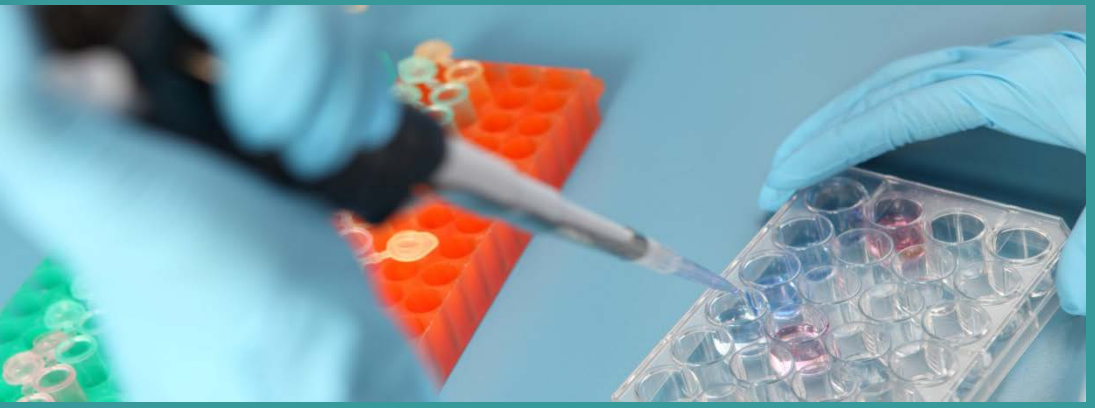
SCANCELL

A NEW FRONTIER IN IMMUNO-ONCOLOGY

16 February 2018

LSE: SCLP.L



AGENDA

Dr Cliff Holloway	Scancell overview & strategy
Prof Lindy Durrant	Moditope® therapies
Mr Gerben Moolhuizen	Amplivant® technology and new generation immunotherapeutics
Dr Peter Brown	ImmunoBody® SCIB2 for lung cancer
Prof Poulam Patel	ImmunoBody® SCIB1 for melanoma
Q & A	

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DIFFERENTIATED IMMUNO-ONCOLOGY CLINICAL STAGE OPPORTUNITY

- Scancell is developing innovative immunotherapies for the treatment of cancer
- Immuno-oncology is one of the fastest growing sectors in the biopharmaceutical industry
- Scancell is transitioning towards commercialisation of key assets
- **2 PLATFORMS, 4 LEAD PRODUCTS, MULTIPLE CANCER INDICATIONS**
- **IMMUNOBODY®** and **MODITOPE®** immunotherapies stimulate the immune system by presenting cancer antigens to trigger potent killer T-cell activation

IMMUNOBODY®

- SCIB1 – melanoma (Phase 1/2 study complete)
- SCIB2 – non-small cell lung cancer (NSCLC) and other solid tumours

MODITOPE®

- Modi-1 – triple negative breast cancer (TNBC), ovarian cancer and sarcoma
- Modi-2 – multiple solid tumours including oesophageal, gastric, pancreatic, colorectal

TWO DIFFERENTIATED INNOVATIVE PLATFORMS

IMMUNOBODY®

- DNA-based platform for the generation of high avidity CD8 anti-tumour cells

MODITOPE®

- Modified citrullinated peptides that deliver potent killer CD4 T-cells to target neo-epitopes

Ref: Chen and Mellman 2013

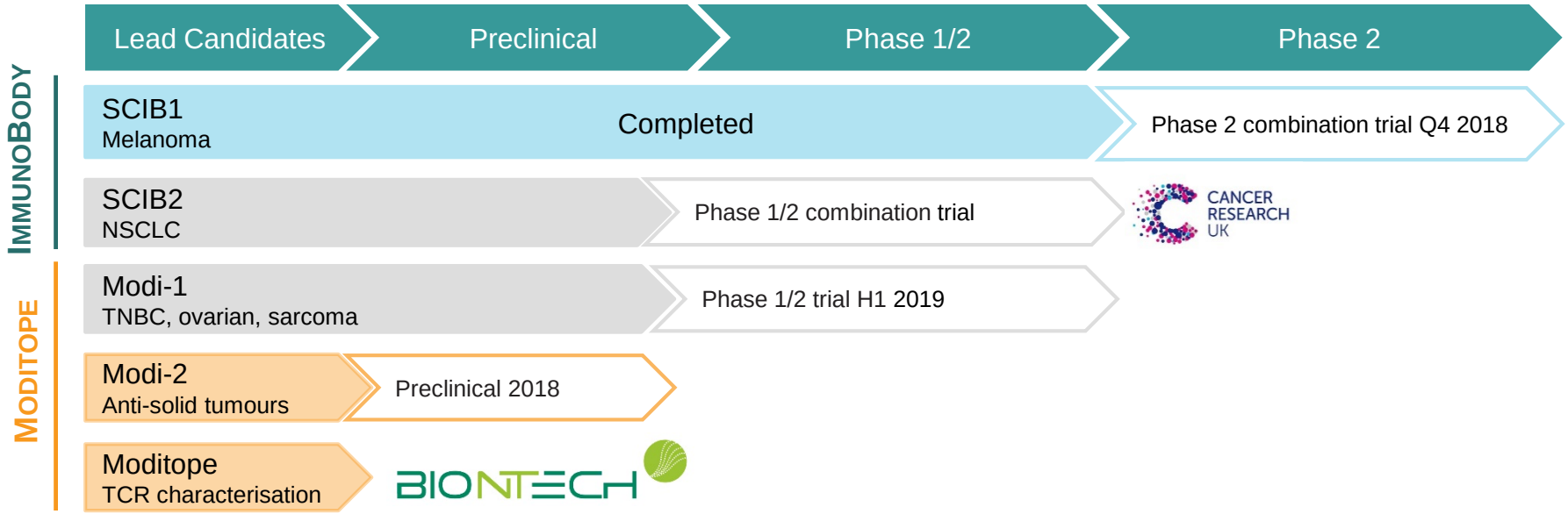
DEVELOPMENT PIPELINE

IMMUNOBODY®

- **SCIB1:** Targets malignant melanoma. Phase 1/2 study completed with strong survival data. Phase 2 combination trial with immune checkpoint inhibitor planned for Q4 2018.
- **SCIB2:** Targets NSCLC. Phase 1/2 combination trial with immune checkpoint inhibitor to be funded and sponsored by CRUK.

MODITOPE®

- **Modi-1:** Manufacturing process development initiated. Phase 1/2 trial in TNBC, ovarian and sarcoma planned for 1H 2019.
- **Modi-2:** Targets multiple solid tumours. Preclinical development of selected epitopes planned 2018.
- **TCR collaboration:** To clone and characterise T cell receptors against Modi-specific epitopes.



OPPORTUNITIES FOR NEW CANCER IMMUNOTHERAPIES

OPPORTUNITIES

- Replace or combine with current standard of care (SOC) treatments
- Provide therapies with an improved safety profile
- Demonstrate efficacy in cancer patients with high unmet needs
- Demonstrate durable response to treatment
- Delay/prevention of disease recurrence

IMPLEMENTATION

- Identify new cancer targets and/or therapeutic approaches to known targets
- Improve understanding of immune system and role in cancer
- Synergies with new targeted therapies
- Synergies with other immunotherapies (e.g., checkpoint inhibitors)
- Focus on traditionally hard-to-treat cancers and unmet needs in disease management

IDENTIFIED OPPORTUNITIES IN A RANGE OF TREATMENT SETTINGS

IMMUNOBODY®

SCIB1

- In combination with checkpoint inhibitors in patients with late stage disease to increase efficacy without compromising safety
- As monotherapy in patients with resected disease (adjuvant setting) to delay or prevent recurrence

SCIB2

- Lung cancer represents a huge unmet medical need; deaths per year greater than melanoma, colon, breast and prostate cancers combined
- Checkpoint inhibitors less effective in lung cancer, with 80% of patients requiring a better SOC

MODITOPE®

Modi-1 & Modi-2

- Innovative mechanism of action potentially targets all solid tumours
- Broad patent filing offers potential to dominate the use of citrullinated peptides for the treatment of cancer
- Modi-1 and Modi-2 will target tumours that are unresponsive to checkpoint inhibitor therapy (turning “cold” tumours to “hot”)
- Identification of Modi-specific TCRs provides a novel pathway for CD4-based TCR therapy

VALIDATION AND ENDORSEMENT

- Clinical Research UK (CRUK) clinical trial partnership announced December 2017
- BioNTech research collaboration announced January 2018

CRUK (SCIB2)

- CRUK is one of the world's leading cancer charities
- CRUK responsible for manufacture, regulatory submissions and conducting clinical trial
- Key terms:
  - Scancell will have the option to acquire the rights to the data on completion of the study
  - Revenue share agreement if option not exercised

BioNTech (MODITOPE®)

- BioNTech is Europe's largest private biotech company
- Initial research focus on Modi-1 epitopes (vimentin and enolase)
- Incorporates BioNTech platform for cloning and characterisation of TCRs
- BioNTech exclusive option to license identified TCRs
- Extensive commercial interest in T-cell therapies e.g., Gilead's USD11.9Bn acquisition of Kite Pharma

CANCER RESEARCH UK

SIGNIFICANT ENDORSEMENT OF SCANCELL'S TECHNOLOGY BY RENOWNED ONCOLOGY PARTNERS

BIONTECH

PROGRESS SINCE LAST FUNDING (MAY 2017, £5m)

- External validation of ImmunoBody® and Moditope® immunotherapy platforms
- Internal projects advanced and expanded

IMMUNOBODY®

- Clinical Development Partnership with CRUK for SCIB2 in non-small cell lung cancer (Dec 2017)
- SCIB1 advancing to IND submission (Ichor Trigrid 2.0 Master File submitted to FDA Feb 2018)
- Publication of SCIB1 Phase1/2 study (Feb 2018)
- Excellent 5-year survival data in late stage resected melanoma patients (Feb 2018)

MODITOPE®

- BioNTech research collaboration to develop T-cell based therapies (Jan 2018)
- CRUK Grand Challenge shortlist (Feb 2018)
- EPO notice of allowance for Moditope® patent (Feb 2018)
- Licensing of ISA Pharmaceuticals' Amplivant® technology (Feb 2018)
- Citrullinated peptides identified for inclusion in Modi-2 vaccine (Dec 2017)
- GMP manufacturers identified for production of Modi-1 (Jan 2018)

PRODUCTS, PATIENTS, PATENTS and PARTNERSHIPS

ANTICIPATED SHORT–MEDIUM TERM MILESTONES

IMMUNOBODY®

2018

- Q2: SCIB1 IND filed
- Q2: SCIB2 manufacturing development starts
- Q4: SCIB1 Phase 2 starts
- Q4: SCIB2 toxicology studies start

2019

- 1H: SCIB1 Phase 2, Part 1 complete
- 1H: SCIB2 toxicology complete
- 2H: SCIB1 Phase 2, Part 2 complete

MODITOPE®

2018

- Q1: Modi-1 GMP manufacture starts
- Q1: Start evaluation of Modi-specific TCRs
- Q4: Modi-1 CTA filed

2019

- 1H: First patient in Modi-1 clinical trial
- 1H: Modi-2 development candidate characterised
- 1H: Complete initial evaluation of Modi-specific TCRs
- 1H: Modi-2 GMP manufacturing starts

2020

- 1H: Modi-1 clinical trial completed

EXPERIENCED MANAGEMENT TEAM

CHAIRMAN **DR JOHN CHIPLIN**	John is MD of Newstar Ventures Ltd, an investment and advisory firm. Recent transaction experience includes Benitec Biopharma (US IPO), Adalta and Sienna Cancer Diagnostics (Australian IPOs), Medistem (acquired by Intrexon), Arana (acquired by Cephalon) and Domantis (acquired by GSK).
CEO **DR CLIFF HOLLOWAY**	Cliff has worked in the life science industry for over 25 years and has expertise in the development and commercialisation of emerging technologies and drug products. He is joined Scancell in January 2018 from Benitec Biopharma (ASX and NASDAQ listed), where he held the position of Chief Business & Operating Officer.
CSO **PROF LINDY DURRANT**	Lindy is an internationally recognised immunologist in the field of tumour therapy and co-founder of Scancell. She has worked for over 25 years in translational research, developing products for clinical trials including monoclonal antibodies & vaccines. She has a Chair in Cancer Immunotherapy at the University of Nottingham.
DIRECTOR **DR RICHARD GOODFELLOW**	Richard ran international clinical trials on Astra's gastrointestinal and cardiovascular products before becoming Director of International Product Marketing. He co-founded Paradigm and was a Board Director of Enact Pharma prior to joining Scancell as co-founder in 1998 and CEO until Dec 2017.
DEVELOPMENT DIRECTOR **DR SALLY ADAMS**	Sally has over 25 years of experience in drug development, including vaccine and cancer immunotherapy development, both in senior management positions within the biotechnology industry and as an independent consultant. Sally was appointed Development Director in May 2014.
CONSULTANT **DR PETER BROWN**	Former Vice President and Global Head of Oncology at Teva Pharmaceuticals and previously Vice President of Clinical Oncology and Experimental Medicine at Cephalon. Peter has over 25 years of experience in the development of cancer therapeutics from early stage to FDA and EMA approval.
FINANCE DIRECTOR **KEITH GREEN**	During the past thirteen years, Keith has had numerous consultancy and interim finance roles for private and AIM listed companies in the life science sector. He started working for Scancell on a part-time basis in January 2010 and took up this full-time role in September 2016.

NEAR TO MEDIUM TERM VALUE DRIVERS

2 PLATFORMS, 4 LEAD PRODUCTS + 5 CORE ACTIVITIES

CLINICAL DATA:	Generate meaningful clinical data to address unmet needs: 2 clinical read-outs (SCIB1 Phase 2 & Modi-1 Phase1/2) anticipated in next 2 years
PIPELINE EXPANSION:	Extend utility of Moditope platform beyond Modi-1 and Modi-2 in association with key industry players e.g., TCR's (BioNTech) and pending CRUK Grand Challenge
TECHNOLOGY PARTNERSHIPS:	Evaluate and implement enabling technologies to de-risk development e.g., TriGrid (Ichor) and Amplivant (ISA Pharmaceuticals)
CLINICAL PARTNERSHIPS:	Establish relationships with key opinion leaders and clinical networks to ensure utility in clinical practice e.g., CRUK and patient advocacy groups (Addario)
INDUSTRY PARTNERSHIPS:	Explore synergies with large Pharma/Biotech companies in identifying combination therapies for optimal outcomes e.g., checkpoint inhibitors

BIONTECH

ichor medical systems

ISA Pharmaceuticals

CANCER RESEARCH UK

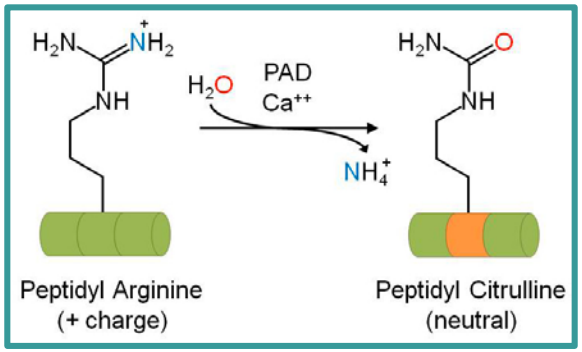
LUNG CANCER FOUNDATION

Moditope® therapy

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*
  - *Citrullinated epitopes presented on MHC class II*



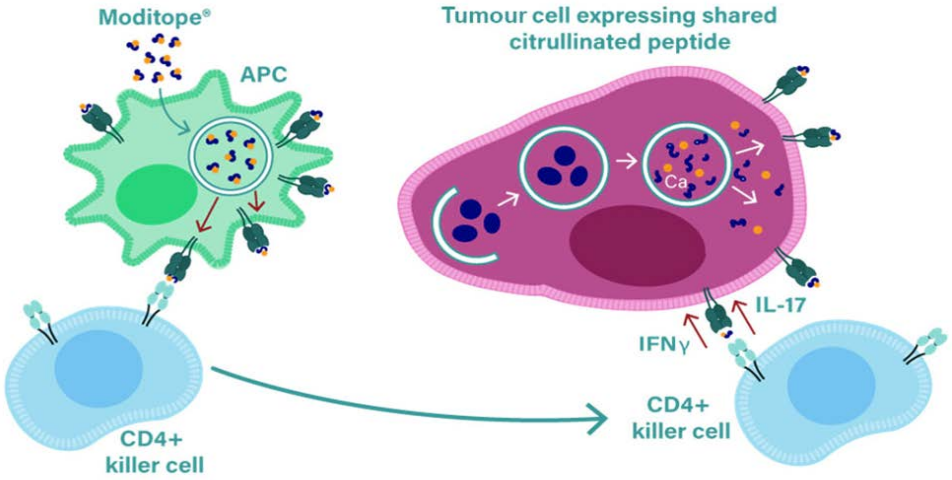
PAD = peptidylarginine deiminase

- The Moditope® platform is based on exploiting this normal immune response to stressed cells, which is largely mediated by cytotoxic CD4 T cells
- The novelty of the technology is harnessing this mechanism to eradicate tumour cells by immunizing with citrullinated peptides
- Intention to grant European patent for the use of any citrullinated epitope for the treatment of cancer
- Patents in other jurisdictions still being examined

MODE OF ACTION

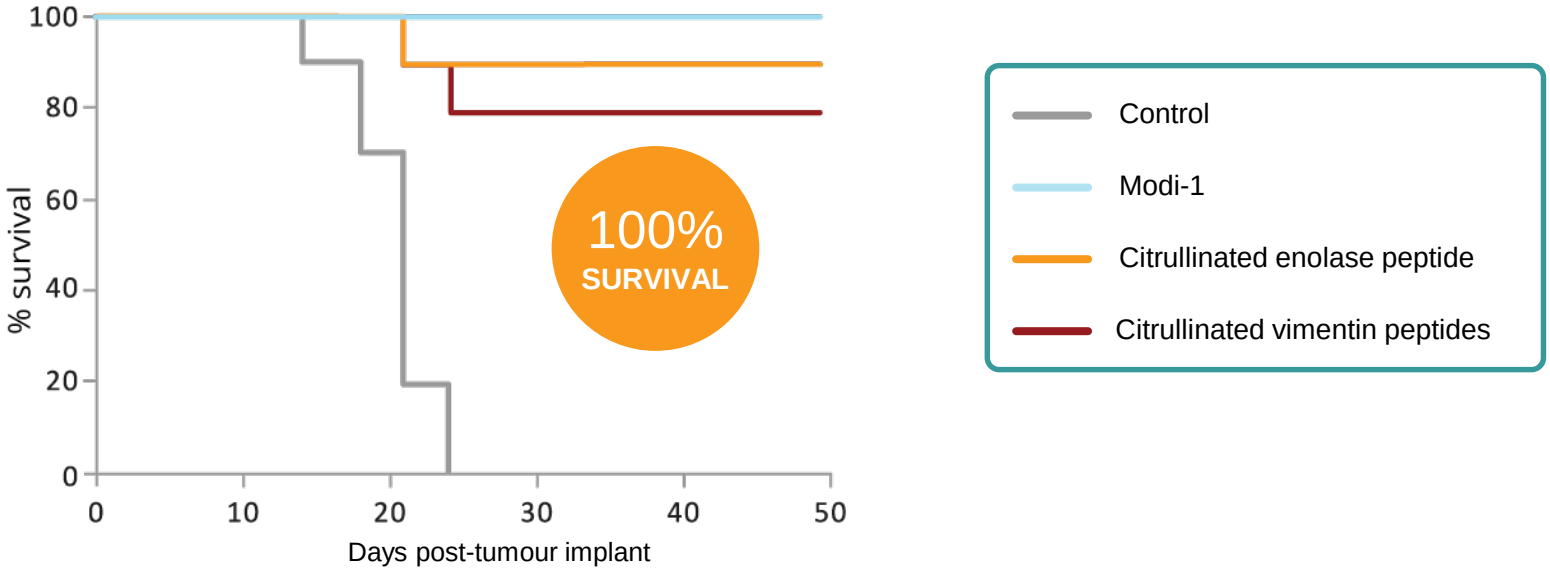
CITRULLINATED PEPTIDES (MODITOPE®) ACTIVATE KILLER T-HELPER CELLS THAT SEEK AND DESTROY CANCER CELLS

- Citrullinated tumour-associated peptides (Moditope® peptides) are administered with adjuvant to activate antigen presenting cells (APCs)
- Moditope peptides are taken up by activated APCs
- APCs present peptides to CD4 killer T-cells
- Primed CD4 killer T-cells enter the tumour
- Stressed tumour cells undergo autophagy and produce citrullinated proteins which can be taken up by APCs
- CD4 T cells recognise citrullinated epitopes presented by APCs and release IFNγ which induces expression of MHC-II on tumour cells
- Primed CD4 killer T-cells destroy cancer cells



Modi-1

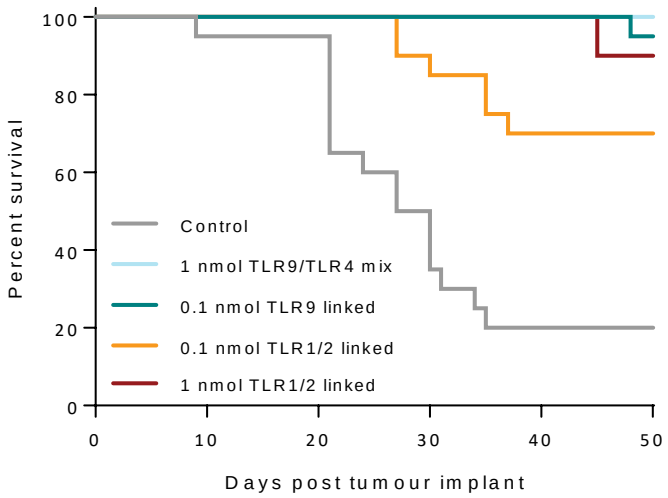
- Consists of:
  - Two citrullinated vimentin peptides (Vim-1 and Vim-2)
  - One citrullinated enolase peptide (Eno-1)
- Vimentin and enolase targets are highly expressed in triple negative breast cancer (90%), ovarian cancer (95%), and sarcoma (100%) - all with high unmet medical need
- Modi-1 induced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



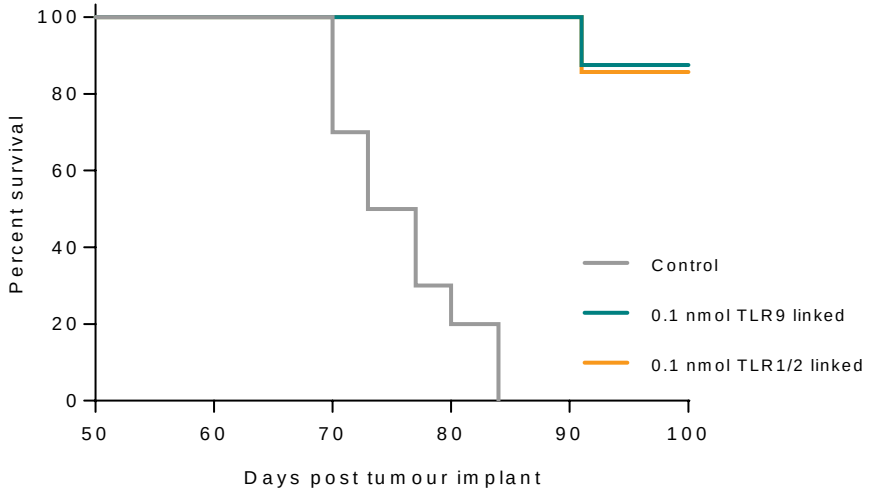
MODI-1 DEVELOPMENT: ISA COLLABORATION

- Conjugation of peptide to Amplivant® (ISA Pharmaceuticals) enhances responses 10-100 fold
- Low dose TLR agonist-linked peptides induce responses that show efficient tumour therapy and establish immunological memory to protect from tumour recurrence
- Peptide-TLR agonist conjugates enable better scaling of dose into human studies

TUMOUR RESPONSE



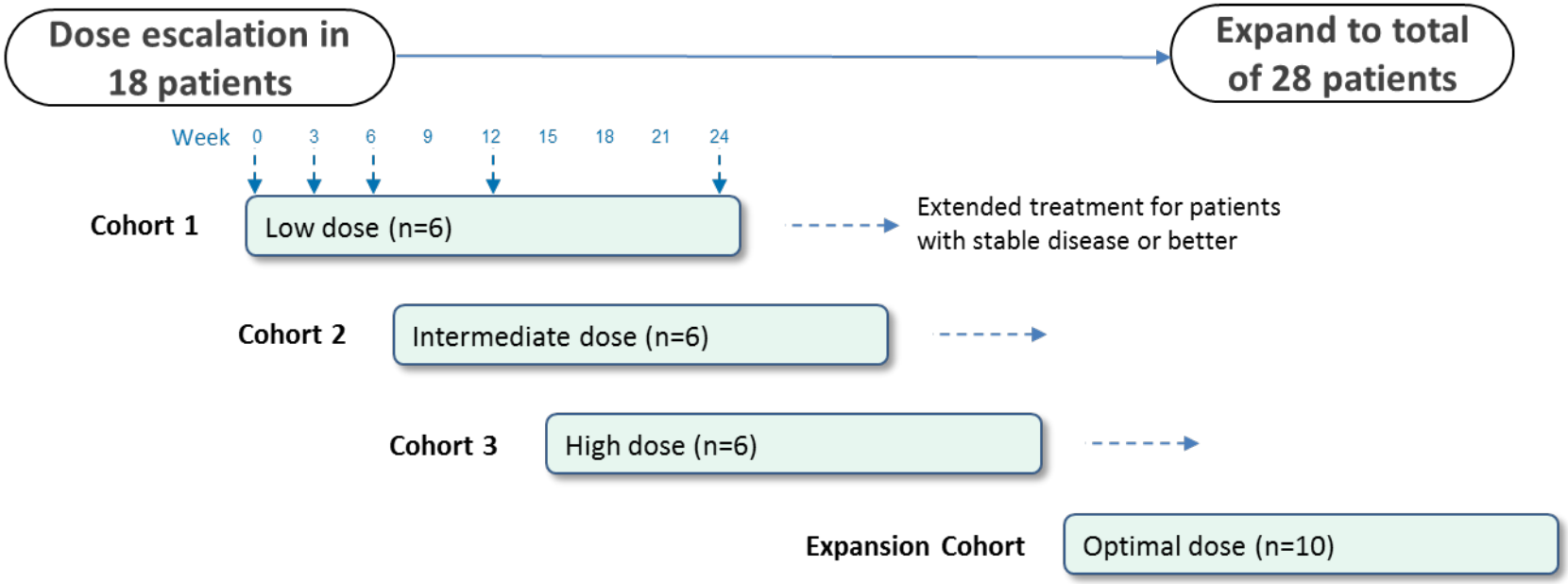
RE-CHALLENGE



MODI-1 FIRST IN HUMAN STUDY

PATIENT POPULATION

- Patients with tumours with high vimentin or enolase expression (*e.g.,* sarcoma, TNBC, ovarian)
- Failed or intolerant to standard of care therapies



First patient treated 1H19

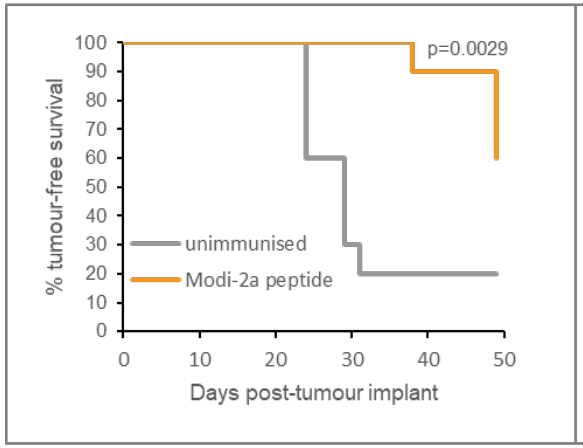
First efficacy and safety data 1H20

Trigger to advance development ≥3 RECIST responses in 16 patients

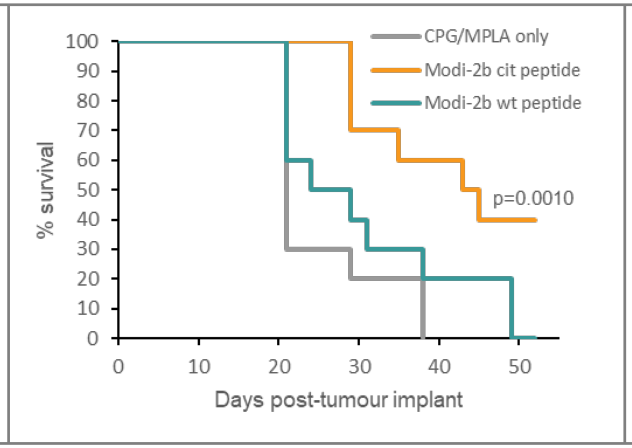
DEVELOPMENT CANDIDATE Modi-2

- Consists of:
  - Citrullinated Modi-2a peptide
  - Citrullinated Modi-2b peptide
  - Citrullinated Modi-2c peptide
  - Citrullinated Enolase peptide
- Targets are highly expressed in oesophageal, gastric, colorectal, breast (non-TNBC), cervical, prostate, liver, renal, endometrial, bladder and thyroid tumours – opportunity to tackle huge unmet need in cancer

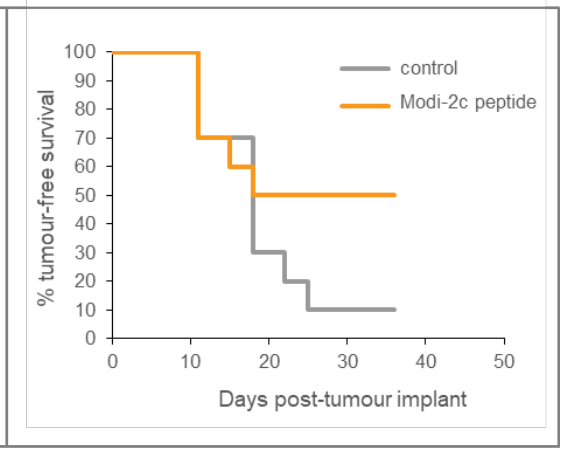
Modi-2a peptide



Modi-2b peptide



Modi-2c peptide



CRUK GRAND CHALLENGE AWARD

- Grand Challenge award recognises research proposals that tackle some of the toughest questions in cancer
- Team's proposal seeks to leverage a tumour vaccine approach to build a blueprint for effective personalised therapy for patients with most types of cancer
- Prof Lindy Durrant, Chief Scientific Officer of Scancell, to lead the multidisciplinary team of eminent cancer immunotherapy scientists, in partnership with BioNtech, ISA and Genentech
- Modi-3 generated from Scancell's proprietary Moditope® platform forms a central element of the approach
- The project focus will be on head and neck cancer, glioblastoma, lung and pancreatic cancer - all of which currently have a poor prognosis
- Treatment with Modi-3 will be assessed alongside vaccines targeting new mutations within individual patients' tumours
- Shortlisting of proposal represents a significant scientific endorsement of Scancell's technology
- £20 million for the whole consortium
- Announced autumn 2018

VALIDATION AND ENDORSEMENT

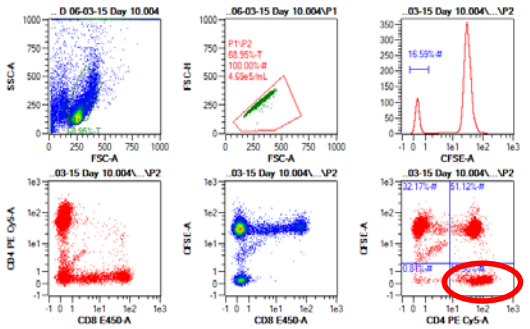
BioNTech research collaboration announced January 2018

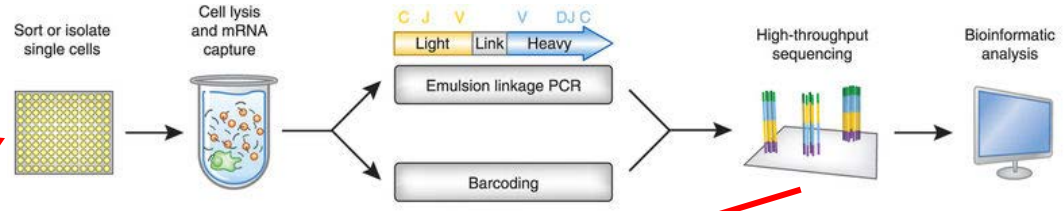
BioNTech (MODITOPE®)

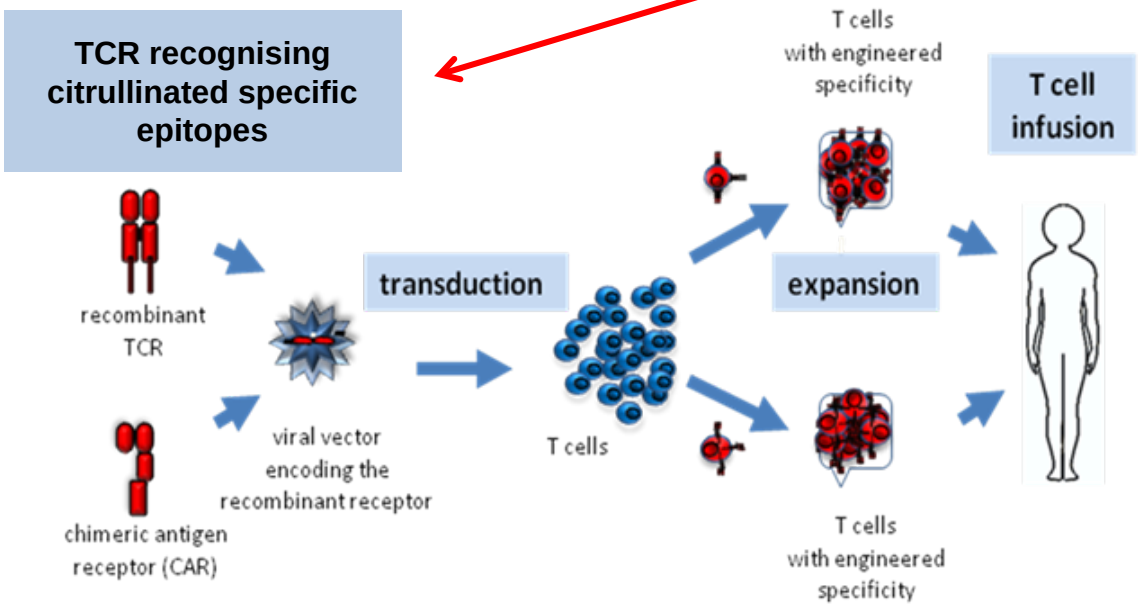
- BioNTech is Europe's largest private biotech company
- Initial research focus on Modi-1 epitopes (vimentin and enolase)
- Incorporates BioNTech platform for cloning and characterisation of TCRs
- BioNTech exclusive option to license identified TCRs
- Extensive commercial interest in T-cell therapies e.g., Gilead's USD11.9Bn acquisition of Kite Pharma

SIGNIFICANT ENDORSEMENT OF SCANCELL'S TECHNOLOGY BY RENOWNED ONCOLOGY PARTNER

TCR TRANSDUCTION AND ADOPTIVE T CELL TRANSFER







Advantages of citrullinated antigen specific TCRs

- Citrullinated antigens are expressed by a wide range of tumours
- Citrullinated antigen-specific T cells recognise the non-polymorphic HLA-DP4 so are applicable to at least 70% of patients
- Citrullinated antigen-specific T cells stimulate potent anti-tumour immunity

SUMMARY

EXTERNAL VALIDATION OF MODITOPE® IMMUNOTHERAPY PLATFORM

INTERNAL PROJECTS ADVANCED AND EXPANDED

MODITOPE®

- Research collaboration to develop T-cell based therapies established with BioNTech
- Collaboration agreed with ISA Pharmaceuticals for development of Amplivant® Modi-1 conjugate therapy
- GMP manufacturers identified for production of Modi-1 using Amplivant®; UK-based study expected to start in 1H19
- Citrullinated peptides identified for inclusion in new Modi-2 vaccine targeting multiple solid tumours
- Shortlisted for CRUK Grand Challenge award

ISA Pharmaceuticals

Next Generation Immunotherapeutics

February 2018

CONFIDENTIAL

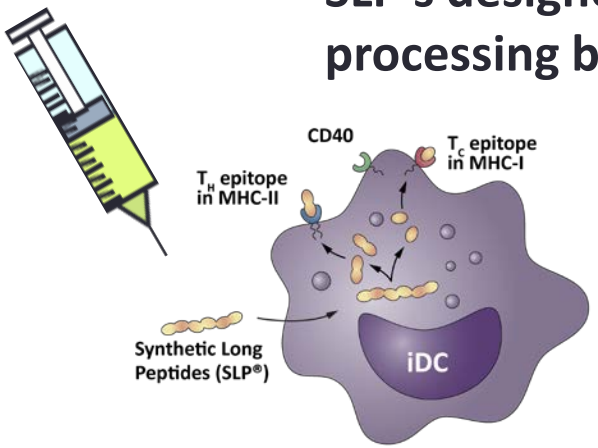
ISA: A pioneer in immunotherapy

- Rationally designed therapeutic vaccines against **cancer** and **persistent viral infections** (e.g., HPV-induced diseases) based on the pioneering work by prof **Kees Melief** (Leiden University)
- Two versatile, proprietary **drug development platforms** (SLP®; AMPLIVANT®) targeting **viral-** and **neo-antigens**
- Fully synthetic compounds with **well-understood mechanism of action**
- **Clinical PoC** with lead program ISA101 established
- Validation through recent **strategic partnership** with REGENERON on ISA101-aPD1 combination; **randomized trials to start in 2018** in late stage HPV16+ cervical cancer and SCCHN
- Lead **proprietary** product to enter **pivotal trials** in **2019**

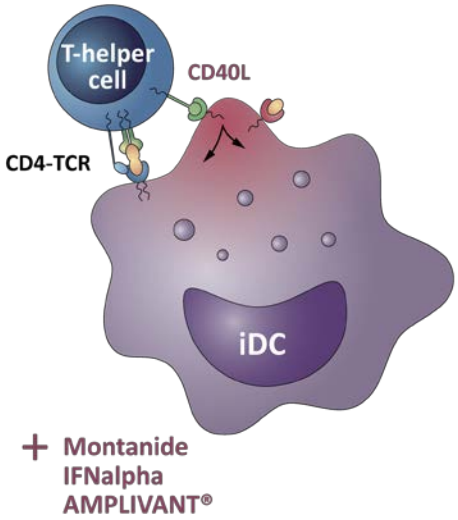
Synthetic Long Peptides (SLP®) induce robust long-lasting cell-mediated immunity

SLP's injection

SLP's designed for efficient uptake and processing by Dendritic Cells (DC's)



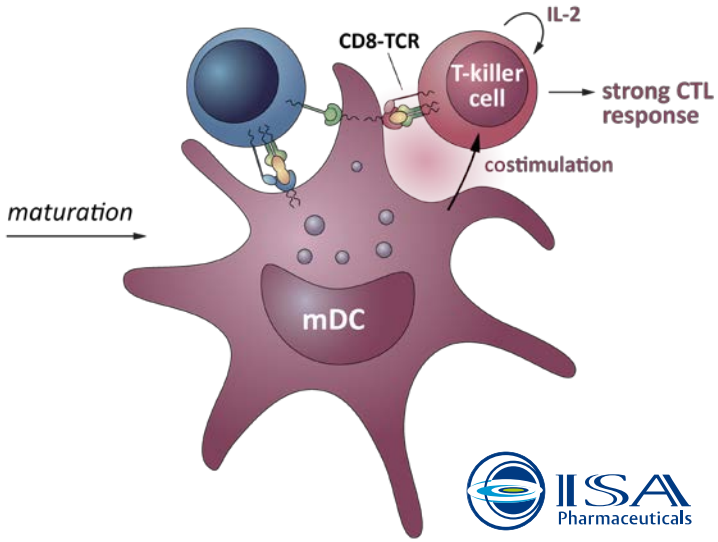
T-helper cell activation



Activation of Cancer Target specific T-cells

Killer and Helper T- cells

T-killer cell activation



ISA101 – aPD1 combination trial in HPV16+ SCCHN at MD Anderson

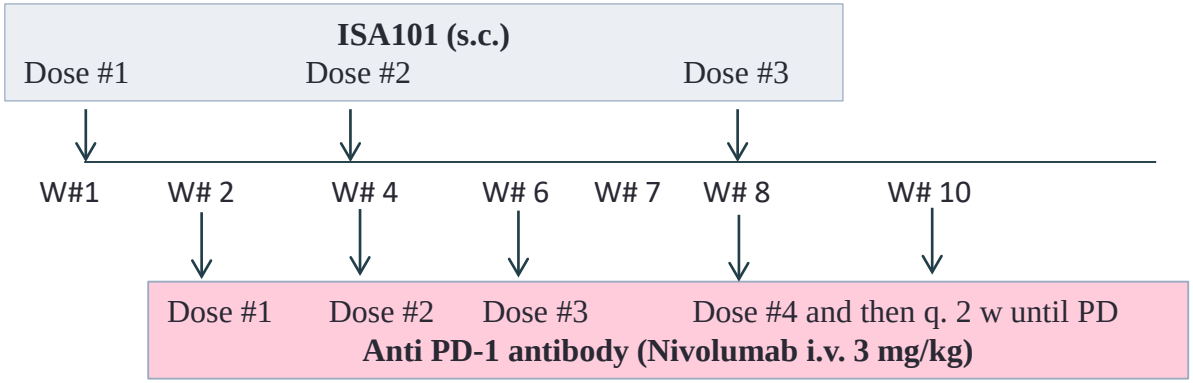
- ISA101: set of SLP's targeting HPV16
- HPV16 main cause of head- and neck cancer (SCCHN)
- Anti-PD1 monotherapy is SoC in 2L SCCHN; HPV+ pts:
  - ORR 15.9%
  - Median Overall Survival 9.1 mo (7.2 – 10.0)
- Trial: combining ISA101 with Nivolumab (aPD-1)

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

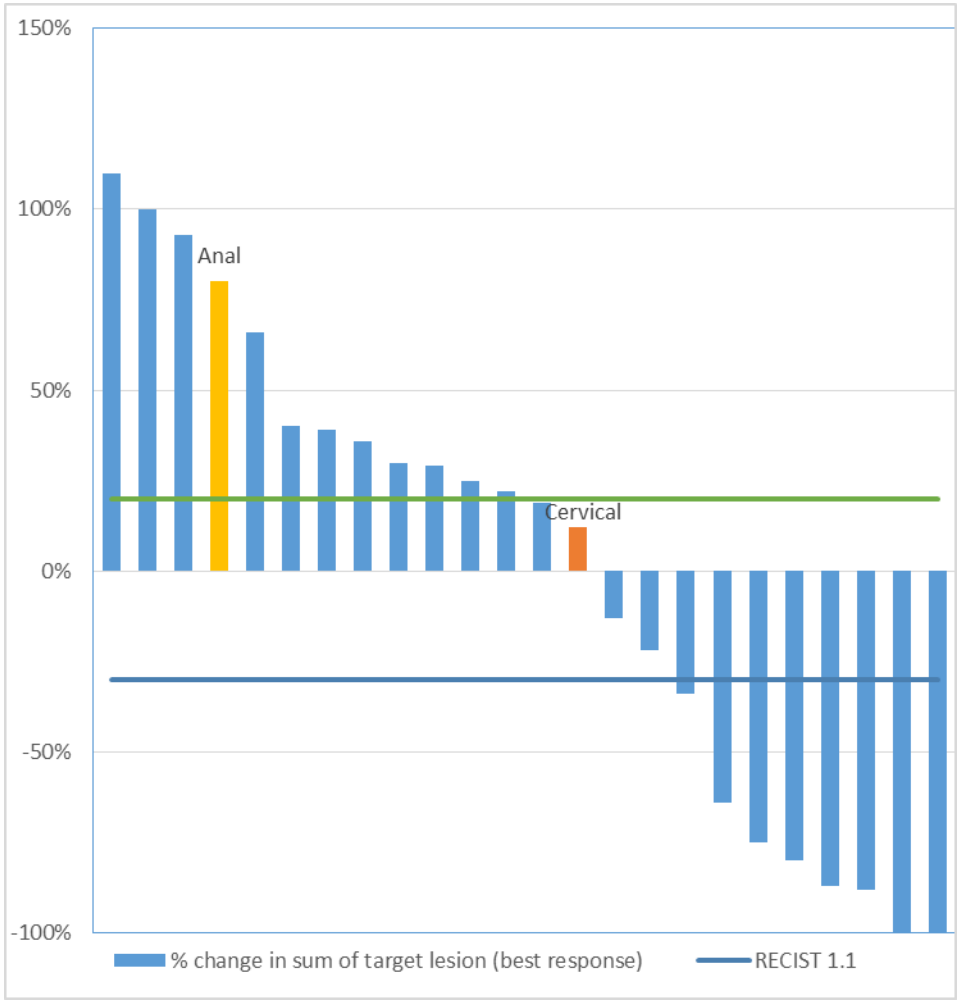
Nivolumab for Recurrent Squamous-Cell Carcinoma of the Head and Neck

R.L. Ferris, G. Blumenschein, Jr., J. Fayette, J. Guigay, A.D. Colevas, L. Licitra, K. Harrington, S. Kasper, E.E. Vokes, C. Even, F. Worden, N.F. Saba, L.C. Iglesias Docampo, R. Haddad, T. Rordorf, N. Kiyota, M. Tahara, M. Monga, M. Lynch, W.J. Geese, J. Kopit, J.W. Shaw, and M.L. Gillison



W=week; PD=disease progression

Intermediate results show > 2x efficacy over nivolumab monotherapy



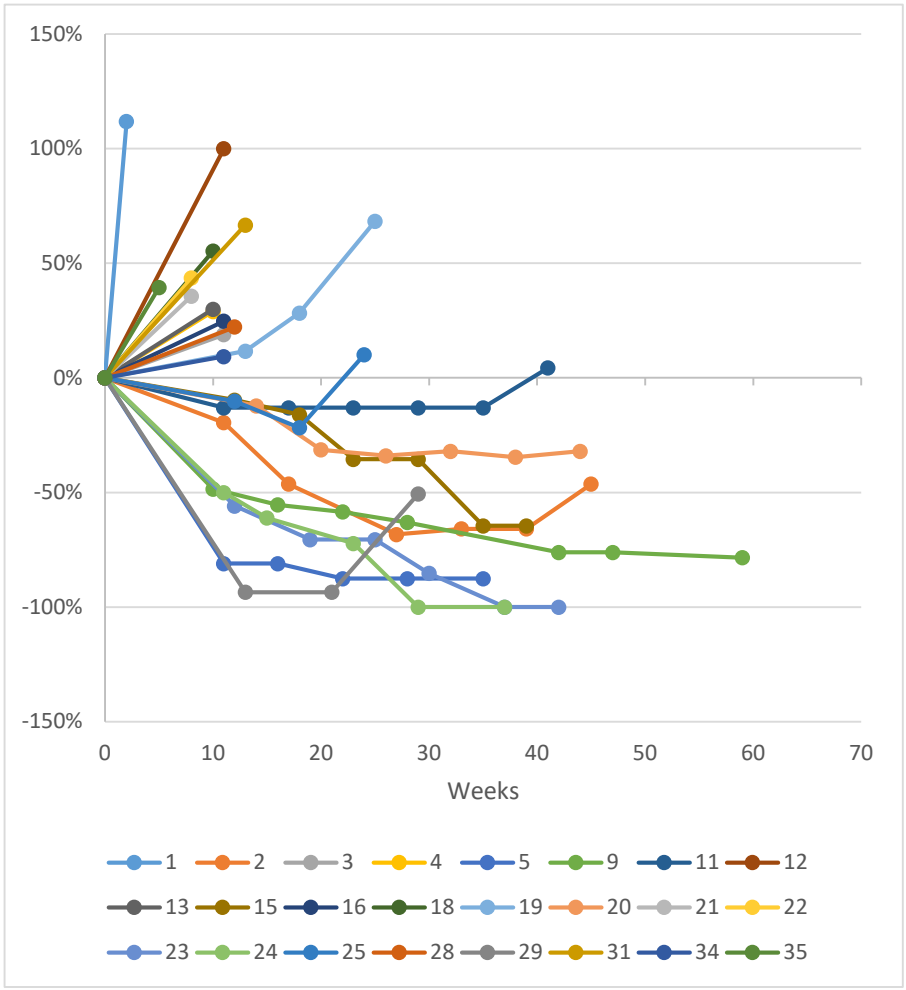
Response RECIST 1.1	% (N) All pts (24)	% (N) OPC (22)
ORR	33 (8)	36 (8)
CR	8 (2)	8 (2)
PR*	25 (6)	25 (6)
SD	13 (3)	8 (2)
PD	54 (13)	55 (12)

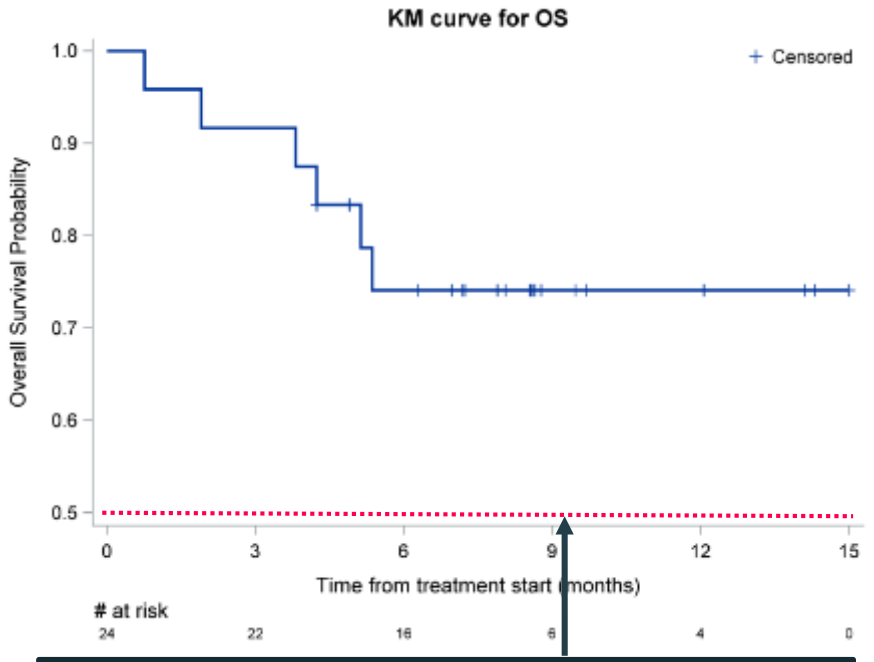
* 1 unconfirmed; OPC, oropharynx cancer; R, refractory

Presented by Bonnie Glisson at 2017 ESMO Congress. Abstract 11360.

ISA Pharmaceuticals

Durable clinical responses induced and encouraging overall survival with ISA101





Nivolumab monotherapy in SCCHN:
Median Overall Survival 9.1 mo (7.2 – 10.0) in HPV+ pts (63)

Ferris et al. (NEJM 2016) / ESMO 2016

Presented by Bonnie Glisson at 2017 ESMO Congress. Abstract 11360.

ISA Pharmaceuticals

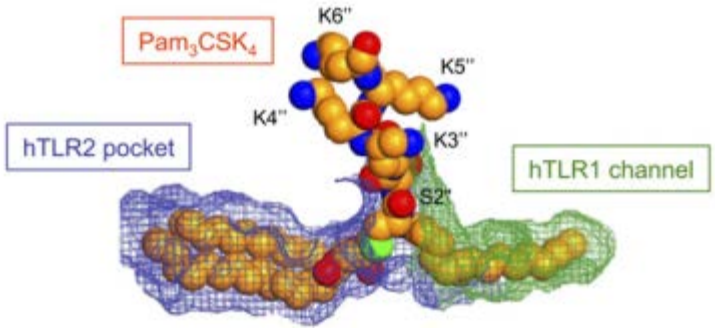
Strong pipeline with lead SLP product entering late stage trials

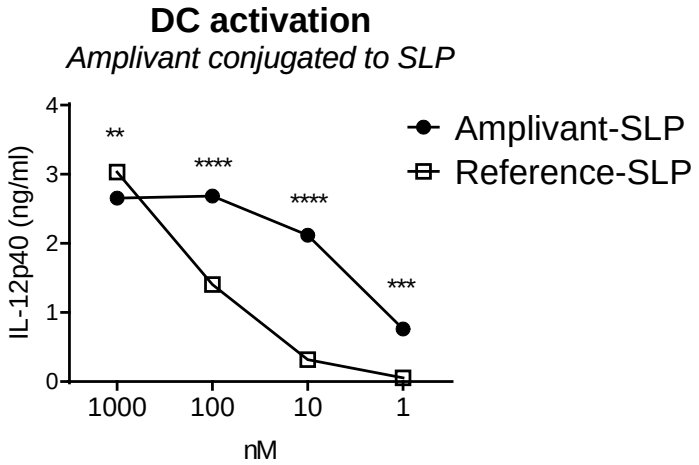
Product	Indication	Pre clinical	Phase 1	Phase 2	Phase 3	Partner
ISA101 (HPV16)	Cervical Cancer	Cemiplimab (aPD1) combo (start 2018)				REGENERON
	SCCHN (2L)	Cemiplimab (aPD1) combo (start 2018)				
	SCCHN (1L; IST)	41BB combo (start 2018)				
ISA201 (HPV16)	SCCHN/Cervical Cancer (Amplivant conjugates; IST)	HESPECTA – ongoing				
HPV- X Orphan indications	Cervical cancer, SCCHN, other	Pivotal trials start 2019				
NEO (Neoantigens)	Personalized therapies*	Anticipated start 2018H2				
ISA203 (PRAME)	Multiple cancer indications					
ISA204 (HBV)	Chronic Hepatitis B					

Amplivant® is an optimized adjuvant for SLP cancer immunotherapy

AMPLIVANT® — Synthetic Long Peptide (SLP®)

AMPLIVANT®: TLR1/2 ligand-based adjuvant technology



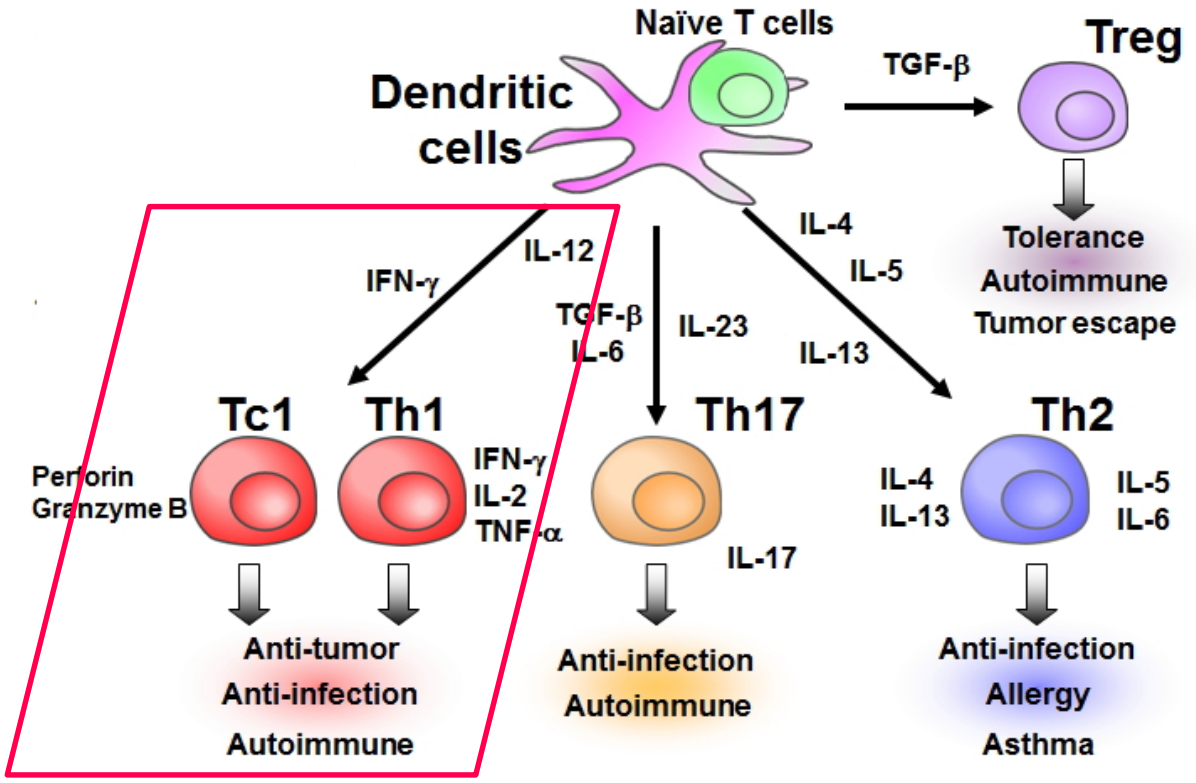


AMPLIVANT® conjugation to SLP® improves

- DC targeting & maturation
- CD8+ (CTL) responses
- in vivo T cell priming and anti tumor response

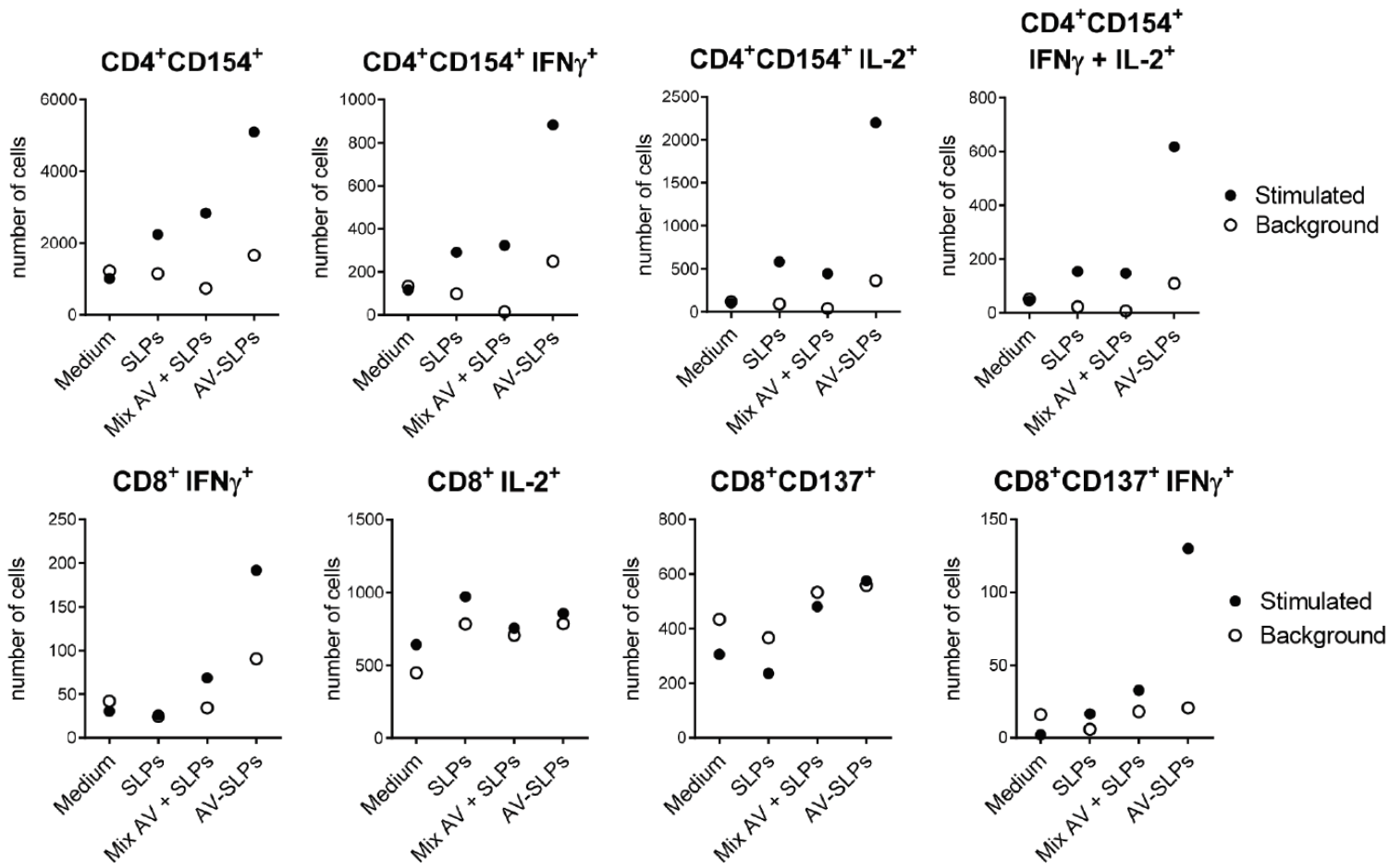
Willems et al; J Med Chem 2014
Zom et al, Oncoimmunol 2014

Th1-type immune response is essential for cancer immunotherapy



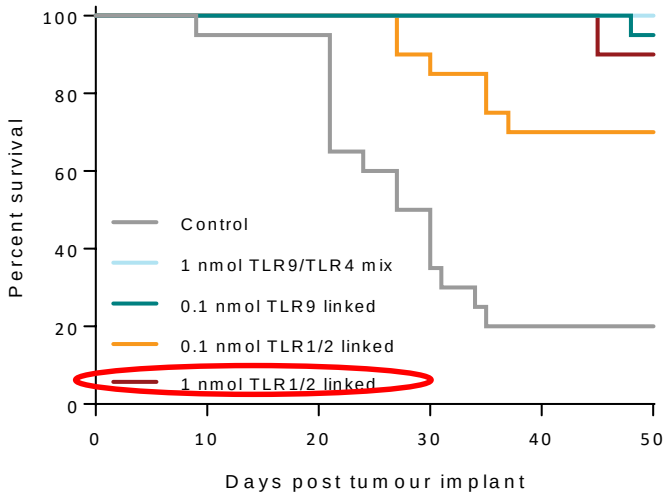
Amplivant® SLP-conjugates induce Th1-type T cell activation

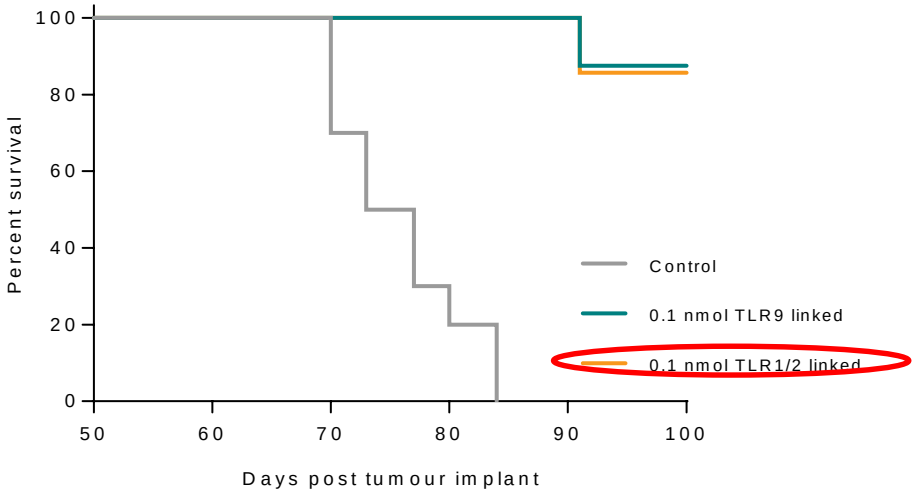
Stimulation of HPV16-induced cancer patient-derived lymph node cells with Amplivant-SLP conjugates



Zom et al, *Oncotarget 2016*

In vivo results with Amplivant-Moditope conjugate encouraging



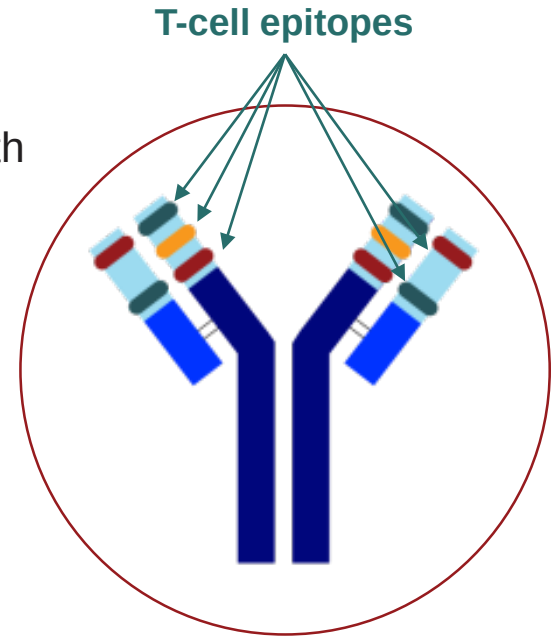


ISA Pharmaceuticals

SCIB2 ImmunoBody®
for lung cancer

MEETING THE NEED FOR AN EFFECTIVE THERAPEUTIC CANCER VACCINE

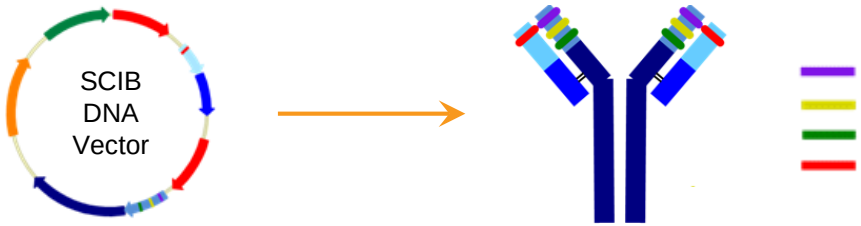
- Key challenge is to stimulate an effective T cell response to reject or kill the growing tumour
- Most vaccine strategies only stimulate low frequency, low avidity T cell responses that fail to control tumour growth
- Avidity is a measure of the overall strength of the interaction between a T cell and its target
- Only high avidity cytotoxic T lymphocytes:
  - are selected into the memory pool
  - mediate tumour eradication



ImmunoBody® is a simple, novel approach that stimulates **high avidity**, **high frequency** CD8 and CD4 T cells that efficiently kill tumours

MEETING THE NEED FOR AN EFFECTIVE THERAPEUTIC CANCER VACCINE

- Proprietary patent protected platform
- Several cancer associated T cell epitopes are engineered into a human antibody framework to make a genetic antigen/antibody complex
- Delivered as a DNA plasmid using electroporation



Cancer antigen sequences inserted into CDRs of ImmunoBody®

- Nano-vesicle delivery under evaluation
- Novel dual mechanism of action based on **direct** and **cross-presentation**
- SCIB1 for melanoma: Phase 1/2 clinical trial complete, Phase 2 planned
- SCIB2 for lung cancer: Clinical development partnership with CRUK

THE IMMUNOBODY® PLATFORM

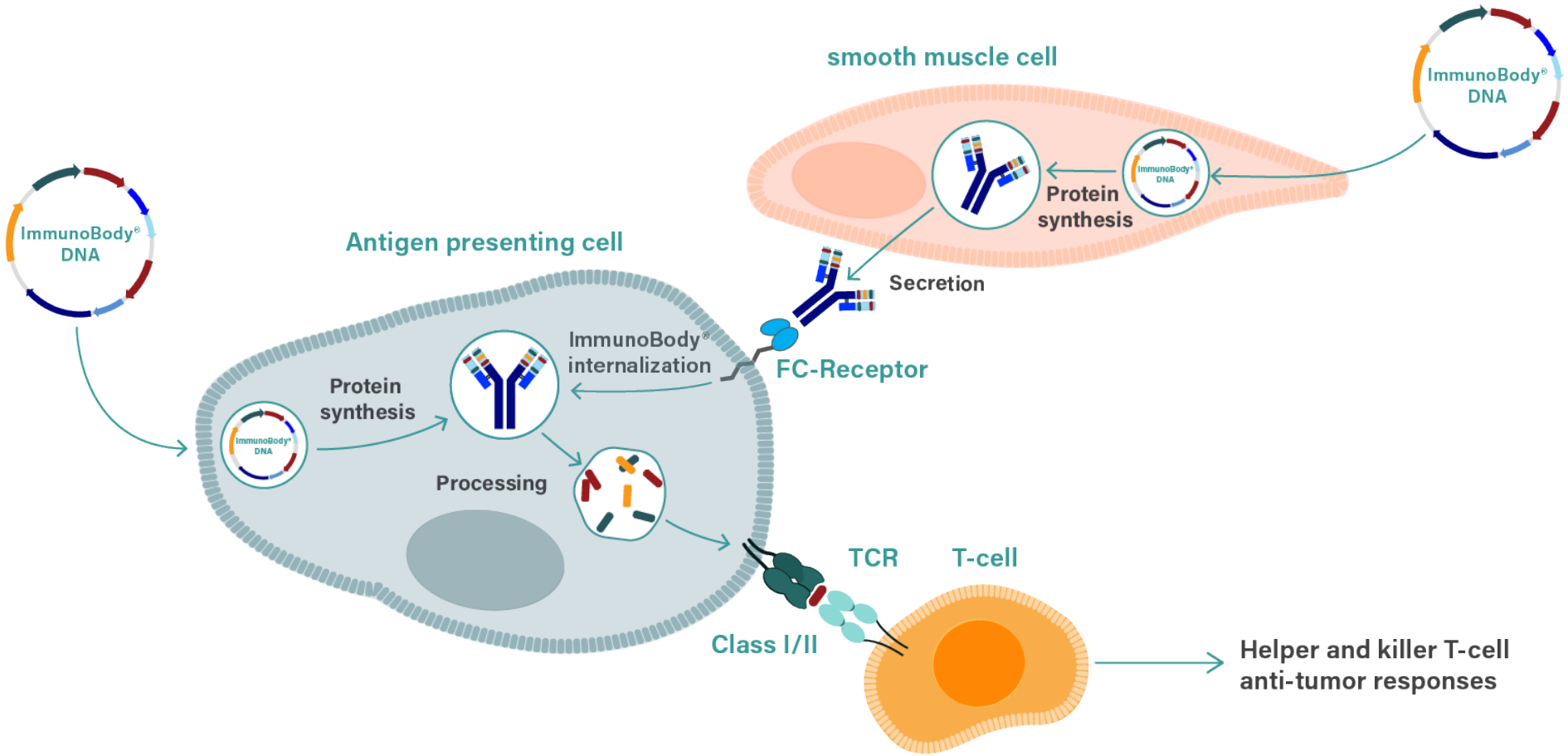
PATHWAY 1

Conventional Direct DNA uptake and antigen presentation by APCs

PATHWAY 2

Cross Presentation amplification pathway

Cross presentation increases potency 100-fold over direct presentation



SCIB2 FOR LUNG CANCER

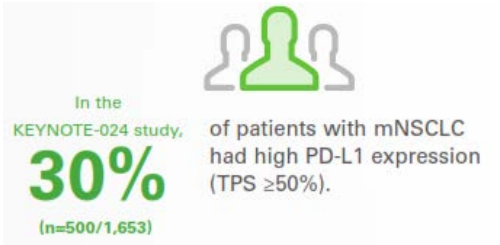
SCIB2 IMMUNOBODY®

- SCIB2 targets the highly immunogenic **NY-ESO-1** cancer antigen, a validated cancer target
- SCIB2 is broadly applicable to many cancer types, including **non-small cell lung cancer**, synovial sarcomas, melanoma, oesophageal, liver, gastric, prostate, ovarian, renal and bladder cancers
- To date, several trials conducted with NY-ESO-1 based vaccines but only induced weak immune responses
- SCIB2 designed to induce high avidity T cell responses
- CD4 epitopes cover 90% of HLA types; CD8 epitopes cover 95-100% of HLA types
- **Potential to induce a more potent therapeutic effect**

NEED FOR IMPROVED THERAPY

- Two main forms of lung cancer: non-small cell (NSCLC; 95% of lung cancers) and small cell (SCLC)
- Account for 22% of all UK cancer deaths
- Checkpoint blockade with pembrolizumab (KEYTRUDA®) has changed the treatment of NSCLC . . . "Better than chemotherapy"
- But the majority of NSCLC patients will not respond to checkpoint blockade

Only 1 in 3 newly diagnosed NSCLC patients will be suitable for pembrolizumab

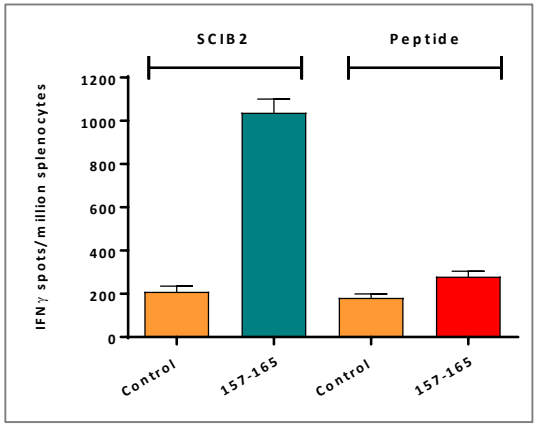


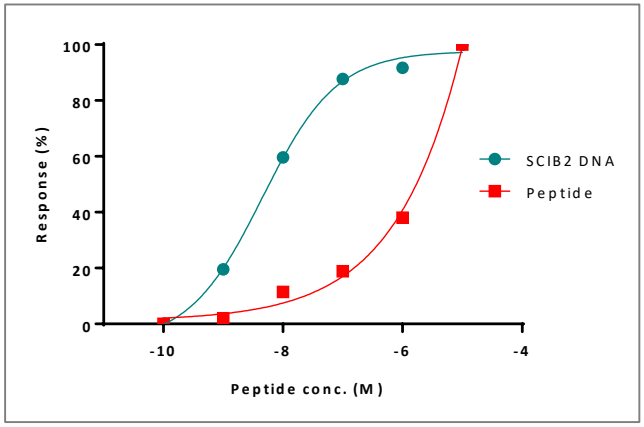
And only 45% of these patients will respond

- Success rates are lower still in second-line treatment with pembrolizumab
- Failure is related to a lack of an immune response to the cancer
- **There is a strong rationale to combine checkpoint inhibitors with an effective therapeutic vaccine**

SCIB2 INDUCES SUPERIOR RESPONSES COMPARED TO PEPTIDE VACCINE

- Responses induced in HHDII mice immunised with SCIB2 or NY-ESO-1 peptide
- SCIB2 induced **higher frequency** responses than peptide immunisation (p=0.0004)
- SCIB2 generated a 100-fold **higher avidity** than peptide

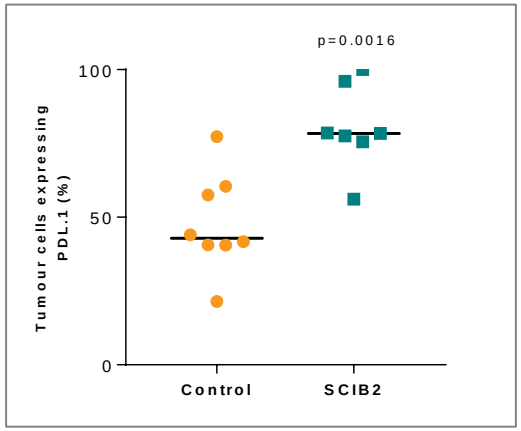


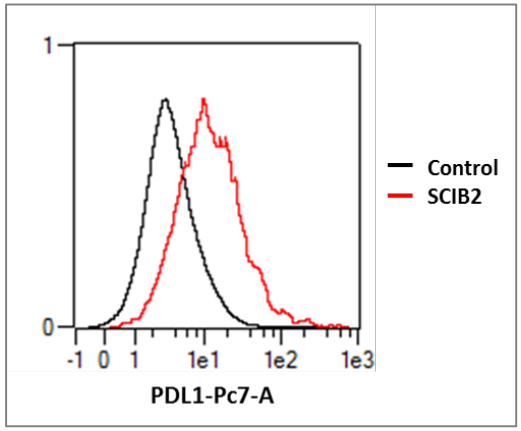


Xue *et al.* Oncoimmunology 2016;5(6):e1169353-13

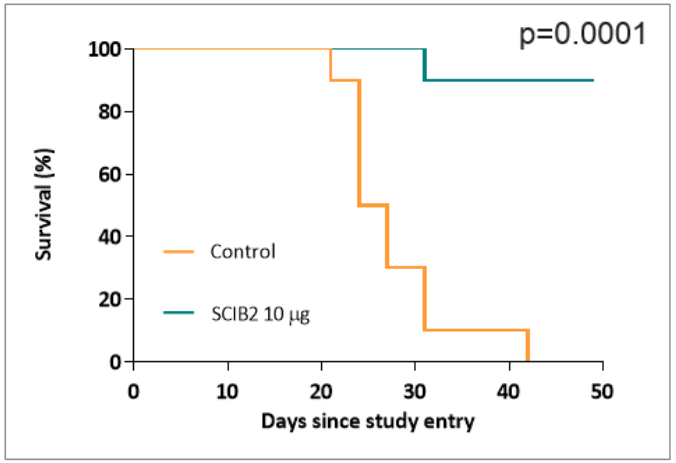
SCIB2 DEVELOPMENT

SCIB2 induces **PD.L1** expression on tumour cells

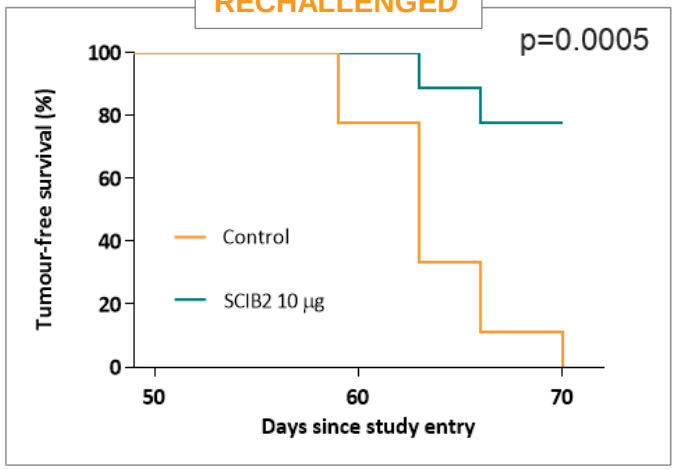




Nano-vesicle delivery of SCIB2 induces strong **anti-tumour responses** and generates a **memory response**

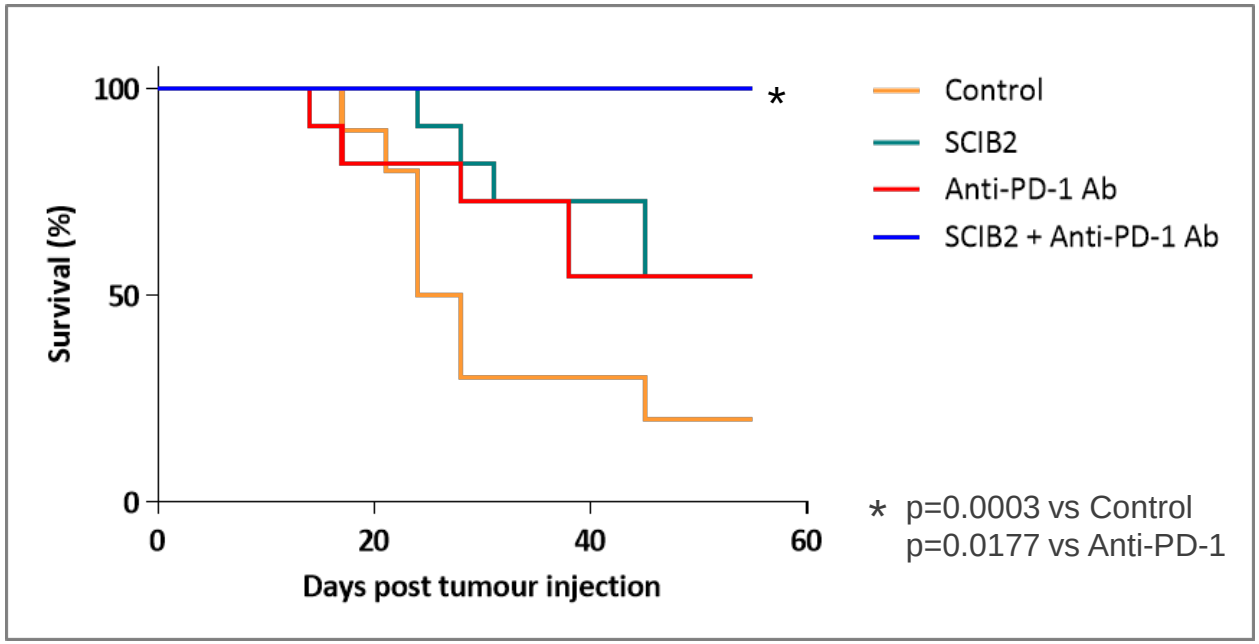


RECHALLENGED



EXPERIMENTAL DATA SUPPORT THE USE OF SCIB2 IN COMBINATION WITH A CHECKPOINT INHIBITOR

- SCIB2 boosts the effect of a PD.1 antibody in HHDII mice implanted with NY-ESO-1 positive tumour cells
- 100% survival rates were seen when SCIB2 treatment was combined with anti-PD.1



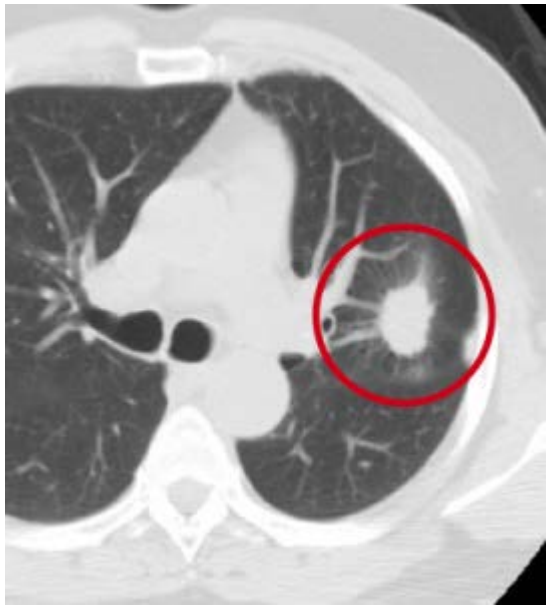
Xue *et al.* 2016

SCIB2 CLINICAL DEVELOPMENT

- Clinical Development Partnership formed with Cancer Research UK (CRUK) to fund and manage a Phase 1/2 study with SCIB2 in combination with a checkpoint inhibitor in NSCLC
- CRUK responsible for manufacture, regulatory submissions and conducting clinical trial
  - Scancell will have the option to acquire the rights to the data on completion of the study
  - Revenue share agreement if option not exercised

OPPORTUNITY TO OBTAIN CLEAR EFFICACY AND SAFETY SIGNALS

- Clinical trial would be in 25-33% of NSCLC positive for NY-ESO-1
- Clinical benefit in NSCLC is readily determined by CT scan measurement of disease
- Trial would set targets for exceeding expected objective response rate for checkpoint inhibitor alone
- Other efficacy endpoints would include progression-free and overall survival at 1 year
- Rate of severe immune related adverse reactions would be a key measure of safety for the combination
- Progress could be assessed rapidly in an open-label trial design



Duke Lung Cancer Screening Service

SUMMARY

- Although checkpoint inhibitors are important new therapies – only a relatively small proportion of lung cancer patients will respond to them
- Failure to respond is related to failure of the patient's immune system to recognize the cancer and mount an effective response
- ImmunoBody® is an ideal agent to combine with checkpoint inhibitors
  - Induces high avidity T cell responses that are selected into the memory pool
  - Induces PD.L1 expression in cancer lesions
- SCIB2 does this by targeting the NY-ESO-1 cancer antigen
- The combination of SCIB2 and PD.1 blockade results in 100% survival in tumour-bearing mice
- The combination of checkpoint inhibitor and SCIB2 should increase the rate and durability of objective response in NSCLC patients

The University of Nottingham

SCIB-1 in melanoma

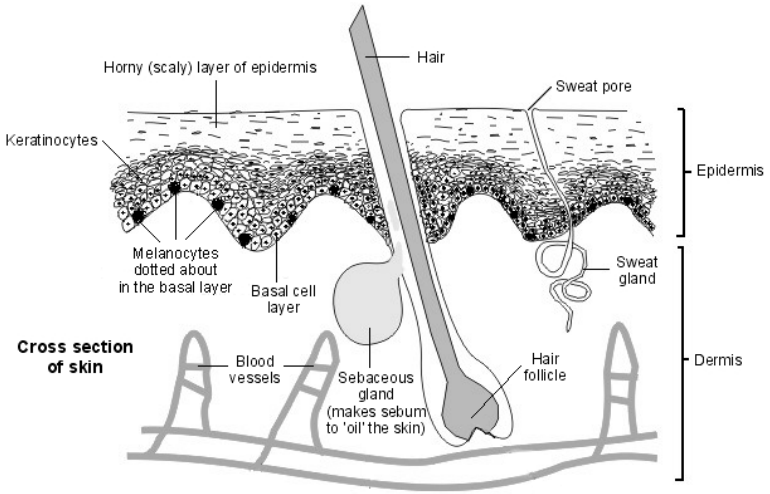
Poulam Patel
Prof of Clinical Oncology
University of Nottingham

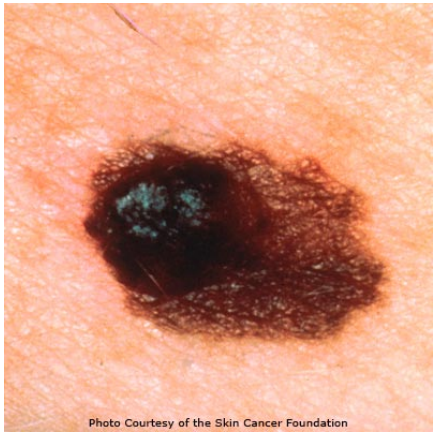
Cancer Research Nottingham

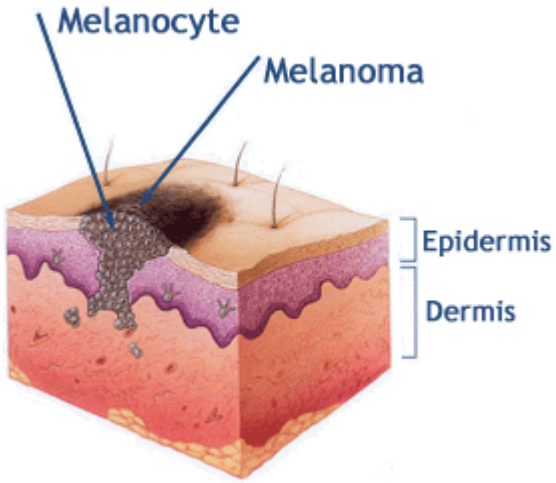
Nottingham University Hospitals NHS
NHS Trust

Background

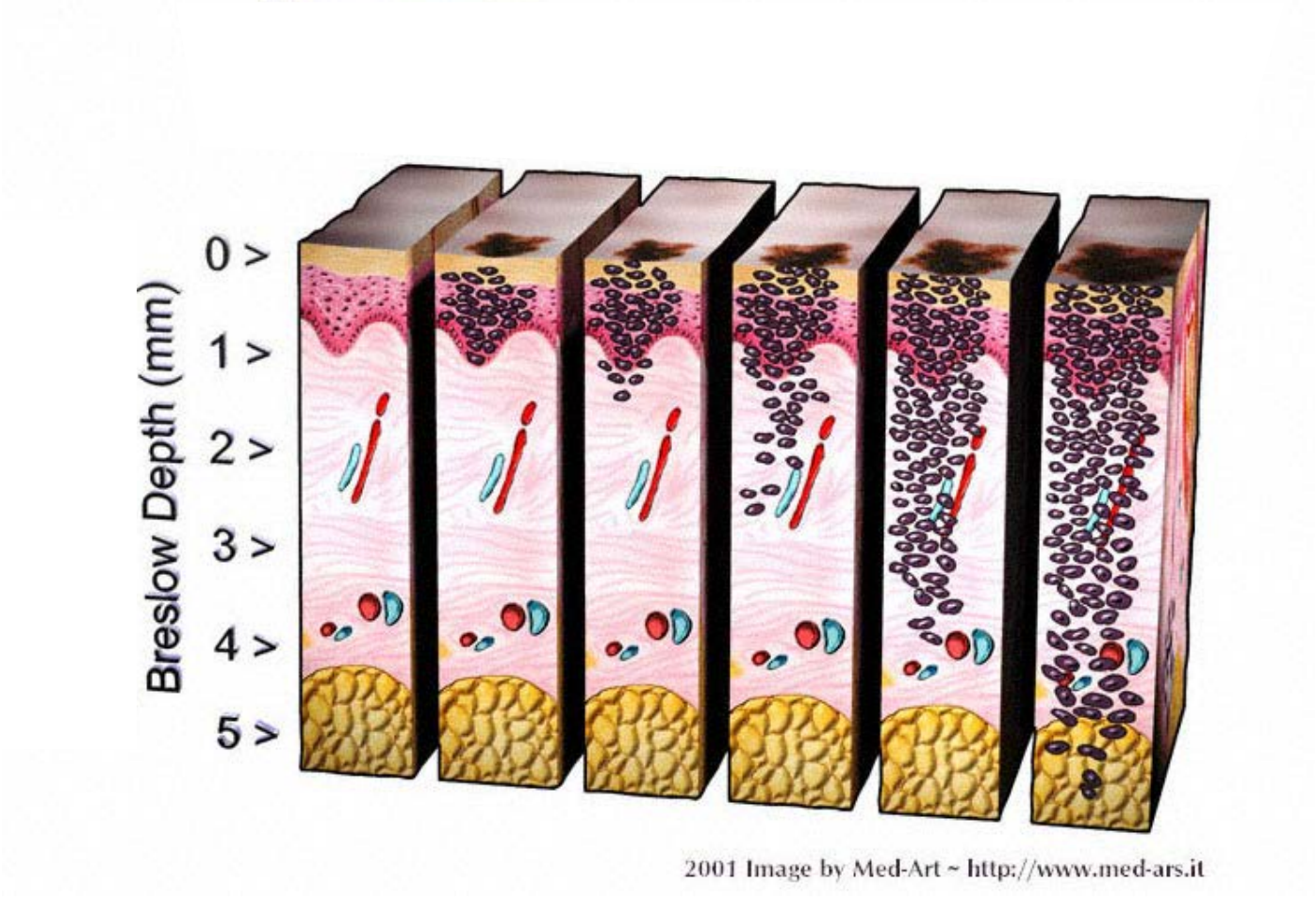
- Cancer of melanocytes
- 14,509 new cases/year UK
- 2,459 deaths/year
- Increasing incidence







Melanoma


Breslow Depth (mm)
0 >
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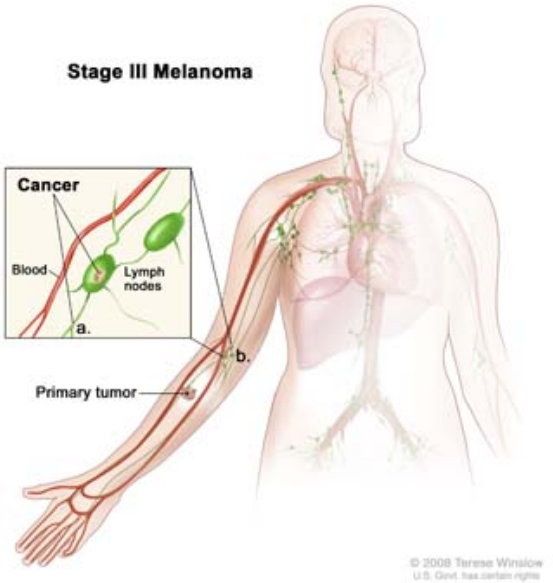
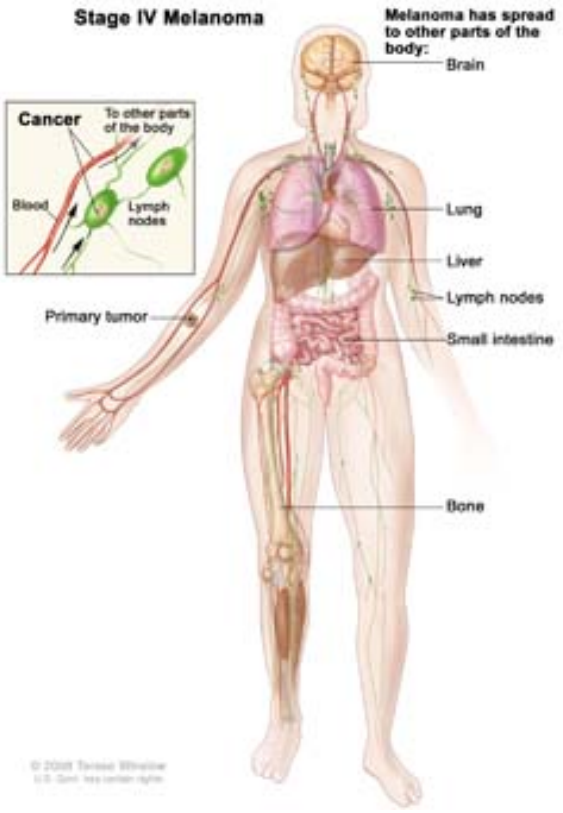
4 >
5 >
2001 Image by Med-Art ~ http://www.med-ars.it

Melanoma can spread

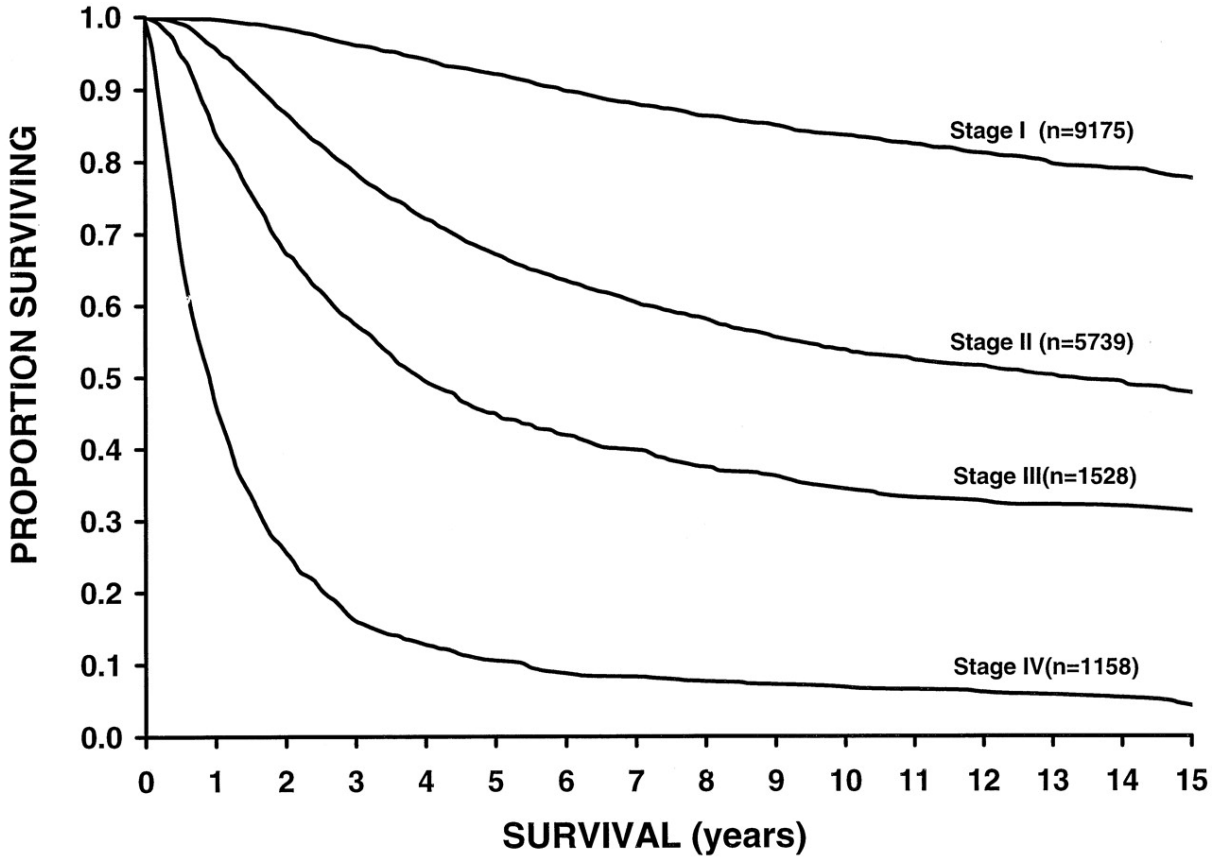
- Lymphatic spread
  - lymph nodes



- Blood borne spread
  - lung, liver, brain, skin



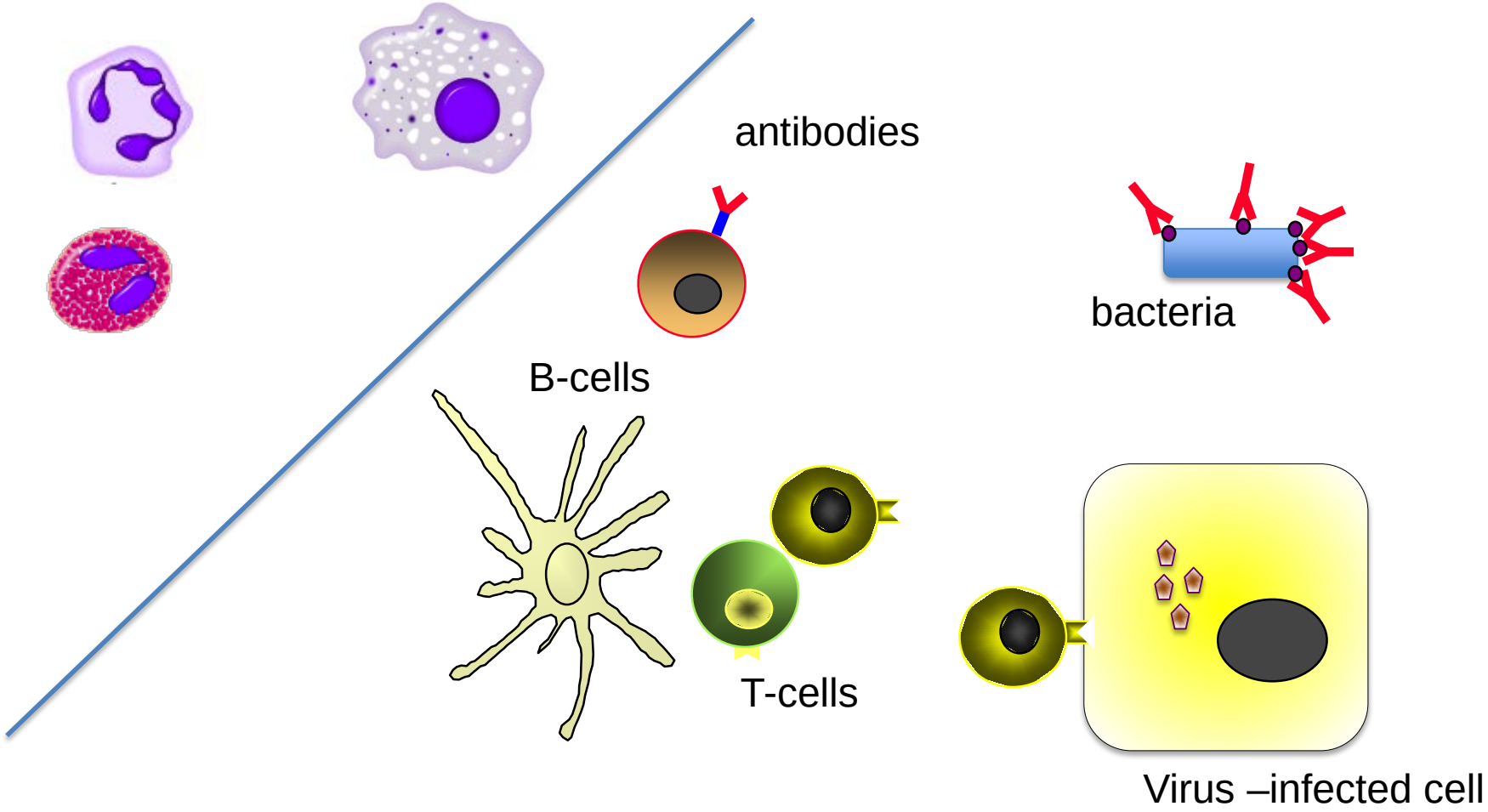
Survival from melanoma



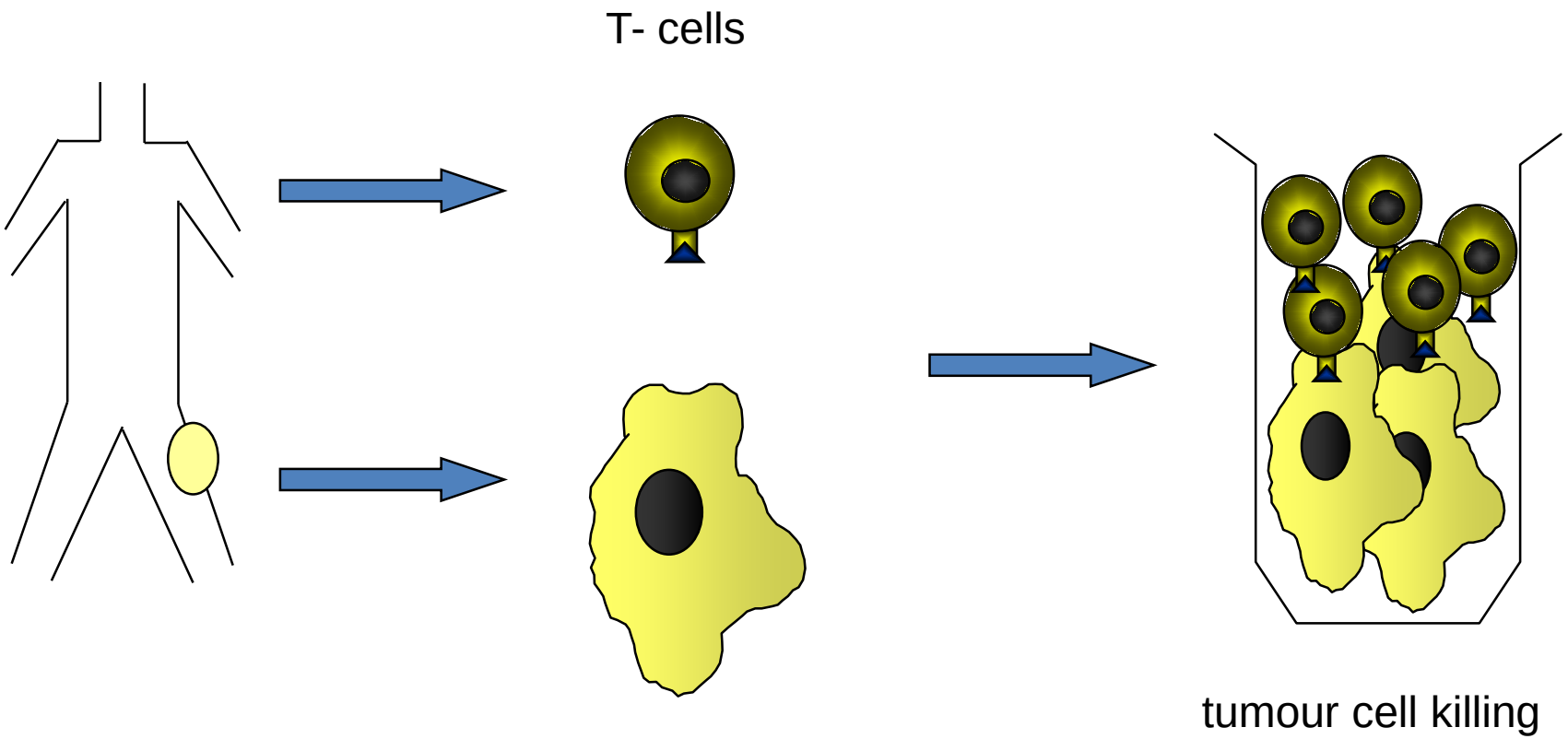
Cancer Immunotherapy

- New anti-cancer immuno-therapies licensed
- Many more in development
- Long term remissions

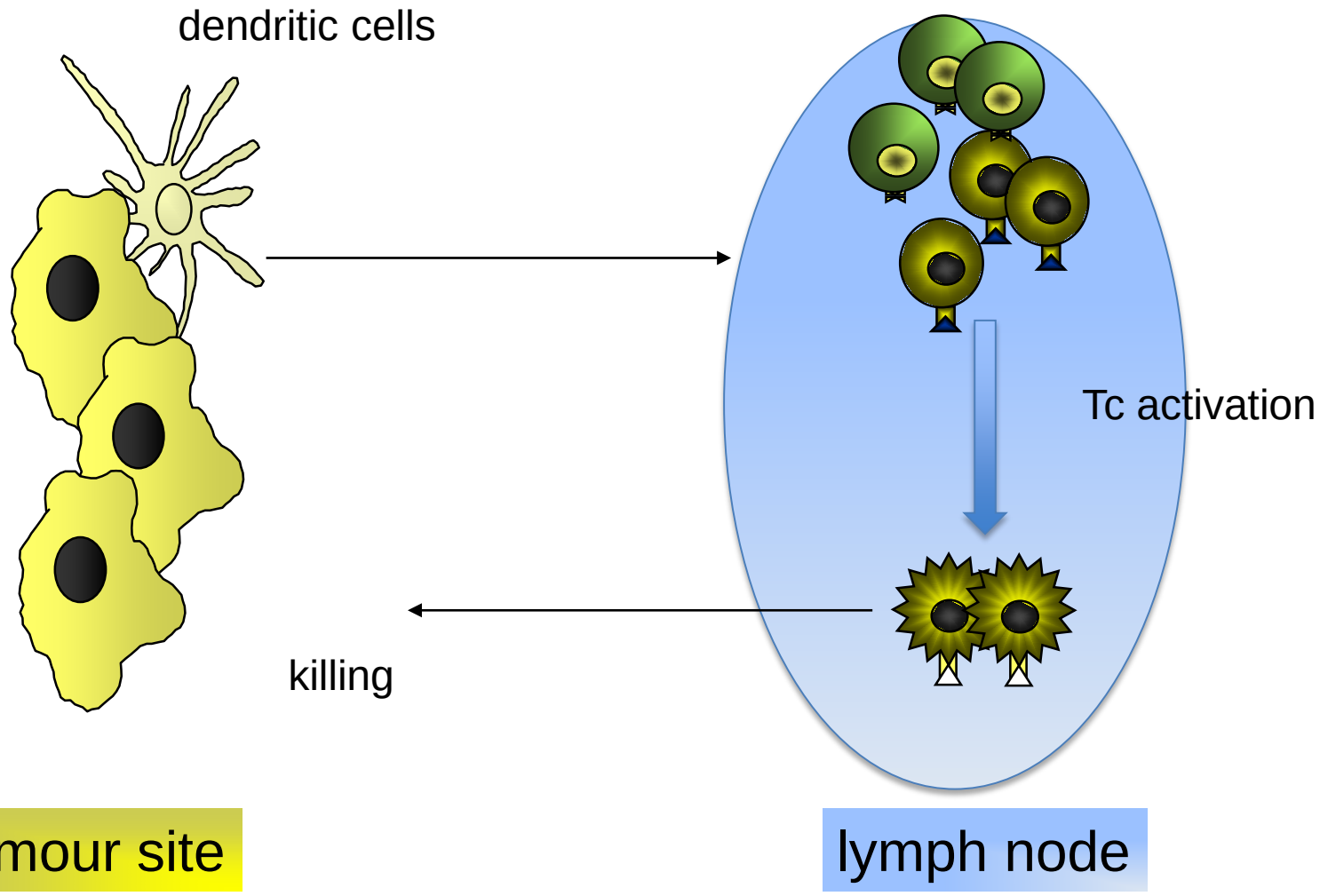
Cells of the immune system



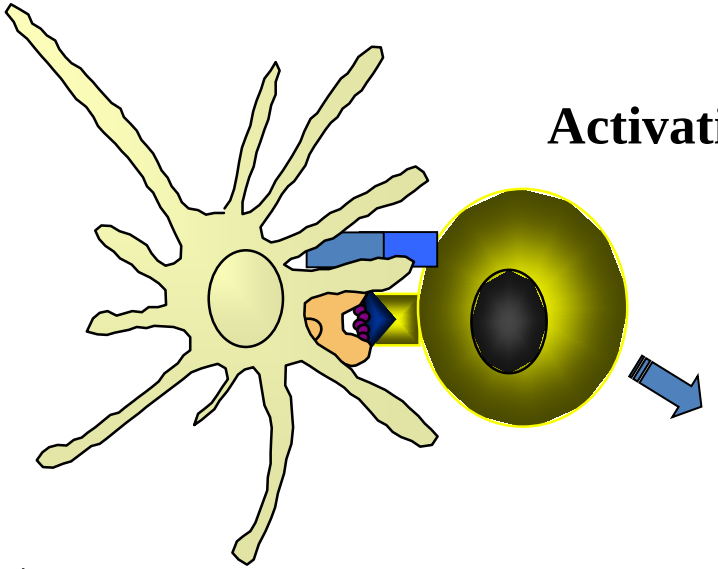
Immune cells can kill cancer



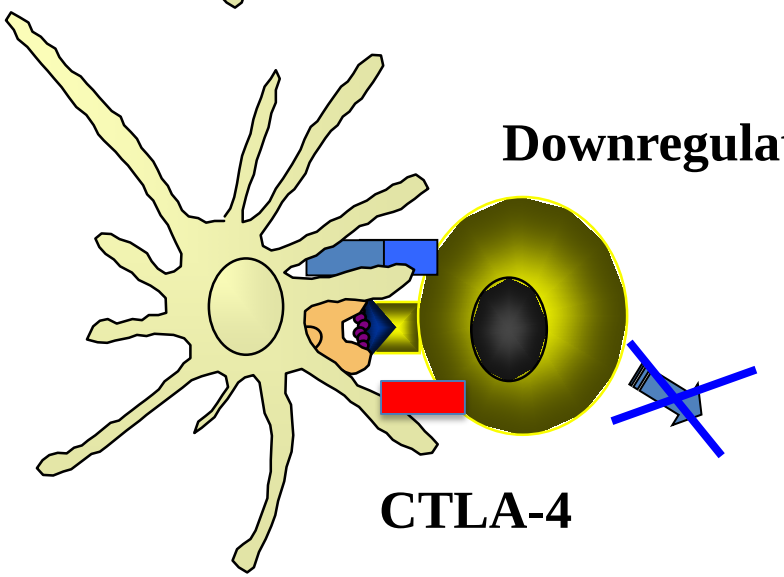
Immune response to cancer

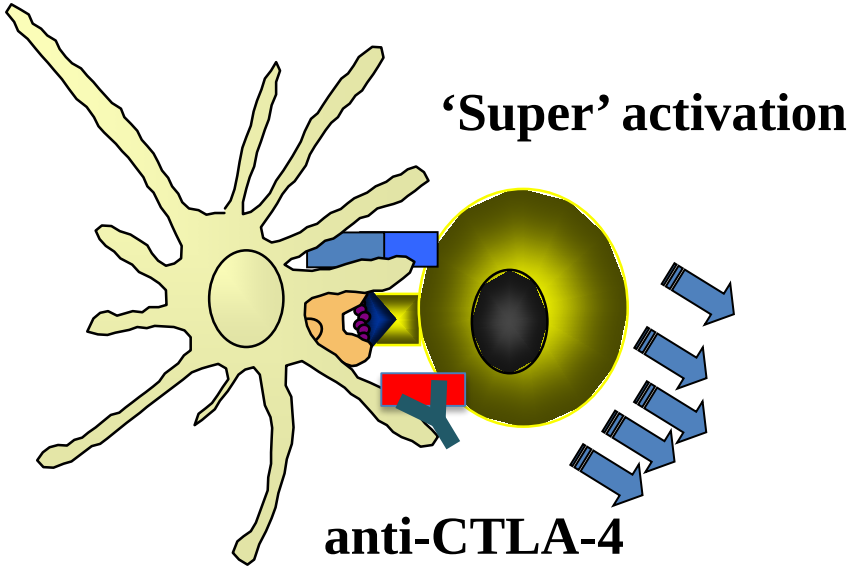


The immune system has ‘brakes’



Taking the ‘brakes off’





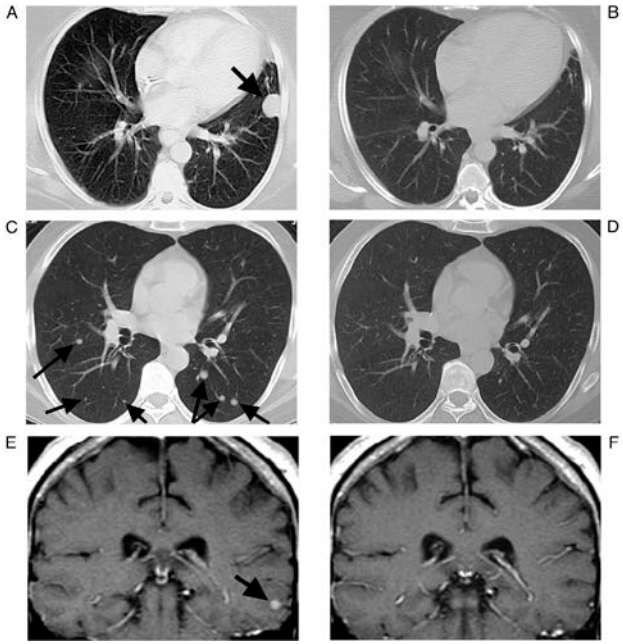
Anti-CTLA4

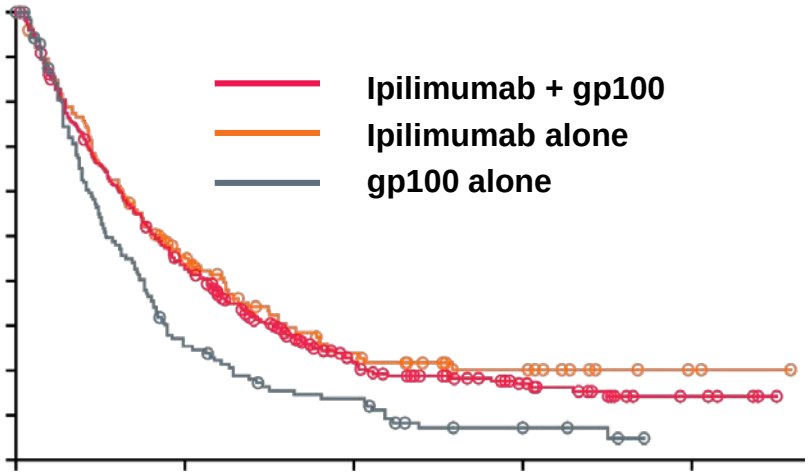
Cancer regression and autoimmunity induced by cytotoxic T lymphocyte-associated antigen 4 blockade in patients with metastatic melanoma

Giao Q. Phan[†], James C. Yang[†], Richard M. Sherry[†], Patrick Hwu[†], Suzanne L. Topalian[†], Douglas J. Schwartzentruber[†], Nicholas P. Restifo[†], Leah R. Haworth[†], Claudia A. Seipp[†], Linda J. Freezer[†], Kathleen E. Morton[†], Sharon A. Mavroukakis[†], Paul H. Duray[‡], Seth M. Steinberg[§], James P. Allison[¶‖], Thomas A. Davis[‖], and Steven A. Rosenberg[†,††]

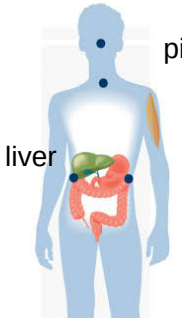
[†]Surgery Branch, [‡]Laboratory of Pathology, and [§]Biostatistics and Data Management Section, National Cancer Institute, National Institutes of Health, Bethesda, MD 20892; [¶]Howard Hughes Medical Institute, Department of Molecular and Cell Biology, University of California, Berkeley, CA 94720; and [‖]Medarex, Inc., Princeton, NJ 08540

Contributed by James P. Allison, May 27, 2003



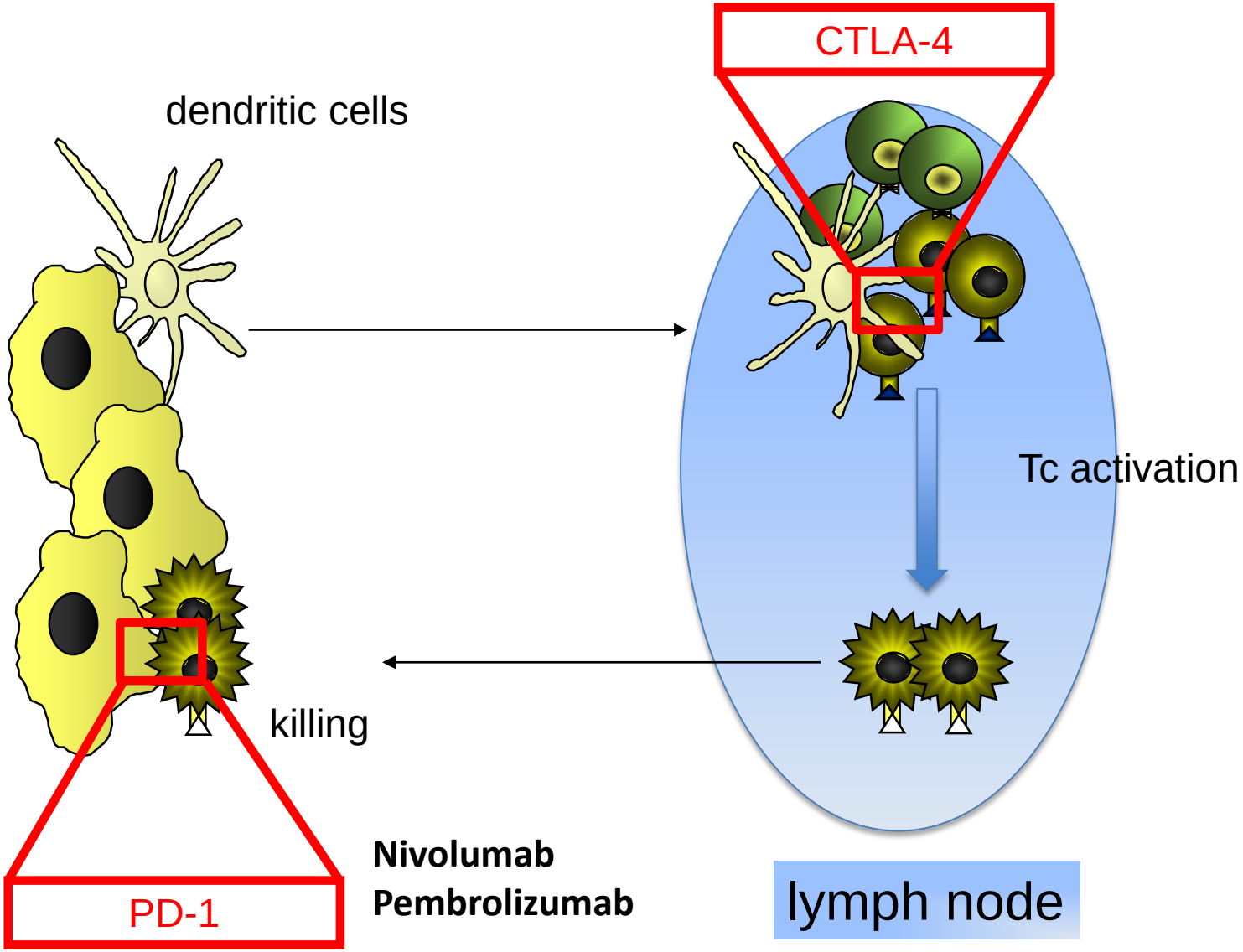


Immune-related side effects

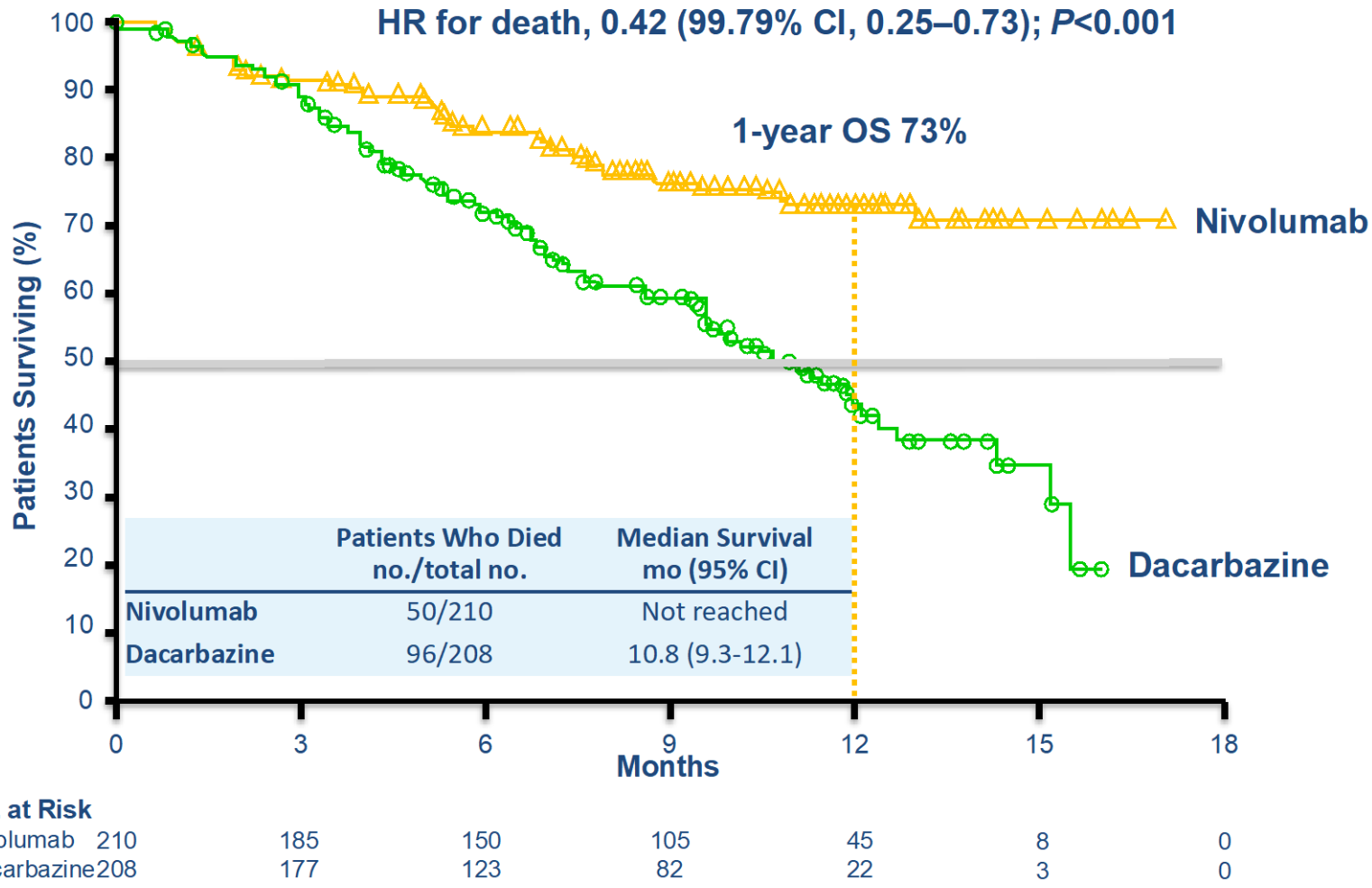


2011 **Ipilimumab** licensed for treatment of advanced melanoma

Immune response to cancer



Anti-PD1 - Nivolumab



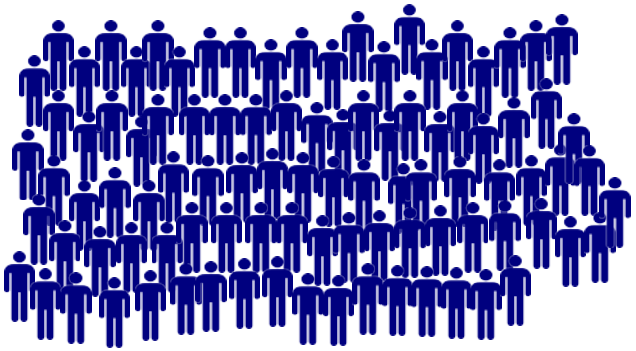
Robert C, et al. N Engl J Med. 2015;372:320-330

Anti-PD1 checkpoint inhibitors licenced

Pembrolizumab
2014

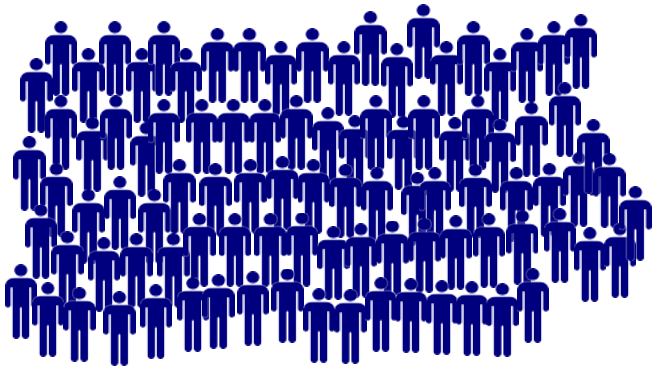
Nivolumab
2014

Checkpoint inhibitors in melanoma

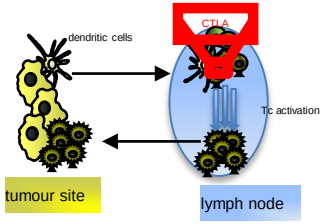


Chemotherapy

1 year ~ 30%
2 year ~ 10%
5 year ~ 4 %

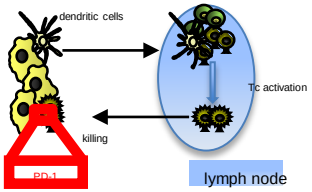


Ipilimumab

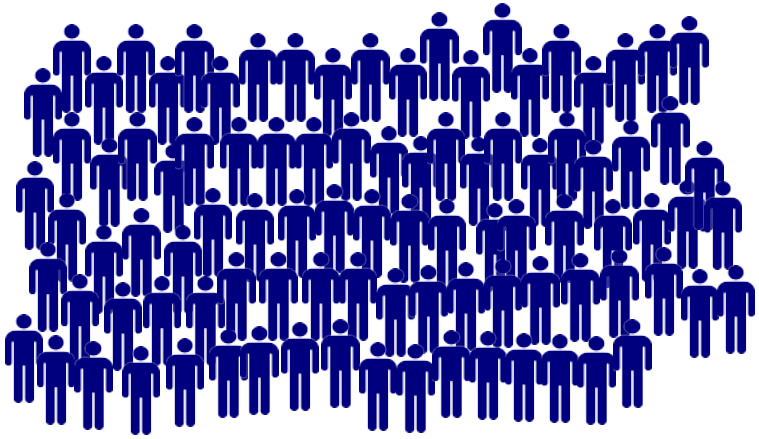


1 year ~ 50%
2 year ~ 25%
5 year ~20%

Anti-PD-1



Pembrolizumab

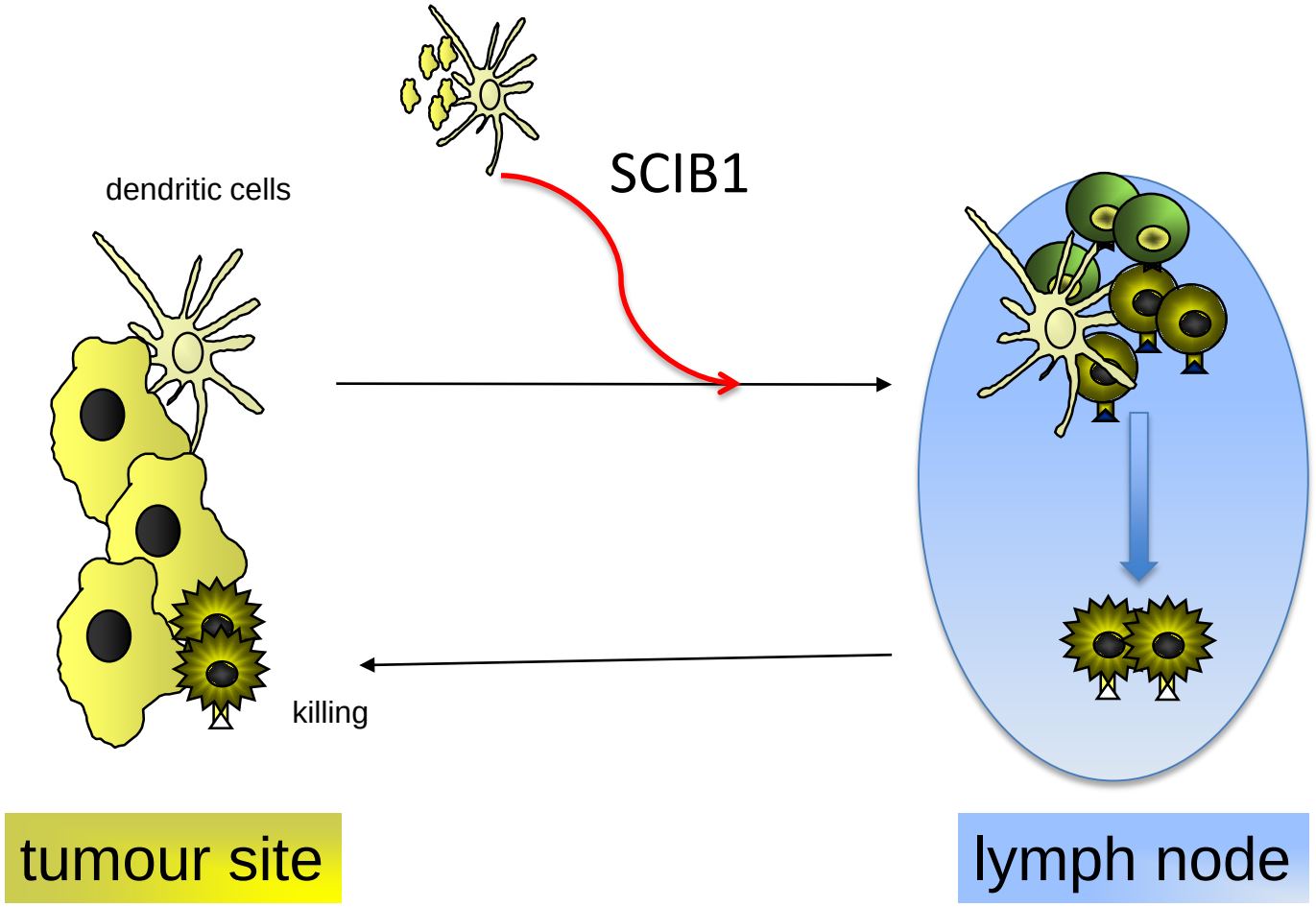


1 year survival ~ 70%

2 year survival ~ 50%

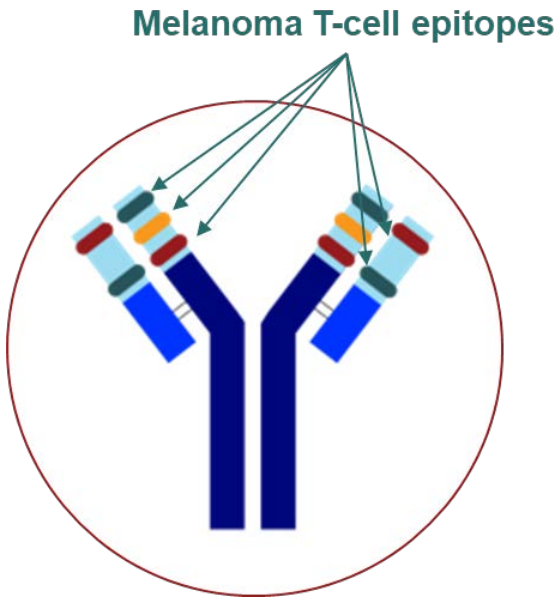
5 year survival ~? 40%

SCIB1 vaccination



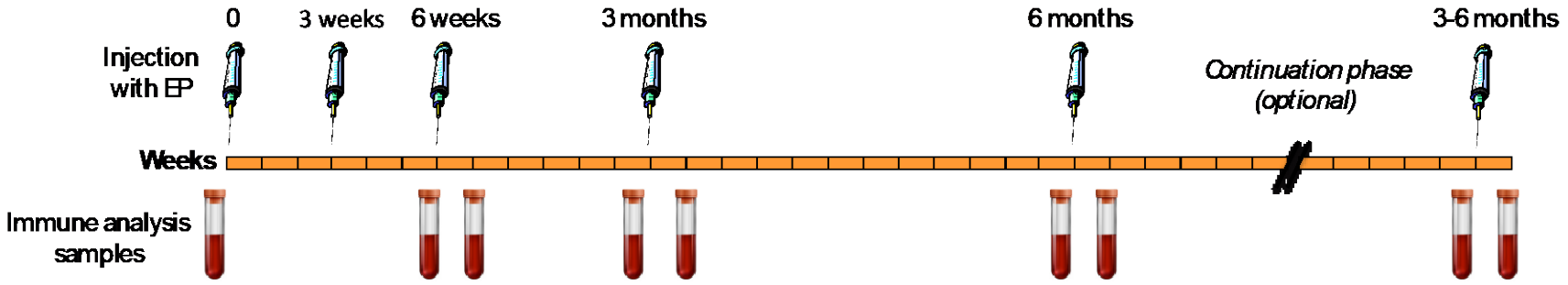
SCIB1

- Several melanoma associated T cell epitopes engineered into a human antibody framework
- Induces high avidity T cell responses compared with conventional approaches
- Novel dual mechanism of action based on direct and cross-presentation
- Delivered as a DNA plasmid using electroporation (EP)



SCIB1-001: PHASE I/II TRIAL

- UK study: Nottingham, Southampton, Leeds, Newcastle, Manchester, Guildford
- Open label, non-randomized study to determine the safety and tolerability of SCIB1 administered intramuscularly
- Patients with stage III/IV metastatic melanoma
- Part 1: dose escalation phase (0.4 mg, 2 mg, 4 mg, 8 mg)
- Part 2: expansion phase (4 mg, 8 mg)
- 15 patients had tumour present
- 20 patients had tumours resected within 12 months of study entry

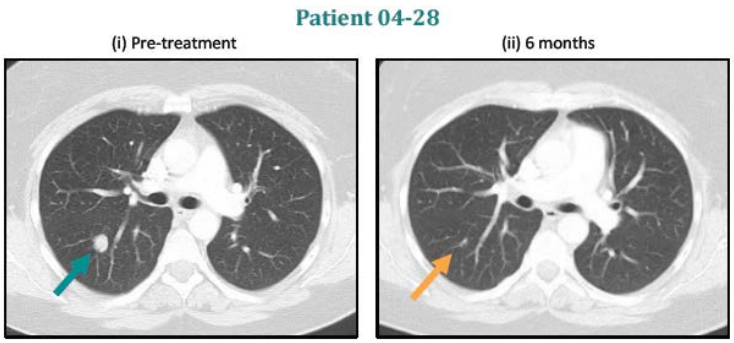


RESULTS

SCIB1 has an excellent safety profile with no dose-limiting toxicities and no serious adverse events related to study drug or delivery device

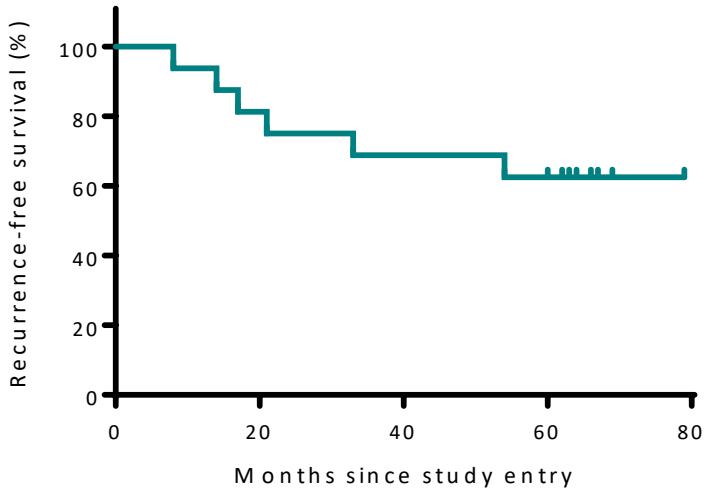
TUMOUR RESPONSE

Patient with tumour received 8 mg SCIB1 and showed a marked reduction in size of detectable lung lesions



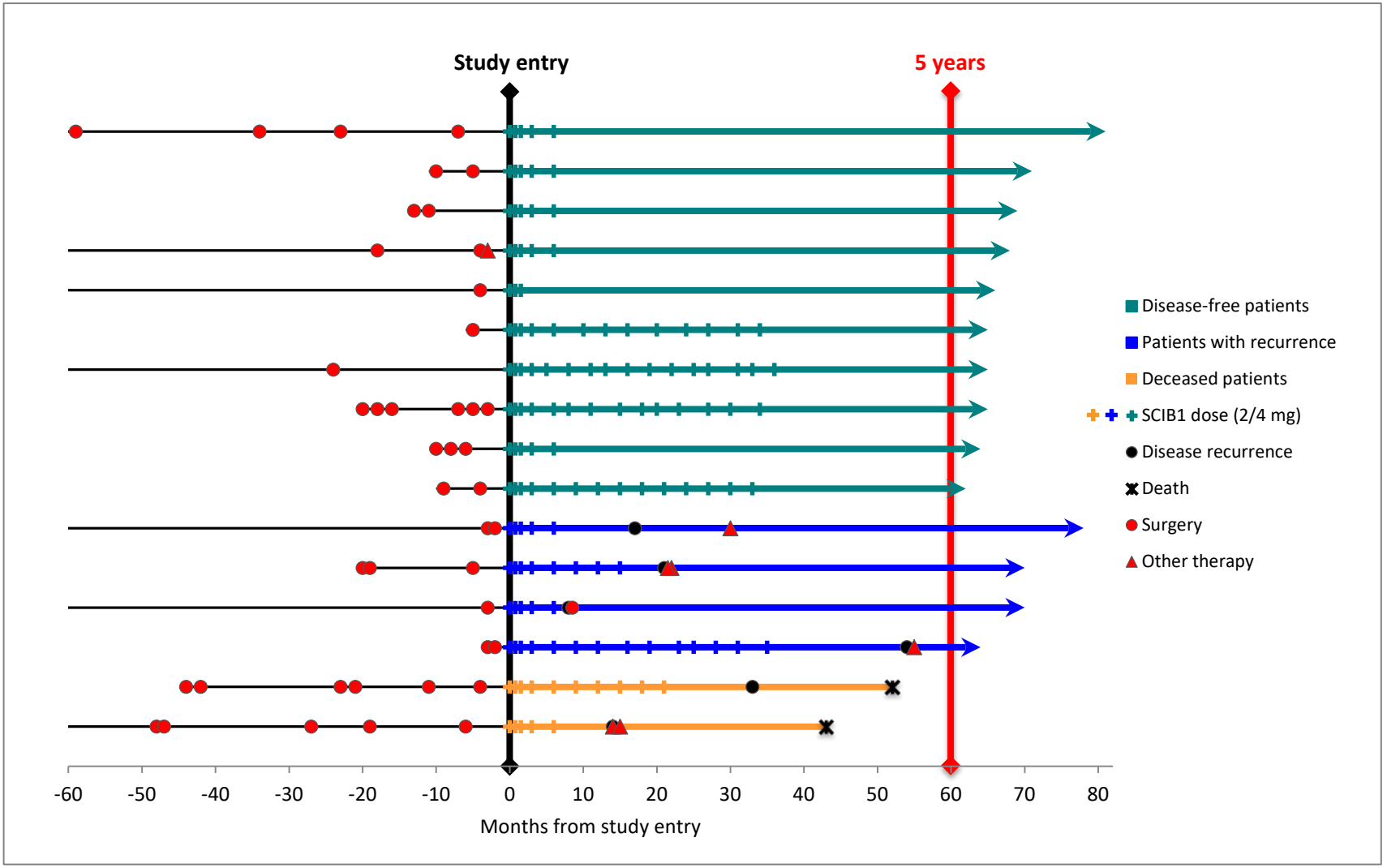
SURVIVAL IN RESECTED PATIENTS

- Overall survival with SCIB1 treatment superior to historical survival rates
- 14 of 16 resected patients receiving 2-4 mg doses have survived for more than 5 years (February 2018)
- Melanoma recurrence rates are lower in SCIB1-treated patients than historical controls



RESULTS

PATIENTS WITHOUT TUMOUR PRESENT AT STUDY ENTRY



COMPARISON TO RECENT STUDIES IN ADJUVANT MELANOMA

Study:		SCIB1-001	EORTC 18071 [a]		CheckMate 238 [b]		COMBI-AD [c]	
Treatment		SCIB1	Ipilimumab	Placebo	Nivolumab	Ipilimumab	Braf‡	Placebo
Female (%)		56	38	38	43	41	55	55
Median Age (yr)		61	51	52	56	54	50	51
Disease Stage (%)	IIIA	19	21	18	0	0	19	16
	IIIB	12	45	43	36	33	39	43
	IIIC	25	34	38	45	48	41	38
	IV	44	0	0	18	19	0	0
2-Year RFS (%)		75.0	51.5	43.8	66.4 (18 mo)	52.7 (18 mo)	67.0	44.0
2-Year OS (%)		100.0	82.0	75.0	-	-	91.0	83.0
5-Year RFS (%)		62.5	40.8	30.3	-	-	58.0 (3yr)	39.0 (3yr)
5-Year OS (%)		87.5	65.4	54.4	-	-	86.0 (3yr)	77.0 (3yr)

RFS – recurrence-free survival; OS – overall survival; ‡ dabrafenib & trametinib

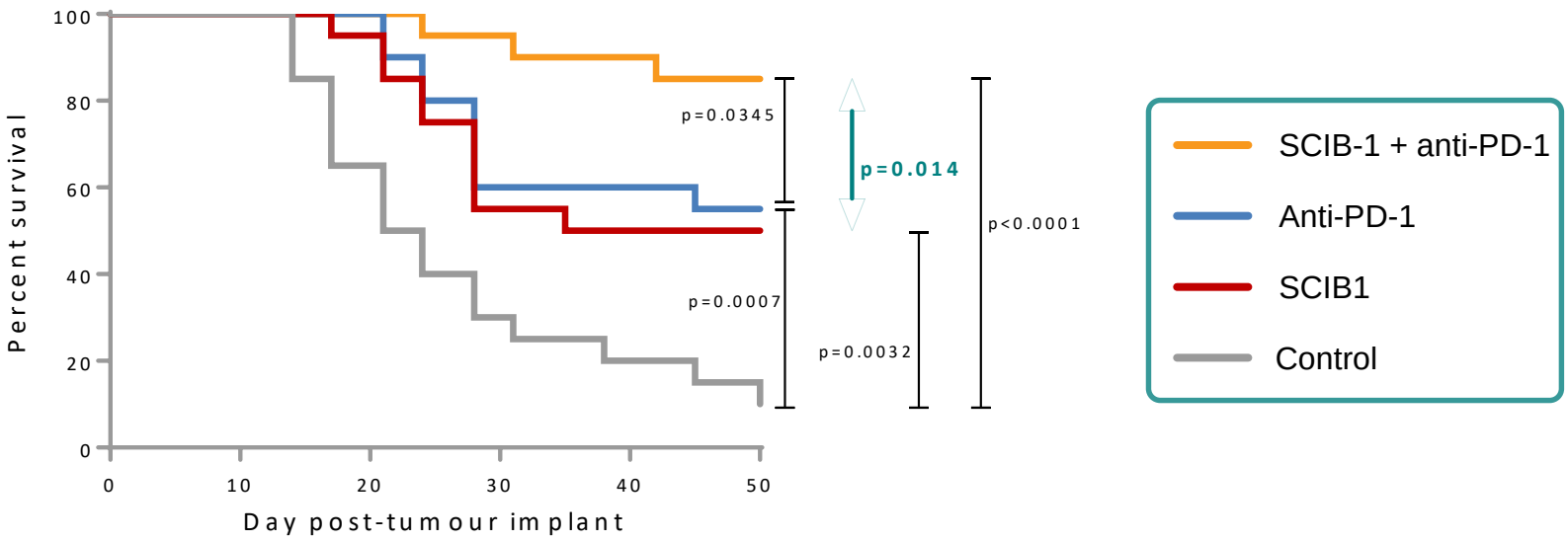
[a] Eggermont et al Lancet Oncol. 2015;16:522 and Eggermont et al N Engl J Med. 2016;375:1845

[b] Weber et al N Engl J Med. 2017;377:1824 [c] Long et al N Engl J Med. 2017;377:1813

SCIB1 BOOSTS IMMUNE CHECKPOINT THERAPY

IN A MOUSE MELANOMA MODEL, SURVIVAL RATES WERE SIGNIFICANTLY BOOSTED WHEN ANTI-PD-1 THERAPY WAS COMBINED WITH SCIB1 TREATMENT

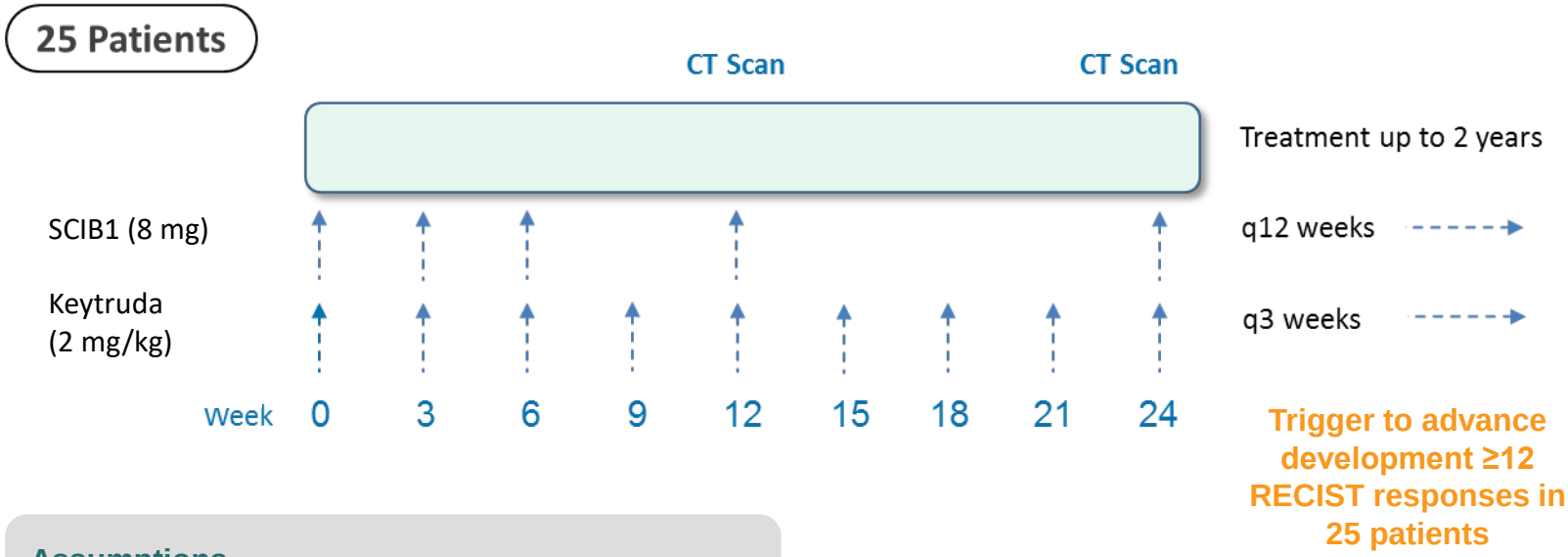
- Survival rates for SCIB1 ImmunoBody® monotherapy ≈ anti-PD-1
- Monotherapy viable option for resected melanoma patients
- Combination therapy resulted in an 85% survival rate
- SCIB1 also upregulates PD-L1 expression and memory response



SCIB1 PLUS CHECKPOINT INHIBITOR COMBINATION PHASE 2 STUDY DESIGN

PATIENT POPULATION

- Histologically confirmed, unresectable AJCC stage III or stage IV melanoma
- No prior systemic treatment for advanced disease
- Suitable for treatment with Keytruda (pembrolizumab), with measurable disease
- Part 1 – safety run-in (n=6); Part 2 – additional 19 patients; total = 25 patients



Trigger to advance development ≥12 RECIST responses in 25 patients

Assumptions

- Response rate to Keytruda = 30%
- Response rate of interest for combination = 55%