IMMUNE DESIGN
The *in vivo* generation of cytotoxic CD8 T cells (CTLs)
Forward-looking Statements

This presentation contains forward-looking statements with respect to, among other things, our business, financial condition, strategy and prospects, and has been prepared solely for informational purposes. All statements, other than statements of historical fact, regarding our strategy, potential future products, prospects, plans, opportunities and objectives constitute “forward-looking statements.” These statements are not guarantees of future performance and involve a number of unknown risks, assumptions, uncertainties and factors that are beyond our control. Given these risks, assumptions and uncertainties, you should not place undue reliance on these forward-looking statements.

Important factors that could cause actual results to differ materially from those indicated by such forward-looking statements include, among others, our history of net losses and expected net losses for the foreseeable future, that we have no product candidates approved for commercialization and may never achieve profitability, that we will require additional capital to finance our operations, that we may not be able to successfully develop, obtain regulatory approval and commercialize our product candidates, all of which are novel and in early clinical development, and those other risks that will be set forth under the header “Risk Factors,” “Note Regarding Forward-Looking Statements” and “Management’s Discussion and Analysis of Financial Condition and Results of Operations” in our periodic reports filed with the Securities and Exchange Commission, including our Annual Report for the period ended March 31, 2015. All statements contained in this presentation are made only as of the date of this presentation and are subject to uncertainty and changes. Except as required by law, we expressly disclaim any responsibility to update such forward-looking statements, whether as a result of new information, future events or otherwise.
<table>
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<tr>
<th>Setting Immune Design Apart</th>
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<tr>
<td><strong>T Cells in vivo</strong></td>
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<td><strong>Broad Immuno-Oncology Potential</strong></td>
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<tr>
<td><strong>2015 Data</strong></td>
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<td><strong>Strategy</strong></td>
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<td><strong>Team</strong></td>
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Immune Design: How we focus in Immuno-Oncology

Two Main I-O Categories

CD8 T cells (CTLs) tumor killing

Remove the Blockade
(checkpoint inhibitors)

Two types of CTL based Therapies

Off-the-shelf, \textit{in vivo} CTL generation

Adoptive T cell transfer (CAR-T, TCR)
(personalized, ex vivo)

Two Immune Design Approaches

Antigen Specific (NY-ESO-1)

Intratumoral Immune Activation

Immuno-Oncology (I-O)
The next pillar of cancer treatment

Tumor-induced Immune Blockade
TWO DISCOVERY PLATFORMS:
ZVex AND GLAAS
The *in vivo* “Prime-Boost” of ZVex™ and GLAAS™

**Four Key Points for Effective Immune-mediated Tumor Killing:**

1. The Dendritic cell (DC) educates naïve T cells to recognize tumor antigens
2. CD8 T cells (CTLs) generated from antigen gene delivery to the DC (ZVex)
3. CD4 T cells ("Helper" T cells) generated from antigen protein delivery to the DC (GLAAS)
4. CD4 T cells “help” boost CTLs to kill tumors
First *in vivo* DC Targeting Gene Delivery Vector

**ZVex**

**Sindbis**

**Lenti**

- Sindbis envelope provides selective *in vivo* DC targeting
- Lack of prior immunity allows for multiple dosing
- Integration-deficient and replication-incompetent for safety

**Capacity for substantial genetic payload = new potential products**

*Immune Design data.*
Highly Potent and Safe DC Activation *in vivo*

GLAAS: *GLA at the Core*

- Activation of innate immunity (TH1 cytokines, chemokines and NK cells)
- De novo induction of Ag-specific CD4 T and B cells and boosts pre-existing Ag-specific CTLs
- Expanding favorable safety and efficacy database (>1,200 subjects)
- Potential in oncology, and in infectious and allergic diseases

*Immune Design and IDRI data; Lambert et al., PLoS One, 2012*
Combination immunotherapy with ZVex and GLAAS results in increased immunogenicity (CD4 and CD8 T cells, other) and pre-clinical efficacy.

**Immunogenicity (model antigen)**

<table>
<thead>
<tr>
<th>Day0:</th>
<th>Day21:</th>
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<tr>
<td>none</td>
<td>GLA+protein</td>
</tr>
<tr>
<td>none</td>
<td>ZVex-RNA</td>
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<tr>
<td>GLA+Protein</td>
<td>ZVex-RNA</td>
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- % Ag specific T cells (ICS)
  - CD4
  - CD8

- 0.8 < 0.1
- 3.2 < 1
- 15.7

**GLAAS + NY-ESO1 protein (G305 P1)**

**ZVex- NY-ESO1 RNA (LV305 P1)**

**CMB305**

Immune Design, unpublished.
CMB305 PRODUCT CANDIDATE:
NY-ESO-1 SPECIFIC
CMB305: Building the Blocks to Maximum CTLs in vivo

**STEP 1**
Individual Building Blocks
- G305
- LV305

**STEP 2 (STARTED)**
Test Combination “Prime-Boost”
- CMB305
- CPI

**STEP 3**
CMB305 Combined w/ Checkpoint Inhibitors (CPI)
Building Towards CMB305: G305 and LV305 Ph1s

Each component safely produced predicted IG with signs of clinical benefit

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<thead>
<tr>
<th>Immunogenicity</th>
<th>G305</th>
<th>LV305</th>
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<tbody>
<tr>
<td>CD4: 5/11</td>
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<tr>
<td>CD8: 2/10</td>
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<td>Ab: 9/12</td>
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<tr>
<td>n=12</td>
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<tr>
<th>Safety</th>
<th>Grade 1-2 AEs Only</th>
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<tr>
<td>Stable disease:</td>
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<tr>
<td>67% (8/12) pts d70 (end Tx)</td>
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<tr>
<td>Median 245 d (161-365+)</td>
<td>Median 208 d (139-347+)</td>
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<tr>
<td>One CA125 response (GCIG Criteria)*</td>
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<th>Clinical Benefit</th>
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<tr>
<td>Median 208 d (139-347+)</td>
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<tr>
<td>Progression impact:</td>
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<tr>
<td>4/6 pts stopped progression and tumor regression of 14% in one pt w/ SD at 347+d</td>
<td>PFR (Progression free rate): 67% (3 months) and &gt;42% (6 months)</td>
<td></td>
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</tbody>
</table>

*CA125 response 600(D0) → 281(D70) → 207(D242)
LV305 Ph1: NY-ESO-1 T-cell Responses compared with Published Studies

Percentage NY-ESO-1-specific T-cell responses in Patients (CD4 and CD8, ELISPOT/ICS/Tetramer)

- **LV305 2015 (n=12)**
  - ZVex

- **Odunsi 2012 (n=47)**
  - Fowlpox
  - + Vaccinia

- **Dhodapkar 2014 (n=34)**
  - DEC-205 mAb/NY-ESO-1/
  - + Resiquimod/Poly-I:C

- **Chen 2015 (Arm A, n=18)**
  - NY-ESO-1 prot/IMX
  - + Fowlpox

LV305 Ph1: Progression Free rate (PFR) in STS trials

LV305’s PFR at 3 and 6 months compares favorably to historical PFR

- PFR can guide active vs inactive treatments in Soft Tissue Sarcoma Trials*
- LV305 patients had at least 1 prior treatment and <10cm in tumor size

CMB305: Early Development and Readouts

- LV305 DE (ZVex-NY-ESO-1 RNA)
- G305 DE (GLAAS+ NY-ESO-1 protein)

- Completed LV305 and G305 DE per plan
- CMB305 Phase 1 dose escalation (DE) underway
- LV305 expansion study at high dose underway in sarcoma, ovarian, lung and in melanoma NR to anti-PD1
  - CMB305 Phase 1 dose expansion in sarcoma, melanoma, ovarian, lung at optimal dose (n=32) planned to commence Q3’15
G100 PRODUCT CANDIDATE:
I.T. IMMUNE ACTIVATION
Three Key Points for Intratumoral Immune Activation:
1. Tumor lysis (e.g., local tumor radiation) releases neo tumor antigens.
2. Intratumor administration of G100 activates peri-tumor DCs to uptake neo antigens AND boost pre-existing peri-tumor CTLs or tumor infiltrating lymphocytes (TILs)
3. Tumor site administration of G100 combined with local radiation may eliminate both local/treated tumor and distal (non-treated) tumors (abscopal effect)

G100 Programs: Intratumoral Immune Activation

G100: MCC Ph1 - Orphan; n=10
G100: NHL Ph1 - Orphan; n=30

Two Pilot Ph1 Trials

Q2’15
Q4’15
G100 in Merkel Cell Carcinoma (MCC): Combined Treatment ORR of 50%

- **Cohort A**: 2/2 pts with locoregional disease completed G100 followed by surgery plus RT and are free of recurrence (336+ & 467+ days).
  - Pt 002 had a pathologic CR following the G100 injections alone.
- **Cohort B**: 2/6 patients with metastatic disease have an ongoing PR after 2 cycles of therapy and are in follow-up.
  - Pt 006 had 28% regression in the injected tumor following G100 alone; this regressed completely after the second cycle consisted of RT plus G100.

---

**Locoregional**

**Cohort A**

- Pt 002 had a pathologic CR following the G100 injections alone.
- Pt 006 had 28% regression in the injected tumor following G100 alone; this regressed completely after the second cycle consisted of RT plus G100.

**G100 CLINICAL RESPONSE**

**Locoregional**

**Metastatic**

Rx: d0,7 (LR) & d21 (Met, each cycle) Radiation + 6 weekly doses cycles 2-4
**First-in-class Immunotherapy Pipeline**

<table>
<thead>
<tr>
<th>Immuno-Oncology</th>
<th>Pre-clinical</th>
<th>Phase 1</th>
<th>Approach</th>
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<tbody>
<tr>
<td>G305 (GLA + NY-ESO-1 protein)</td>
<td></td>
<td></td>
<td>SPECIFIC ANTIGEN</td>
</tr>
<tr>
<td>LV305 (Zvex- NY-ESO-1 RNA)</td>
<td></td>
<td></td>
<td>NY-ESO-1 specific (Soft tissue sarcoma, melanoma, ovarian, lung)</td>
</tr>
<tr>
<td>G100 (intratumoral GLAAS) MCC</td>
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<td></td>
<td>I.T. IMMUNE ACTIVATION</td>
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<tr>
<td>G100 (intratumoral GLAAS) NHL</td>
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<td>G100 alone and in combo w/ radiation</td>
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<thead>
<tr>
<th>Infection &amp; Allergy (GLAAS)</th>
<th>Preclinical</th>
<th>Phase 1</th>
<th>Partner</th>
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<tbody>
<tr>
<td>RSV Vaccine</td>
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<td>Exclusive License</td>
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<tr>
<td>Food Allergy Vaccine</td>
<td>Exclusive License</td>
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<tr>
<td>G103 (HSV-2 Vaccine)</td>
<td>Joint Program</td>
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</table>

**Specific Antigen**
- NY-ESO-1 specific
  - Soft tissue sarcoma, melanoma, ovarian, lung

**I.T. Immune Activation**
- G100 alone and in combo w/ radiation

**Partners**
- MedImmune
- SANOFI
- SANOFI PASTEUR

**Approach**
- **G100 (intratumoral GLAAS) MCC**
- **G100 (intratumoral GLAAS) NHL**
- **CMB305 (LV305 + G305)**
# Financial Highlights and Upcoming 2015 Milestones

- **Cash as of March 31, 2015**: $60.2 million
- **April 2015 following-on offering**: $74.2 net proceeds
- **Expected 2015 net operating cash burn**: $33-37M
- **Total shares outstanding (April 2015)**: ~19.9 million

## Milestones: Data

<table>
<thead>
<tr>
<th>Anticipated Timing</th>
<th>Milestones: Data</th>
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<tr>
<td>Q2’15*</td>
<td>✓ Phase 1 data on LV305 and G305 dose-escalation in solid tumors at ASCO</td>
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<tr>
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<td>✓ Phase 1 data on G100 in Merkel Cell carcinoma at ASCO</td>
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<tr>
<td>YE’15</td>
<td>• Phase 1 data on CMB305 dose escalation</td>
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## Milestones: Clinical Development

<table>
<thead>
<tr>
<th>Timing</th>
<th>Milestones: Clinical Development</th>
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<tbody>
<tr>
<td>Q1’15</td>
<td>✓ Initiate Phase 1 study of CMB305 dose-escalation in solid tumors</td>
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<tr>
<td></td>
<td>✓ Initiate Phase 1 LV305 study expansion in solid tumors</td>
</tr>
<tr>
<td>Q2’15</td>
<td>• Initiate Phase 1 study of G100 + XRT in NHL</td>
</tr>
<tr>
<td></td>
<td>• Initiate Phase 1 LV305 study expansion with α-PD1 in melanoma NRs to α-PD1</td>
</tr>
<tr>
<td>H2’15</td>
<td>• Initiate Phase 2 randomized study of CMB305 in sarcoma</td>
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<tr>
<td>2015</td>
<td>• Establish additional non-oncology collaborations</td>
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*Abstracts for the LV305, G305 and G100 MCC Phase 1 studies have been presented at the ASCO 2015 Annual Meeting.*
Broad Development Potential in Immuno-Oncology

Current clinical development programs. Potential development opportunities.

Stand-alone

ZVex/GLAAS Prime-Boost (CMB305)

Intratumoral activation w/GLAAS (G100)

ZVex 2nd Gen:
- Multiple Ags
- Neo Ags
- Immune-modulators

ZVex/GLAAS Prime-Pull

Combination

Check point inhibitors + LV305/CMB305 and G100

Radiation + G100

Adoptive T Cell Therapy (CAR-T, TCR) + ZVex/GLAAS

Oncolytic Virus + G100

- Two product discovery platforms w/ first-in class product candidates driving CTLs in vivo
- Potential to complement/synergize with multiple other I-O approaches