Off-The-Shelf, Engineered Gamma Delta γδ T cell Therapy for Oncology

Anil Singhal, President and CEO

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Adicet Bio: Two Compelling Platforms for Cell Therapy

Leading the Next Generation of CAR-T Therapies

• Founded in 2015 with $51M Series A funding - 60 employees
• Potent off-the-shelf, engineered γδ T cell therapy for oncology and other indications
• Proprietary intracellular tumor-selective targets from TCR-L platform for treatment of solid tumors
• IND for ADI-001 planned in Q4’19 for non-Hodgkin’s lymphoma and CLL
• Robust, cost-effective, cGMP-compliant manufacturing from healthy donors
• Strategic collaboration with Regeneron
• Experienced leadership team and top tier investors
Our Goal: Improve Cancer Immunotherapy

Engineered γδ T Cells Solve Key Challenges of Current Cellular Therapies

• Autologous CAR-T have demonstrated remarkable efficacies in heme malignancies, however...
  • Cumbersome, high manufacturing cost of patient-specific therapies
  • Current therapies are compromised by patient’s immune system dysfunction
  • Existing cell therapies present challenging safety profiles
  • Loss of target from current cell therapies leading to relapses
  • Unsuccessful treatment of solid tumors due to lack of selective targets
Adicet Advantages

γδ T Cells: The Foundation of Superior ‘Off-The-Shelf’ T Cell Therapies

- Allogeneic without gene editing
  - Bind tumor antigen without MHC complex
- Highly potent against solid and liquid tumors
  - Provide both innate and adaptive immunity
- No risk of GvHD
- Actively traffic to solid tumors and tissues
- Potent γ-IFN production
- Able to redose on demand

γδ T cells express multiple tumor-recognizing receptors
Improving Cancer Immunotherapy

γδ T Cells Strongly Correlate with Positive Clinical Outcomes

Pan-Cancer: Improved Overall Prognosis

Post-HSCT Improved Survival

Improved Disease Free Progression Colorectal Cancer

Gentles et al. 2015
Godder et al. 2007
Meraviglia et al. 2017
### Building a Broad Pipeline in Cancer

<table>
<thead>
<tr>
<th>Program</th>
<th>Indication</th>
<th>Discovery</th>
<th>Target Optimization</th>
<th>Preclinical γδ cells</th>
<th>Manufacturing &amp; IND-enabling studies</th>
<th>Initiate Phase 1</th>
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<tbody>
<tr>
<td>CD20</td>
<td>NH Lymphoma</td>
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** UT: Undisclosed Targets Derived from TCR-L platform
ADI-001 Cells Potently Kill Multiple Lymphoma Cell Lines in vitro

- Innate and CAR-mediated activity of γδ T cells is superior to published results of competitor products
- CD20 CAR potentiates innate tumor recognition and killing
- Effective killing of HLA-Class 1 null (Daudi) cells
- Effective killing of cell lines expressing low CD20 levels

* Adicet Study
ADI-001 Cells Effectively Control Aggressive Lymphoma Tumors in Mice

- $\gamma\delta$ T cell treatment initiated* at $T=0$, s.c. tumor volume $\geq 200\text{mm}^3$
- 2nd generation CD20 CAR-modified $\gamma\delta$ T cells effectively control multiple disseminated (iv) and localized (sc) tumors

*Adicet Study
ADI-001 Cells Effectively Control Secondary Challenge Tumors

- Control of secondary tumor challenge strongly indicates persistence, potency & lack of exhaustion

Subcutaneous Raji Tumor Growth*

Mice with no / low tumor burden at Day 55-60 were rechallenged with tumor

* Adicet Study
CD20 CAR γδ T Cells Proliferate in Response to Activation in Tumors

Substantial target-mediated proliferation of CD20 CAR γδ T cells in localized lymphoma tumors at 6 days post treatment
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CD20 CAR γδ T Cells Proliferate in Response to Activation in Tumors

Substantial target-mediated proliferation of CD20 CAR γδ T cells in localized lymphoma tumors at 6 days post treatment
Absence of GvHD with ADI-001 Cells

- No GvHD observed in mice treated with γδ cells
- No gene editing required to overcome GvHD
- Deaths in the αβ CAR T cell group due to GvHD

†SRG-15 mice express human IL-15 transgene
* Adicet study
Adicet Advantages: Robust, Large-Scale Manufacture of γδ T Cells

Selection of Optimal Healthy Donors
Able to selectively expand different γδ T cell subsets

Manufacturing Process < 1 Month
• Robust activation using Adicet’s γδ TCR mAbs
• Viral transduction

• Large-scale closed-system perfusion bioreactor-based expansion
• Excellent post cryopreservation viability & function

Batch Sizes of 2E11 Cells
~1000s of doses per batch

Simplify for Robustness, Partner for Capability and Capacity
Clinical Development of ADI-001

• Target product profile of ADI-001 (CD20 CAR γδ T cells derived from healthy donor)
  – Highly effective (ORR, PFS/OS) in CD20 expressing NHL and CLL
  – No GvHD
  – Significantly lower CRS

• Phase 1 Study
  – NHL, CLL patients relapsing from 2 or more prior lines of treatment
  – 2-3 cohorts for dose escalation/safety
  – Up to 30 patients at the selected dose
  – Single treatment with ADI-001

• Pivotal study likely in DLBCL and/or MCL
ADI-001 Timeline

✓ GMP Manufacturing initiated: 4Q’18
✓ Pre-IND meeting Q1’ 2019
  • IND filing: 4Q’19
  • Phase 1 initiation: 1Q’20
  • Clinical data: 1H’21
TCR-Like monoclonal antibodies (TCRL)
Adicet Advantages: Unlocking the Intracellular Proteome

**CHALLENGE**

- Lack of disease-specific cell surface targets in solid tumors (80% of proteins are intracellular)

**SOLUTION**

- Ability to target disease-specific intracellular proteins highly expands the target pool
- Unlikely to express on normal cells
- TCR-Like (TCR-L) antibodies are specific to peptide-MHC complexes and have multiple applications
  - Mimic TCR specificity with mAb affinity
  - scFv for chimeric antigen receptors for cellular therapy
  - Bispecific T-cell engaging antibodies
Tyrosinase TCR-Ls Effectively Control Melanoma Growth

- Tyr CAR γδ T cells effectively controls subcutaneous growth of melanoma cell line

- Tyr-CD3 bispecific antibodies effectively control subcutaneous growth of melanoma cell line

*Adicet Study
Additional Opportunities for Adicet Platform Technologies

• Potential to treat severe infectious disease with γδ T cells

• Potential to eradicate autoreactive B-cells with CAR γδ T cells

• Growing portfolio of internally-validated tumor-specific TCR-like antibody targets
  — Able to develop TCR-like antibodies as T cell engaging antibodies
Strong IP Portfolio: 11 Patent Families Worldwide

**Patent portfolio on γδ T cell technology**
- Composition of matter for engineered γδ T cells
- Selective expansion of γδ T cell populations and compositions thereof

**Family of patents on TCRL technology**
- TCRL technology and use in cancer, viral infection, and autoimmune disease
- Specific TCRL Antibodies and their targets
- Class I major histocompatibility complexes
Key Terms of the Collaboration with Regeneron in Oncology

Structure of the agreement:

- Multiple targets
- REGN has option to license a defined number of product candidates at IND
  - REGN optioned products: Adicet has option to co-develop/co-commercialize OR receive royalties
- Adicet products: royalties to REGN

γδ T cells engineered with CARs and TCRs for oncology
Generate a pipeline of liquid and solid tumor product candidates

Five year research collaboration; Initiated 7/2016
### Adicet: Leader in CAR and TCR Engineered γδ T cells

<table>
<thead>
<tr>
<th>Company</th>
<th>γδ Subtype</th>
<th>Engineering</th>
<th>Partner</th>
<th>Stage (engineered ACT)</th>
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<td>CAR/TCR</td>
<td>Regeneron</td>
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<td>FPI 2H2019?</td>
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- Other players, not directly competing with Adicet, include: Gadeta (αβT, autologous), Phosphogam (Vδ2), American Gene Technologies (viral activation of Vγ9Vδ2 cells), potentially Universal Cells/Adaptimmune
Experienced Team with Proven Track Record

Stewart Abbot, Ph.D.
Chief Scientific and Operating Officer

Anil Singhal, Ph.D.
President and CEO

Brian Hogan
Chief Financial Officer
Investment Opportunity

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Back up
# Engineered γδ T Cell Product Development Timeline

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<th>Indication</th>
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