The PACT Vision

Curative T Cell Therapies for Cancer, Tailored for Each and Every Patient
Solid Cancers Represent the Vast Majority of all Cancers and are Patient-Specific

- Each person’s cancer is **personal and unique** with highly specific mutations, thereby limiting treatment options.

- Neoepitopes (neoE) are peptides originating from tumor-specific mutations that bind to the patient’s HLA. These neoE-HLA constructs are highly specific targets for T cells.

- **Only <1%** of neoE-HLA targets are the same among individuals with solid cancer.
The PACT Approach to Developing Personalized T-Cell Therapies

**Personalized NeoTCR Discovery & Validation Process**
(while patient is on standard of care therapies)

**Clinic**
- **Step 1**: Collect tumor biopsy & blood samples
- **Step 2**: Predict & Prioritize targets from tumor mutation sequencing
- **Step 3**: Generate Target Library of bar-coded, patient-specific, neoE-HLA proteins ('Bar-coded Snares')
- **Step 4**: Capture neoE-HLA specific T cells from patient blood
- **Step 5**: Functional Verification of neoTCR therapeutic candidates
- **Step 6**: Select Products for up to 3 neoTCRs considering:
  1. Functionality
  2. NeoE truncality
  3. NeoE diversity
  4. HLA diversity

**GMP NeoTCR-T Cell Product Mfg**
- **Step 7**: TrifectaR™ cell mfg

**Clinic**
- **Step 8**: Infuse patient-specific, polyclonal (up to 3 neoTCRs) neoTCR-T cell product

**Patient Leukapheresis**

= Steps performed outside of PACT
Our NeoTCR Discovery and Validation Process Is Designed to Capture and Verify Patient Specific Polyclonal Products

- **1000s of tumor-specific targets**
- **Prioritize mutations**
- **100s of bar-coded snares**
- **Capture patient T cells**
- **10s of engineered T cell product prototypes**
- **Validate & select products**

Next Generation Sequencing of tumor biopsy & blood samples

Predict & Prioritize* targets from tumor mutation sequencing

Generate Target Library of bar-coded, patient-specific, neoE-HLA proteins

Capture neoE-HLA specific T cells from patient blood

Functional Verification of neoTCR product candidates

Product Selection for up to 3 verified neoTCRs considering:
- Functionality
- NeoE truncality
- NeoE diversity
- HLA diversity

* AACR 2021: Abstract # 2177

Tumor Neoantigen Profiling with Validated Patient-Specific NeoTCR Characterization to Improve Neoepitope Prediction
TrifeCtaR™ Cell Manufacturing Process

- CD4 & CD8 Enrichment Day 0
- Activation Day 0
- Electroporation Day 2
- T cell Expansion Day 2-13 D8 split
- Harvest/Fill/Finish Day 13

Leukapheresis Day -1
**TrifeCtaR™ Process** Leverages our Precision Genome Engineering Technology to Allow for Enhanced T Cell Functionality and Trafficking

**PACT Precision Genome Engineering**
- Knock-out of endogenous TCR
- Precision insertion of PACT neoTCR

**PACT final product:**
- Under control of native TCR gene regulation
- No competition for CD3
- **Normal functioning T cell**

Platform allows for knock-in, knock-out, surface secreted, and TCR induced payloads

**Typical Viral-based Manufacturing Approach**
- Random viral vector insertion
- No copy number control

**Final product:**
- Under control of artificial TCR gene regulation
- Competes with endogenous TCR for CD3
- **Less functional T cell**

Platform limited to insertion of new payloads
Step 7 – **TrifeCtaR™** Process Designed to Engineer T Cells with Increased Activity and Persistence

**T Cell Evolution**

- Naïve \((T_N)\)
- Memory stem cell \((T_{MSC})\)
- Central memory \((T_{CM})\)
- Effector memory \((T_{EM})\)
- Effector \((T_E)\)

**‘Young’ Phenotypes**

**TrifeCtaR™ Cell Manufacturing Process**

- Optimized growth medium
- No IL2

- Final product mainly consists of memory stem cell and central memory T cells
- Increased persistence *in vivo*
- Robust engraftment potential based on third party preclinical studies

**Traditional Cell Manufacturing Approach**

- Rapid expansion
- High level IL2

- Final product mainly consists of effector T cells
- Short lifespan *in vivo*
- Requires high dosing
## The Production of a Cell Therapy Product Poses Unique Challenges/Opportunities in the Autologous Cell Therapy Commercialization Process

<table>
<thead>
<tr>
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<th>Challenges</th>
<th>Opportunities</th>
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<tbody>
<tr>
<td>Manufacturing</td>
<td>Complex and resource-intensive manufacturing technology</td>
<td>Automate manufacturing processes to lower cost of goods, meet market demand, and reduce excessive manpower</td>
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<td>Supply Chain</td>
<td>Each patient is a unique batch; requires chain of identity and chain of custody</td>
<td>Optimize business systems with predictive analytics to drive standardized process efficiencies throughout the network</td>
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<td>Timing and scheduling are critical</td>
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<td>Raw Material</td>
<td>Single suppliers and the Pandemic environment</td>
<td>Collaborative partnerships with vendors to increase reliability of raw material supply</td>
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<td>Process Development</td>
<td>Variability in incoming patient cells reduces manufacturing consistency</td>
<td>Continue to generate sufficient knowledge-base of apheresis material</td>
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<td>Safety and Efficacy</td>
<td>Adverse events need to be minimized and managed</td>
<td>Established efficacy in cancers for patients with limited options</td>
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Manufacturing Strategy to Scale Out Over Time on Clinical Results

Centralized

- Optimal model for near term clinical mfg operations & launch of first commercial product
- Logistical coordination across large geographical area

US: Downstream Manufacturing Centers

- Optimal model for patient treatment of multi-disease & US scale out
- Logistical coordination within regional population

International Manufacturing Centers

- Optimal model for patient treatment of multi-disease & international scale-out
- Logistical coordination within regional population
Scaling Internal Capabilities to Support Anticipated Clinical and Commercial Needs

In-house capabilities for discovery and manufacturing

- Current capability ~150 patients/year
- Continuous improvement
- Highly experienced manufacturing team

Designing ~55,000 square feet in support of commercial scale

- Anticipated ramp to ~3,000 patients/year
- Technology partnerships
- Fully enclosed, fully automated
Thank you!
www.pactpharma.com