About Immunomic Therapeutics (ITI)

Privately-held clinical stage biotechnology company

Developing next generation vaccines based on the patented LAMP Technology

Lead product is JRCLAMP-vax, an allergy immunotherapy to treat pollen allergies caused by Japanese red cedar

ITI Has Achieved Significant Accomplishments

Phase I study of JRC-LAMP-vax demonstrated excellent safety and a positive indication of immunogenicity – 100% of allergic Japanese-native patients converted from positive to negative skin test at the end of the Phase Ib

2012 IND filed for JRC-LAMP-vax Phase I; study initiated in Japanese patients

2011 Animal health collaboration with top 5 pharma company

2005 Sublicensed LAMP to major biopharma company for use in a cancer vaccine
Patented LAMP Technology: A Platform for Developing Potent Next Generation Vaccines

Applied in Multiple Clinic Trials

**Allergy:**
Completed Phase Ia and Ib studies in 24 subjects for pollen allergy

**Cancer:**
Prostate, melanoma, glioblastoma & AML studies have shown immune activation, safety, and trend towards positive survival in over 100 patients to date

**Literature:**
Over 70 publications on therapeutic LAMP vaccines and the mechanism of action
### Human Health Pipeline

**Internal & External Development**

<table>
<thead>
<tr>
<th>Antigen</th>
<th>Design</th>
<th>Validation</th>
<th>Pre-clinical</th>
<th>Ph. I</th>
<th>Ph II</th>
<th>Ph. III</th>
<th>Commercial Partner (P) / Academic (Co)</th>
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<tbody>
<tr>
<td><strong>Allergy Immunotherapy</strong></td>
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<tr>
<td>JRC-LAMP-vax (Jap. Red Cedar)</td>
<td>Cry j1, j2, j3</td>
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<td><em>Internal Development</em></td>
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<tr>
<td>JCC-LAMP-vax (Global Cedar, Juniper, Cypress)</td>
<td>CryJ1, j2, j3</td>
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<td>ARA-LAMP-vax (Peanut)</td>
<td>Ara h1, 2, 3</td>
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<td>Mt. Sinai (Co)</td>
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<td>Multi-LAMP-vax (Multivalent)</td>
<td>Undisclosed</td>
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<td>GRNVAC1 (Prostate Cancer)</td>
<td>hTERT</td>
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<td><em>BioTime / Asterias (P)</em></td>
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<td>GRNVAC1 (AML)</td>
<td>hTERT</td>
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<td><em>BioTime / Asterias (P)</em></td>
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<td>GRNVAC2 (AML and Other)</td>
<td>hTERT</td>
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<td><em>BioTime / Asterias (P)</em></td>
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<td>TriMix DC Therapy (Melanoma)</td>
<td>MAGE-A3 / C2 tyrosinase, gp100</td>
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<td>U. Brussels (Co)</td>
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<td>Td+pp65 DC (Glioblastoma)</td>
<td>pp65</td>
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<td>Duke University (Co)</td>
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<td>TMZ/anti IL-2/LAMP+ pp65 DC Therapy (Glioblastoma)</td>
<td>pp65</td>
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<td>University of Florida (Co)</td>
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### Infectious Disease Vaccines

<table>
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<tr>
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<th>Design</th>
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<tbody>
<tr>
<td>HIV-LAMP-vax</td>
<td>Gag-pol-nef-tat-vif</td>
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<td><em>Internal Development</em></td>
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<td>HIV Clade B mRNA DC Therapy</td>
<td>Tat, rev, nef</td>
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<td>U. Brussels (Co)</td>
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## Summary of Phase I Clinical Studies of JRC-LAMP-vax to Date

<table>
<thead>
<tr>
<th>Efficacy &amp; Safety Goals for JRC-LAMP-vax</th>
<th>Phase 1a Results</th>
<th>Phase 1B</th>
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<tbody>
<tr>
<td><strong>EFFICACY:</strong></td>
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<td></td>
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<tr>
<td>Elimination of JRC/Mtn C/CryJ2 skin test reactivity</td>
<td>14 of 16 subjects</td>
<td>100% conversion</td>
</tr>
<tr>
<td>Conversion skin test from positive to negative</td>
<td>15 of 16 subjects</td>
<td>100% conversion</td>
</tr>
<tr>
<td><strong>SAFETY:</strong></td>
<td></td>
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<tr>
<td>No anaphylactic / allergic responses</td>
<td>Achieved</td>
<td>Maintained</td>
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<tr>
<td>(CryJ2 sequestered intracellular no leakage)</td>
<td></td>
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<tr>
<td>No anti LAMP antibody generation</td>
<td>Achieved</td>
<td>Maintained</td>
</tr>
<tr>
<td>No severe adverse reactions</td>
<td>Achieved</td>
<td>Maintained</td>
</tr>
<tr>
<td>Skin test negative patients remain negative</td>
<td>8 of 8 subjects</td>
<td>Maintained</td>
</tr>
<tr>
<td>IgE levels stable or decreasing</td>
<td>Achieved</td>
<td>TBD</td>
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</table>
ARA-LAMP-vax - ITI’s peanut allergy product

- Over 1.5 million Americans suffer symptoms from peanut allergy (PA), an IgE-mediated food allergy
  - Over 50% of food-induced anaphylaxis fatalities are due to peanuts
  - An estimated 100-200 deaths each year in US are believed to be due to peanuts
- A safe and effective therapeutic is urgently needed to improve the life of PA subjects by inducing desensitization and antigen tolerance
- ARA-LAMP-vax is a 3 plasmid formulation designed for the major peanut allergens, Ara h 1, Ara h 2, and Ara h 3 within LAMP
- Aim is to rebalance the immune system in favor of IgG / Th1 response, instead of allergic IgE / Th2 response
Highlights of Cancer Immunotherapy Products in Development
About GRNVAC1

GRNVAC1 is an autologous immunotherapeutic product candidate that comprises mature dendritic cells (DCs) transfected with messenger RNA encoding the catalytic subunit of human telomerase (hTERT)

– hTERT is encoded with a portion of the lysosomal targeting signal from LAMP to enhance immune stimulatory capacity.

– GRNVAC1 aims to induce an immune cell mediated response targeted against tumor cells expressing telomerase antigen on their surface.

GRNVAC1 Clinical Program

- Two clinical studies to date

- **Phase I** head-to-head study between hTERT mRNA loaded DCs and hTERT-LAMP-1 mRNA loaded DCs in 20 patients with late stage prostate cancer that showed addition of LAMP greatly improved CD4 activity

- **Phase I / II** study of hTERT-LAMP-1 mRNA loaded DCs in 21 AML patients, which showed strong immune responses correlating with improvements in interim overall survival
GRNVAC1 Phase II AML Study & Summary of Results

**Phase II** Acute Myeloid Leukemia Study

- 21 patients received VAC1

**Patient Response**

- Median of 17 (3-32) doses administered with a median follow-up of 13.2 mo
- 15 in CR (12 in CR1, 3 in CR2) and 6 relapsed
- 9 of 11 patients at high risk for relapse in complete remission at trial conclusion
- 14 of 15 CR patients in extended boost phase, now in long-term follow-up
- Suggested a survival benefit of 5 months greater than existing standard of care

**Immunological Response**

- hTERT specific immune response observed by ELISPOT in 55% of patients
- Immunological response correlated with control of WT-1 expression and disease progression

**Safety**

Vaccine Well Tolerated and Demonstrated Safety
The Future of GRNVAC Program and LAMP Technology

- Findings by Gilboa et. al. provided a rationale for further development of hTERT-transfected DC vaccines in the treatment of prostate and other cancers and led to Geron license in 2006
  - Clearly showed benefit and MoA of LAMP-vax vs vectors not containing LAMP
- GRNVAC program shows efficacy, provides commercial opportunity for LAMP Technology through existing license
- GRNVAC2 provides opportunity for development of next generation, non-autologous-DC-based immunotherapies
- Immunomic Therapeutics is preparing for discussions with Asterias to propose additional applications of GRNVAC2 lines in order to build on existing clinical immunotherapies using LAMP, integrating next generation delivery to meet market needs
University of Brussels’ Tumor Program Utilizing LAMP + TriMix

About TriMix-LAMP Immunotherapy

- A novel protocol for improving antigen specific DC functions in vivo
- Enhances CD4 and CD8 immune responses

TriMix is delivered as mRNA, encoding:

- **Tumor antigen(s)** of interest encoded with **DC-LAMP**
- **CD40L** for helper T-cell activation
- **Constitutively active TLR4** for innate immune activation
- **CD70** for enhanced T-cell proliferation and cytolytic activity

[Diagram showing antigen presentation by DCs and immunostimulatory capacity]

Bonehill, A et al. Mol Ther, 2008
The combination of TriMix and a cancer antigen has shown to produce relevant immunological results for treating cancer patients

- DC-LAMP is a critical component of the immunotherapy to ensure sufficient CD4 helper T-cell and CD8 cytotoxic T-cell proliferation

- The Brussels group, led by Drs. Kris Thielemans and Aude Bonehill are translating the promising work using autologous dendritic cells into a commercially viable mRNA vaccine platform for easier, more commercially-scalable delivery

- The mRNA program enables a new class of adjuvants to be safely administered, taking advantage of the rapid degradation of mRNA in vivo

- The future of the TriMix program is in cancer indications of high unmet need of the various maturation methods, TriMix is possibly the most intriguing, and can be formulated with additional LAMP-tumor-associated antigen (TAA) constructs to target other cancer types
### Duke University

- Studies at Duke Univ. have Employed Human autologous DC generation for vaccination and production of pp65-LAMP/A64 mRNA
- Results from a recent Ph I clinical trial reveal that DC migration in the context of priming with Td (tetanus toxoid) prior to an immunotherapeutic LAMP/DC vaccine induces superior clinical outcomes in patients with malignant brain tumors.
- ITI is currently planning **future preclinical studies** with J. Sampson’s group at Duke Univ. to employ the Td pre conditioning strategy, but deliver pp65-LAMP DNA plasmid intradermally rather than pp65-LAMP-mRNA via DCs, in order to move to an easier, more commercially viable delivery methodology.

### University of Florida

- D. Mitchell has conducted numerous trials employing LAMP-pp65 mRNA vectors in Glioblastoma with therapeutic success for example:
- Results from the recent REGULATE trials demonstrate that his strategy which includes anti–IL-2Rα mAb administration during recovery from lymphodepletive TMZ in patients with GBM reduced TReg frequency (48% reduction; P<.0061) while permitting vaccine-stimulated antitumor effector cell expansion. Further, 4 of 6 patients displayed an increase in pp65-specific T cells after vaccination with a mean 4-fold increase in tetramer-positive CD8+ T cells.
- Dr. Mitchell is currently exploring further applications of this and other vaccine strategies.
- ITI is engaged in a collaboration to produce vectors utilizing LAMP and targeting various key antigens in a nanoliposomal mRNA formulation in glioblastoma that may obviate the need for DC therapy in this context.
Rationale for Next-generation Immunotherapies Based on LAMP Technology

- Promising pipeline based on proprietary programs and numerous academic, investigator-sponsored research programs
- Clinical data in well over 100 patients shows that LAMP
  - Solves a major problem in nucleic acid vaccines through direct activation of helper T-cells
  - Generates robust CD8 cytotoxic T-cell responses
  - Is safe and well tolerated in humans
- The diverse pipeline positions in a mature and exciting allergy program with the potential to revolutionize the allergy field AND in the unfolding promise of cancer immunotherapies with a potent immunomodulator