ex-US site) who had rapidly progressed through three lines of therapy (including a first-generation CAR-T) in the six months prior to MT-3724 dosing
  - Subject experienced grade 2 CLS after two doses of MT-3724 which had resolved prior to resuming dosing

- First grade 5 CLS event across all MT-3724 studies
  - All prior occurrences of CLS across all MT-3724 studies were grade 2 or below

- Elevated $C_{\text{max}}$ exposure observed in last 5 of 6 subjects dosed on MT-3724 monotherapy study
  - Higher than expected pharmacokinetic (beyond pharmacokinetic projections) observed in these 5 subjects
  - All five subjects received drug from the same single lot of MT-3724 drug product
  - $C_{\text{max}}$ exposures observed in these five subjects were higher than has been observed in any other subjects or studies with MT-3724
  - Elevated $C_{\text{max}}$ exposures have not been observed with 2nd generation ETB programs

- Investigation ongoing and MT-3724 studies put on partial clinical hold by the FDA on Nov 4, 2020
  - No new enrollment; patients on drug and benefiting will continue to receive MT-3724; lot in question held until investigation is complete

- Other MTEM studies continue and are not affected
  - TAK169, MT-5111 and planned MT-6402
2nd-Generation ETBs

Increased Potency; Better Safety
2nd-gen ETBs Designed to Have Improved Potency and Reduced Toxicity

First-gen ETB
Wildtype SLTA payload

- NHP Tox: HNSTD < 150 ug/kg
- In-vitro potency (IC₅₀): ~sub-nanomolar

Next-gen ETBs
Proprietary De-immunized SLTA payload

- NHP Tox: HNSTD > 500 ug/kg
- In-vitro potency (IC₅₀): ~pico to sub-picomolar

MT-3724 utilizes wild-type SLTA payload with intact innate receptor interaction (TLR4)

ETBs utilize next-gen SLTA payload de-immunized to reduce adaptive and innate immunogenicity

ETB structural modifications (orientation) greatly improve potency (more efficient intracellular routing)
2nd-Generation ETBs
MT-5111 / HER2
MT-5111: A 2nd-Generation HER-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-Gen ETB Targeting HER2

### HER2-targeting Agents

<table>
<thead>
<tr>
<th>Mab: Herceptin, Perjeta</th>
<th>Engineered Toxin Body (MT-5111)</th>
</tr>
</thead>
<tbody>
<tr>
<td>ADC: Kadcyla</td>
<td></td>
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<tr>
<td>TKI: Tykerb, Nerlynx</td>
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</tr>
</tbody>
</table>

### MOA

- **Signal transduction blocker (Mabs, TKIs)**
- **Direct cell kill (ADC)**
- **Direct cell kill (enzymatic ribosome inactivation)**

### HER2 target interaction

- **Binding and internalization**

### Limitations

- **Target persists but the modalities ultimately fail**
- **New modality with activity after other modalities have failed**

### MOA

- **HER2 amplification is associated with poor prognosis**
- **New modalities needed to overcome resistance**
  - Patients progressing from trastuzumab (Mab) can receive lapatinib (TKI) or T-DM1 (ADC)
- **Other modalities currently being explored, but success may be limited**
  - T-cell engagement in solid tumor setting may be difficult limiting use of CAR-Ts and bispecifics
  - Bi-paratropic antibodies rely on the same mechanisms of tumor destruction as Mabs
- **MT-5111 has a wholly unique MOA that does not appear subject to the resistant mechanism associated with Mabs, TKIs, or ADCs**
- **MT-5111 Phase 1 ongoing; update in 4Q20**
MT-5111: Early Clinical Data

Update provided in June 2020

- Ongoing two-part Phase 1: Part 1 is dose escalation; Part 2 (dose expansion) after MTD or rec. Ph. 2 dose established
- 10 subjects with a median of 5 prior lines of tx and a median of 2 prior HER2-targeting tx treated with MT-5111 (metastatic cholangiocarcinoma n=5, MBC n=4, metastatic GE junction n=1)
- No DLTs have been observed in any cohort; no cardiotoxicity or abnormalities to date
- 4 subjects remained on treatment from the second (1 μg/kg/dose) and third cohorts (2 μg/kg/dose)
- AEs that may be causally related included: one grade 1 chills, one grade 1 hypophosphatemia, one grade 1 nausea, and one grade 2 AST↑. The grade 2 AST↑ occurred in a subject in cohort 1 with disease progression in hepatic met; no causally related AST/ALT elevations noted in any other subjects to date.
- The ongoing subject from cohort 2 (45 y/o female with MBC) had stable disease and remained on treatment (in cycle 5). One subject in cohort 3 with MBC with stable disease at the end of cycle 2
- Six subjects had discontinued for disease progression and two subjects were too early to evaluate
- Cohort 4 was opened (3 mcg/kg)
2nd-Generation ETBs
TAK-169 / CD38
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**
Primary mechanism of cell-kill - enzymatic ribosome destruction. pM potency against CD38+ cells.

**Other Properties**
Fusion protein; no linker chemistry. Short serum half-life; irreversible intra-cellular effects.
## TAK-169: 2nd-Gen ETB Targeting CD38

<table>
<thead>
<tr>
<th>CD38-targeting Agents</th>
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</thead>
<tbody>
<tr>
<td><strong>Mab:</strong> Darzalex</td>
<td><strong>Engineered Toxin Body:</strong> TAK-169</td>
</tr>
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</table>

### MOA

<table>
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<tr>
<th></th>
<th>Indirect CDC cell kill</th>
<th>Direct cell kill (enzymatic ribosome inactivation)</th>
</tr>
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### CD38 target interaction

<table>
<thead>
<tr>
<th></th>
<th>Binding</th>
<th>Binding and internalization</th>
</tr>
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### Limitations

<table>
<thead>
<tr>
<th></th>
<th>CD55/59 upregulation in failures, inhibiting immune response</th>
<th>None identified</th>
</tr>
</thead>
</table>

### Limitations

- CD38 is a poorly-internalizing receptor central to disease in multiple myeloma
- TAK-169 efficiently internalizes and destroys low- or high-expressing CD38
- TAK-169 activity is retained in the presence of daratumumab in preclinical models
- TAK-169 active in patient samples (including dara-refractory)
- TAK-169 has shown activity in xenograph models when dosed weekly or bi-weekly
- Reduced ADA and innate response (de-immunized STLA scaffold)
- HNSTD of 750 mcg/kg in NHPs (150 mcg/kg for MT-3724)
- Phase I in rel/ref myeloma patients with weekly dosing started at 50 mcg/kg
3rd-Gen ETBs / Novel Approach to IO

2nd-Gen Scaffold + antigen seeding
3rd-Gen Antigen Seeding: Altering the Tumor Immunophenotype

- ETBs localize to ER/cytosol to “seed” tumors with foreign non-self antigens
- Antigen cleaved intracellularly and 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
- Fundamental alteration of immunophenotype on tumor with foreign viral antigens to redirect T-cell response
MT-6402: Potent Activity Against PD-L1+ Tumor Cells

Potent effect on PD-L1+ tumor cells

- Direct cell-kill against PD-L1+ tumors through two diverse MOAs (ribosomal destruction and antigen seeding)
- Ribosomal destruction is independent of tumor microenvironment conditions
- Strong evidence that CMV-specific T-cells are present in tumor microenvironments (Rosato et al, *Nature Comm* 2019)

**MOA1 (ribosomal destruction)**

**MOA1 + MOA2 (AST)**
ETBs and IO: PD-L1 ETB Moving to Clinic; 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
- Novel alteration of cancer cell immunophenotype for pre-existing, synaptic T-cell recognition of tumor (MOA2)
- Early in vivo and in vitro data suggest potent activity on PD-L1 immune cells and activation of immune system

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

- CTLA4 lead development work underway; lead selection expected in 2020
- Potential safety and efficacy benefits around direct cell-kill of CTLA4+ T cells vs blocking
Engineered Toxin Bodies

Putting the scaffold in context
### ETB Scaffold Opportunity: Inherent Value Of Scaffolds In Oncology

<table>
<thead>
<tr>
<th>CAR-T</th>
<th>Bispecific</th>
<th>ETB</th>
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<tbody>
<tr>
<td><strong>Efficacy</strong></td>
<td>Potent activity with conditioning therapy</td>
<td>Yes (extracellular effects)</td>
</tr>
<tr>
<td><strong>Active against non-internalizing targets</strong></td>
<td>Yes (extracellular effects)</td>
<td></td>
</tr>
<tr>
<td><strong>Novel MOA</strong></td>
<td>T-cell engagement</td>
<td>T-cell engagement</td>
</tr>
<tr>
<td><strong>Combination</strong></td>
<td>Unclear</td>
<td>Unclear</td>
</tr>
<tr>
<td><strong>Solid tumor</strong></td>
<td>Unlikely</td>
<td>Unlikely</td>
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<tr>
<td><strong>Payload delivery</strong></td>
<td>No</td>
<td>No</td>
</tr>
<tr>
<td><strong>Companies</strong></td>
<td>Multiple</td>
<td>Multiple</td>
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- **MT-3724+Gem/Ox (Phase 2)**
- **MT-3724+ Len (Phase 2)**
- **MT-5111 in HER2+ tumors (Phase 1)**
- **MT-6402 in PDL1+ tumor (2020 IND)**
- **MT-6402 antigen seeding (2020 IND)**
# Robust Clinical Pipeline Driving Value of Drugs and Platform

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<thead>
<tr>
<th></th>
<th>2H20</th>
<th>1H21</th>
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<tr>
<td>MT-3724</td>
<td>Update on investigation of safety and PK</td>
<td>Possible resolution of partial clinical</td>
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<td>pertaining to partial clinical hold</td>
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<td>Phase 2 studies</td>
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<td>MT-5111</td>
<td>Phase 1 dose escalation data update</td>
<td>Completion of dose escalation</td>
<td>Potential interim dose expansion data</td>
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<td>Validation of de-immunized 2nd-Gen scaffold</td>
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