Creating Smarter T-Cells to Transform Treatment and Change Lives

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Forward-looking statements

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.

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The human T-cell is the most potent drug ever discovered by mankind
Focused on saving and improving lives of patients with devastating diseases

First financial investment seed $10M
Technologies exclusive to Tmunity

2015

Series A $135M Funding
Moving very quickly into a clinical stage company

The right leadership with unmatched expertise
Leased our own state-of-the-art manufacturing facility

Licensed 12+ additional assets from Penn
Tmunity is a cancer immuno-oncology focused T cell engineering biotechnology company

Today
Challenges in delivering next-gen T-cell therapies

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

**LEARNING FROM PATIENTS**
Embedding key learnings from patients in early-stage trials

**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

**BREAKTHROUGH THERAPIES**
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

MANUFACTURING THE RIGHT PRODUCT
Efficient manufacturing processes

UTILIZE LEARNINGS
to optimize delivery of T-cell therapies

LEARNING FROM PATIENTS
Rapid learning in the clinic
Tmunity’s potential therapies are designed to overcome tumor microenvironment challenges

OPTIMIZE TARGETING

OPTIMIZE SIGNALING

OVERCOME IMMUNOSUPPRESSION

M Castellariuet al., Gene Therapy (2018) 25:165–175
## Innovative pipeline of potentially transformative therapies*

<table>
<thead>
<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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<td>NY-ESO-1 TCR-T -Triple Knockout TCR (NYCE**) MYELOMA, MELANOMA, SYNOVIAL SARCOMA</td>
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</table>

* Full pipeline not shown   ** NYCE- New York CRISPR edited   ***In collaboration with UCSF

June 2019
Prostate specific membrane antigen (PSMA) CAR-T in Phase 1 clinical trials
Key differentiator: TGFβ (Transforming 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

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

TGFβ DNR-II has a truncated component:
- Preventing coupling with TGF β R-I
- Blocking signaling within T-cell
Phase I trial: CART-PSMA-TGFβRDN 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/TGFβ-resistant CAR modified autologous T-cells (CART-PSMA-TGFβRDN cells) in patients with metastatic castrate-resistant prostate cancer.

ClinicalTrials.gov Identifier: NCT03089203

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

Follow-up:
- Safety and research
- CT c/a/p staging, bone scan research studies, PSA
- Month 2
- Month 3
- Month 6
- Follow-up every 3 months until 2 years; long term follow-up until 15 years

* Enrollment will follow in succession from Cohort 1 to Cohort 3.
Tn MUC-1 CAR-T – a novel CAR-T in liquid & solid tumors
Changes in mucin1 expression, polarization and glycosylation generate the TnMUC1 tumor target

Normal tissue heavily glycosylated mucin1

Normal glycosylated mucin1

Normal carbohydrate chains

Cancer with aberrant “stumpy” TnMUC1

Under-glycosylated mucin1

Abnormal carbohydrate chains

Gastric epithelial cell: TnMUC1 only found in the Golgi complex as a precursor to the epithelial lining (mucin1)

Ovarian cancer cell: Stumpy mucin1 (TnMUC1) generated as the enzyme process to glycosylate the mucin1 protein backbone is disabled

COSMC mutations thought to enhance the process of metastasis by permitting easy slippage of transformed cells to the extracellular space
Protein glycosylation is initiated with the covalent linkage of glycans to following amino acids:
- asparagine residues (N-linked)
- serine (Ser) or threonine (Thr) residues (O-linked)

Tmunity targeting the O-linked glycosylation pathway
- The most prevalent aberrant glycoforms found in cancer are
  - **Tn** (GalNAca1-O-Ser/Thr) and
  - Sialyl-Tn (STn) (NeuAca2-6-GalNAca1-O-Ser/Thr)
- Dysregulation of a chaperone protein COSMC is implicated

Tn and STn antigen expression is correlated with adverse outcome and decreased patient survival in breast cancer, gastric cancer, endometrial cancer, and oral squamous cell carcinoma, among other cancers

Tmunity specifically targeting the Tn glycoform epitope of MUC1 with an antibody with recognition of a short peptide sequence with one or two Tn O-glycans on the Ser/Thr residues
**TnMuc1 CAR-T: Construct**

**Autologous T cells**

- Transduced with a lentivirus encoding the anti-TnMuc1 CAR composed of:
  - Murine anti-human TnMuc1 scFv
  - CD8$\alpha$ hinge and transmembrane domains
  - CD2 and CD3$\zeta$

Comparison of 41BB and CD2 CARs
Challenges in the development of CART therapies in solid tumors include:

- Driving the persistence of the CART despite little or no antigen stimulation in the long-term setting
- Preventing CART cell exhaustion

Studies of T cell exhaustion and persistence of pathogenic autoreactive T cells in autoimmune disease indicate that those T cells signaling via the CD2 costimulatory pathway persist without exhaustion markers.

Targeted manipulation of the CD2 co-stimulation pathway has led to enhanced persistence in murine studies of CART.

- In the clinic, a CD2-based CART is hypothesized to lead to enhanced CART cell persistence while maintaining CART activation.

McKinney EF et al., T cell exhaustion, co-stimulation and clinical outcome in autoimmunity and infection. Nature 2015
H3.3K27M TCR in DIPG
H3.3K27M TCR: potential to address high unmet need in DIPG

- Diffuse Intrinsic Pontine Glioma (DIPG) is a devasting disease, has seen little medical progress over the past several decades and has no approved therapies.

- DIPG affects approximately 300 children a year in the US, largely between the ages of 5 and 7

- Children diagnosed with DIPG have an average life expectancy of 8-10 months, with fewer than 10% surviving more than 2 years

- DIPG refers to a tumor originating from glial cells that is not well contained and is found in the Pons

- The Pons are a vital part of the brainstem responsible for breathing, bladder control, balance and other vital functions

ZS Chheda, et.al. The Journal of Experimental Medicine, 4Dec17, p141
https://vivianrosedipg.org/dipg-facts/overview/what-is-the-prognosis-for-a-child-diagnosed-with-dipg/
Realizing the plan
Tmunity’s proprietary manufacturing facility

Quality by design

Cost effective & scalable

Flexible & 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

June 2019
Autologous & Allogeneic Manufacturing
Tmunity is developing a modular approach to both

**Autologous CAR-T Product Manufacturing Strategy**

1. **BIOLOGICAL SOURCE MATERIAL**
   - Patient cells collected (precursor cell product) for manufacturing material

2. **SCREENING AND SOURCE MATERIAL**
   - Donor cells collected and screened

3. **MANUFACTURING FACILITY**
   - Final ‘personalized’ product shipped from manufacturing facility to the local clinical center

4. **CLINICAL CENTER**
   - Patient infused with autologous CART-T cells

**Allogeneic CAR-T Product Manufacturing Strategy**

1. **BIOLOGICAL SOURCE MATERIAL**
   - Patient evaluation

2. **SCREENING AND SOURCE MATERIAL**
   - Donor cells collected and screened.

3. **MANUFACTURING FACILITY**
   - Final ‘targeted’ product ready to be shipped from cryogenic storage in manufacturing facility or other distributed location to the targeted local clinical center

4. **CLINICAL CENTER**
   - Patient infused with allogeneic CART-T cells

5. **CLINICAL CENTER**
   - Patient infused with allogeneic CART-T cells
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