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): November 10, 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)	(I.R.S. Employer Identification No.)

9301 Amberglen Blvd, Suite 100
Austin, Texas 78729
(Address of Principal Executive Offices) (Zip Code)

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

(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 obligation 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 2.02. Results of Operations and Financial Condition.

On November 10, 2022, Molecular Templates, Inc. (the "Company") announced its unaudited financial results for the third quarter of 2022 ended September 30, 2022. The full text of the press release issued in connection with the announcement is furnished as Exhibit 99.1 to this Current Report on Form 8-K.

The information contained in this Item 2.02 and in the press release furnished as Exhibit 99.1 to this Current Report on Form 8-K shall not be deemed "filed" for purposes of Section 18 of the Securities Exchange Act of 1934, as amended or Sections 11 and 12(a)(2) of the Securities Act of 1933, as amended. The information contained in this Item 2.02 and in the press release furnished as Exhibit 99.1 to this current report on Form 8-K shall not be incorporated by reference into any filing with the U.S. Securities and Exchange Commission made by the Company whether made before or after the date hereof, regardless of any general incorporation language in such filing.

Item 7.01. Regulation FD Disclosure.

Attached hereto as Exhibit 99.2 and incorporated by reference herein is the November 11, 2022 Society for Immunotherapy of Cancer (SITC) 37th Annual Meeting presentation of the Company.

The information contained in this Item 7.01 and in the accompanying Exhibit 99.2 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.

99.1	Press Release dated November 10, 2022
99.2	Society for Immunotherapy of Cancer’s 37th Annual Meeting Presentation, dated November 11, 2022
104	Cover Page Interactive Data File (embedded within the Inline XBRL document)

SIGNATURE

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: November 10, 2022

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

EXHIBIT 99.1

Molecular Templates, Inc. Reports Third Quarter 2022 Financial Results

AUSTIN, Texas, Nov. 10, 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), to create novel therapies with potent and differentiated mechanisms of action for cancer and other serious diseases, today reported financial results and business updates for the third quarter of 2022.

"We are excited with the progress we continue to make across all our clinical and pre-clinical programs. We have now seen evidence of monotherapy clinical activity with MT-6402, MT-5111, and MT-0169 in heavily pretreated relapsed/refractory patients -- in both solid and hematological cancer settings -- demonstrating the broad potential utility of this novel scaffold," said Eric Poma, PhD., Chief Executive and Chief Scientific Officer of Molecular Templates. "We look forward to providing further updates on our MT-6402, MT-5111, and MT-0169 programs throughout 2023 and look forward to our anticipated IND submission for MT-8421 all while we continue to advance our development of additional ETB candidates targeting TROP2, TIGIT, and BCMA."

Company Highlights and Upcoming Milestones

Corporate

- MTEM expects to provide periodic updates on MT-6402, MT-5111, MT-8421, and MT-0169 throughout 2023.
- Dose escalation continues with MT-6402 with dose dependent pharmacodynamic (PD) effects observed. One patient in cohort 1 (16 mcg/kg) with non-small cell lung cancer (NSCLC) and osseous metastases demonstrated tumor regression. This patient is the only patient treated thus far with high tumor PD-L1 expression and HLA-A*02/ CMV+.
- MT-5111 has declared Maximum Tolerated Dose (MTD) at 23 mcg/kg with a dose limiting toxicity (DLT) of grade 3 rash. The HER2-positive breast cancer (BC) dose expansion cohort (DEC) continues to enroll patients at a dose of 10 mcg/kg. Three of five evaluable BC patients treated at 10 mcg/kg have had prolonged Stable Disease for 40, 22, and 22 weeks, respectively. One of the patients treated for 22 weeks has experienced a 43% reduction in mediastinal lymphadenopathy and a halt in the growth of her pulmonary lesions. Overall, the patient has had a 14% reduction in index lesions. This patient has been previously treated with multiple HER2-targeting therapies including trastuzumab, pertuzumab, trastuzumab emtasine, lapatinib, trastuzumab deruxtecan, and tucatinib.
- MT-0169 completed the 5 mcg/kg dose escalation cohort (N=4) without any cardiac adverse events (AEs) or DLTs and is enrolling at 10 mcg/kg. One patient with IgA myeloma treated at 5 mcg/kg has had a marked reduction in IgA serum protein, conversion from immunofixation positive to negative and marked improvement of hemoglobin to normal values, demonstrating at least a Partial Response. A PET scan is pending to determine if the patient is in a Complete Response.
- Of the over 80 patients treated across MTEM's three clinical programs to date, there has been no instance of capillary leak syndrome (CLS). One patient treated at 63 mcg/kg with MT-6402 showed a grade 2 decrease in albumin that may potentially represent a subclinical manifestation of CLS.
- All toxicities seen to date appear to be target-mediated and unrelated to the underlying scaffold.

ETB Technology

ETBs represent a novel platform with unique biology for therapeutic development in oncology. ETBs have the target specificity of antibodies, can force their own internalization, even against non-internalizing receptors, and can induce tumor cell death through the novel mechanism of enzymatic and irreversible ribosomal destruction. Because of this unique biology, ETBs to targets like HER2 and CD38 have the potential to drive clinical benefit in patients that have progressed after all available therapeutics. ETBs also represent a unique approach to immuno-oncology. Unlike current approaches to PD-L1 that only block the steric interaction of PD-1 and PD-L1, MT-6402, MTEM's ETB targeting PD-L1, is designed to directly kill PD-L1+ tumors cells, destroy immune cells that inhibit T-cell function and propagate tumor growth, and alter the immunophenotype of tumor cells.

MT-6402 (PD-L1 ETB with Antigen Seeding Technology)

- The Phase 1 study of MT-6402 is a multi-center, open-label, dose escalation and dose expansion trial. Patients with confirmed PD-L1 expressing tumors or confirmed PD-L1 expression in the TME are eligible for enrollment, irrespective of HLA genotype or CMV status.
- As of November 2022, 19 patients with relapsed/refractory tumors that express PD-L1 have been treated across four dose cohorts: 16 mcg/kg (n=6), 24 mcg/kg (n=6), 32 mcg/kg (n=4), and 42 mcg/kg (n=3). One DLT of grade 2 rash was observed in cohort 2 whereas no DLTs were reported in cohorts 1, 3 and 4. Enrollment continues in cohort 5 at 63 mcg/kg.
- One patient in cohort 1 (16 mcg/kg) with NSCLC demonstrated tumor regression of osseous metastases. This patient is the only patient treated thus far with high tumor PD-L1 expression and who is also HLA-A*02/ CMV+.
- MTEM continues to observe PD effects not seen with PD-L1 antibodies and consistent with the dismantling of the TME including PD-L1+ immune cell depletion and T cell activation, as well as cytokine changes in TNF-α, IL-2, and vascular endothelial growth factor (VEGF) in all dose escalation cohorts evaluated to date. The extent and timing of these PD effects appear dose-dependent with higher dose levels showing more rapid and profound PD effects, including MDSC depletion and T cell activation. These effects were seen across the majority of patients irrespective of HLA genotype or level of tumor or immune cell PD-L1 staining.
- Treatment-related AEs including immune related AEs have been largely restricted to grade 1-2.

MT-5111 (HER2 ETB)

- As of November 2022, the Phase 1 study of MT-5111 has enrolled 48 patients across 10 dose escalation cohorts ranging from 0.5 mcg/kg

to 23 mcg/kg. One DLT of grade 3 acneiform rash was observed at 23 mcg/kg, which improved to grade 1 with topical steroids, and the patient continued treatment at the same dose. 23 mcg/kg has been declared the MTD.

- Serum concentration of MT-5111 showed predictable and dose-proportional increasing exposure starting at 6.75 mcg/kg doses and higher.
- The HER2-positive BC DEC continues to enroll patients at a dose of 10 mcg/kg. Six patients have been treated, three of whom for 40, 22, and 22 weeks, respectively, at 10 mcg/kg.
- One of the patients treated for 22 weeks came on study with two nodal lesions and two non-nodal necrotic pulmonary lesions. The patient has seen a continued reduction in her nodal lesions while on therapy with a 43% reduction in mediastinal lymphadenopathy and a halt in the growth of her pulmonary lesions. Overall, the patient has had a 14% reduction in index lesions. This patient has been previously treated with multiple HER2-targeting therapies including trastuzumab, pertuzumab, trastuzumab emtasine, lapatinib, trastuzumab deruxtecan, and tucatinib. The next monotherapy cohort for BC patients is planned at 17 mcg/kg.
- No clinically significant cardiac AEs have been observed at any dose; grade 1 hs-troponin elevations have been observed at various doses.

MT-0169 (CD38 ETB)

- The Phase 1 study in patients with relapsed/refractory multiple myeloma (MM) or non-Hodgkin's lymphoma explores MT-0169 at doses lower than the initial dose of 50 mcg/kg to reduce the risk of AEs and to enable patients to continue MT-0169 therapy for a longer duration that may drive tumor benefit.
- The 5 mcg/kg cohort completed recruitment (N=4) and analysis with no related AEs higher than grade 1. CD38+ Natural Killer (NK) cell depletion was observed in cycle 1 and in cycle 2 for patients continuing therapy. Nadir levels of NK cells were delayed and lower in magnitude than observed at 50 mcg/kg. Enrollment at 10 mcg/kg has commenced.
- One patient with IgA myeloma treated at 5 mcg/kg has had a marked reduction in IgA serum protein, conversion from immunofixation positive to negative and marked improvement of hemoglobin to normal values, demonstrating at least a Partial Response. A PET scan is pending to determine if the patient is in a Complete Response.

Research and Development

- Preclinical data from MTEM's MT-8421 program targeting CTLA-4 was featured in an abstract at the 2022 Society for Immunotherapy of Cancer (SITC) annual meeting held November 8-12, 2022, in Boston, Massachusetts. Clinical studies for MT-8421 are expected to commence in mid-2023.
- MTEM continues to expand its unique approach to immuno-oncology targets with lead optimization ongoing for several targets.
- Lead optimization continues on ETBs targeting TROP-2 incorporating Antigen Seeding Technology, a TIGIT-targeting ETB and BCMA.

Upcoming Conferences

- MTEM will present four posters (736, 764, 817, and 1379) and provide an in-person R&D Day presentation at the SITC annual meeting, Friday, November 11, 2022, 11:30am – 12:30pm ET. SITC posters can be accessed via MTEM's corporate website. The webcast can be accessed here.
- MTEM will present a fireside chat at the virtual ISI HealthCONx Conference, Wednesday, November 30, 2022, at 9:15am ET. The webcast will be live-streamed and can be accessed here.
- MTEM will present at the 2022 San Antonio Breast Cancer Symposium (SABCS) taking place December 6 – December 10, 2022, in San Antonio, Texas.
- MTEM will participate at the American Society of Hematology's 64th annual meeting taking place December 10 – 13, 2022 in New Orleans, Louisiana. One-on-one meetings may be scheduled directly with MTEM.

Financial Results

The net loss attributable to common shareholders for the third quarter of 2022 was $24.6 million, or $0.44 per basic and diluted share. This compares with a net loss attributable to common shareholders of $30.4 million, or $0.54 per basic and diluted share, for the same period in 2021.

Revenues for the third quarter of 2022 were $4.2 million, compared to $2.4 million for the same period in 2021. Revenues for the third quarter of 2022 were comprised of revenues from collaborative research and development agreements with Bristol Myers Squibb.

Total research and development expenses for the third quarter of 2022 were $22.0 million, compared with $22.9 million for the same period in 2021. Total general and administrative expenses for the third quarter of 2022 were $5.9 million, compared with $9.0 million for the same period in 2021.

As of September 30, 2022, MTEM's cash and investments totaled $79.4 million.

For more details on MTEM's financial results for the third quarter 2022, refer to Form 10-Q filed with the SEC.

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 "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 MT-6402, MT-5111, MT-0169, and MT-8421 and Molecular Templates' next-generation ETBs; statements relating to the development of MT-6402, MT-5111, MT-0169, and MT-8421 and next-generation ETBs; the expected timing for submitting various IND applications and conducting studies, opening sites and generating data; the expected participation and presentation at upcoming conferences; the expected timing for providing updates on MT-6402, MT-5111, MT-0169, and MT-8421, including any pre-clinical or clinical data as well as Molecular Templates' pipeline of ETBs; statements relating to the progress of our collaboration agreement; Molecular Templates' future cash needs and the length of time for which Molecular Templates' cash resources are expected to be sufficient; 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 for cancer and other serious diseases.

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.

Contacts:
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Head of Investor Relations
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Molecular Templates, Inc.
CONDENSED CONSOLIDATED STATEMENTS OF OPERATIONS
(in thousands, except share and per share data)
(unaudited)

	Three Months Ended September 30,		Nine Months Ended September 30,	
	2022	2021	2022	2021
Research and development revenue, related party	$ —	$ —	$ —	$ 13,136
Research and development revenue, other	4,240	2,379	17,143	7,597
Total revenue	4,240	2,379	17,143	20,733
Operating expenses:				
Research and development	21,973	22,881	64,835	65,328
General and administrative	5,934	9,027	20,120	26,178
Total operating expenses	27,907	31,908	84,955	91,506
Loss from operations	23,667	29,529	67,812	70,773
Interest and other income, net	307	175	563	308
Interest and other expense, net	(1,252)	(1,033)	(3,394)	(2,301)
Net loss	24,612	30,387	70,643	72,766
Provision for income taxes	26	—	26	—
Net loss attributable to common shareholders	$ 24,638	$ 30,387	$ 70,669	$ 72,766
Net loss per share attributable to common shareholders:				
Basic and diluted	$ 0.44	$ 0.54	$ 1.25	$ 1.32

Weighted average number of shares used in net loss per share calculations:				
Basic and diluted	56,350,858	56,174,644	56,328,664	54,958,365

Molecular Templates, Inc.
CONDENSED CONSOLIDATED BALANCE SHEETS
(in thousands, except share and per share data)

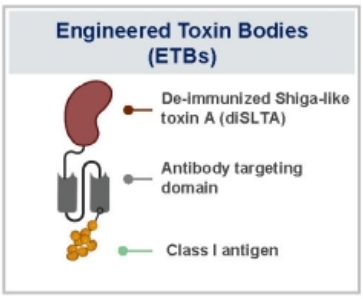
	September 30, 2022(unaudited)	December 31, 2021
ASSETS		
Current assets:		
Cash and cash equivalents	$ 22,277	$ 24,983
Marketable securities, current	57,168	118,061
Prepaid expenses	3,729	3,917
Other current assets	4,011	1,254
Total current assets	87,185	148,215
Marketable securities, non-current	—	8,986
Operating lease right-of-use assets	11,120	8,608
Property and equipment, net	16,347	19,309
Other assets	3,994	7,244
Total assets	$ 118,646	$ 192,362
LIABILITIES AND STOCKHOLDERS' EQUITY		
Current liabilities:		
Accounts payable	$ 1,085	$ 1,612
Accrued liabilities	8,890	9,515
Deferred revenue, current	38,290	32,937
Other current liabilities	1,957	2,606
Total current liabilities	50,222	46,670
Deferred revenue, long-term	14,641	33,350
Long-term debt, net of current portion	35,940	35,491
Operating lease liabilities	12,422	9,564
Other liabilities	1,269	1,625
Total liabilities	114,494	126,700
Commitments and contingencies		
Stockholders' equity		
Preferred stock, $0.001 par value:		
Authorized: 2,000,000 shares at September 30, 2022 and December 31, 2021; issued and outstanding: 250 shares at September 30, 2022 and December 31, 2021	—	—
Common stock, $0.001 par value:		
Authorized: 150,000,000 shares at September 30, 2022 and December 31, 2021; issued and outstanding: 56,351,647 shares at September 30, 2022 and 56,305,049 shares at December 31, 2021	56	56
Additional paid-in capital	427,042	417,704
Accumulated other comprehensive loss	(227)	(48)
Accumulated deficit	(422,719)	(352,050)
Total stockholders' equity	4,152	65,662
Total liabilities and stockholders' equity	$ 118,646	$ 192,362

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-6402, MT-5111, MT-0169, and MT-8421 and our next generation ETBs and 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 providing updates on our pipeline, including MT-6402, MT-5111, MT-0169 and MT-8421, and our earlier stage pipeline of ETBs; 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.

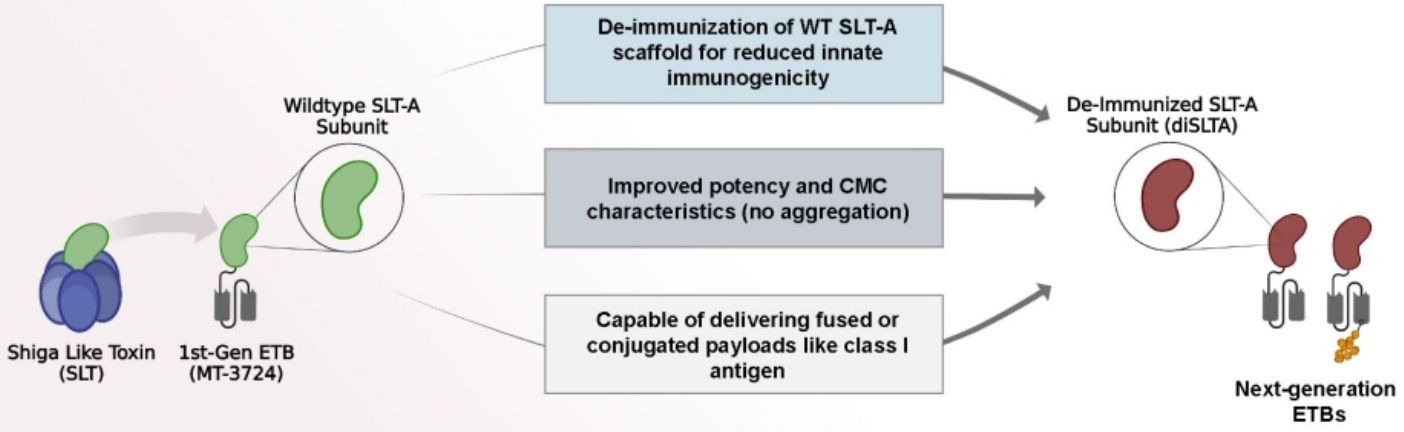
MTEM Platform: Engineered Toxin Bodies (ETBs) leverage novel MoAs for oncology

- **ETBs are next generation immunotoxins that leverage the unique biology of Shiga toxin to:**
  - Force internalization of non-internalizing receptors
  - Traffic intracellularly to the cytosol with potential to deliver other payloads like class I antigen
  - Induce potent direct-cell kill via the enzymatic and irreversible destruction of ribosomes
- **MTEM's first-gen ETB, MT-3724, provided clinical PoC around forced internalization, safety, and efficacy, but limited by innate immunogenicity / capillary leak syndrome (CLS) and aggregation**
- **Next-gen ETBs are more potent, de-immunized, and have improved CMC properties**
  - 80+ patients treated to date with de-immunized ETB scaffold across three clinical programs with no instance of CLS observed to date
- **Novel approach to I/O with next-gen ETBs**
  - Direct cell-kill and depletion of "bad actor" immune cells with ETBs to key checkpoint targets vs steric inhibition of checkpoint targets with current approved antibodies
  - Delivery of foreign class I antigen to alter tumor immunophenotype and redirect resident antigen-specific T-cells to the tumor ("Antigen Seeding")
- **Continued progress against validated oncology targets with next-gen ETBs**
  - Unique biology of ETBs can drive benefit in relapsed or refractory cancer patients



Next-Gen ETBs incorporate a proprietary deimmunized SLTA scaffold

- **Clinical validation provided by 1st-Gen ETB (MT-3724) targeting CD20 but limitations around innate immunogenicity / capillary leak syndrome and aggregation**
- **Next-Gen ETBs scaffold goes beyond addressing limitations of 1st-Gen ETB scaffold**



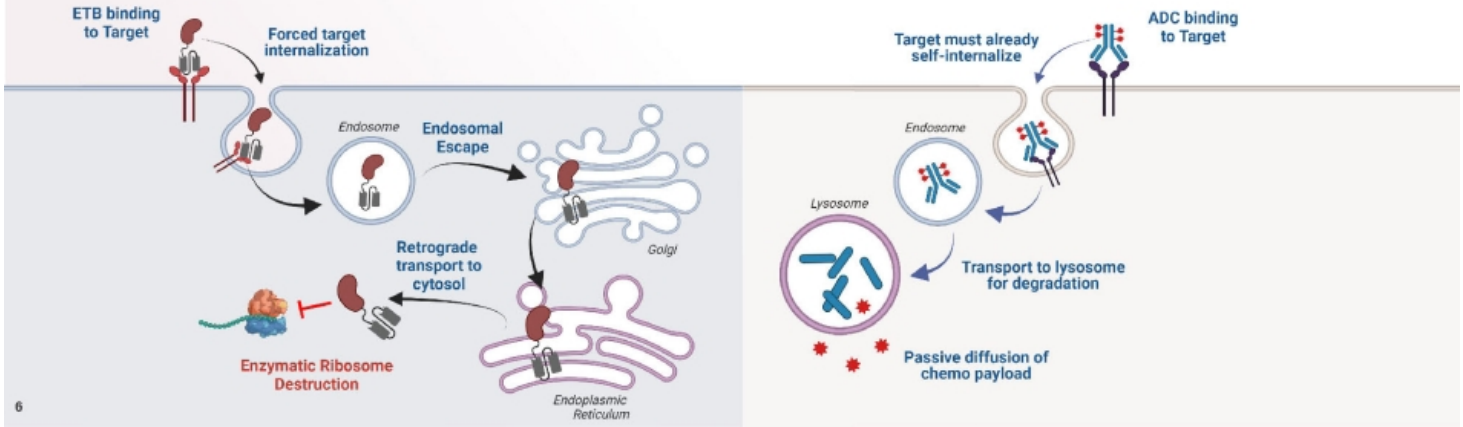
Next-Gen ETBs do not have innate immune AE of capillary leak syndrome (CLS)

- **Genetic engineering to de-immunize SLTA allows for unprecedented reduction of innate immunity in a bacterial protein**
- **In 80+ patients treated with next-gen ETBs, there has not been a case of CLS**
  - One noted case of Grade 2 albumin decrease (potential subclinical manifestation of CLS) on MT-6402 at 63 mcg/kg
  - No Grade 4 or Grade 5 events seen with diSLTA; no off-target heme toxicity seen with diSLTA
  - Unlike with ADCs, no release of payload seen with ETBs; may explain lack of systemic toxicity

	Treatment	Scaffold	Dose level	CLS (all grades)
Approved Immunotoxins	Elzonris	IL-3 diphtheria fusion	12 mcg/kg	55% (52/94)
	Ontak	IL-2 diphtheria fusion	9 or 18 mcg/kg	33% (76/234)
	Lumoxiti	CD-22 scFv pseudomonas fusion	40 mcg/kg	34% (44/129)
1st-Gen ETB	MT-3724 (Monotherapy)	CD20 scFv wild-type SLTA fusion	5 through 100 mcg/kg	53% (20/38)
Next-Gen ETBs	MT-6402	PD-L1 scFv de-immunized SLTA fusion	16 through 63 mcg/kg (dose escalation ongoing)	**0% (0/23)**
	MT-5111	HER2 scFv de-immunized SLTA fusion	0.5 through 23 mcg/kg (MTD declared at 23 mcg/kg)	**0% (0/48)**
	MT-0169	CD38 scFv de-immunized SLTA fusion	5 and 50 mcg/kg (dose escalation ongoing)	**0% (0/9)**

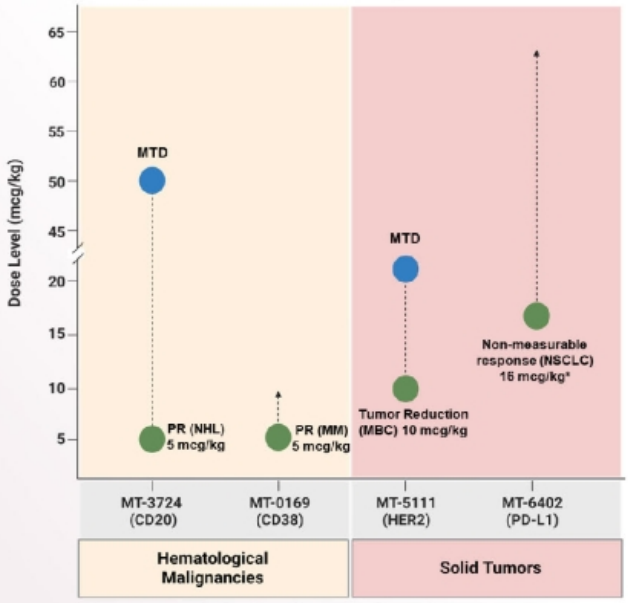
ETBs have differentiated biology and MOAs compared to ADCs

	ETBs	Antibody Drug Conjugates (ADC)
Amenable Targets	Internalizing or non-internalizing	Targets must readily internalize
Intracellular Routing	Endosomal escape and self-routing to cytosol	No endosomal escape; shuttled to lysosome
Cytosolic/ER Delivery	Yes	No
MOA	Enzymatic ribosome inactivation	Chemo; stoichiometric
Off-Target Payload Release	No	Yes



ETBs demonstrate pharmacodynamic and clinical activity in hematological and solid tumors at low doses

Higher dose levels may be required for solid tumors to penetrate the TME vs hematological tumors



** Response likely due to antigen seeding activity*

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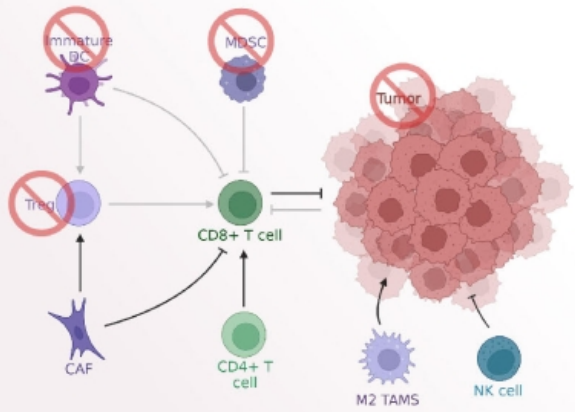
tem

Novel approach to I-O targets

Dismantling the TME and altering tumor immunophenotype

A novel approach to immuno-oncology

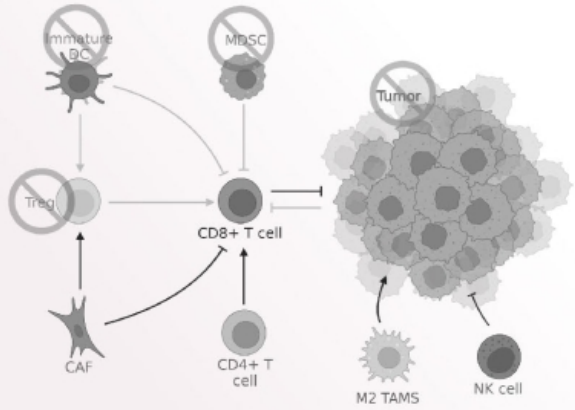
Dismantling the TME



ETBs are designed to potently destroy tumor and immune cells to dismantle the TME

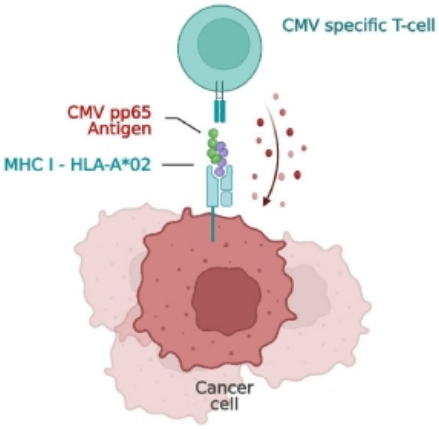
A novel approach to immuno-oncology

Dismantling the TME



ETBs are designed to potently destroy tumor and immune cells to dismantle the TME

Altering Tumor Immunophenotype

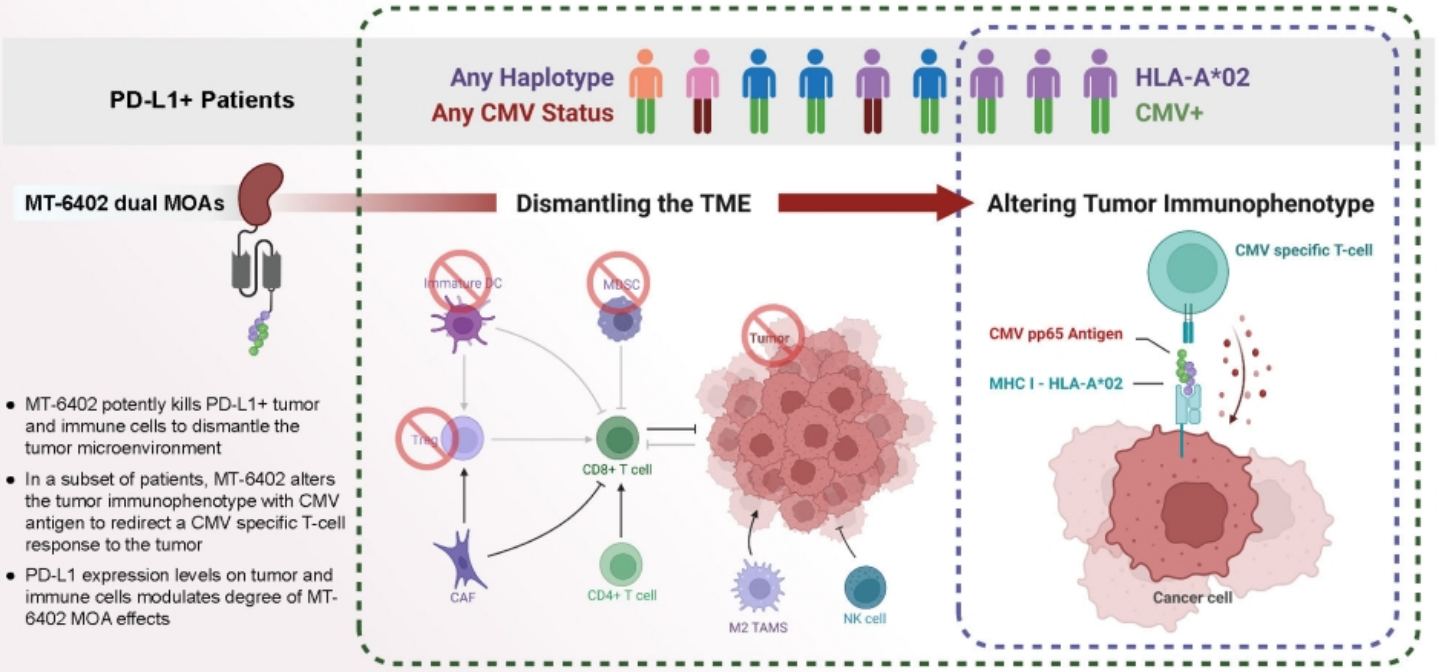


ETBs can deliver foreign antigens to alter the tumor's immunophenotype and redirect pre-existing antigen specific T-cells to destroy tumor ("Antigen Seeding")

MT-6402: A novel approach to PD-L1

Part 1 – Altering tumor immunophenotype

MT-6402 targets PD-L1 with dual mechanisms of action



- MT-6402 potently kills PD-L1+ tumor and immune cells to dismantle the tumor microenvironment
- In a subset of patients, MT-6402 alters the tumor immunophenotype with CMV antigen to redirect a CMV specific T-cell response to the tumor
- PD-L1 expression levels on tumor and immune cells modulates degree of MT-6402 MOA effects

MT-6402 clinical overview

- **Four dose escalation cohorts completed (16, 24, 32, and 42 mcg/kg)**
  - Patients with any solid tumor type expressing any level of PD-L1 on either the tumor or immune cells
  - Patients do not have to be CMV+ and/or HLA-A*02
  - Patients with a tumor type indicated for checkpoint therapy must have progressed after checkpoint therapy
  - 63 mcg/kg dose cohort currently enrolling
- **Immune related AE's of grade 2 severity observed (CRS, fever, IRR, rash)**
  - One Grade 3 event of back pain during infusion at 16 mcg/kg (treated with ibuprofen), considered a manifestation of an IRR; one grade 3 IRR at 63 mcg/kg
  - One Grade 3 event of elevated lipase/amylase at 42 mcg/kg in the setting of intra-abdominal disease progression and porta hepatis compression
  - One Grade 2 rash at 24 mcg/kg
- **Clinical efficacy in an evaluable patient at 16 mcg/kg with near resolution of NSCLC osseous metastases with duration on treatment of approximately 8 months**

MT-6402 Phase I: Patient demographics, PD-L1 expression, and haplotype / CMV status

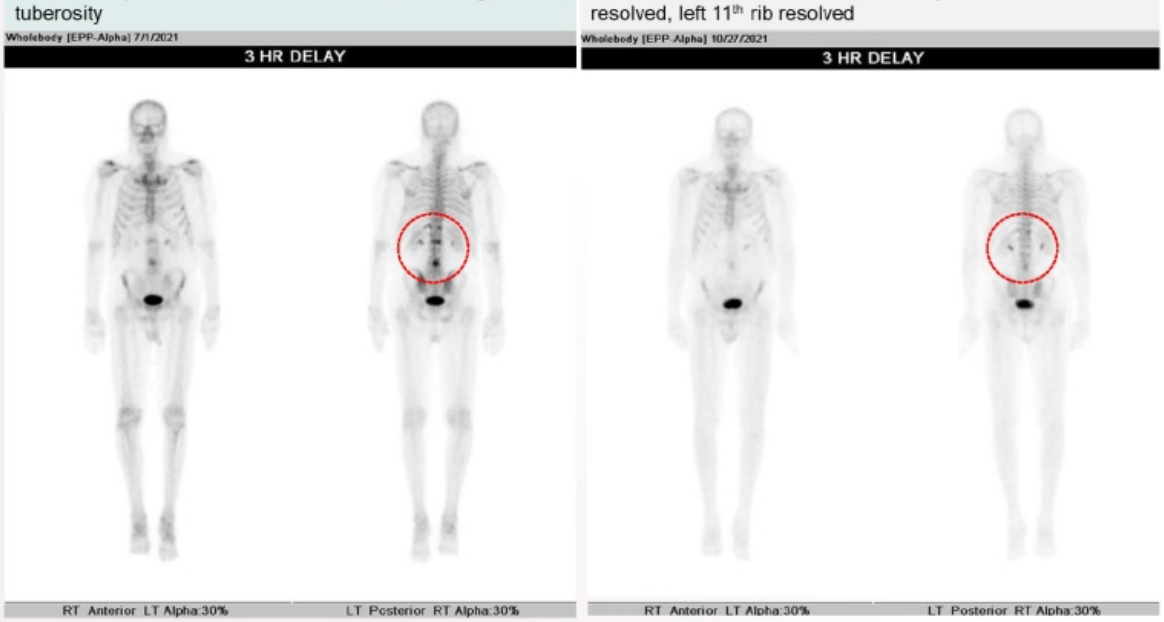
	Patient ID	Disease	Lines of Tx	Prior CPI	Best Response to prior CPI	PD-L1 Expression	Antigen Seeding Engaged (HLA-A*02/CMV+)
Cohort 1 (16 µg/kg)	1008-001	NSCLC	1	Nivo+Ipi 1L	Unk (1Y)	**TPS 80%**	Yes
	1004-002	NSCLC	3	Pem 1L	Unk	**TPS 70%**	No
	1001-001	Melanoma	3	Pem Adjuvant Nivo 1L	Adjuvant	n.a	No
	1002-003	Ovarian	2	--	--	CPS > 1	Unk
	1005-002	Solid tumor	4	--	--	TPS 10%	No
	1004-003	NSCLC	3	Pem 1L & PD-1 + TIM-3	PD	CPS > 1	Yes
Cohort 2 (24 µg/kg)	1007-005	Esophageal	3	Pem 2L	PD	CPS 10	Yes
	1004-004	Solid tumor	5	Nivo 2L	SD	TPS 20%	N/A
	1001-002	NSCLC	2	Pem 1L	PD	TPS 10%	No
	1001-004	RCC	4	Nivo + Ipi 1L	PD	TPS 1%	No
	1008-002	Pancreatic	5	--	--	TPS 5%	No
	1001-005	CSCC	9	Cemi 4 & 5L	Unk	CPS 3	Yes
Cohort 3 (32 ug/kg)	1005-005	Colon	4	--	--	n.a	No
	1005-007	Esophageal	2	Nivo + Ipi maintenance	Unk	TPS ≥ 1%	No
	1001-006	Breast	9	Pem 7L	PD	CPS 10	No
	1005-008	Pancreatic	4	CD47 Mab	--	TPS 1-20%	Yes
Cohort 4 (42 ug/kg)	1017-001	Peritoneal Meso	4	Pem 2L	PD	TPS 10%	No
	1024-001	Colon	3	--	--	IC 20%	Yes
	1017-002	GEJ	1	Nivo 2L	PD	CPS 25-35	No

- *Green shaded patient is able to engage Antigen Seeding MOA (HLA-A*02+/CMV+) and has high PD-L1 expression*
- *Yellow shaded patients are able to engage Antigen Seeding MOA but have low PD-L1 expression*
- *Median age: 63 years (min 33, max 81); 13 male (72.0%), 6 female (28.0%)*
- *Historical tumor biopsy evidence of PD-L1 by FDA-approved assays (22C3, 28-8, SP263, SP142) per local institution*

Subject 1008-001 (16 mcg/kg – HLA-A*02/CMV+): Resolution/decrease of osseous lesions

Jul 01, 2021
Metastatic uptake: L1, T11, left 11th rib, left 5th rib, right ischial tuberosity

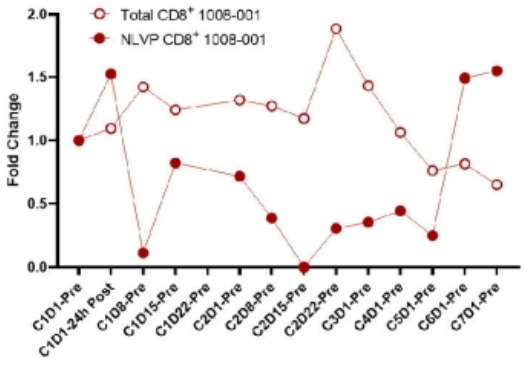
Oct 27, 2021
Interval decrease of T11, L1 has mostly resolved, left 5th rib resolved, left 11th rib resolved

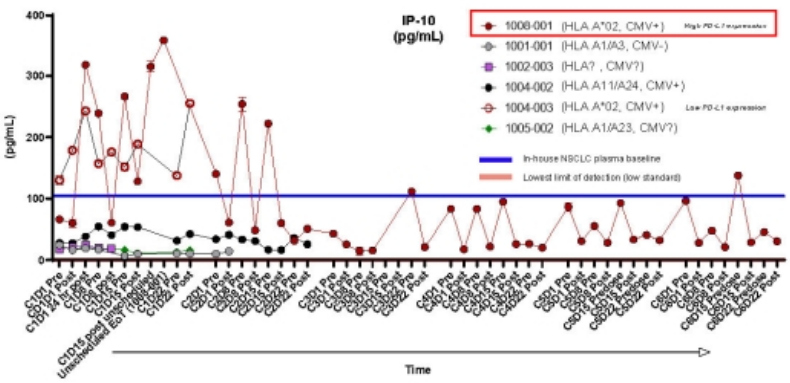


Patient 1008-001

- NSCLC w/only osseous disease
- HLA-A*02, CMV+ - Antigen Seeding available
- High PD-L1 tumor staining
- Progressed after Ipi/Nivo
- Not eligible for chemo
- NSCLC patients with bone metastases substantially less likely to respond to I/O

CMV-specific T-cells leave the periphery and IP-10 is elevated in subject 1008-001 (high PD-L1)





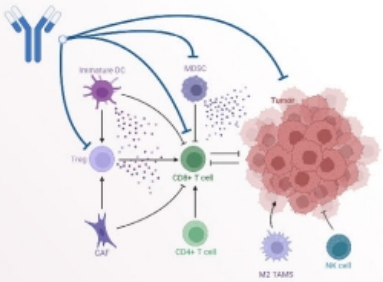
- **Trafficking of CMV-specific CD8 T cells observed only in HLA-A*02/CMV+ patients**
- **Changes in IP-10, which functions to mobilize T-cells,-correlate with extravasation in HLA-A*02/CMV+ patients**
- **General CD8 T cells (non-CMV specific) increase, indicating a likely general T cell expansion due to checkpoint break**

MT-6402: A novel approach to PD-L1

Part 2 – Dismantling the TME

Checkpoint blockade does not deplete immunosuppressive immune cells in TME

Antibody mediated checkpoint blockade



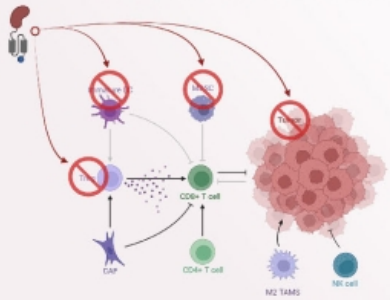
Avelumab, a PD-L1 Mab w/ effector function, does not eliminate peripheral MDSCs or Tregs (or any other immune cell type)[1]

Table 3 Effect of avelumab on classic and PD-L1^{+} classic immune cell subsets

	Pre vs 1 cycle				Pre vs 9 cycles			
Subset	Increase	Minimal change	Decrease	P-value	Increase	Minimal change	Decrease	P-value
A. Classic subsets								
CD4	0 (0%)	18 (95%)	1 (5%)	0.0230 (†*, 0.2070)	0 (0%)	12 (75%)	4 (25%)	0.0063 (‡*, 0.0567)
CD8	1 (5%)	16 (84%)	2 (11%)	0.1447 (=)	3 (19%)	11 (68%)	2 (13%)	0.9799 (=)
Tregs	7 (37%)	10 (53%)	2 (10%)	0.2253 (=)	2 (12%)	7 (44%)	7 (44%)	0.0934 (=)
NK	5 (26%)	10 (53%)	4 (21%)	0.8268 (=)	0 (0%)	9 (56%)	7 (44%)	0.0182 (‡*, 0.1456)
NK-T	2 (11%)	15 (78%)	2 (11%)	0.2413 (=)	1 (6%)	12 (75%)	3 (19%)	0.1046 (=)
B cells	5 (26%)	12 (63%)	2 (11%)	0.7381 (=)	6 (38%)	5 (31%)	5 (31%)	0.8209 (=)
cDC	3 (16%)	15 (79%)	1 (5%)	0.3955 (=)	6 (37%)	7 (44%)	3 (19%)	0.7436 (=)
pDC	6 (32%)	8 (42%)	5 (26%)	0.4900 (=)	6 (38%)	9 (56%)	1 (6%)	0.0833 (=)
MDSC	8 (42%)	8 (42%)	3 (16%)	0.1232 (=)	8 (50%)	7 (44%)	1 (6%)	0.0833 (=)

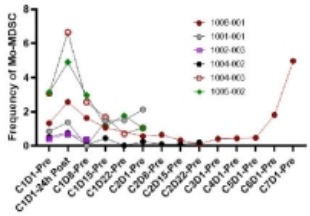
1. Donahue R, et al. Analyses of the peripheral immunome following multiple administrations of avelumab, a human IgG1 anti-PD-L1 monoclonal antibody. J Immunother Cancer 2017;5: 20

ETB-mediated immune cell clearance

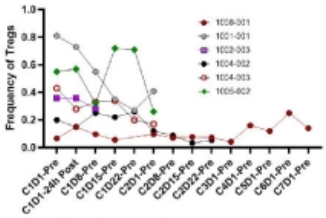


ETB-mediated destruction of MDSCs and Tregs

Cohort 1 (16 mcg/kg) – Mo-MDSC (frequency of live cells)



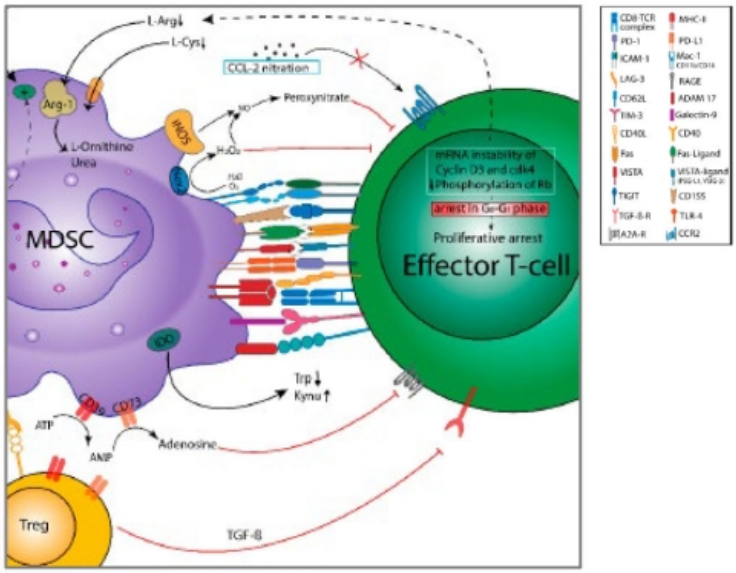
Cohort 1 (16 mcg/kg) – Tregs (frequency of CD45+ cells)



- MDSCs and Tregs are important biomarkers of non-response to ICIs
- MT-6402 inducing shift toward "responder" phenotype

MDSCs block T-cell function and promote tumor growth

- Peripheral expression of MDSC correlates with poor prognosis and low likelihood of response to PD-1 therapy[1,2]
  - Multiple interactions between MDSCs and T-cells beyond PD-1/PD-L1
- MDSCs inhibit immune surveillance, induce angiogenesis, and promote metastasis[3]
- Expression ADAM17 on MDSC decreases CD62L expression on CD8+ T cells inhibiting trafficking
- Can MT-6402 destruction of peripheral MDSCs restore T-cell functionality / trafficking?

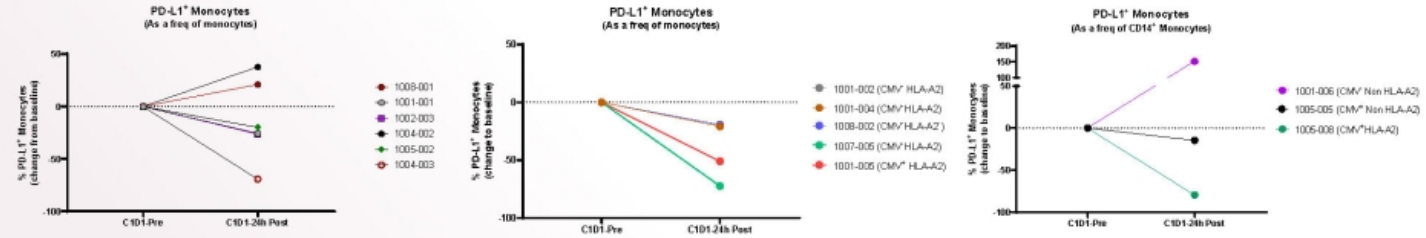


1. Koh et al, Eur J Immunol. 2020 Nov; 50(11): 1810–1819
2. Ostrand-Rosenberg Annual Review of Cancer Biology. Vol 5. 2021
3. Weber et al, Front Immunol. 2018; 9: 1310
4. Haist et al, Cancers 2021: 13(2)

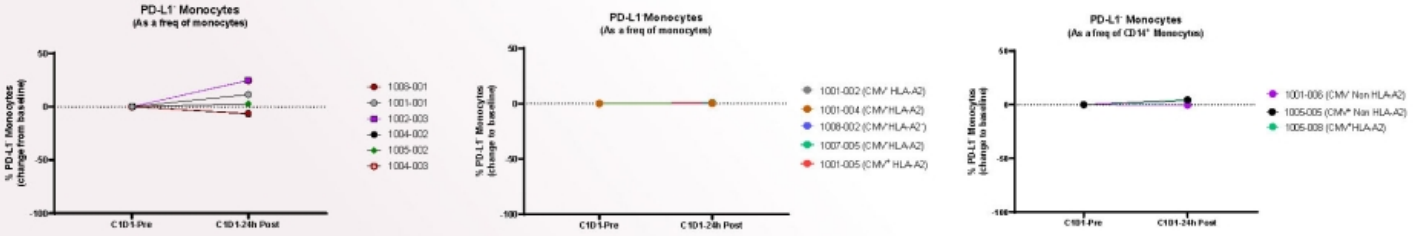
MT-6402 depletes PD-L1+ peripheral monocytes

Cohort 1 (16 ug/kg) | Cohort 2 (24 ug/kg) | Cohort 3 (32 ug/kg)

PD-L1 positive monocytes



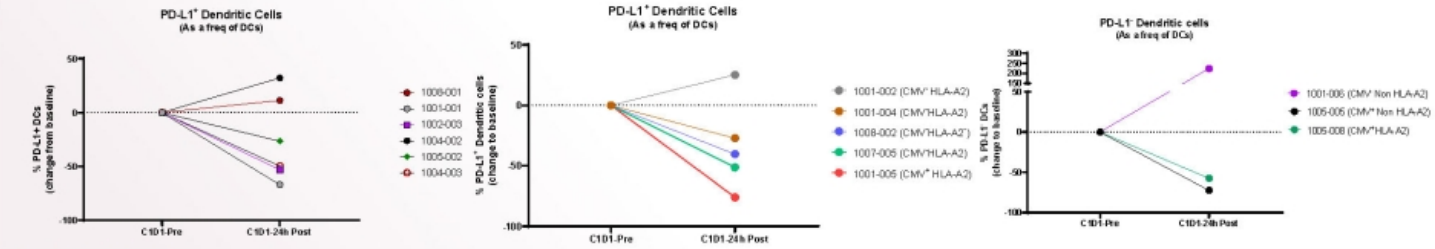
PD-L1 negative monocytes



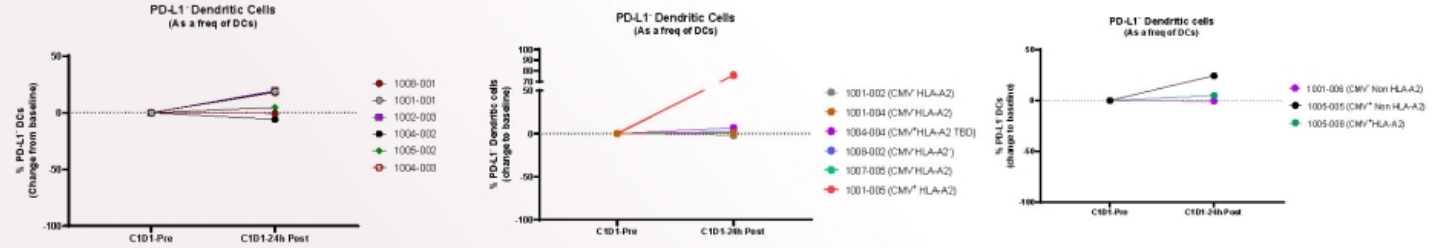
MT-6402 depletes PD-L1+ peripheral dendritic cells

Cohort 1 (16 ug/kg) | Cohort 2 (24 ug/kg) | Cohort 3 (32 ug/kg)

PD-L1 positive DCs

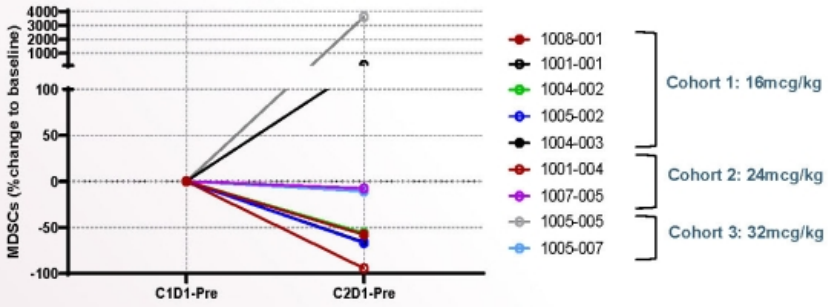


PD-L1 negative DCs



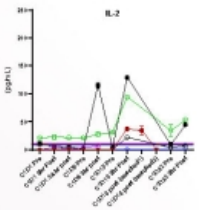
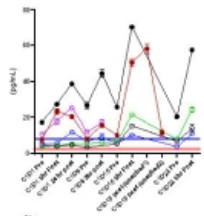
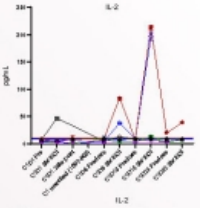
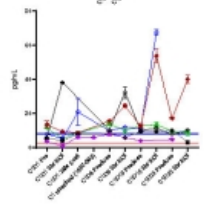
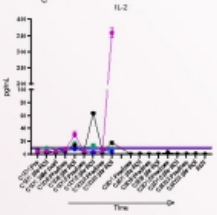
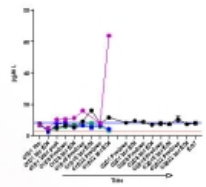
MT-6402 depletes MDSCs in the periphery

- **MDSCs are depleted in the periphery after one cycle of treatment in 7/9 patients**
  - MDSCs not sorted based on PD-L1 positivity
- **Pre- and post-treatment tumor biopsies will be conducted once RP2D is established to assess depletion in TME**



Increases in “good” cytokines associated with immunological anti-tumor responses

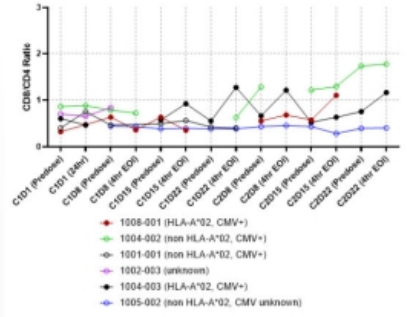
IL-2 and TNF-α can drive T cells toward an activated/proliferative phenotype

	IL-2	*IL-2 spike*	TNF-α	*TNF-α spike*
Cohort 1 (16μg/kg)		2/6 (33%)		2/6 (33%)
Cohort 2 (24μg/kg)		2/6 (33%)		3/6 (50%)
Cohort 3 (32μg/kg)		2/4 (50%)		1/4 (25%)

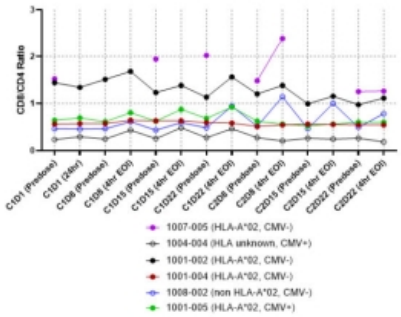
CD8/CD4 T cell ratio increases with each MT-6402 dosing: shift toward “effector” phenotype

- Increased CD8/CD4 ratio is a hallmark of “re-awakening” T cell responses
- CD8/CD4 ratios continue elevations in all higher dose cohorts

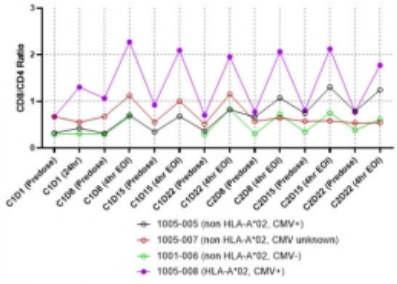
16 μg/kg



24 μg/kg

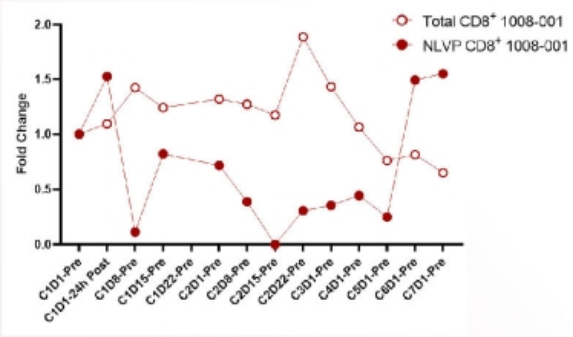


32 μg/kg

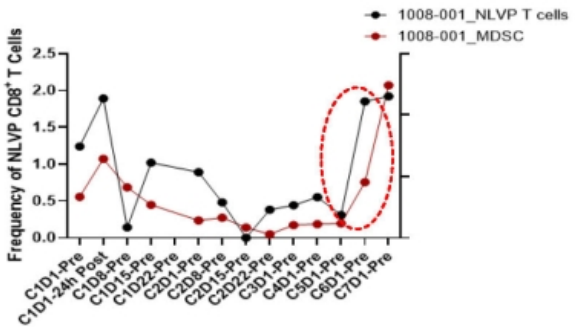


Anti-tumor T-cell effect dependent on MDSC clearance via MT-6402

NLVP T-cell Trafficking vs Total T-cell Trafficking



NLVP T-cells Trafficking vs MDSC Levels



- Trafficking of CMV specific CD8 T cells caused by antigen seeding of NLVP antigen in tumor and PD-L1+ cells
- MDSCs are known to inhibit T-cell trafficking and trafficking of antigen specific T-cells are only observed when MDSC levels are low
- Patient had disease progression at cycle 8 following return of MDSCs and inhibition of T-cell trafficking

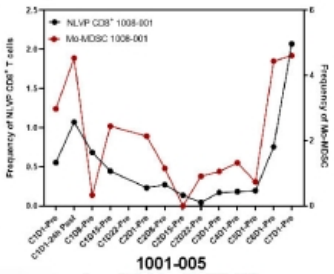
Monotherapy activity appears dependent on MDSC clearance to restore T-cell activity

Even in low PD-L1 expressing patients, evidence that MT-6402 can eliminate MDSCs and restore T-cell trafficking

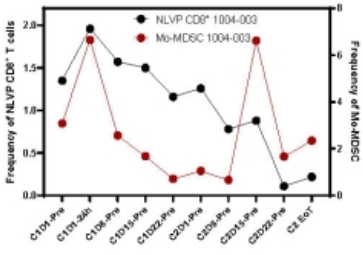
T-cell trafficking/biology is dependent on MDSC clearance

- Trafficking of NLVP specific T-cells correlates with reduction in MDSCs
- Trafficking not observed in patients when peripheral MDSCs are high

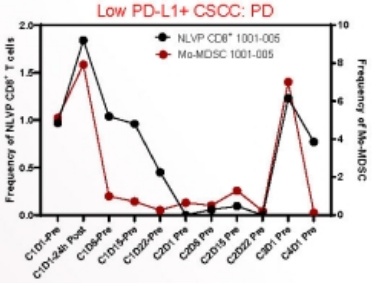
1008-001
High PD-L1+ NSCLC: tumor reduction



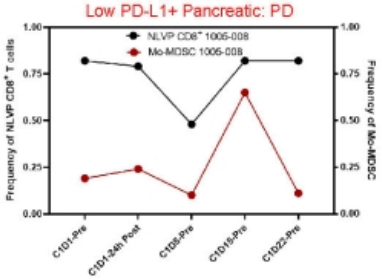
1004-003
Low PD-L1+ NSCLC: PD



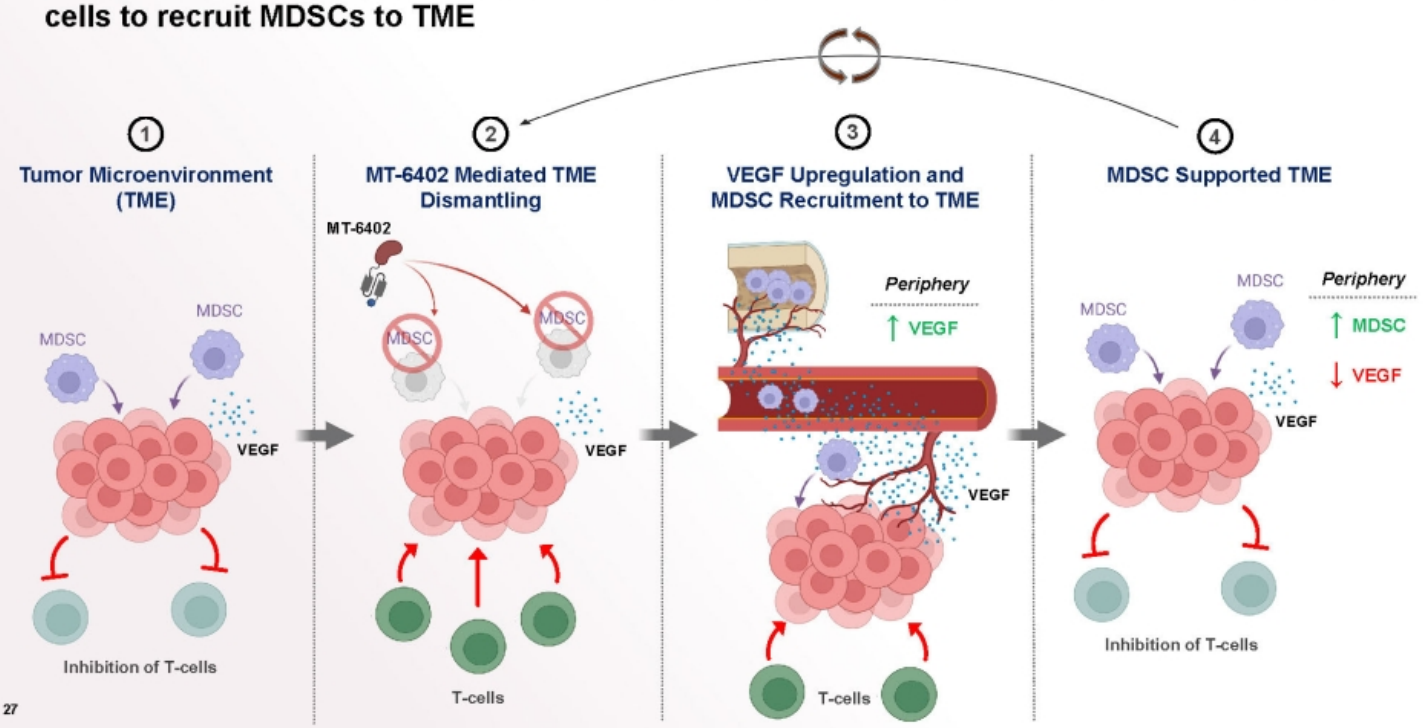
1001-005
Low PD-L1+ CSCC: PD



1005-008
Low PD-L1+ Pancreatic: PD



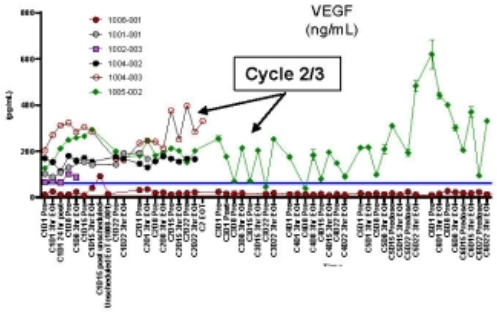
MT-6402 depletes MDSCs and may result in a compensatory upregulation of VEGF by tumor cells to recruit MDSCs to TME



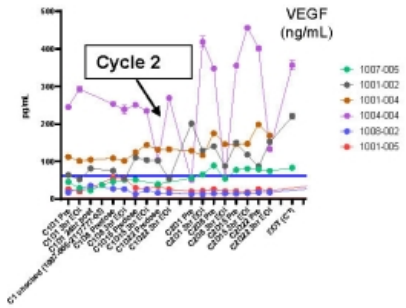
Tumors secrete VEGF to attract MDSCs as cornerstone of the TME

- **Patients treated with MT-6402 show pronounced dose-dependent changes in serum VEGF**
  - Patients demonstrate a "sawtooth" pattern of changes in serum VEGF; onset appears dose-dependent
  - Increases in VEGF may represent the tumor's attempt at re-establishing MDSCs in the TME
  - Modulation of VEGF has not been observed with other ICI therapies

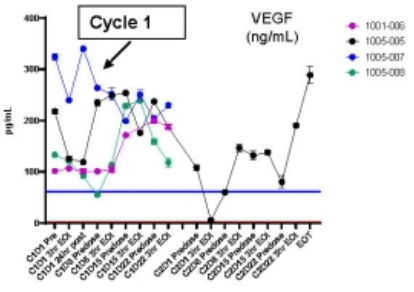
Cohort 1: 16 mcg/kg



Cohort 2: 24 mcg/kg



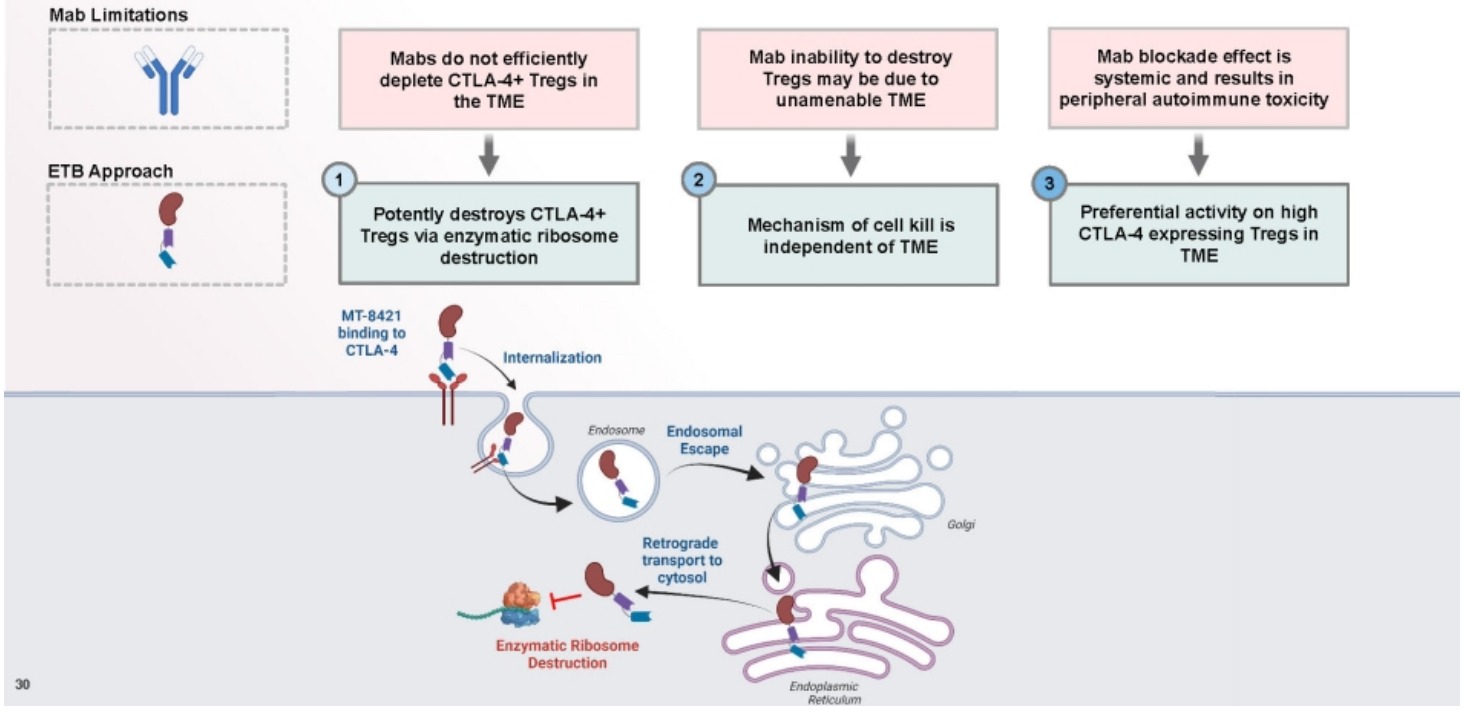
Cohort 3: 32 mcg/kg



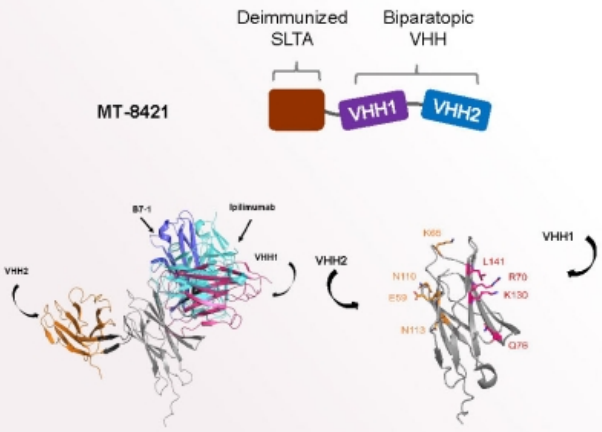
MT-8421

ETB with novel MOA targeting CTLA-4

MT-8421: ETB dismantling the TME by destroying CTLA-4+ Tregs

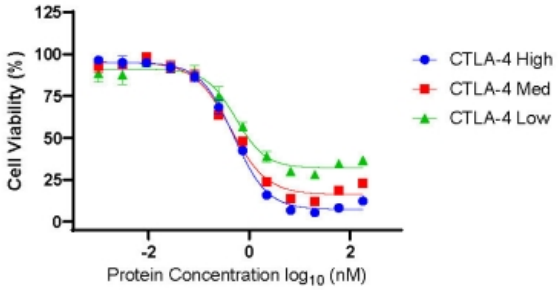


MT-8421: CTLA-4 targeting ETB



Docked structure is superimposed on crystal structure of complex of CTLA-4 with Fv of ipilimumab (PDB: 5TRU, cyan) and B7-1 (PDB: 1I8L, blue). CDR3 loop of VHHs are colored black. Docking supports that VHH1 competes with Ipilimumab for a similar epitope region, while VHH2 binds in a distinct epitope region

Potency is specific and dependent on receptor density

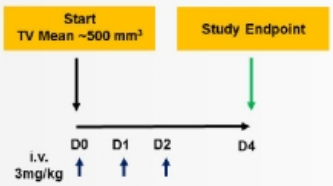


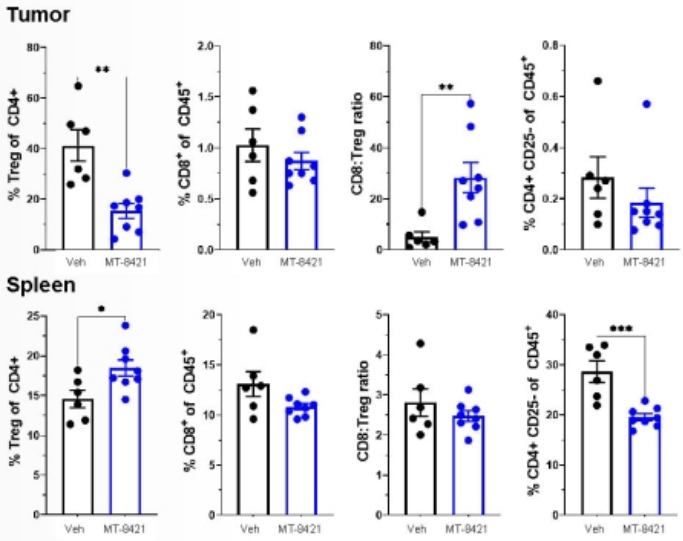
Cell Line	Approx. Receptors/Cell	ETB IC50 [nM]	% Viability at Max Dose
High	4510	0.49	12.4
Med	2617	0.42	22.9
Low	1262	0.54	36.5

Viability of various cell lines was measured 96 hours after ETB addition to cells. IC50 values reported in nM. The cell lines represent different subclones of the same parental hCTLA-4-CHOK1 monoclonal cell line; each subclone was selected to represent a different range of CTLA-4 Expression.

MT-8421 Pharmacodynamic activity in MC38 mouse model

T cell Immunophenotyping in a tumor-bearing syngeneic humanized mouse model



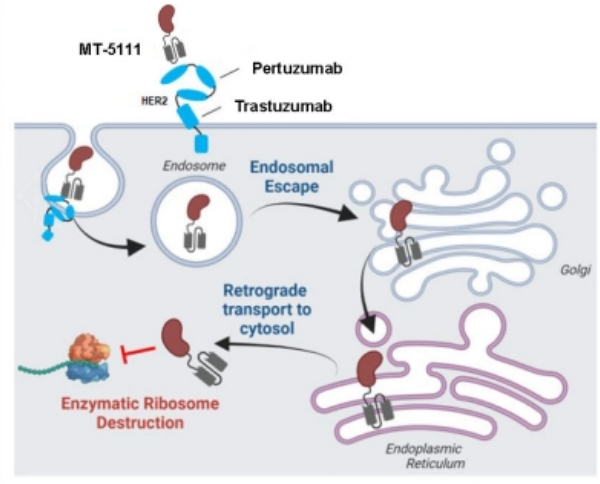


Human CTLA-4 knock-in HuGEMM mice (Biocytogen) were inoculated with MC38 tumors. When the tumors reached 500 mm³, ETB was dosed at 3 mg/kg for 3 consecutive days. On day 4, the tumors and spleens were harvested and processed for immunophenotyping. The % CD4+ effectors, CD8+ CTLs and Tregs from the tumor and spleen are displayed on the graphs.

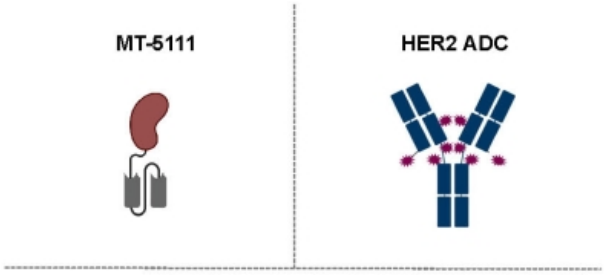
MT-5111

ETB with novel MOA targeting HER2

MT-5111: Anti-HER2 modality with differentiated biology



- MT-5111 binds HER2 at a distinct epitope from trastuzumab and pertuzumab
- Potent direct cell kill (pM) against HER2 expressing cancer cells through ribosomal destruction
- No inhibition of HER2 signal transduction effects



- Potent MOA of ribosomal destruction that is not subject to resistance mechanism of Mabs or ADC chemo payloads
- Distinct HER epitope binding allows for combination potential with Mabs and ADCs
- Lack of hematological toxicity
- Smaller size (monomer – 55kDa) may allow for improved tumor penetration

MT-5111 activity at 10 mcg/kg in breast cancer

- **MTD reached at 23 mcg/kg as part of dose escalation cohort**
  - One patient with Grade 3 acneiform rash, treated with topical steroids and improved quickly to Grade 1
  - Several patients with Grade 1 hs-troponin elevations without symptoms, EKG changes, or reductions in LVEF
- **Mean serum concentration of MT-5111 increases in a dose-proportional manner at doses ≥ 6.75 mcg/kg**
  - Breast cancer expansion cohort initiated at 10 mcg/kg based on PK data
- **5 evaluable pts treated on breast cancer expansion cohort at 10 mcg/kg; 2 patients remain on study**
  - One breast cancer patient (6101-001) has completed 13 cycles
  - One breast cancer patient (1009-005) has a 14% total reduction in tumor size (~43% reduction in two nodes and no growth in two non-nodal lesions)

Subject ID	HER2 Status	Dose (mcg/kg)	Last Dose Received	Best Response	Prior Rx (# of lines)	Prior HER2-targeting Rx (duration on selected prior Rx)
6101-001	IHC 3+	10	C14D8 (40 w) On-Rx	SD (+5.7%)	4	TRA, PER, T-DM1 (8 mo)
1009-004	IHC 2+	10	C9D1 (24 w) Off-Rx	SD (+4.5%)	9	TRA, PER, TUC, DHES0815A, T-DXd (3 mo)
1009-005	IHC 2+	10	C8D8 (22 w) On-Rx	SD (-14%)	10	TRA, PER, T-DM1 (5 mo), T-DXd (21 mo), TUC (10 mo)

***Abbreviations**: TRA-Trastuzumab; PER-Pertuzumab; T-DM1-ado-Trastuzumab emtansine; T-DXd-fam-trastuzumab deruxtecan; TUC-Tucatinib; DHES0815A-Investigational HER2-directed ADC; Inv mAb- Investigational mAb.*

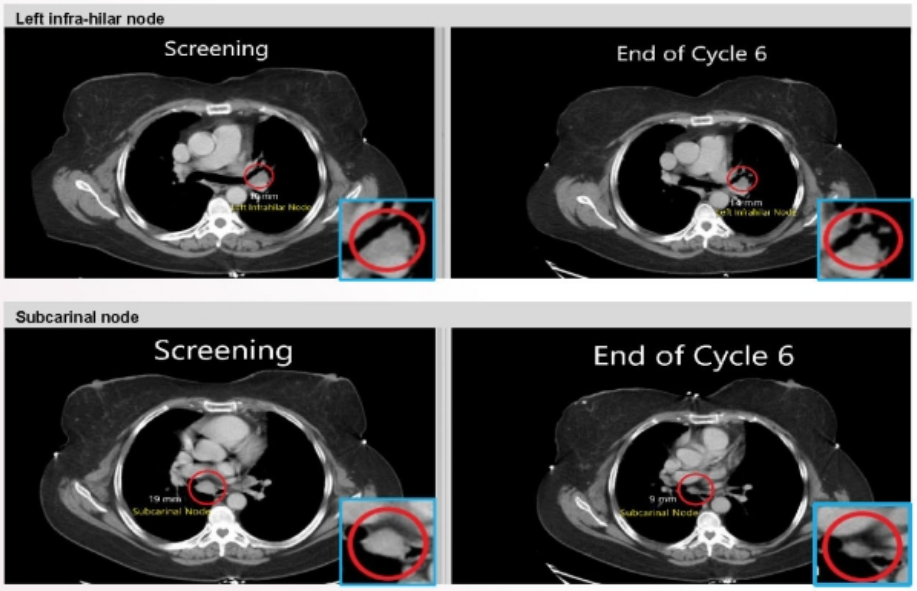
Spotlight on Subject 1009-005

- **Patient diagnosed with Stage IV metastatic breast cancer since October 2015**
  - HER2 IHC 2+, ISH amplified, moderately differentiated invasive ductal carcinoma of the right breast with multiple metastases to the lung and mediastinal lymphadenopathy including left infra-hilar, subcarinal and right paratracheal nodes
- **10 previous lines of tx including trastuzumab, pertuzumab, trastuzumab emtansine, lapatinib, trastuzumab deruxtecan, and tucatinib**
- **Response to treatment: Total target tumor size has progressively decreased by 14% after six cycles of therapy**
  - The two nodal lesions (i.e., left infra-hilar node and subcarinal node) have significantly decreased in size **(~43% reduction)**
  - The non-nodal lesions (i.e., necrotic LUL and RLL masses) have remained stable in size.
  - Per the treating physician, these lesions grew in the past and the patient had pulmonary symptoms.

Target Lesion	Screening 20 May 22	Assessment 1 12 Jul 22	Assessment 2 22 Aug 22	Assessment 3 04 Oct 22
LUL mass (lung)	31 mm	31 mm	31 mm	31 mm
Left Infra-hilar LN	18 mm	18 mm	18 mm	**14 mm (-22%)**
Sub-Carinal LN	22 mm	22 mm	**13 mm (-41%)**	**9 mm (-59%)**
RLL mass (lung)	51 mm	51 mm	51 mm	51
Total % Change	122 mm	122 mm	**113 mm (-7.4%)**	**105 mm (-14%)**

Spotlight on Subject 1009-005

Patient diagnosed with Stage IV metastatic breast cancer



MTem

MT-0169

ETB with novel MOA targeting CD38

Initial MT-0169 starting dose of 50 mcg/kg exceeded therapeutic window

- **Five heavily pretreated R-R MM patients were treated at the initial Phase I starting dose of 50 mcg/kg**
  - Highest starting dose of any ETB clinical program
- **Two patients had asymptomatic and reversible cardiac DLT's**
  - Grade 2 reversible myocarditis and Grade 3 reversible non-ischemic cardiomyopathy
  - All patients demonstrated very rapid clearance of CD38+ NK cells within hours of 1st dose of MT-0169
  - CD38 expressed at low levels on myocardial endothelial cells; high starting dose may have inadvertently targeted myocardial endothelial cells
- **Only one patient in 50 mcg/kg was evaluable for response and had PD**
  - Two of the patients were non-evaluable due to DLTs, and two patients progressed during cycle 1
- **Five patients tested at 50 mcg/kg not sufficient to assess utility of forced internalization and novel MOA targeting CD38**

MT-0169 Phase I restarted at 5 mcg/kg with one of four patients in a clinical response

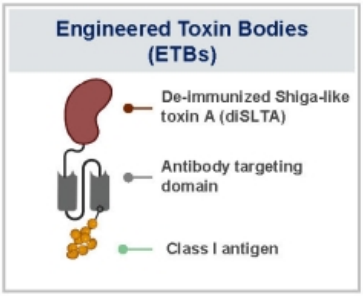
- **Four heavily pre-treated R/R MM patients have been treated at 5 mcg/kg**
  - Additional tests added to the protocol to extend cardiac safety monitoring
- **No toxicity observed at 5 mcg/kg cohort; 10 mcg/kg cohort is enrolling**
- **CD38+ NK cell depletion noted but less profound and rapid than what was observed at 50 mcg/kg**
- **One patient remains on treatment with a partial response at end of cycle 2; PET scan planned to determine if patient is in a CR**
  - Patient progressed after six lines of therapy including multiple proteasome inhibitors, multiple IMiDs, Dara, and a BCMA/CD3 bispecific
  - Patient's lab parameters have improved significantly with serum free light chain lambda and IgA spike showing marked decrease
  - Serum immunofixation has converted from positive to negative
  - CRP has improved considerably and likely explains the patient's improvement from a hemoglobin of 10 g/dL to 14 g/dL
- **Patient clinical response suggests therapeutic index is between 5 mcg/kg and 50 mcg/kg**

ETB Pipeline and Platform

Diversified ETB pipeline with novel MOAs

MTEM Platform: Engineered Toxin Bodies (ETBs) leverage novel MoAs for oncology

- **ETBs are next generation immunotoxins that leverage the unique biology of Shiga toxin to:**
  - Force internalization of non-internalizing receptors
  - Traffic intracellularly to the cytosol with potential to deliver other payloads like class I antigen
  - Induce potent direct-cell kill via the enzymatic and irreversible destruction of ribosomes
- **MTEM's first-gen ETB, MT-3724, provided clinical PoC around forced internalization, safety, and efficacy, but limited by innate immunogenicity / capillary leak syndrome (CLS) and aggregation**
- **Next-gen ETBs are more potent, de-immunized, and have improved CMC properties**
  - 80+ patients treated to date with de-immunized ETB scaffold across 3 clinical program with no instance of CLS observed to date
- **Novel approach to I/O with next-gen ETBs**
  - Direct cell-kill and depletion of "bad actor" immune cells with ETBs to key checkpoint targets vs steric inhibition of checkpoint targets with current approved antibodies
  - Delivery of foreign class I antigen to alter tumor immunophenotype and redirect resident antigen-specific T-cells to the tumor ("Antigen Seeding")
- **Continued progress against validated oncology targets with next-gen ETBs**
  - Unique biology of ETBs can drive benefit in relapsed or refractory cancer patients



Novel Mechanisms of Action with focus on validated targets create new axes for pipeline differentiation

		Target	Stage and Timeline
Immuno-Oncology Targets	MT-6402	PD-L1	Phase 1 Ongoing *Data presented at SITC 4Q2022*
	MT-8421	CTLA-4	*Phase 1 Start 1H2023*
	ETB Candidate	TIGIT	Lead Selection
Oncology Targets	MT-5111	HER2	Phase 1 Ongoing *Data to be presented at SABCS 4Q2022*
	MT-0169	CD38	Phase 1 Ongoing
	ETB Candidate	TROP-2	Lead Selection
	ETB Candidate	BCMA	Lead Selection
	BMS Partnership	Various Undisclosed	Preclinical