Delivering clinically proven epigenetically programmed memory TCR-T cells to fight cancer

Mongoose Bio, Inc.
Executive Summary

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Overview

Mongoose Bio, Inc is an emerging clinical-stage biopharmaceutical company revolutionizing precision oncology with first-in-class T cell receptor T cell (TCR-T) therapies. Leveraging our proprietary and extensive antigen discovery pipeline with memory T cell reprogramming technology, Mongoose Bio is poised to deliver unprecedented coverage of common and rare solid tumors and provide long-lasting immunoprotection.

The science and broad intellectual property behind Mongoose Bio were developed by Dr. Cassian Yee, a leading medical oncologist and faculty member at the renowned MD Anderson Cancer Center in Houston, Texas. Dr Yee is an Endowed Professor of the Department of Melanoma Medical Oncology and Immunology, Division of Cancer Medicine and Director of the Solid Tumor Cell Therapy Program, Center for Cancer Immunology Research at MDACC. Mongoose Bio was spun out of MD Anderson in late 2023 and was recently awarded over $10.5M from the Cancer Prevention and Research Institute of Texas (CPRIT).

The Company is preparing to initiate its first Phase 1 study later this year with its lead candidate, MGB-001, in patients with advanced, recurrent/relapsed lung, gastric, and esophageal cancer. Additional programs in the pipeline address other cancers including prostate, triple negative breast, lung, colorectal, bladder and thyroid. The Company has identified one of the leading oncologists at MD Anderson to oversee the Phase 1 study.

Management

Mongoose Bio has assembled a team of world-class experts to manage the clinical development and commercialization of its products. In addition to Dr. Yee, the Founder and CSO, Neil Warma, the Company's President and Chief Executive Officer, will oversee the strategic and commercial development of all drug products, financing and business development. Mr. Warma has over 25 years of expertise in the life science arena having built and run companies in the US, Europe and Asia from early to commercial stage. The team is rounded out by experts in drug development, clinical operations, regulatory affairs and CMC.

The Promise:

Adoptive T cell therapy offers the prospect of treating all cancers by targeting tumor antigens with *ex vivo* expanded T cells.

The Problem and Unmet Need

The most popular form of adoptive therapy using CAR-T cells achieves complete responses in many patients with B cell malignancies but fails to deliver long-term responses and has been largely unsuccessful for the treatment of solid tumors. **Currently, only 3% of all cancer patients are eligible for T cell therapy**.

Mongoose Bio, backed by 20 years of research in TCR target identification and the epigenetics of T cell memory, advances a therapeutic approach that will fulfill the promise of T cell therapy for patients with solid tumors by addressing two major challenges limiting the efficacy and broader applicability of conventional T cell therapy:

1) **Novel targets for TCR-based cell therapy**
2) **T cell persistence**

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The Solution and Impact

Mongoose Bio addresses both major challenges by advancing an approach based on TCRs directed against important immunogenic pan-cancer antigens and a memory programming module that will confer *in vivo* longevity to transferred T cells.

1. Targets for T cell therapy: The most common cell therapy modality is CAR-T cell therapy, however, CAR-T cells often have serious toxicities, lack selective tumor recognition and only target a very limited portfolio of liquid tumors. In contrast to CAR-T cell therapy (that uses antibodies as the recognition domain), TCR-T therapies utilize the T cell receptor (TCR) to engage tumor targets. Because TCRs recognize surface MHC presented fragments of protein (peptides) that can originate from any cellular compartment, TCR targets can be a transcription factor, oncogene, cancer-testis antigen, DNA repair gene, chemoresistance gene or any of the thousands of tumor-associated proteins found in solid tumors. Indeed, the focus of our work over the last 12 years has been to (i) identify and catalog 11 million target peptide spectra that we have eluted from the MHC of several solid tumor types and (ii) deconvolute these data into 250 highly curated, tumor-selective antigens for TCR-T therapy. The majority of the discovered antigens are actually novel TCR targets, and they cover more than 80% of common and rare tumors for 90% of HLA alleles found in the global cancer patient population.

   Mongoose Bio has interrogated its database of peptide target spectra and we have selected the highest-ranking antigens for our drug development portfolio. These top four antigens were selected on the basis of tumor selectivity, (i.e. they are expressed at very low or undetectable levels in normal tissues), tumorigenicity (i.e. they are known to be functionally associated with chemo, radio and/or immune resistance, proliferation, obviating antigen-loss), immunogenicity (i.e. they elicit high affinity TCRs) and broad tumor prevalence so that the same TCR can be used to target multiple tumor types.

   Our lead program, MGB-001, targets a classic cancer-testis antigen that is not a previously known TCR target. The expression pattern of the MGB-001 target is highly tumor selective and the target itself is known to be tumorigenic (i.e. it is associated with epithelial mesenchymal transformation (EMT) and DNA repair). MGB-001 is expressed at high levels across multiple common and rare cancers with a prevalence of >60% in breast cancer, 45% in lung, gastric, ovarian, bladder, head/neck cancers, and is presented by both HLA-A2 and A3/A11 subtypes that represent >60% of all Western & Asian cancer patients. HLA-A2 is the most common subtype among the Arab population (25.2% Emirati population) followed by HLA-A3 (9.1% Emirati population).

2. T cell memory: The second major challenge to effective T cell therapy has always been the limited persistence *in vivo* of the adoptively transferred T cells, leading to relapse rates as high as 60% despite patients achieving complete remission following CAR-T cell therapy. In large part, this is attributable to the absence of "T cell memory" in the transferred cells – a feature absent from almost every cell therapy modality to date.

   To address this challenge, Mongoose Bio has incorporated a proprietary epigenetic reprogramming protocol, pioneered by Dr. Yee, that locks T cells into the central memory highly persistent "state". Indeed, in 2020 the Yee Lab successfully reprogrammed differentiated effector T cells via epigenetic modification and this breakthrough enabled *ex vivo* reversion of TCR-Ts to a stable memory phenotype (T_{cm}) that has demonstrated three very important properties: (i) superior clinical efficacy, (ii) marked *in vivo* persistence, and (iii) durable patient responses.

Taken together, the Mongoose Bio approach is differentiated from conventional thinking in current T cell therapy approaches by applying first principles of immunogenic TCR target identification

enabling near comprehensive coverage of all solid tumors, and T cell memory reprogramming technology to ensure long- lasting responses, thereby creating patient-centric, tumor agnostic T cell-based therapy for cancer.

As a consequence, the Mongoose Bio therapeutic approach now obviates the requirement for highly toxic immuno- depletion regimens that typically accompany other cell therapy modalities. Not only does this render Mongoose Bio TCR-T therapy a significantly safer modality, but it also facilitates a second wave "antigen spreading" responses by the hosts' endogenous immune repertoire and provides a singularly unique opportunity for the Mongoose Bio TCR-T product to be administered in combination with other approved therapies known to further "shape" the immune response.

Novelty of Technology and Competitive Advantage

- There are only 5 TCR targets in current clinical use by current biotech companies and these only address a very small fraction of cancer patients (vs. Adaptimmune, T-Knife, Immatics, Immunocore). **Mongoose Bio accessed 250 highly curated MS-defined epitopes and selected 4 high value targets expressed across several common (lung, breast, prostate, head and neck, bladder, ovarian, colorectal) and rare cancers (gastric, esophageal, chordoma, glioblastoma, anaplastic thyroid cancer).** We expect to have a very broad market share and our strategic plan is to obtain breakthrough status for rare tumor indications in the US, allowing for TCR targets to be shared for common indications globally**.** All TCR targets are shared tumor-selective antigens providing universal eligibility for matching any given tumor and HLA allele.
- **The TCR targets chosen by Mongoose Bio were empirically identified by mass spectrometry and validated experimentally for immunogenicity.** Almost all TCR targets among competitors were predicted *in silico* with little or no immunogenic validation (vs. T-scan, 3T Biosciences, immunoSCAPE).
- **The TCRs in Mongoose Bio are *naturally occurring* T cell receptors,** obviating the possibility of target cross- reactivity and requiring no affinity maturation (vs. Affini-T)
- **Mongoose Bio TCR-Therapy uses a clinically proven, epigenetically programmed memory module**. No such memory programming is being developed by any biotech cell therapy company.
- **The memory TCR-T cell product from Mongoose Bio will not require high dose lymphodepletion (vs. all TCR-T and CAR-T companies),** eliminating serious toxicities, permitting outpatient therapy and combinational strategies.

Conclusion

Mongoose Bio is a clinical stage company developing novel technology based on years of research conducted at the world renowned MD Anderson Cancer Center. It is a Delaware-based C-corp. and is preparing to enter the clinic later this year having resolved what it believes to be two critical issues which have stood in the way of effective cancer treatment for years; 1) identifying novel pan cancer, TCR targets and 2) creating T-cells that persist and survive to provide long term tumor killing capability.

With an experienced management team with global drug development expertise, Mongoose Bio has identified and licensed multiple pan-cancer TCR targets that are implicated in numerous rare and common cancers. This novel approach is broadly protected with a vast patent estate and has the ability to transform the treatment of cancer.