# Immunocellular Therapeutics Ltd.



## Forward-Looking Statements

This presentation contains forward-looking statements. All statements other than statements of historical facts contained in this presentation, including statements regarding our plans, timelines, prospects, objectives, expectations and intentions with respect to the potential for success of our potential products, cancer immunotherapy research, development efforts and timelines, regulatory status, business, operations, intellectual property, financial condition and other statements that are not historical in nature, are forward-looking statements.

You should consider forward-looking statements carefully because they may include statements regarding our future expectations or projections about future events. These statements involve known and unknown risks, uncertainties, assumptions and other factors, including those described in our filings with the Securities and Exchange Commission (SEC).

You are cautioned that forward-looking statements are not guarantees of future performance. The forward-looking statements included in this presentation are made only as of the date of this presentation, and, except as required by law, we assume no obligation to update these forward-looking statements publicly, or to update the reasons why actual results could differ materially that those anticipated in the forward-looking statements, even if new information becomes available in the future.



## ImmunoCellular is Building a Cancer Immunotherapy Company, Leading with the Phase 3 GBM Program

- Multiple opportunities for building shareholder value in 2015-2016
  - Initiate registrational Phase 3 program for ICT-107 in US, Canada and EU in newly diagnosed glioblastoma; US sites opening now
  - Stem-to-T-cell program driving toward a clinical candidate; research collaboration with MD Anderson
  - ICT-121 phase 1 trial in recurrent glioblastoma enrolling; potential data in 2016
  - Continued evaluation of inbound opportunities to build our pipeline



# Immunotherapy Strategies are Leading the Fight Against Cancer





# IMUC Advantage: Two Therapeutic Approaches to Achieve T-Cell Killing of Cancer Cells





# **IMUC** Pipeline

Program Name (Developmental Focus)	Pre Clin	Phase 1	Phase 2	Phase 3
ICT-107 (Newly Diagnosed Glioblastoma)				US Sites Open
<ul> <li>6 antigen DC-based immunotherapy for HLA-A2 patients</li> </ul>				op on
ICT-121 (Recurrent Glioblastoma)		Enrolling		
<ul> <li>1 antigen / 2 epitope DC-based immunoth patients</li> </ul>	erapy for HLA	4-2		
Stem-to-T-Cell Therapy (Cancer)	Research Commenced			
<ul> <li>New program using hematopoietic stem c create antigen-specific T-cell therapies</li> </ul>	ells to			
ICT-140 (Ovarian Cancer)			Ph 1/2 On ho	old*
<ul> <li>7 antigen DC-based immunotherapy for HLA-2 patients</li> </ul>				
Resource dependent - awaiting partnership or other financing Copyrig	ht November 2015			6

## ICT-107 for the Treatment of Newly Diagnosed GBM

ICT-107 Dendritic Cell Presenting to T-cell



## Efficient, Cost-Effective Manufacturing: One Run from Patient's Own Cells Yields 20-50 Doses





# The Phase 2 Trial Identified a Major Subgroup Where ICT-107 Benefit was Clear



- ICT-107 showed trend benefit in overall survival and statistical benefit in progression free survival
- The ICT-107 treatment effect was concentrated in HLA-A2 patients



- Patient's MGMT methylation status predicts their response to chemotherapy and their survival time
- ICT-107 appears to have effect in both groups



# The Phase 2 Survival (OS and PFS) Results in the Predefined Subgroups Supports Moving to Phase 3

Group (n)	Statistic	Value	Sta	
ITT (124	OS – log rank p-value	0.436	Mad	
patients, 81 active 43	OS – HR	0.846	ivieu	
control)	PFS – log rank p-value	0.033	Madi	
	PFS – HR	0.640	ivieai	
PP HLA-A2*	OS – log rank p-value	0.326	Mad	
MGMT UnMeth (24 active, 14 control)	OS – HR	0.704	wea	
	PFS – log rank p-value	0.364	Madi	
	PFS – HR	0.720	wear	
PP HLA-A2* MGMT Methylated (17 active, 14 control)	OS – log rank p-value	0.645	Mad	
	OS – HR	0.800	ivied	
	PFS – log rank p-value	0.004	Madi	
	PFS – HR	0.257	iviedi	



\* Includes HLA-A1/A2 dual positive patients

Note: p-values and HRs are stratified for age and MGMT where appropriate; OS data are from October 2015 update; PFS data are from October 2014 update



# The Phase 2 ELISPOT Immune Response Data Inform Improvements in the Phase 3 Design

Comparison	Results	Implications for phase 3
Immune response association with HLA status	<ul> <li>HLA-A2+ patients have a higher immune response rate (50%) than HLA-A1+ (34%)</li> <li>Fisher's exact p=0.0578</li> </ul>	<ul> <li>Supports phase 3 population of HLA-A2+ only</li> </ul>
Immune response association with OS	<ul> <li>Log rank test of survival difference in HLA-A2+ patients for immune responders vs non-responders is statistically significant with p=0.0084</li> </ul>	<ul> <li>Additional doses may help drive higher immune responses</li> </ul>
Immune response association with treatment group	<ul> <li>HLA-A2+ ICT-107 treated patients have a higher immune response rate (60%) than controls (36%)</li> <li>Fisher's exact p=0.0512</li> </ul>	<ul> <li>Changing control to monocytes which are less effective than DCs at driving an anti-tumor response</li> </ul>
ICT-107 immune responders associated with survival	<ul> <li>ICT-107 HLA-A2+ patients with an immune response have median OS of 22.5 months versus non-responders with median OS of 15.2 months</li> <li>Log rank test of survival is statistically significant with p=0.0147</li> </ul>	<ul> <li>Additional dose may help drive higher immune responses</li> </ul>
DC IL-12 secretion association with immune response	<ul> <li>For HLA-A2+, 70% of high IL-12 patients were immune responders compared with 43% of low IL-12 patients</li> <li>Fisher's exact p=0.0419</li> </ul>	<ul> <li>Changing control to monocytes which are less effective than DCs at driving an anti-tumor response</li> </ul>
Immune response not associated with MGMT	<ul> <li>No statistical difference in immune response rates between MGMT methylated and unmethylated patients</li> </ul>	<ul> <li>Supports phase 3 population that includes both MGMT types</li> </ul>



### Phase 3 Design: Special Protocol Assessment Reached with FDA; Key Design Elements De-Risked

#### Design

- Double blind, placebo-controlled phase 3; placebo is patient's own monocytes
- ~120 US, Canada, EU sites in collaboration with cancer cooperative groups

#### Population

- ~400 HLA-A2 patients post-surgery and chemoradiation
  - Similar entry criteria to phase 2 design with reconfirmed stable disease at randomization
  - Stratified for age, MGMT, and resection status

#### Endpoints

- **s** Overall survival registrational endpoint recommended by FDA/EMA
  - Overall survival in MGMT subgroups
  - Progression-free survival
  - Safety
  - Disease progression determination by iRANO criteria

#### Regimen

- SOC +/- ICT-107 immunotherapy
- Induction immunotherapy (4 in month 1) and maintenance (monthly through month 12 or progression)

#### Duration •

- 2 years to enroll
- 2-3 years to follow-up
- Futility interim analysis at 33% of events (~2 yrs)
- Efficacy interim analysis at 60% of events (~2.5 yrs)



## ICT-107 is Positioned Well in the Competitive Immuno-Oncology Landscape for Newly Diagnosed Glioblastoma

Company	Program	Status	Comment
ImmunoCellular	<ul> <li>ICT-107</li> <li>6-antigen DC-based immunotherapy for HLA-A2 patients</li> </ul>	<ul> <li>Completed <u>controlled</u> phase 2 trial with <u>OS</u> endpoint</li> <li>Entering phase 3 with <u>OS</u> endpoint</li> </ul>	Only controlled phase 2 immunotherapy trial to show benefit on a clinical outcome (PFS)
Northwest Bio	<ul> <li>DCVax-L</li> <li>Tumor lysate DC vaccine</li> </ul>	<ul> <li>Completed <u>uncontrolled</u> phase 1</li> <li>Enrolling phase 3 with <u>PFS</u> endpoint</li> </ul>	Phase 3 modified multiple times and has PFS primary endpoint - FDA and EMA specify OS as registrational endpoint
Agenus	<ul> <li>Prophage</li> <li>Tumor lysate and heat shock protein</li> </ul>	<ul> <li>Completed <u>uncontrolled</u> phase 2 with <u>OS</u> endpoint</li> <li>Planning phase 3</li> </ul>	Indicated that they are looking for a partner
Celldex	<ul> <li>Rindopepimut</li> <li>EGFRV3 antigen vaccine for patients expressing EGFRV3</li> </ul>	<ul> <li>Completed <u>uncontrolled</u> phase 2 with <u>PFS</u> endpoint</li> <li>Fully enrolled phase 3 with <u>OS</u> endpoint</li> </ul>	Well-designed phase 3 program that addresses <15% of GBM market; 745 patients in 22 countries in trial
BMS	<ul> <li>Checkpoint inhibitors</li> </ul>	<ul> <li>Testing in <u>newly diagnosed</u> and <u>recurrent</u> GBM for safety and <u>OS</u></li> </ul>	Testing CTLA4 and PD1 alone and in combination
Merck	<ul> <li>Checkpoint inhibitors</li> </ul>	<ul> <li>Testing in phase 1/2</li> </ul>	Unknown patient population



## DC-based Immunotherapy Development Pipeline

Program	Description	Status
ICT-121	<ul> <li>HLA-A2 restricted immunotherapy for the treatment of recurrent glioblastoma</li> <li>1 antigen – 2 variants of CD133</li> </ul>	<ul> <li>Enrolling phase 1</li> <li>20 patients to be treated at 6 US sites</li> <li>Enrollment continuing; update in 2016</li> </ul>
ICT-140	<ul> <li>HLA-A2 restricted immunotherapy for the treatment of ovarian cancer</li> <li>7 antigens</li> </ul>	<ul> <li>IND and protocol for phase 1/2 trial allowed by FDA</li> <li>6 sites in the US identified</li> <li>Program start awaiting partnership or other financing</li> </ul>



# Novel Stem-to-T-Cell Technology In-Licensed from David Baltimore's Lab at Caltech



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## **Overview of Stem Cell Program Current Thinking**



- 1. Prioritize antigens/tumors
- License existing TCR and/or commence discovery research program sponsored research at MD Anderson announced and underway
- 3. Develop process to create product and file for patents as able
- 4. Commence human cell line work to show killing of tumor cells
- 5. Commence animal model work to validate system
- 6. Understand and complete FDA requirements for IND
- 7. File IND and commence human testing



### Potential Advantages of IMUC's Stem-to-T-Cell Technology

Technology	Description	Assessment
CAR-T	<ul> <li>Introduce an antibody-like receptor via virus into T-cells isolated from patient to create therapy</li> <li>Requires targeting of surface antigens</li> </ul>	<ul> <li>Restricts targets to surface antigens</li> <li>HLA independent</li> <li>"Cytokine storm" needs to be managed as does off-target tox</li> </ul>
Engineered T-cell	<ul> <li>Introduce an antigen-specific TCR via virus into T-cells isolated from the patient to create a therapy</li> </ul>	<ul> <li>Broad range of potential targets</li> <li>Requires TCR discovery</li> <li>HLA dependent</li> <li>May require <i>ex vivo</i> cell expansion</li> <li>Therapies may have a time-limited effect</li> </ul>
TILs	<ul> <li>Isolate tumor infiltrating lymphocytes from the patient's tumor and expand <i>ex</i> <i>vivo</i> to make the therapy</li> </ul>	<ul> <li>Customized to patient's tumor</li> <li>Requires significant <i>ex vivo</i> cell expansion</li> <li>Therapies may have a time-limited effect</li> </ul>
IMUC Stem- to-T-cell	<ul> <li>Isolate hematopoietic stem cells, use virus to deliver TCR, and return to patient as therapy</li> </ul>	<ul> <li>Broad range of potential targets</li> <li>Requires TCR discovery</li> <li>HLA dependent</li> <li>Does not require <i>ex vivo</i> expansion</li> <li>Stem cells produce constant supply of T-cells so therapy is robust over time</li> <li>Potentially lower COGS</li> </ul>



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## **Anticipated Program Milestones**



## Current Balance Sheet – As of 9/30/15

Cash \$24.4 million

2015 burn (9 months) \$13.2 million

Outstanding debt None

Shares outstanding 90.3 million

Warrants outstanding 28.2 million

**Options outstanding** 10.7 million with an average exercise price of \$1.19

The \$19.9 million CIRM award will be received by the Company over the duration of the trial as specified milestones are achieved



### ImmunoCellular is a Compelling Investment Opportunity

- Our mission is to build a leading cancer immunotherapy company:
  - Broad technology platform, pipeline of differentiated therapies
  - Changing cancer treatment paradigms; improving outcomes for patients with intractable lethal cancers that represent high unmet medical needs
- We aim to create value for all our stakeholders
  - Patients and families
  - Shareholders and partners
  - Employees
  - Medical and scientific community
- We are accomplished, driven, focused and committed to achieving our goals and having a beneficial impact on human health

