



## A NEW FRONTIER IN T-CELL ACTIVATION AND TARGETING

AGM PRESENTATION 18 Oct 2016

Dr John Chiplin: Executive Chairman

**Dr Richard Goodfellow:** CEO **Professor Lindy Durrant:** CSO

LSE AIM Symbol: SCLP.L



## FORWARD LOOKING STATEMENT

Today's presentation includes forward-looking statements intended to qualify for the safe harbor from liability established by the Private Securities Litigation Reform Act of 1995. These forward-looking statements, including statements regarding our planned pre-clinical studies and clinical trials, regulatory approval process, and demand for our product candidates are subject to risks, uncertainties, and other factors that could cause actual results to differ materially from those suggested by our forward-looking statements.

These factors include, but are not limited to, the following: we have incurred significant net losses and anticipate that we will continue to incur significant net losses for the foreseeable future; we have never generated any revenue from product sales and may never be profitable; we will need to raise additional funding in the future, which may not be available on acceptable terms, or at all; no product candidates utilizing ImmunoBody® and Moditope® technology have been approved for commercial sale in the United States, and our approach to the development of ImmunoBody® and Moditope® technology may not result in safe, effective, or marketable products; we are early in our product development efforts and may not be able to obtain regulatory approvals for the commercialization of some or all of our product candidates; our ability to develop and successfully commercialize product candidates may be compromised by other companies developing their technologies or product candidates for our target indications more rapidly than we do or if their technologies are more effective; we may not be able to obtain exclusivity or intellectual property rights for our product candidates or prevent others from developing similar competitive products.

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### **SCANCELL IMMUNO-ONCOLOGY**

### TWO PLATFORMS

- IMMUNOBODY® Potent innovative DNA-based immunotherapy platform for the generation of ultra-high avidity anti-tumor T-cells
- MODITOPE® Citrullinated peptides that deliver potent killer helper T cells during autophagy

### **THREE PRODUCTS**

SCIB1, SCIB2, Modi-1

### **FIVE CANCER INDICATIONS**

Melanoma, Lung Cancer, Breast Cancer, Ovarian Cancer, Osteosarcoma



### **DRUG PIPELINE**

### LEAD CANDIDATES

**IMMUNOBODY® SCIB1:** Targets malignant melanoma. Phase 1/2 study completed with promising results. Phase 2b combination trial with immune checkpoint inhibitor planned for Q3 2017.

IMMUNOBODY® SCIB2: Targets non-small cell lung cancer (NSCLC). Phase 1/2, combination trial with immune checkpoint inhibitors planned for Q1 2018.

**MODITOPE® Modi-1:** Targets variety of solid tumors. Phase 1/2 trial in breast, ovarian, and osteosarcoma planned for Q1 2018.

| Lead Candidates                    | Preclinical                      | Phase 1/2          | > | Phase 2b                        |   |
|------------------------------------|----------------------------------|--------------------|---|---------------------------------|---|
| ImmunoBody® SCIB1<br>Anti-melanoma | Completed                        |                    |   | Phase 2b combination trial 2017 | > |
| ImmunoBody® SCIB2<br>Anti-NSCLC    | Phase 1/2 combination trial 2018 |                    |   |                                 |   |
| Moditope® Modi-1 Anti-solid tumors | Pha                              | ase 1/2 trial 2018 |   |                                 |   |



### THE IMMUNOBODY® PLATFORM

# MEETING THE NEED FOR AN EFFECTIVE THERAPEUTIC CANCER VACCINE

- Successes in the cancer vaccine space include preventative anti-viral vaccines such as Gardasil®, Cervarix®, and Recombivax HB® and therapeutic vaccines such as Provenge® and Imlygic®
- Therapeutic anti-cancer vaccine development has, however, been hampered by high failure rates that can, in large measure, be attributed to a failure to trigger the induction of high avidity (a measure of how well a T cell responds to an antigen) multi-targeted anti-tumor T-cell responses
- Preclinical studies have confirmed that the ImmunoBody® platform delivers ultra-high avidity tumor killing T-cell responses that are superior in magnitude to those generated by current anticancer vaccines
- The ImmunoBody® platform is a highly customizable multi-epitope delivery system that ensures multi-targeted T-cell responses
- Genentech's recent \$310 M upfront and near term milestones for in-licensing of BioNTech's cancer vaccine platform provides further validation of the vaccine approach



### PROMISING PHASE 1/2 TRIAL RESULTS IN MELANOMA PATIENTS

### SURVIVAL "WELL BEYOND ESTABLISHED NORMS"\*

- Of the 20 patients with resected stage III and IV melanoma enrolled in the trial, 95% remain alive today (16 enrolled 2011-2013; 4 enrolled 2014-2015)
- Overall survival (OS) or recurrence-free survival (RFS) with SCIB1 treatment is superior to historical survival rates, including those seen in:
  - Untreated stage IV patients
    - Deaths: 14% SCIB1 versus 64% untreated
  - Stage III and IV patients treated with a peptide-based vaccine
    - Deaths: 6% SCIB1 versus 21% peptide treated

Historical comparisons for the first 16 patients with long-term follow-up

| Fully resected melanoma patients | Proportion of Patients with Melanoma Recurrence at 3 years (%) |                                 |             |                      |                        |  |  |  |
|----------------------------------|--|---------------------------------|-------------|----------------------|------------------------|--|--|--|
|                                  | SCIB1  | Peptide<br>Vaccine <sup>1</sup> | lpilimumab² | Placebo <sup>2</sup> | Untreated <sup>3</sup> |  |  |  |
| Stage III & IV                   | 31   | 48                              |             |                      |                        |  |  |  |
| Stage III                        | 33   |                                 | 54          | 65                   |                        |  |  |  |
| Stage IV                         | 29   |                                 |             |                      | 84                     |  |  |  |

<sup>&</sup>lt;sup>1</sup> Slingluff et al. 2011; <sup>2</sup> Eggermont et al 2015; <sup>3</sup> Sosman et al 2011

\*Dr Keith Flaherty; Massachusetts General Hospital



### **RESULTS OF PHASE 1/2 TRIAL RESULTS IN MELANOMA PATIENTS**

### SURVIVAL "WELL BEYOND ESTABLISHED NORMS"\*

- Median observation time since trial entry is 4 years for 16 patients with resected tumors and receiving 2–4 mg doses
  - Only five patients had disease recurrence and one died
- Median observation time since trial entry is 17 months for 4 patients with resected tumors and receiving 8 mg doses
  - None have had disease recurrence and none have died

\*Dr Keith Flaherty; Massachusetts General Hospital



### **UPCOMING CLINICAL TRIALS**

#### PHASE 2b COMBINATION STUDY

SCIB1 + Anti-PD-1 immune checkpoint inhibitor in melanoma

#### PHASE 1/2 COMBINATION STUDY

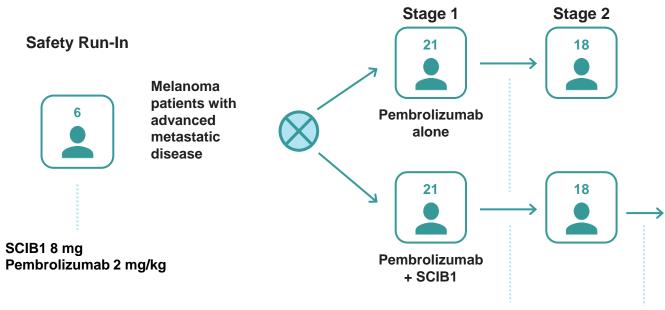
SCIB2 + Anti-PD-1 immune checkpoint inhibitor in non-small cell lung cancer

# RATIONALE FOR THE SCIB1 PHASE 2b COMBINATION TRIAL IN MELANOMA

- Anti-PD-1 checkpoint inhibitors can significantly extend the survival of previously untreatable late stage melanoma patients but response rates are only about 28–33%
- Therapeutic cancer vaccination and T-cell activation provide a means to increase the immunogenicity of cancers and subsequently the response rate to immune checkpoint therapy
- SCIB1 boosts the effect of a PD-1 antibody to significantly enhance response rates and survival times in preclinical animal models of melanoma



#### DESIGN FEATURES OF THE SCIB1 PHASE 2b COMBINATION TRIAL



#### Design

Randomize at start of pembrolizumab

Null response rate 35%, improved to 55%

Total study size: 21 + 18 per group plus 6 run-in = **84 patients** 

Alpha = 0.05 (two-sided); power = 80%

For each group ≥9 RECIST responses required to progress to Stage 2

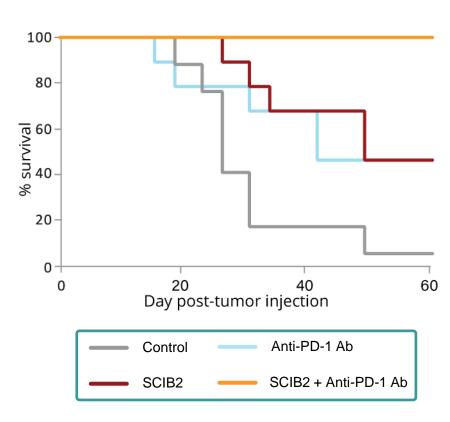
Considered worthy of further study if ≥19 RECIST responses in a group of 39

- Principal investigator Dr Keith Flaherty, with additional sites at MSK and University of Colorado
- Enrollment expected to begin in Q3 2017



# RATIONALE FOR THE SCIB2 PHASE 1/2 COMBINATION TRIAL FOR LUNG CANCER

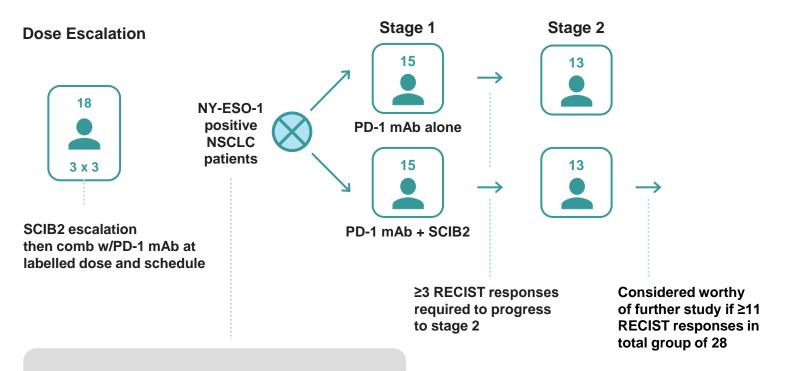
- 80% of patients with non-small cell lung cancer (NSCLC) fail to respond to anti-PD-1 inhibitors because their tumours are insufficiently immunogenic
- Therapeutic cancer vaccination and T-cell activation may serve to increase the immunogenicity of lung cancers and subsequently the response rate to immune checkpoint therapy
- In a mouse lung cancer model, survival rates achieved with the SCIB2 ImmunoBody® were comparable to that seen with anti-PD-1 immune checkpoint therapy¹
- Survival rates were boosted to 100% when anti-PD-1 therapy was combined with SCIB2 treatment¹



1.Xue et al., Oncoimmunology. 2016 Apr 22;5(6):e1169353. [Epub Ahead of Print]



### DESIGN OF THE SCIB2 PHASE 1/2 COMBINATION TRIAL IN NSCLC



#### **Patient Populations**

Pembrolizumab all patients (19% ORR) or Pembrolizumab <50% PD-L1 +ve (13% ORR)\* or Nivolumab Squamous <10% PD-L1 +ve (16% ORR) or Nivolumab Non-Squam. <10% PD-L1 +ve (11% ORR) \* off-label

#### **Assumptions**

Response rate to PD-1 mAb = 15% Response rate of interest for combination = 35% Total study size:**74 patients** 



### THE COMMERCIAL LANDSCAPE

### MARKET OPPORTUNITIES FOR SCIB1/SCIB1 PLUS

#### COMBINATION WITH CHECKPOINT INHIBITORS IN METASTATIC SETTING

- Stage III/IV patients are indicated for checkpoint inhibitor therapy
- There are a growing number of available patients as approved use broadens to include larger segments of the market
- Increase efficacy to 55% of patients

#### MONOTHERAPY IN ADJUVANT SETTING

The majority of melanoma is treated surgically; however, approximately 22%\* of patients have stage IIB, IIC, and III melanoma and are at high risk of recurrence without an acceptable standard of care

- The only FDA-approved therapies, interferon-α and Yervoy®, have severe side effects resulting in discontinuation of therapy in up to 50%\*\* of patients despite RFS benefits
- There is a significant market opportunity
  - ≥ 220,000 patients with stage IIB, IIC, and III melanoma, of which 45% can be treated with SCIB1\*\*\* at an estimated annual cost of \$40k representing a \$4b market in the U.S. alone
- SCIB1 is designed to offer an improved efficacy and safety benefit above the current standard of care

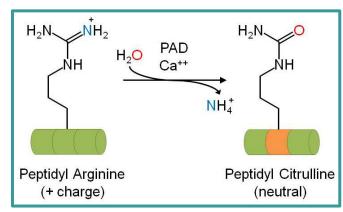
<sup>\*</sup>Cancer Research UK 2014 \*\* Eggermont et al, 2015 \*\*\* "MHC Ligands and Peptide Motifs" by Hans-Georg Rammensee et al, 1997



## THE MODITOPE® PLATFORM

## A NOVEL IMMUNOTHERAPY THAT OVERCOMES IMMUNOSUPPRESSION AND DELIVERS UNPRECEDENTED KILLER T-HELPER CELL RESPONSES

- Post-translational modifications of proteins occur under conditions of cellular stress
- One such modification involves the process of citrullination
  - Involves the alteration of proteins due to enzymatic conversion of arginine residues to citrulline
  - Citrullination occurs as a result of a degradation and 'recycling' process called autophagy\* that is induced in stressed cells including cancer cells
    - \* 2016 Nobel Prize in physiology/medicine awarded to Prof Ohsumi for discovery of autophagy mechanisms



PAD = peptidylarginine deiminase

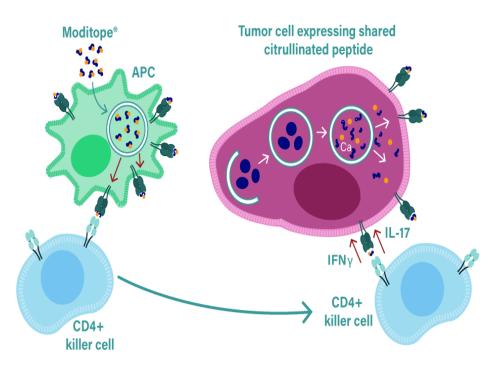
- Increased citrullination of proteins is observed in autoimmune diseases and results in the expression of 'new' neo-antigens that become targets of powerful autoimmune responses
- Scancell has discovered that the potent immune responses unleashed in response to the detection of citrullinated proteins can be harnessed and redirected in order to destroy cancer cells
- The powerful anti-tumor effect observed does not require checkpoint inhibition and offers a completely new highly customizable approach in immunotherapy

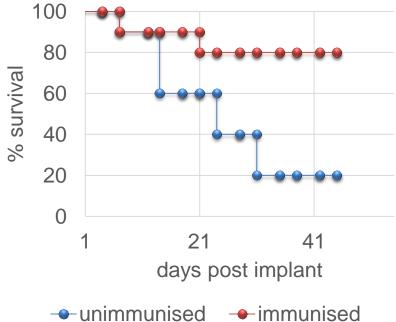


## THE MODITOPE® PLATFORM

# CITRULLINATED PEPTIDES (MODITOPE®) ACTIVATE KILLER T-HELPER CELLS THAT SEEK AND DESTROY CANCER CELLS - update

- Identified new targets
- Identified a new modification
- Published in Cancer Research and Autophagy
- Optimized formulation (reduced dose by 100 fold)
- Showed worked in 3 other mouse models (ID8ovarian cancer)



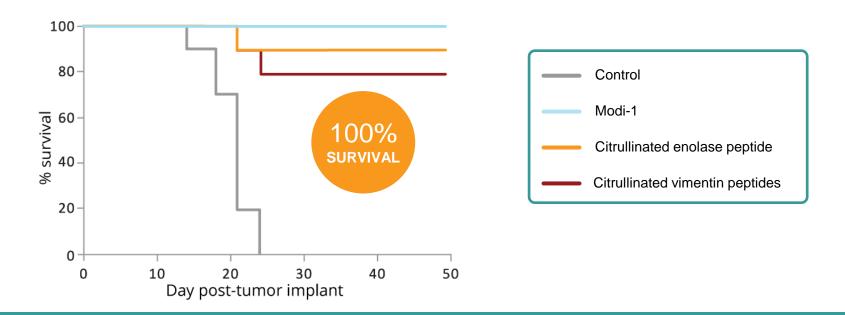




### THE MODITOPE® PLATFORM

### **LEAD MODITOPE® CANDIDATE MODI-1**

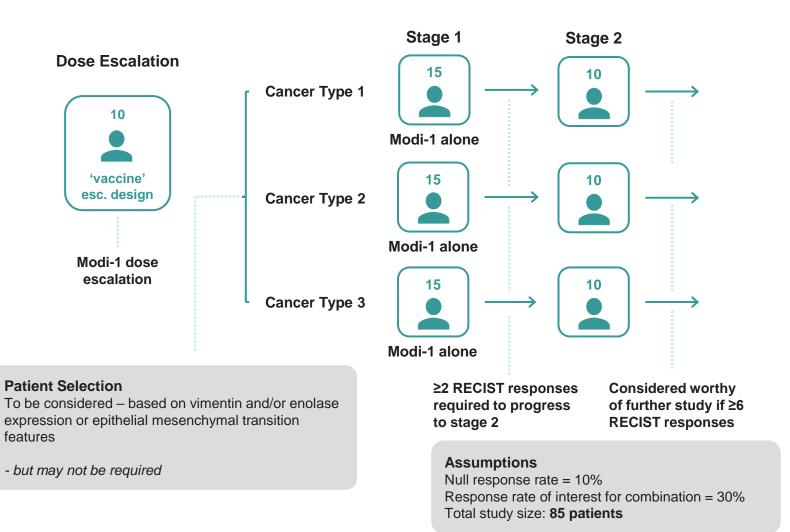
- Consists of:
  - Two citrullinated vimentin peptides (Vim-1 and Vim-2)
  - One citrullinated enolase peptide (Eno-1)
- Vimentin and enolase targets are highly expressed in triple negative breast cancer (90%), ovarian cancer (95%), and osteosarcoma (100%)
- Modi-1 induced potent anti-tumor responses in mice with established melanoma (B16)
- A single immunization of Modi-1 resulted in a 100% survival rate





## THE MODITOPE® CLINICAL DEVELOPMENT PLAN

### **DESIGN OF THE MODI-1 PHASE 1/2 TRIAL**





### **ANTICIPATED NEWS FLOW: 2016-2018**

#### 2016

**Q4** 

SCIB1 phase 1/2 final Clinical Report completed
SCIB1 phase 1/2 survival update
Start Modi-1 manufacture

#### 2017

Q1

SCIB1 IND filed

Q2

SCIB1 IND approval

Start SCIB2 manufacture

Q3

First patient treated in SCIB1 combo trial

Modi-1 CTA filed

SCIB2 IND filed

Quarterly

SCIB1 phase 1/2 survival update

#### 2018

Q1

Safety data on SCIB1/checkpoint inhibitor combination released

First patient treated in Modi-1 trial

First patient treated in SCIB2 combo trial

**Q4** 

First efficacy data from SCIB1 combo trial

Go/No Go decision on Part 2 of SCIB1 combo trial

Quarterly

SCIB1 phase 1/2 survival update