Overview of Cell Medica

**Mission:** Transform the treatment of cancer with cellular immunotherapy

- Founded 2007 as T cell immunotherapy company
- Treating patients since 2008 – significant manufacturing experience
- London, Zurich, Houston
- Three oncology product platforms – lead product in Phase II
- Experienced Management Team and Board of Directors

Patient’s immune cells activated or engineered to kill cancer cells

**Shareholders**

![Shareholders logos](image-url)
Experienced Management and Board

**Board**

- Gregg Sando
  Founder & CEO
- Thomas Hecht, MD,
  Chairman
  Amgen Europe
- Maina Bhaman
  Touchstone
  Innovations
- Nigel Burns, PHD
  Cambridge Antibody
  Technology
- Andrea Ponti
  Partner & Founder
  GHO Capital
- Allan Marchington
  Takeda/Millennium
  Pharma

**Senior Management Team**

- Karren Hodgkin
  COO
- Kurt Gunter, MD
  Chief Medical Officer
- Tim Anderson
  Group Finance Director
- Ross Durland
  SVP, Development
- Stefanos Theoharis
  SVP, Corporate Dev. & Partnering
- Alain Pralong
  SVP, Manufacturing
- Lynn Lester
  SVP, HR
Three high-value oncology product platforms

Leading-edge proprietary technology

With pre-eminent research partners

And strong focus on solid tumours

<table>
<thead>
<tr>
<th>Activated EBV+ T cells</th>
<th>CAR-NKT Cells</th>
<th>Engineered TCRs</th>
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<tr>
<td>Native T cells activated against viral antigens</td>
<td>NKT cells modified to express chimeric antigen receptors</td>
<td>T cells modified to express Dominant TCRs</td>
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<tr>
<td>Phase II – Interim Q4 2017</td>
<td>Planned Phase I by Q2 2018</td>
<td>Planned Phase I by Q4 2018</td>
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- Baylor College of Medicine
- University of North Carolina
- University College London

- EBV+ Lymphoma
- EBV+ Nasopharyngeal Carcinoma
- Small Cell Lung Cancer
- Hepatocellular Cancer
- Triple Negative Breast Cancer
- Acute Myeloid Leukemia
- Pancreatic Cancer
- Ovarian Cancer
Activated EBV+ T cells

For treatment of
- EBV+ Lymphomas
- EBV+ Nasopharyngeal carcinoma
- EBV+ Gastric cancer
CMD-003 in Phase 2 for EBV+ Malignancies

18% of cancers are associated with pathogenic infections

**World Health Organization**

CMD-003 Mechanism of Action

- Activated T cells which kill EBV+ cancer cells

Hodgkin lymphoma cells
expressing EBV antigens (LMP1)

Indications
- NKT cell lymphoma (100%)
- Hodgkin’s Lymphoma (30%)
- Nasopharyngeal carcinoma (95%)

Key Product Attributes

- Autologous – naturally occurring
- Targets “non-self antigens” expressed by cancer cells – no harm to healthy cells
- Recognizes 100s of epitopes preventing cancer escape
- Safety profile is optimal for combination with anti-PD1s (EBV upregulates PD1)
GRALE Trial at Baylor College of Medicine

GRALE Study = Investigator-led at Baylor College of Medicine

- Product nearly identical to CMD-003
- Patients with range of EBV+ lymphomas
- Responses determined by independent radiologist

**Patients with active disease (N=8)**

- 3 complete responses
- 2 partial responses
- 1 stable disease
- 2 no response

62.5 % ORR
Durations up to 29 months

**Patients in remission with high risk of relapse (N=18)**

- 13* remain in remission
- 2 relapse
- 3 pending assessment

86.7% Remain in Remission
Durations up to 26 months

*1 death in remission due to cerebral hemorrhage unrelated to therapy
**Cell Medica Trial Targets High Unmet Clinical Need**

**Relapsed NK/T cell lymphoma**

*Extranodal NK/T Cell Lymphoma Patients receiving gemcitabine following relapse after asparaginase-based regimen*  

**Medical Need**
- CITADEL Phase II Trial for patients with relapsed NK/T cell lymphoma who have very poor prognosis
  - PFS = 2.3 months
  - Median OS = 4.9 months

**Regulatory Considerations**
- Fast track designation received Feb. 2017
- Possibility of accelerated approval (FDA) and conditional approval (EMA)

**Orphan drug approval in USA and EU**
- NKT cell Lymphoma
- Post Transplant Lymphoproliferative Disease

*Ahn et al. Invest New Drugs 2013*
CITADEL: Early Efficacy Results

### Patient Responses

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<tr>
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<th>Full Analysis Set (N = 6)</th>
<th>Per Protocol (N = 5)</th>
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<tr>
<td>Disease Control (CR, PR, SD)</td>
<td>4/6</td>
<td>4/5</td>
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<tr>
<td>Responses (CR, PR)</td>
<td>3/6</td>
<td>3/5</td>
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Results to be presented at ASH 2017

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**Baseline**

Patient 502-001

**Week 8 - Partial Response**

Patient 502-001
Objective: Potential synergy of anti-PD1 plus EBV-specific T cells (EBV T cells)

Sponsor: Baylor College of Medicine

Product: EBV-specific T cells similar to Cell Medica’s CMD-003 but made in BCM’s GMP facility

EBV+ Hodgkin Lymphoma
(1) second relapse
(2) first relapse refractory to salvage chemotherapy
(3) primary refractory disease after at least two lines of therapy

EBV+ Non Hodgkin Lymphoma
(1) first relapse refractory to at least one salvage chemotherapy
(2) primary refractory disease after at least two lines of therapy or in second or subsequent relapse
Next Generation CAR NKTs for Solid Tumours

For treatment of
- Small Cell Lung Cancer
- Hepatocellular Cancer
- Triple Negative Breast Cancer
# Cell Medica’s CAR Technologies for Solid Tumours

1. **NKT Cell**
   - Navigate to sites of tumor more effectively than T cells

2. **Humanized scFvs**
   - Improves persistence by preventing rejection

3. **Activating Cytokines**
   - Overcomes tumour microenvironment

4. **Localized anti-PDL1**
   - Prevents inhibitory pathway

5. **High Value Cancer Targets**
   - Targeting large patient populations (solid tumors)
CAR-NKTs Homing to Tumour Superior to CAR-Ts

- Significantly more intra-tumoral CAR-NKT cells compared to CAR-T cells in mouse neuroblastoma model

Source: Heczey et al. (2014), Blood 124:2824.
Big Opportunity: Cell Medica's Off the Shelf Product

CAR-NKTs do not require gene-editing to delete the endogenous T cell receptor – **much more simple to manufacture**

NKT Cells recognize a specific glycolipid antigen which is not associated with Graft vs Host Disease (GVHD) – **safety is increased**

Off-the-shelf CAR-T cells may attack patient’s body as “non-self” relative to donor (GVHD).

**NKT cells avoid GVHD!**

Off-the-shelf product may be rejected by patient’s immune system as “non-self”, limiting therapeutic window.

Patient conditioning before treatment can reduce rejection.
CAR NKTs avoid GVHD risk of Off the Shelf Products

Invariant NKT cells with chimeric antigen receptor provide a novel platform for safe and effective cancer immunotherapy

Andras Heczey,1 Daofeng Liu,1 Gengwen Tian,2 Amy N. Courtney,1 Jie Wei,1 Ekaterina Marinova,1 Xiuhua Gao,1 Linjie Guo,1 Eric Yvon,3 John Hicks,2 Hao Liu,4 Gianpietro Dotti,2,3 and Leonid S. Metelitsa1,2,3

1Texas Children’s Cancer Center, Department of Pediatrics, 2Department of Pathology and Immunology, 3Center for Cell and Gene Therapy, and 4Division of Biostatistics, Dan L. Duncan Cancer Center, Department of Medicine, Baylor College of Medicine, Houston, TX

BLOOD, 30 OCTOBER 2014 • VOLUME 124, NUMBER 18

Summary

- GD2-specific CAR renders NKT cells cytotoxic against NB cells
- Potent in vivo antitumor activity
- Without graft-versus-host disease (histology performed 4-5 weeks following therapy)
Next Generation Engineered T Cell Receptors

For treatment of
- Pancreatic Cancer
- Ovarian Cancer
High TCR expression levels enhance antigen-specific activation

T cells with normal TCRs are usually expressed at too low levels to achieve activation and are therefore ineffective.

Key:
- Normal TCR
- Dominant TCR
- MHC/Target Complex

Natural T-cell activation requires multiple TCR-MCH binding events.

- Recognition of cancer targets expressed at low levels, or rare mutations, even when levels of HLA presentation are reduced (common in tumours)
- Reduced mispairing with endogenous TCR
- Validated with multiple TCRs
High Expression Levels Enable Improved Function

Dominant TCR allows activation at much lower target concentration
Cells display considerably improved target-specific functionality
Clinical Value Inflection Points 2017 – 2019

Clinical development programmes for six cell therapy products
Important clinical endpoints by 2019

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<th>2017</th>
<th>2018</th>
<th>2019</th>
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<td>EBV</td>
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<td>CMD-003: CITADEL Data</td>
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<tr>
<td>CMD-003: CIVIC Data</td>
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<td>EBV-CTLs: PREVALE Data –Nivolumab</td>
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<td>CMD-008: “ABC”-Dominant TCR</td>
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<tr>
<td>CMD-009: Survivin Dominant TCR</td>
<td>IND</td>
<td>CMD-009: Ph I Trial</td>
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Expected News Flow for 2017

**CMD-003**
- Fast Track Designation from FDA
- Orphan Drug for PTLD in USA
- Successful completion of interim stage for Phase II CITADEL Trial
- First patient treated in Phase II CIVIC Trial
- Clinical data from Baylor’s combination study with Nivolumab

**CAR-NKTs**
- Pre-IND Meeting with FDA for GD2-CAR-NKT cells
- Announcement of target for off-the-shelf product

**Dominant TCRS**
- In-licensing new TCRs for application of Dominant TCR platform
- Development collaborations and out-licensing

**Company**
- Additional senior team members
- Expanded manufacturing capability in UK