NexImmune
Directing T-cell function to restore natural immunity

Spring 2019
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Business Overview
## NexImmune Management Team

<table>
<thead>
<tr>
<th>Management</th>
<th>Previous Experience</th>
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<tbody>
<tr>
<td>Scott Carmer</td>
<td>Genentech</td>
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<tr>
<td>President, CEO</td>
<td>AMGEN</td>
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<td></td>
<td>MedImmune</td>
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<tr>
<td></td>
<td>A member of the AstraZeneca Group</td>
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<tr>
<td>Kristi Jones</td>
<td>Genentech</td>
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<tr>
<td>COO</td>
<td>MedImmune</td>
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<td></td>
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<td>Alain Cappeluti</td>
<td>HUMAN GENOME SCIENCES</td>
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<td>CFO</td>
<td>CoGenesys</td>
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<td>TEVA PHARMACEUTICALS</td>
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<tr>
<td>Mathias Oelke, PhD</td>
<td>JOHNS HOPKINS SCHOOL OF MEDICINE</td>
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<tr>
<td>SVP, Cell Biology</td>
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<td>Dan Bednarik, PhD</td>
<td>HUMAN GENOME SCIENCES</td>
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<td>SVP, Prot. Eng.</td>
<td>Intrexon</td>
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<td>Cardiome</td>
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<td>Naimish Pandya, MD</td>
<td>MedImmune</td>
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<tr>
<td>VP, Clinical Dev.</td>
<td>MACROGENICS</td>
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<td>Northern Biologics</td>
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<tr>
<td>Alex Matschiner, MS</td>
<td>MedImmune</td>
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<tr>
<td>VP, Process Dev.</td>
<td>HUMAN GENOME SCIENCES</td>
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<td>BioFactura</td>
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NexImmune
# Board of Directors and Advisors

## Board of Directors

<table>
<thead>
<tr>
<th>Name</th>
<th>Title</th>
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<tbody>
<tr>
<td><strong>Alan S. Roemer, MBA, MPH</strong></td>
<td>Chairman</td>
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<tr>
<td><strong>Scott Carmer</strong></td>
<td>President, CEO</td>
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<td><strong>Tim Bertram, PhD</strong></td>
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<tr>
<td><strong>Paul D’Angio, RPh, MSJ</strong></td>
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<tr>
<td><strong>Robert Spiegel, MD, FACP</strong></td>
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<tr>
<td><strong>Zhengbin (Bing) Yao, PhD</strong></td>
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<tr>
<td><strong>Tony Yao, MD, PhD</strong></td>
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<td><strong>Sol J. Barer, PhD</strong></td>
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## Advisors

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<tr>
<th>Name</th>
<th>Title</th>
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<tbody>
<tr>
<td><strong>Miguel-Angel Perales</strong></td>
<td>Deputy Chief, Adult Bone Marrow Transplant Service</td>
</tr>
<tr>
<td><strong>Jonathan Schneck</strong></td>
<td>Professor, Scientific Co-founder</td>
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<tr>
<td><strong>Paul Richardson</strong></td>
<td>Medical Oncologist</td>
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* Board Observer
### Company Highlights

#### T-Cell Platform
- **Artificial Immune Modulation (AIM) platform generates highest quality in vitro T-cell product:**
  - Artificial Antigen Presenting Cells (aAPCs) function as synthetic dendritic cells to train T cells
  - Enrichment and Expansion (E+E) manufacturing generates optimal T-cell products

#### Differentiated T-Cell Attributes
- 1. Targets multiple tumor-relevant antigens
- 2. Generates optimal T-cell subtypes
- 3. Drives robust in vitro functionality
- 4. Mimics natural immune response

#### Manufacturing
- Fully enclosed scalable manufacturing
- Lack of viral transduction reduces risk of severe toxicities
- E+E delivers cell therapy with pharmaceutical precision

#### Clinical Catalysts
- Three IND submissions mid-2019 (2 AML / 1 MM)
- Three phase 1/2 trials initiating in 2H 2019
- Initial durability data in 1Q 2020

#### Pipeline
- Modular aAPC platform can be rapidly expanded for uses in oncology, autoimmune, and inflammatory disease
- In vivo applications for oncology and autoimmune disease
## Robust Pipeline of Novel T-Cell Therapy Programs

<table>
<thead>
<tr>
<th>Therapy Type</th>
<th>Program</th>
<th>Indication</th>
<th>Lead Site</th>
<th>Discovery</th>
<th>Preclinical</th>
<th>Phase 1</th>
<th>Upcoming Milestones</th>
</tr>
</thead>
</table>
| Allogeneic   | NEXI-001  | AML / MDS                   | Memorial Sloan Kettering Cancer Center |           |             |         | • IND submission 3Q 2019  
• Phase 1/2 initiation 4Q 2019                           |
|              |           | Post-allogeneic transplant  |                                 |           |             |         |                                                          |
| Autologous   | NEXI-002  | Multiple Myeloma            | Dana-Farber Cancer Institute   |           |             |         | • IND submission 3Q 2019  
• Phase 1/2 initiation 4Q 2019                           |
|              |           |                             |                                 |           |             |         |                                                          |
|              | NEXI-003  | AML / MDS                   | MD Anderson Cancer Center       |           |             |         | • IND submission 3Q 2019  
• Phase 1/2 initiation 4Q 2019                           |
|              |           | Transplant Ineligible       |                                 |           |             |         |                                                          |
| Injectable aAPC | AIM 101   | Undisclosed                 |                                 |           |             |         | • IND ready 4Q 2020                                        |
Competitive Landscape: Differentiation Focuses on Cell Therapy Attributes

Only NexImmune delivers a cellular product that combines each key therapeutic attribute.

1. Targets Multiple Tumor-Relevant Antigens
2. Generates Optimal T-Cell Subtypes
3. Drives Robust In Vitro Functionality
4. Mimics Natural Immune Response

No Other Cell Therapy Achieves This Combination of Therapeutic Attributes

<table>
<thead>
<tr>
<th>Category</th>
<th>Genetically Modified</th>
<th>Non-Genetically Modified</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>CAR-T, TCR, and NK-cell</td>
<td>T-cell, NK-cell, TILs, and MILs</td>
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<tr>
<td>Notable Companies</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Allogene Therapeutics (CAR-T)</td>
<td></td>
<td>ATARA Bio (T-cell)</td>
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<tr>
<td>Immatics (TCR)</td>
<td></td>
<td>IOVANCE Biotherapeutics (TILs)</td>
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<tr>
<td>Autolus (CAR-T)</td>
<td></td>
<td>MARKER THERAPEUTICS (T-cell)</td>
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<tr>
<td>Adaptimmune (TCR)</td>
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<td></td>
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<tr>
<td>POSEIDA Therapeutics (CAR-T)</td>
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<tr>
<td>Bristol-Myers Squibb (CAR-T)</td>
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<td></td>
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<tr>
<td>GILEAD (CAR-T)</td>
<td></td>
<td>MANA THERAPEUTICS (T-cell)</td>
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<tr>
<td>NOVARTIS (CAR-T)</td>
<td></td>
<td>CytoSen (NK-cell)</td>
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<tr>
<td>cellectis (CAR-T)</td>
<td></td>
<td>Immatics (T-cell)</td>
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<td>TCR² THERAPEUTICS (TCR)</td>
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<tr>
<td>Fate THERAPEUTICS (NK-cell)</td>
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<tr>
<td>Celyad (CAR-T NKG2D)</td>
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<td>celularity (NK-cell)</td>
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<td>celularity (NK-cell)</td>
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<td>WindMIL THERAPEUTICS (MILs)</td>
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<td>TORQUE (T-cell)</td>
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NexImmune’s Differentiated T-Cell Attributes
Artificial Immune Modulation (AIM™) platform optimizes endogenous T-cells for maximum therapeutic effect

<table>
<thead>
<tr>
<th>1</th>
<th>Targets Multiple Tumor-Relevant Antigens</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Artificial Antigen Presenting Cells (aAPCs) prime T-cells to recognize wide range of tumor-relevant antigens - minimizes potential for antigen escape</td>
<td></td>
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</tbody>
</table>

<table>
<thead>
<tr>
<th>2</th>
<th>Generates Optimal T-Cell Subtypes</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Enrichment and Expansion (E+E) drives expansion and preservation of the less differentiated T-cell subtypes associated with durable anti-tumor activity</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>3</th>
<th>Drives Robust In Vitro Functionality</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Diverse representation of antigen-specific T-cell subtypes generate multiple key cytokines (polyfunctionality) that enhance target-specific killing of tumor cells and generate a natural immune response</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>4</th>
<th>Mimics Natural Immune Response</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Tumor recognition, engagement, and killing mechanisms mimic the natural immune response and minimize risk of toxicity</td>
<td></td>
</tr>
</tbody>
</table>
Proprietary Artificial Immune Modulation (AIM) Platform Overview

Modular aAPCs engage directly with T-cells to drive specific T-cell function

**Core**

**Synthetic nanoparticle**
- Optimized for size, ligand density, orientation
- Utilized for ex vivo and in vivo applications

**Signal 1**

**HLA IgG4 hinge dimer fusion protein**
- Readily modified for multiple HLA-subtypes
- Incorporates multiple antigen peptides unique to tumor

**Signal 2**

**Co-stimulatory or inhibitory ligands**
- Provides T-cell co-stimulation instructions
- Designed to engage both naïve and memory cells

**Artificial Antigen Presenting Cell (aAPC)**
- **Mechanism of Action:**
  - Direct engagement with target T-cells and subsequent activation, suppression, or self-destruction
Proprietary Artificial Immune Modulation (AIM) Platform Overview

Enrichment & Expansion (E+E) process enables rapid generation of multi-antigen-specific T-cells

17 – 20 Days from T-Cell Harvest to Reinfusion

<table>
<thead>
<tr>
<th>T-Cell Harvest</th>
<th>Enrichment and Expansion</th>
<th>Reinfusion</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patient or Donor</td>
<td>14 day process</td>
<td>Therapeutic levels of tumor-specific T-cells</td>
</tr>
</tbody>
</table>

CD8+ T-Cells

Magnetic Column

Discarded Fraction

Elute and Culture Positive Fraction

aAPC

Schneck et al., Johns Hopkins School of Medicine
Section IIa

Differentiated T-Cell Attributes
Acute Myeloid Leukemia (AML) Program

1. Targets Multiple Tumor-Relevant Antigens
2. Generates Optimal T-Cell Subtypes
3. Drives Robust In Vitro Functionality
4. Mimics Natural Immune Response
NexImmune’s aAPCs Targets T-Cells to Multiple Tumor Antigens

Enrichment and Expansion (E+E) system generates T-cell products that are highly antigen specific

- 150+ manufacturing runs have been used to optimize NexImmune’s antigen cocktails for clinical use

- AIM platform generates T-cell products with highly antigen-specific T-cell populations
  - 200 million cells delivered per recommended phase 1/2 dose
  - Approximately 140 million cells (70%) recognize at least two antigen targets

For comparison, endogenous T-cell competitors demonstrate antigen specificity of 1% or less
  - Example competitor data on pages 32-35
Optimal T-Cell Subtypes Required for Durable Response

Central Memory (T_{cm}) and Stem Cell Memory (T_{scm}) T-cells represent the most potent anti-tumor T-cells.

Progressive T-Cell Differentiation

- CD8+ Naïve T-cell
  - Stem Cell Memory T-cell
  - Central Memory T-cell
  - Effector Memory T-cell
  - Effector T-cell

Optimal T-Cell Subtype Characterization

- Potent Anti-Tumor T-Cells
- Subtypes Required for Durable Response
  - Central Memory (T_{cm})
  - Naïve / Stem Cell Memory (T_n & T_{scm})
  - Effector Memory (T_{em})
  - Effector T-Cell (T_{emRA})

T-Cell Differentiation Increases
- Anti-Tumor Efficacy Decreases
- Proliferative Capacity Decreases
- Multi-Potency Decreases
- Self-Renewal Decreases

- Stem cell memory T-cells can overcome the limitations of current adoptive T-cell therapies
  - Inefficient T-cell engraftment
  - Persistence and mediation of prolonged immune attack

Luca Gattinoni*, Christopher A. Klebanoff* and Nicholas P. Restifo; Nature Reviews 2012
NexImmune Controls T-Cell Differentiation and Drives Optimal Subtype

95%+ of T-cells are Memory Subtype and 60%+ are Central Memory (T\textsubscript{cm}) and Stem Cell (T\textsubscript{scm}) Subtype

- **E+E System Drives T-Cell Subtype**

<table>
<thead>
<tr>
<th>Day 0</th>
<th>Day 14</th>
</tr>
</thead>
<tbody>
<tr>
<td>After Enrichment / Before Expansion</td>
<td>Clinical Scale - Batch Epitope Stimulation</td>
</tr>
<tr>
<td><strong>CD62L</strong></td>
<td><strong>CD62L</strong></td>
</tr>
<tr>
<td>10.13% T\textsubscript{cm}</td>
<td>46.82% T\textsubscript{cm}</td>
</tr>
<tr>
<td>21.03% T\textsubscript{scm}/T\textsubscript{n}</td>
<td>17.84% T\textsubscript{scm}/T\textsubscript{n}</td>
</tr>
<tr>
<td>- T\textsubscript{scm} = 5.26%</td>
<td>- T\textsubscript{scm} = 17.48%</td>
</tr>
<tr>
<td>- T\textsubscript{n} = 15.77%</td>
<td>- T\textsubscript{n} = 0.36%</td>
</tr>
<tr>
<td><strong>CD45RA</strong></td>
<td><strong>CD45RA</strong></td>
</tr>
<tr>
<td>33.83% T\textsubscript{em}</td>
<td>32.24% T\textsubscript{em}</td>
</tr>
<tr>
<td>35.01% T\textsubscript{emra}</td>
<td>3.10% T\textsubscript{emra}</td>
</tr>
</tbody>
</table>

- **T-Cell Phenotypes**

  - WT1, PRAME, Cyclin A1
  - n=4

  - Higher Therapeutic Efficacy

  - Therapeutic Efficacy
  - Lower

- 98% T\textsubscript{scm} (stem cell)
  - 2% T\textsubscript{n} (naïve cell)

- For comparison, competitors demonstrate T-cell subtypes comprised primarily of Effector Memory Cells (T\textsubscript{em}) which demonstrate lower therapeutic efficacy than T\textsubscript{scm} and T\textsubscript{cm}
  - Example competitor data on pages 36-41

- ✓ 75% of T\textsubscript{n}/T\textsubscript{scm} cells are naïve
- ✓ Less preferable T-cell composition (T\textsubscript{cm} & T\textsubscript{emra})
- ✓ 98% of T\textsubscript{n}/T\textsubscript{scm} cells stem cells
- ✓ More preferable T-cell composition (T\textsubscript{cm} & T\textsubscript{emra})

T\textsubscript{scm} cells are characterized as CD62L\textsuperscript{*}, CD45RA\textsuperscript{*}, CD95\textsuperscript{*}

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Phenotype of final cellular product after E+E (Day 14) AML cocktail:
- WT1, PRAME, Cyclin A1

For comparison, competitors demonstrate T-cell subtypes comprised primarily of Effector Memory Cells (T\textsubscript{em}) which demonstrate lower therapeutic efficacy than T\textsubscript{scm} and T\textsubscript{cm}
  - Example competitor data on pages 36-41
NexImmune T-Cells Demonstrate Robust Polyfunctionality

The majority of AML-specific T-cells generate multiple distinct cytokines upon non-specific stimulation.

- **Number of AML Cytokines Generated by AML-Specific T-Cells**
  - 57% generate 1 cytokine
  - 19% generate 2 cytokines
  - 15% generate 3 cytokines
  - 5% generate 4 cytokines

- **% T-Cells with Cytokine Function**
  - IL-2: 40% ± 10%
  - TNFα: 80% ± 10%
  - IFNγ: 60% ± 10%
  - CD107a: 70% ± 10%

- **Immune Function of Cytokines Evaluated**
  - **IL-2**: T-cell proliferation and persistence
  - **IFNγ**: HLA / co-stim upregulation
  - **TNFα**: Recruitment of other immune cells
  - **CD107a**: Activation of granzyme / perforin pathway

- **76% of T-cells generate 3 or 4 distinct cytokines**
- **Majority of T-cells generate key cytokines to enhance anti-tumor effect and immune response**

For comparison, a competitor demonstrated that between 20%-55% of TCR transduced T-cells generate 2-3 cytokines upon stimulation.

- Example competitor data on page 42
NexImmune T-Cells Exhibit Effective and Target-Specific Killing

Demonstrated killing across multiple effector:target (E:T) ratios using healthy donor PBMCs

AML-Specific T-Cell-Mediated Tumor Cell Killing

% Tumor Cell Killing

5:1 10:1

AML Cocktail: WT1, PRAME, Cyclin A1
Source: Healthy donor fresh PBMCs. AML Cell Line: U266. Assay time: 6 hours

✓ AML antigen-specific T-cells kill 40%-70% of tumor cells at different E:T ratios

For comparison, a competitor demonstrated that its CD19 directed CAR-T cells killed 32% of primary tumor cells with a 36:1 E:T ratio
  - Example competitor data on page 43
Natural TCR Signaling Mimics a Natural Immune Response

TCR repertoire is comparable between patients and donors

- T-cell clones that survive in vitro expansion are derived from the naïve T-cell subtype
- Breadth of TCR repertoire after expansion is very similar between patient and donor
- TCR repertoire of antigen-specific T-cells mimics a natural immune response
Section III

Manufacturing and Clinical Plan
Clinical Scale E+E Manufacturing Delivers Consistent T-Cell Characteristics
E+E manufacturing consistently generates targeted cell product composition across indications and lots

- Generates >90% target cell population (CD3+/CD4-/CD8+) with >80% viability
- Comprised of >95% memory subtypes including T_{scm} and T_{cm}
- Negligible cells with allo-reactive potential
- Successful transfer to CMO with final process locked
NEXI-001: Acute Myeloid Leukemia and MDS Trial (Allogeneic)

NEXI-001 trial design and key milestones

- Prospective, multi-center, open-label, single-arm phase 1/2 study of adoptively-transferred donor-derived CD8+ T-cells among post-allogeneic transplant AML patients with relapsed disease
- **IND Submission:** 3Q 2019 | **Anticipated FPI:** 4Q 2019
- **AML target antigens:** WT1, PRAME, Cyclin A1
- **Patient population:** HLA*A0201
- **Endpoints:** Safety and tolerability, Efficacy (ORR, MRD conversion, PFS), T-cell persistence, TCR repertoire

**Trial Design**

- **Indication:** Post-allogeneic Matched HSCT MRD+ or Relapsed AML / MDS patients

Dose Level 1 (n=3)

Dose Level 2 (n=3)

Dose Expansion (n=16-20)
NEXI-002: Multiple Myeloma Trial (Autologous)

NEXI-002 trial design and key milestones

- Prospective, multi-center, open-label, single-arm phase 1/2 study of adoptively-transferred patient-derived CD8+ T-cells among relapsed / refractory multiple myeloma patients
- **IND Submission:** 3Q 2019 | **Anticipated FPI:** 4Q 2019
- **MM target antigens:** WT1, CD138, CS1, NY-ES0-1
- **Patient population:** HLA*A0201
- **Endpoints:** Safety and tolerability, Efficacy (ORR, PFS), T-cell persistence, TCR repertoire

### Trial Design

#### Indication: Relapsed / Refractory Multiple Myeloma
- Relapsed / refractory to at least 3 prior lines of therapy
- At least two prior standard regimens, including proteasome inhibitor and thalidomide analog
- Must have measurable disease

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**Dose Level 1 (n=3)**

**Dose Expansion (n=16-20)**
**NEXI-003: Acute Myeloid Leukemia and MDS Trial (Autologous)**

**NEXI-003 trial design & key milestones**

- **Prospective, multi-center, open-label, single-arm phase 1/2 study of adoptively-transferred patient-derived CD8+ T-cells among transplant-ineligible AML patients**

- **IND Submission:** 3Q 2019 | **Anticipated FPI:** 4Q 2019

- **AML target antigens:** WT1, PRAME, Cyclin A1

- **Patient population:** HLA*A0201

- **Endpoints:** Safety and tolerability, Efficacy (ORR, MRD conversion, PFS), T-cell persistence, TCR repertoire

---

**Trial Design**

- **Indication:** Transplant ineligible AML patients that are post induction / consolidation chemo with MRD+ disease

- **Dose Level 1 (n=3)**

- **Dose Expansion (n=16-20)**
Section IV

Adaptable Platform & Future Directions
Modular Nature of aAPCs Enables Rapid Pipeline Expansion

NexImmune’s technology can direct T-cell function to a specific therapeutic goal

**Illustrative Customizable aAPCs**

- **aAPC**
  - **Oncology:** Break T-Cell Tolerance

- **KaAPC**
  - **Autoimmune Diseases:** Induce T-Cell Tolerance

- **Other Diseases:**
  - **Direct Other Immune Cell Types**

**Signals**
- MHC-Ig
- anti-4-1BB
- anti-CD28
- anti-CD2
- B7.1-Ig
- anti-PD1
- anti-Fas
- CD83-Ig
- CD1d-Ig
- anti-CD44

**Synthetic Particle**
- Fe⁺ or PLGA-PEG
Next Generation R&D Efforts Focusing on Injectable aAPCs

Injectable aAPC nanoparticle (e.g. AIM 101) can direct T-cell function in vivo

**Mechanism of Action**
- PLGA-PEG based aAPC nanoparticles decorated with HLA presenting disease-relevant antigens and humanized stimulatory ligands
- To enhance engagement with targeted T cell subtypes, aAPCs can be designed to increase trafficking to – or injected into – lymph nodes
- Demonstrated ability to generate antigen-specific TILs in preclinical models
- Early non-clinical data suggests additive benefit when used in combination with checkpoint inhibitors

**Clinical Plan**
- Being developed for solid tumors in combination with checkpoint inhibitors
- Being developed for autoimmune diseases