Creating Smarter T-Cells to Transform Treatment and Change Lives

37th Annual J.P. Morgan Healthcare Conference
Usman “Oz” Azam, President and CEO

January 8, 2019
This presentation contains forward-looking statements. All statements other than statements of historical facts, including statements regarding our future results of operations or financial condition, business strategy and plans and objectives of management for future operations, are forward-looking statements. In some cases, you can identify forward-looking statements by terminology such as “believe,” “will,” “may,” “estimate,” “continue,” “anticipate,” “intend,” “should,” “plan,” “expect,” “predict,” “could,” “potentially” or other similar expressions. We have based these forward-looking statements largely on our current expectations and projections about future events and financial trends that we believe may affect our financial condition, results of operations, business strategy and financial needs.

These statements involve known and unknown risks, uncertainties, and other factors that may cause our actual results of operation, financial condition, levels of activity, performance or achievements to be materially different from the information expressed or implied by these forward-looking statements. Although we believe that the expectations reflected in the forward-looking statements contained in this presentation are reasonable, we caution you that these statements are based on a combination of facts and factors currently known by us and our projections of the future, about which we cannot be certain. Moreover, we operate in a competitive and rapidly-changing industry in which new risks may emerge from time to time, and it is not possible for management to predict all risks.

We cannot assure you that the forward-looking statements in this presentation will prove to be accurate. Furthermore, if our forward-looking statements prove to be inaccurate, the inaccuracy may be material. In light of the significant uncertainties in these forward-looking statements, you should not regard these statements as a representation or warranty by us or any other person that we will achieve our objectives and plans in any specified time frame, or at all. We do not undertake to update any of the forward-looking statements after the date of this presentation, except to the extent required by law.
The human T-cell is the most potent drug ever discovered by mankind
Challenges in delivering next-gen T-cell therapies

**FINDING RIGHT CONSTRUCTS**
Too many non-validated synthetic biology choices

**MANUFACTURING THE RIGHT PRODUCT**
Optimizing manufacturing

**DISPARATE COMPONENTS**
Currently, challenging to integrate end to end

**TESTING IN PATIENTS**
Efficiently testing in non-clinical settings and in clinical trials

**LEARNING FROM PATIENTS**
Embedding key learnings from patients in early-stage trials
Our approach to delivering next-gen T-cell therapies

FINDING RIGHT CONSTRUCTS
Effective T-cell engineering and synthetic biology

TESTING IN PATIENTS
Successful transition to the clinic

UTILIZE LEARNINGS
To optimize delivery of T-cell therapies

MANUFACTURING THE RIGHT PRODUCT
Efficient manufacturing processes

LEARNING FROM PATIENTS
Rapid learning in the clinic

BREAKTHROUGH THERAPIES
Our model for delivering next-gen T-cell therapies

TMUNITY-PENN LICENSE AGREEMENT
- Primary focus in oncology
- Autoimmune diseases, infectious diseases

TMUNITY-PENN SPONSORED RESEARCH AGREEMENT
TCR-T & CAR-T focus

RAPID AND EFFICIENT creation of next-generation products

MANUFACTURING
- Tmunity labs: fully integrated product development
- Tmunity phase II GMP manufacturing

CLINICAL/REGULATORY
Phase I/II development

STRATEGIC COMMERCIAL

NEW INTELLECTUAL PROPERTY
### Innovative pipeline of potentially transformative therapies*

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<tr>
<th>Program INDICATION</th>
<th>RESEARCH</th>
<th>PRECLINICAL DEVELOPMENT</th>
<th>IND ENABLING</th>
<th>PHASE 1</th>
<th>NEXT ANTICIPATED MILESTONE</th>
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* Full pipeline not shown  ** NYCE- New York CRISPR edited
Tmunity’s potential therapies are designed to overcome tumor microenvironment challenges.

- Optimize Targeting
- Optimize Signaling
- Overcome Immunosuppression

Prostate specific membrane antigen (PSMA) CAR-T in Phase 1 clinical trials
Key differentiator: TGFβ (Transformational growth factor beta)
A potent immunosuppressor of T-Cells expressed in prostate cancer tumor microenvironment

Prostate Cancer Tumor Cell

TGFβ receptor type I and II couple to complete signaling mechanism leading to T-cell immunosuppression and anergy.
PSMA CAR-T & TGFβ dominant negative receptor type II

A dual mechanism of action targeting approach in prostate cancer

The Lentiviral Vector contains coding for both a PSMA CAR-T and a TGFβ dominant negative receptor II (TGFβ DNR-II)

The TGFβ DNR-II has a truncated component preventing coupling with TGF β R-I and blocking signaling within T-cell
Phase I trial: CART-PSMA-TGF\(\beta\)RDN cells for metastatic castrate-resistant prostate cancer (mCRPC)

**Study Design and Planning:** A single center, single arm Phase I study to establish the safety and feasibility of intravenously administered lentivirally transduced dual PSMA-specific/TGF\(\beta\)-resistant CAR modified autologous T-cells (CART-PSMA-TGF\(\beta\)RDN cells) in patients with metastatic castrate-resistant prostate cancer.

- **Confirm mCRPC and tumor PSMA expression**
- **CART cell infusion**
  - 1-3 x 10^7/m^2
  - 1-3 x 10^8/m^2
  - MTD

**CART cell infusion**

- **COHORT 1**
- **COHORT 2**
- **COHORT 3**

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- **CART cell infusion**
  - 1-3 x 10^7/m^2
  - 1-3 x 10^8/m^2

- **MTD**

- **Day 0**
- **Days 1**
- **Days 3**
- **Days 7**
- **Days 10**
- **Days 14**
- **Day 21**

**Follow-up:**

- Safety and research

**ClinicalTrials.gov Identifier:** NCT03089203

- TGF\(\beta\): Transformational Growth Factor Beta
- Cy: Cyclophosphamide
- Flu: Fludarabine
- CT c/a/p: Computer Tomography chest, abdomen, pelvis
- PSA: Prostate Specific Antigen

*Enrollment will follow in succession from Cohort 1 to Cohort 3*
NY-ESO-1 TCR: CRISPR/Cas9 multiplex gene edited product in Phase 1 clinical trials*

* Co-funded with the Parker Institute for Cancer Immunotherapy
Rationale for Tmunity’s CRISPR edited T-cell receptor

1. NY-ESO-1 rarely expressed on normal tissue and widely expressed in many tumors

2. Data indicates that targeting of NY-ESO-1 with transgenic T-cells is safe and has antitumor activity*

3. Gene editing may increase function of transgenic TCRs and increase resistance to exhaustion (PD-1 deficiency)

Mechanism of action for Tmunity's Phase 1 CRISPR gene edited TCR

Mechanism of action for Tmunity's Phase 1 CRISPR gene edited TCR

NY-ESO-1 - New York esophageal squamous cell carcinoma-1, PD1 - Programmed cell death protein 1, PDL1 - Programmed death-ligand 1, MHC - Major Histocompatibility Complex, CRISPR - clustered regularly interspaced short palindromic repeats, CRISPR/CAS9 - CRISPR-associated protein-9 nuclease
Mechanism of action for Tmunity's Phase 1 CRISPR gene edited TCR

NY-ESO-1- New York esophageal squamous cell carcinoma-1, PD1-Programmed cell death protein 1, PDL1-Programmed death-ligand 1, MHC- Major Histocompatibility Complex, CRISPR - clustered regularly interspaced short palindromic repeats, CRISPR/CAS9- CRISPR-associated protein-9 nuclease
Phase I trial of autologous T-cells engineered to express NY-ESO-1 TCR and CRISPR gene edited to eliminate endogenous TCR and PD-1 (NYCE T-cells)

This is a first-in-human trial proposed to test HLA-A*0201 restricted NY-ESO-1 redirected T-cells with CRISPR edited endogenous T-cell receptor and PD-1

**ClinicalTrials.gov Identifier:** NCT03399448

**NY-ESO-1**
New York Esophageal Squamous Cell Carcinoma -1, a well-known cancer-testis antigen (CTA)

**CRISPR**
Clustered Regular Interspaced Short Palindromic Repeats

**HLA**
Human Leukocyte Antigen

**Follow-up every 3 months until 2 years**
Tmunity’s proprietary manufacturing facility

Quality by design

Cost effective and scalable

Flexible and responsive

Fully Integrated Product Development

Tmunity Labs

- Manufacturing & analytical expertise
- Developing partnerships with best-in-class technology providers
- Areas of focus:
  - Fully enclosed, streamlined, scalable manufacturing platform
  - Product and process characterization
  - Systems integration

Late Phase Clinical

Tmunity Launch Facility

- Facility secured
- Investment initiated in cell processing
- Anticipated readiness 2020
- >250 therapies per year, scalable to >1,000
- Vector supply
Advanced planning for commercial success

- Integration of real-world data and health technology assessments
- Implementation of novel pricing and reimbursement models
- Customized selling model focusing on new company capabilities in medical & account management
- Integration of chain of identity to medical center hubs
Founders

Proven, global leaders in T-cell biology, R&D & manufacturing

Carl H. June, MD
Director, UPenn CCI

Bruce Levine, PhD
Director, UPenn Clinical Cell & Vaccine Production Facility

Yangbing Zhao, MD, PhD
Director, UPenn CCI
T Cell Engineering Lab

Anne Chew, PhD
Executive Deputy Director, UPenn CCI

James L. Riley, PhD
Associate Professor of Microbiology, UPenn

Bruce Blazar, MD
Director, UMN Clinical & Translational Science Institute

Unparalleled track record

Executing effective cell & gene therapy clinical trials
Management team

The right experience to advance new technologies to the patient

Unmatched expertise

T-cell biology, cell & gene manufacturing, translational medicine, regulatory affairs, clinical development, commercial model development, strategic, operational and general management life sciences experiences
1H18 Series A Closed: $135M Untranched
Our approach to delivering next-gen T-cell therapies

- Effective T-cell engineering and synthetic biology
- Successful transition to the clinic
- Efficient manufacturing processes
- Rapid learning in the clinic

Optimize delivery of T-cell therapies
Creating Smarter T-Cells to Transform Treatment and Change Lives

THANK YOU!

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