AstraZeneca
What science can do

ASCO 2015 investor science event

Chicago, IL, USA
01 June 2015

Forward-looking statements

In order, among other things, to utilise the 'safe harbour' provisions of the US Private Securities Litigation Reform Act 1995, we are providing the following cautionary statement:

The preliminary announcement contains certain forward-looking statements with respect to the operations, performance and financial condition of the Group. Although we believe our expectations are based on reasonable assumptions, any forward-looking statements, by their very nature, involve risks and uncertainties and may be influenced by factors that could cause actual outcomes and results to be materially different from those predicted. The forward-looking statements reflect knowledge and information available at the date of preparation of the preliminary announcement and AstraZeneca undertakes no obligation to update these forward-looking statements. We identify the forward-looking statements by using the words 'anticipates', 'believes', 'expects', 'intends' and similar expressions in such statements. Important factors that could cause actual results to differ materially from those contained in forward-looking statements, certain of which are beyond our control, include, among other things: the loss or expiration of patents, marketing exclusivity or trademarks, or the risk of failure to obtain and enforce patent protection; the risk of substantial adverse litigation/government investigation claims and insufficient insurance coverage; exchange rate fluctuations; the risk that R&D will not yield new products that achieve commercial success; the risk that strategic alliances and acquisitions will be unsuccessful; the impact of competition, price controls and price reductions; taxation risks; the risk of substantial product liability claims; the impact of any delays in the manufacturing, distribution and sale of any of our products; the impact of any failure by third parties to supply materials or services; the risk of failure to manage a crisis; the risk of delay to new product launches; the difficulties of obtaining and maintaining regulatory approvals for products; the risk of failure to adhere to applicable laws, rules and regulations; the risk that new products do not perform as we expect; the risk of environmental liabilities; the risks associated with conducting business in emerging markets; the risk of reputational damage; the risk of illegal trade in our products; the risk of failure to successfully implement planned cost reduction measures through productivity initiatives and restructuring programmes; the risk that regulatory approval processes for biosimilars could have an adverse effect on future commercial prospects; the impact of failing to attract and retain key personnel and to successfully engage with our employees; the impact of increasing implementation and enforcement of more stringent anti-bribery and anti-corruption legislation; and the risk of failure of information technology and cybercrime.

Agenda

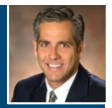
1 **AstraZeneca Oncology**
Mondher Mahjoubi
Head of Oncology, Global Product & Portfolio Strategy

2 **The power of combinations in IO**
Mohammed M. Dar
VP, Oncology Clinical Development, MedImmune

3 **Clinical experience w/MEDI4736 + treme**
Scott Antonia
Moffitt Cancer Center, Tampa, FL, USA

4 **Small-molecule combinations**
Susan Galbraith
Head of Oncology, Innovative Medicines Biotech Unit

5 **Maximising value across tumour types**
Robert Iannone
Head of Immuno-Oncology, Global Medicines Development



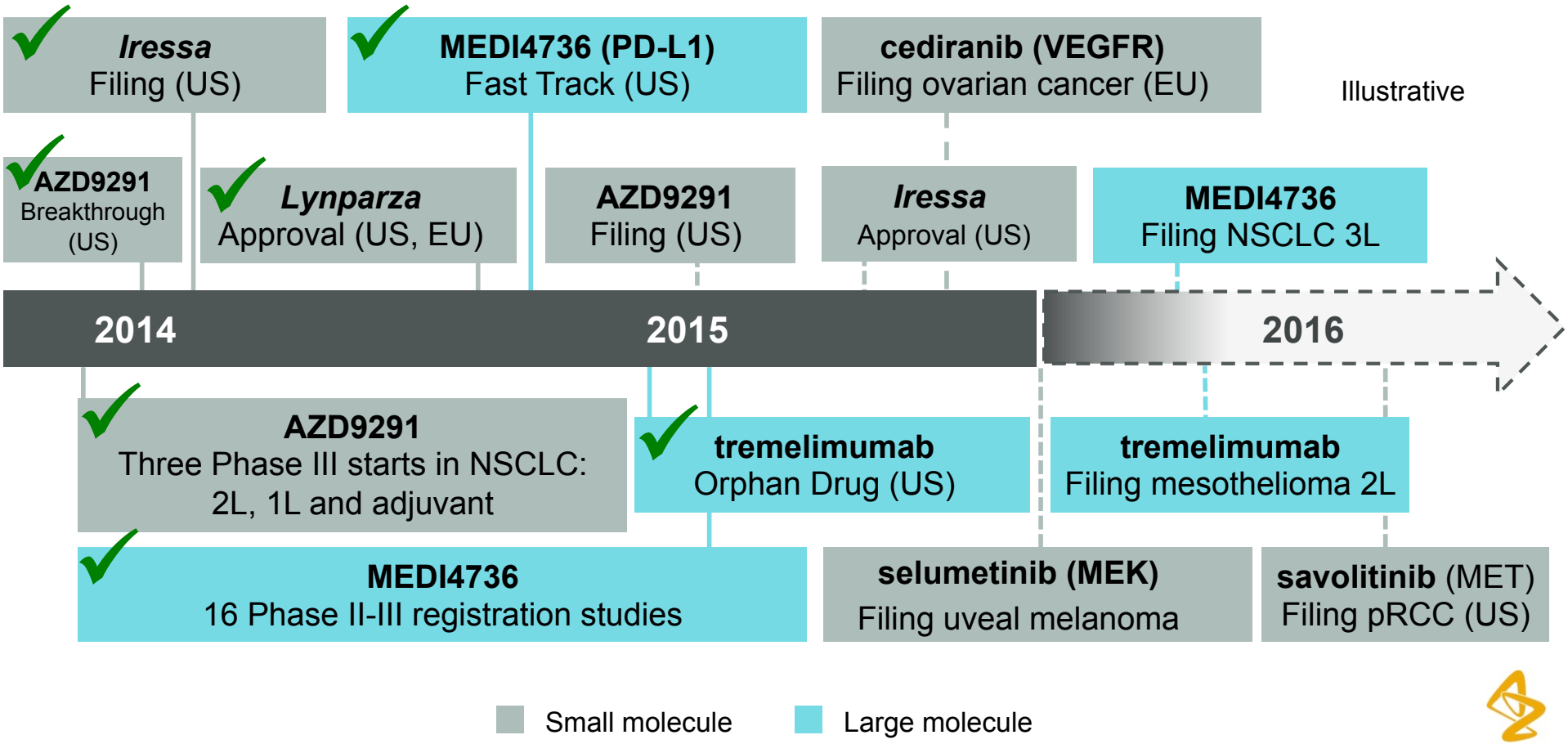
6 **Closing and Q&A**
Pascal Soriot
Chief Executive Officer

AstraZeneca Oncology

AstraZeneca
What science can do

Mondher Mahjoubi
Head of Oncology, Global Product & Portfolio Strategy

Oncology: Achieving scientific leadership



Small molecules (SM): Growing momentum

Genetic drivers of cancer and resistance	**AZD9291** (EGFR)	- Updated PFS of 13.5 months (AURA 2L study) - Encouraging data in EGFR-mutated 1L lung cancer - Combination with savolitinib to overcome resistance
	savolitinib (MET)	- Responses in MET-amplified gastric cancer and papillary renal cancer
	AZD2014 (mTOR)	- Encouraging data in ovarian & lung cancers in combination with paclitaxel
	AZD5363 (AKT)	- Responses in AKT1-mutated tumours, combinations with *Lynparza*, paclitaxel and enzalutamide
DNA damage repair	***Lynparza*** (PARP)	- Promising clinical activity in prostate cancer
	AZD1775 (WEE-1)	- Proof of concept in p53-mutated ovarian cancer

Immuno-Oncology (IO): Building leadership

1. Create a diverse portfolio	2. Maximise value across tumour types	3. Unlock the power of combinations
Optimising T-cell function and memory	Solid tumours	IO-IO combinations
Inhibition by micro-environment	Haematology	IO-SM combinations
Antigen presentation and innate immunity	Early-stage disease	

MEDI4736: Potential against haematological cancers

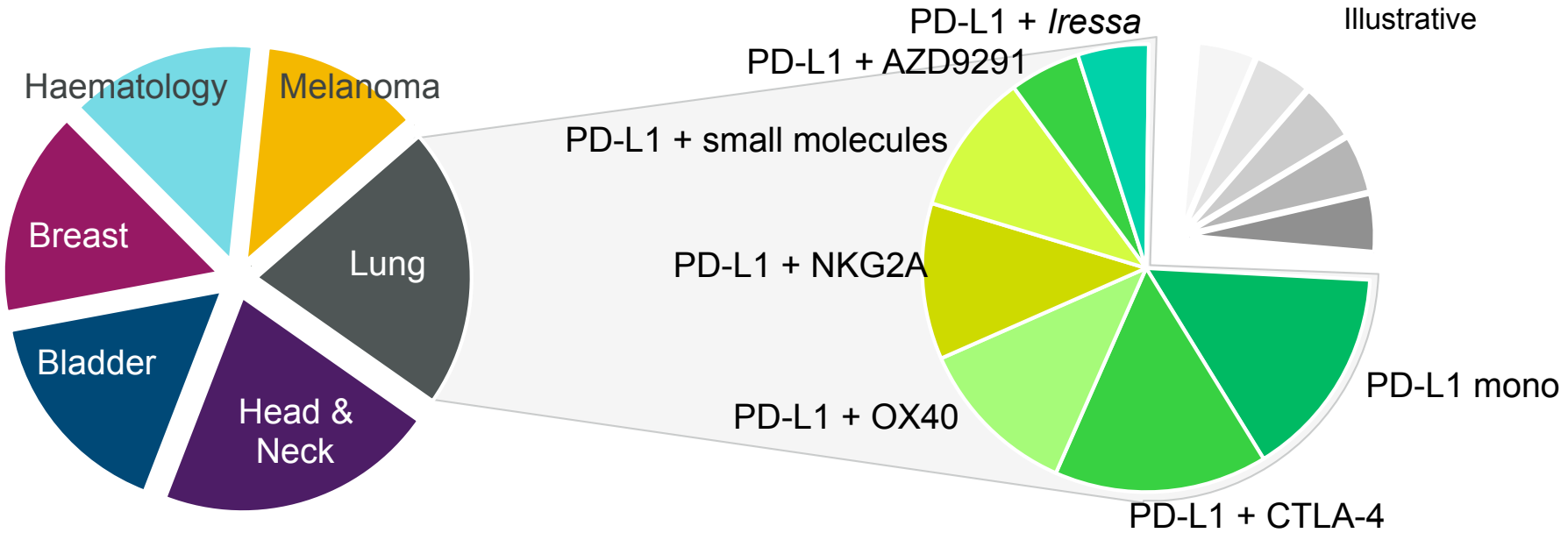
Celgene joint development plan across wide range of uses

Lymphoma	DLBCL[1]	Relapsed / refractory settings
	FL[2]	
Multiple myeloma		Front line
		Relapsed / refractory
Myelodysplastic syndrome		Relapsed / refractory

Further indications and combinations to be determined

1 DLBCL = Diffuse Large B-Cell Lymphoma
2 FL = Follicular Lymphoma

IO: Backbone with various combination partners targeting specific tumour biology - lung cancer example



PD-1/PD-L1: Promise of durable responses in multiple tumour types

Not all lung cancers are the same: Combo therapies will address tumour biology

The power of combinations in IO

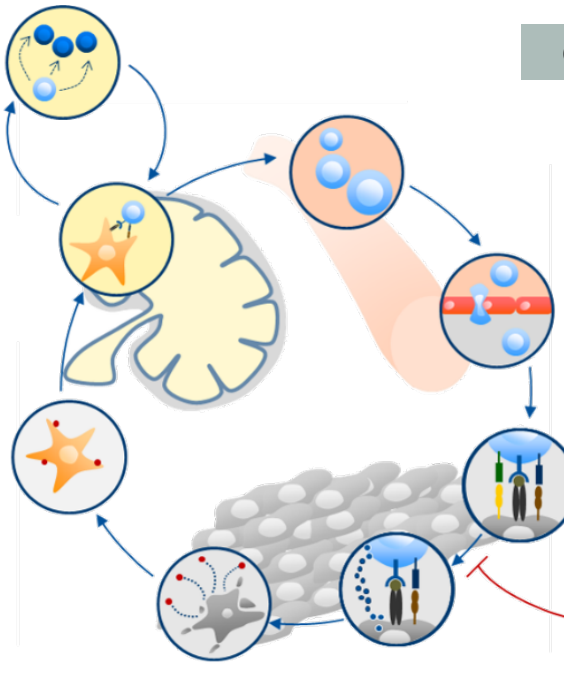
AstraZeneca
What science can do

Mohammed M. Dar
Vice President, Oncology Clinical Development, MedImmune

Optimising anti-tumour immunity

Portfolio addresses major escape mechanisms

Key: New since ASCO 2014



Optimising T-cell function and memory

- PD-L1
- CTLA-4
- OX40 FP
- PD-1
- NME-2015
- OX40 hAb
- mOX40 combos with MEDI4736, treme, rituximab
- OX40 FP combo with MEDI4736
- CART* (Juno)

Antigen presentation

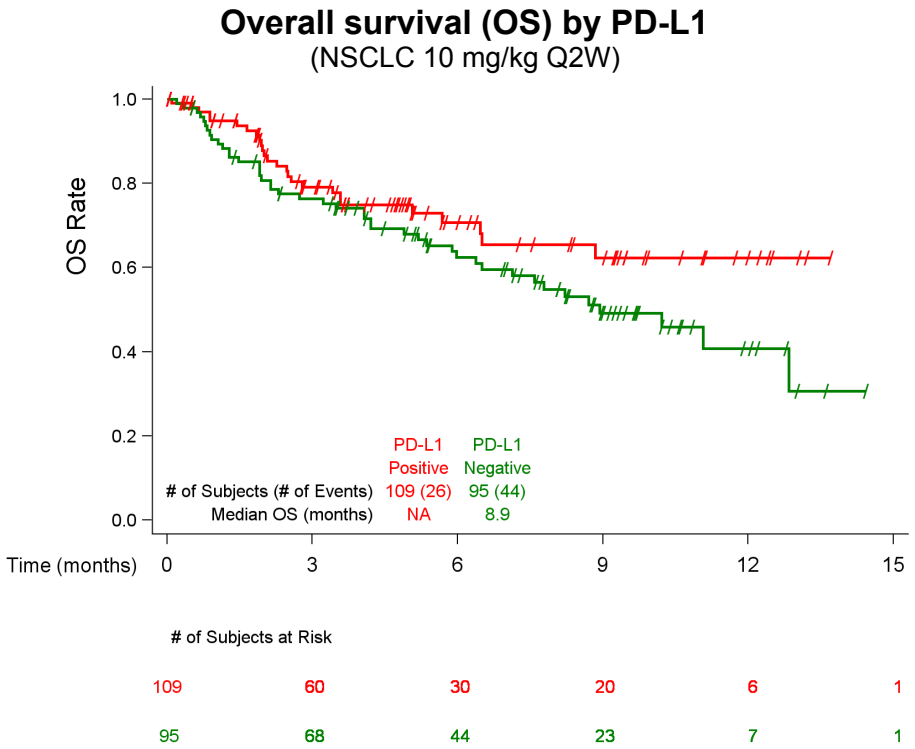
- Chemo
- Oncolytic Virus* (Omnis VSV-Ifnb)
- NKG2A (Innate Pharm)
- Radiotherapy
- NME-2015
- ADC NME-2015
- TKI combos (AZD9291, *Iressa*, BRAF/MEK*) ibrutinib*
- Vaccines (Advaxis*, others)

Inhibition by micro-environment

- IDO*
- CCR4*
- NME-2015
- CXCR2
- STAT3

*Clinical collaboration

MEDI4736: Trend towards overall survival in NSCLC

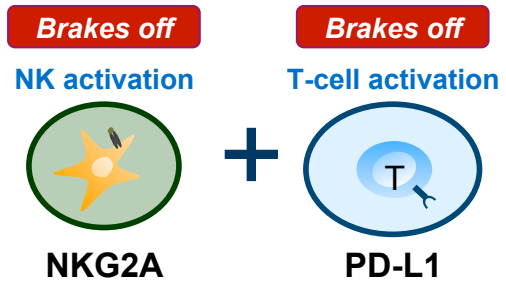


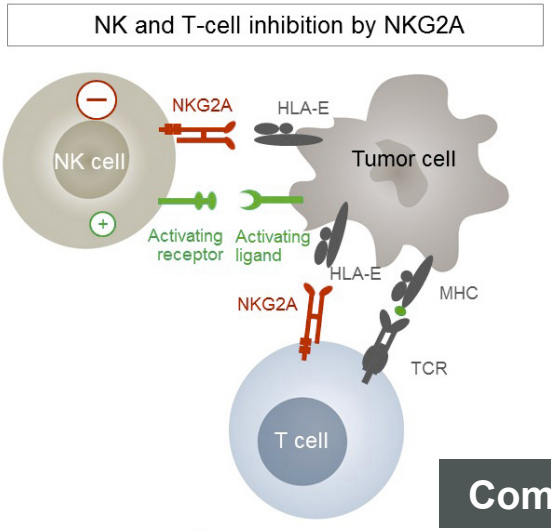
- Preliminary OS data from study 1108 are encouraging and suggest that patients with PD-L1 positive tumours may have improved OS compared to patients with PD-L1 negative tumours

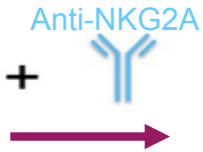
Unmet need remains in PD-L1 negative tumours

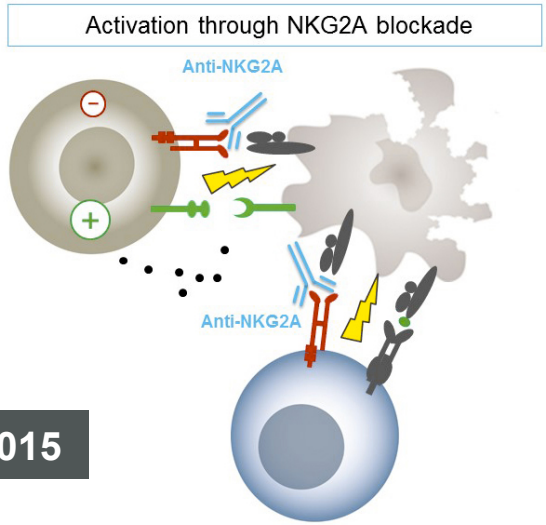
The promise of combinations

Stimulating both innate and adaptive immunity







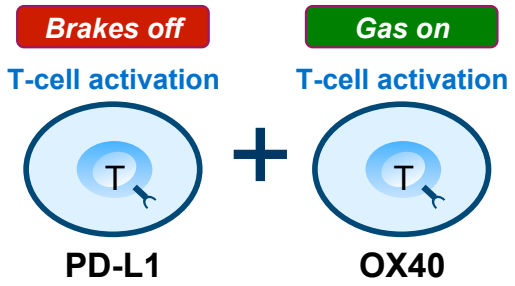


Combination with MEDI4736 planned for H2 2015

- Like T-cells, NK cells are also capable of killing tumour cells
- NKG2A is expressed both on NK and T-cells and acts as checkpoint (different from KIR)
- The ligand, HLA-E, is expressed on multiple solid and liquid tumours (potential selection)

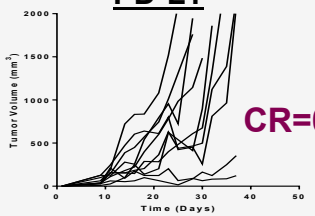
The promise of combinations

PD-L1 + OX40 and CTLA-4 + OX40



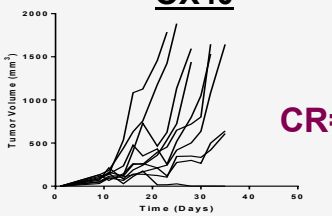
Pre-clinical[1] data with PD-L1

PD-L1



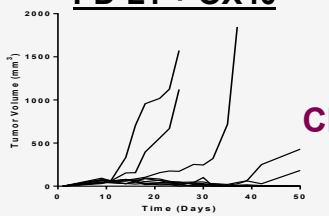
CR=0/10

OX40



CR=1/10

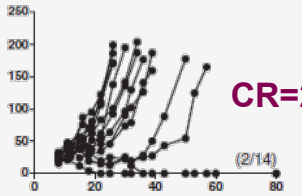
PD-L1 + OX40



CR=5/10

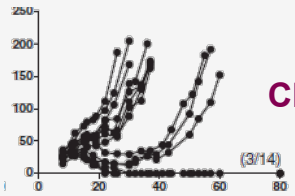
Pre-clinical[1] data with CTLA-4

CTLA-4



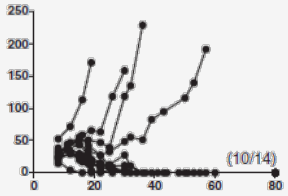
CR=2/14

OX40



CR=3/14

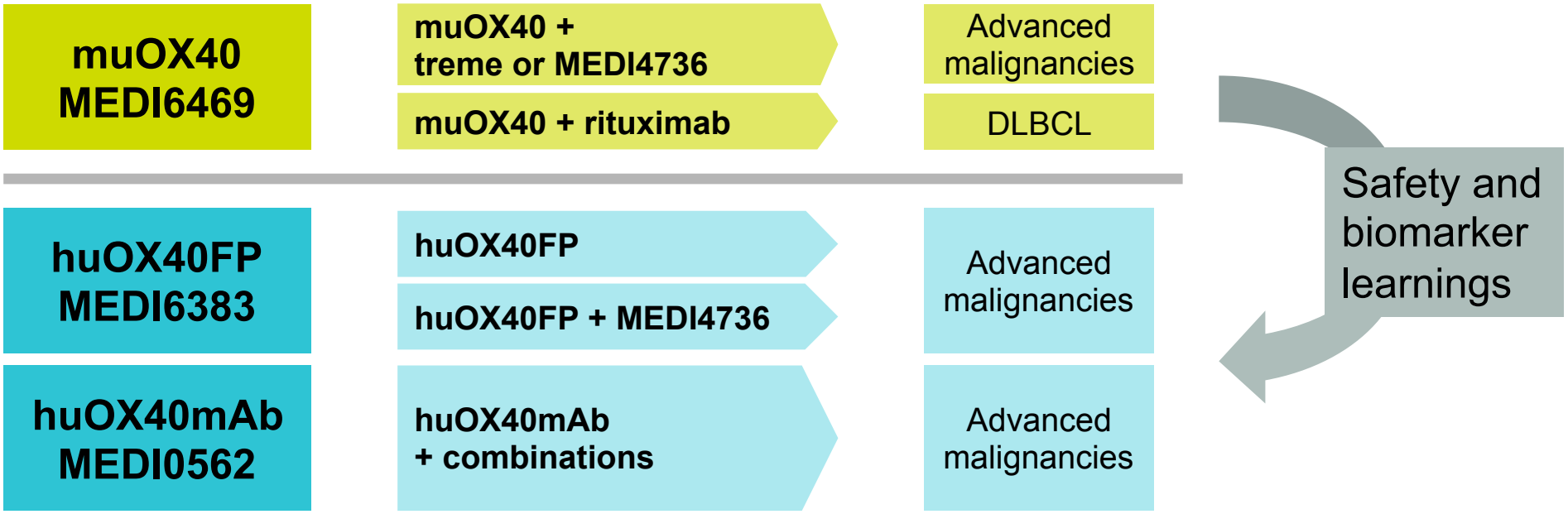
CTLA-4 + OX40



CR=10/14

1 Mouse model used in experiments
CR = complete response
McGlinchey et al. Poster AACR 2014

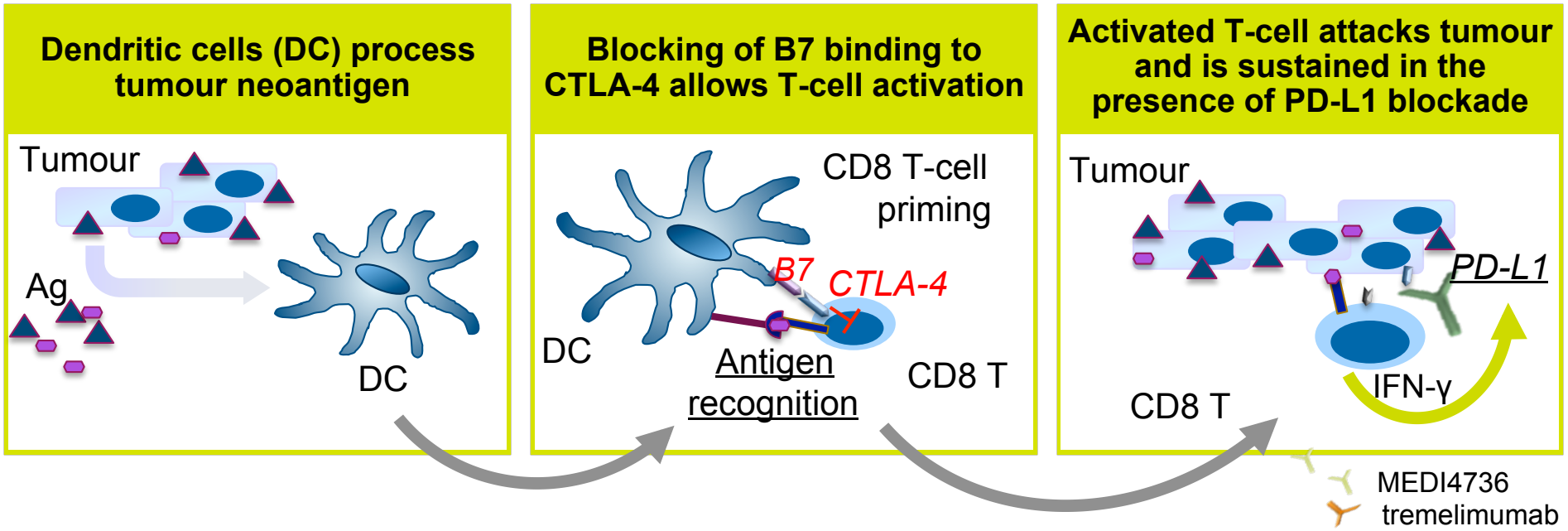
Translation of IO strategy into the clinic: OX40 programme



Optimal OX40 construct to be selected based on clinical efficacy by year end

MEDI4736 + treme target two different escape pathways

Scientific rationale



Study 006: Dose selection for MEDI4736 + treme

Design: Zone-based dose escalation and Phase Ib expansion phase

Population: Stage III-IV NSCLC patients who have failed systemic therapy (no restrictions on # of prior therapies)

1st endpoint:	2nd endpoint:	Exploratory endpoints:
Safety (28-day DLT period)	Efficacy (RECIST response Q8 wks)	Peripheral pharmacodynamics, tumour PD-L1 status

MEDI4736 + treme show efficacy regardless of PD-L1 status

Treme doses beyond 1 mg/kg do not increase efficacy

	M10-20 Q4/2W T1 mg/kg	M10-20 Q4/2W T3 mg/kg	M15 Q4W T10 mg/kg	All cohorts
All evaluable subjects[1] (n)	**27**	24	9	63[2]
ORR[2] - n (%)	**9 (33%)**	6 (25%)	2 (22%)	17 (27%)
95% CI	**(17% - 54%)**	(10% - 47%)	(3% - 60%)	(17% - 40%)
PD-L1 positive (n)	**9**	5	4	18
ORR[2] - n (%)	**3 (33%)**	2 (40%)	1 (25%)	6 (33%)
95% CI	**(7% - 70%)**	(5% - 85%)	(1% - 81%)	(13% - 59%)
PD-L1 negative (n)	**13**	14	4	33[2]
ORR[2] - n (%)	**5 (38%)**	3 (21%)	1 (25%)	9 (27%)
95% CI	**(14% - 68%)**	(5% - 51%)	(1% - 81%)	(13% - 46%)
PD-L1 unknown (n)	**5**	5	1	12[2]
ORR[2] - n (%)	**1 (20%)**	1 (20%)	0 (0%)	2 (17%)
95% CI	**(1% - 72%)**	(1% - 72%)	(0% - 98%)	(2% - 48%)

Dose selected for Phase III studies

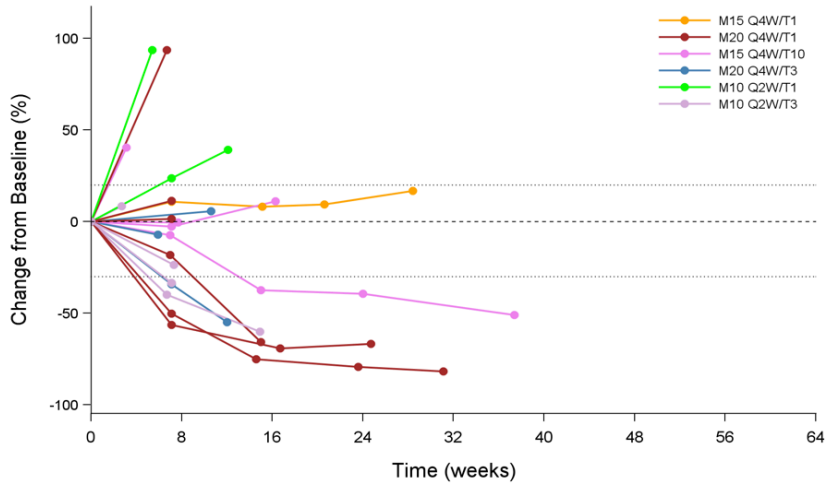
1 Includes confirmed and unconfirmed complete response (CR) or partial response (PR). In patients with measurable disease at baseline, ≥1 follow-up scan + those that discontinued due to PD or death without any follow-up scan. All subjects were dosed ≥sixteen weeks prior to the cut-off date.

2 Includes three subjects (two PD-L1 negative and one PD-L1 unknown) treated at M3 Q4W + T1 mg/kg

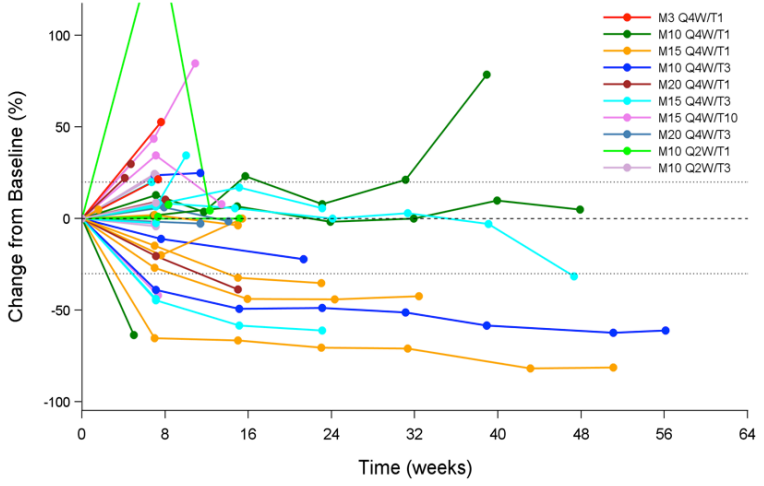
Responses with MEDI4736 + treme: Rapid and durable

Similar activity across PD-L1 positive and negative subsets

PD-L1 positive



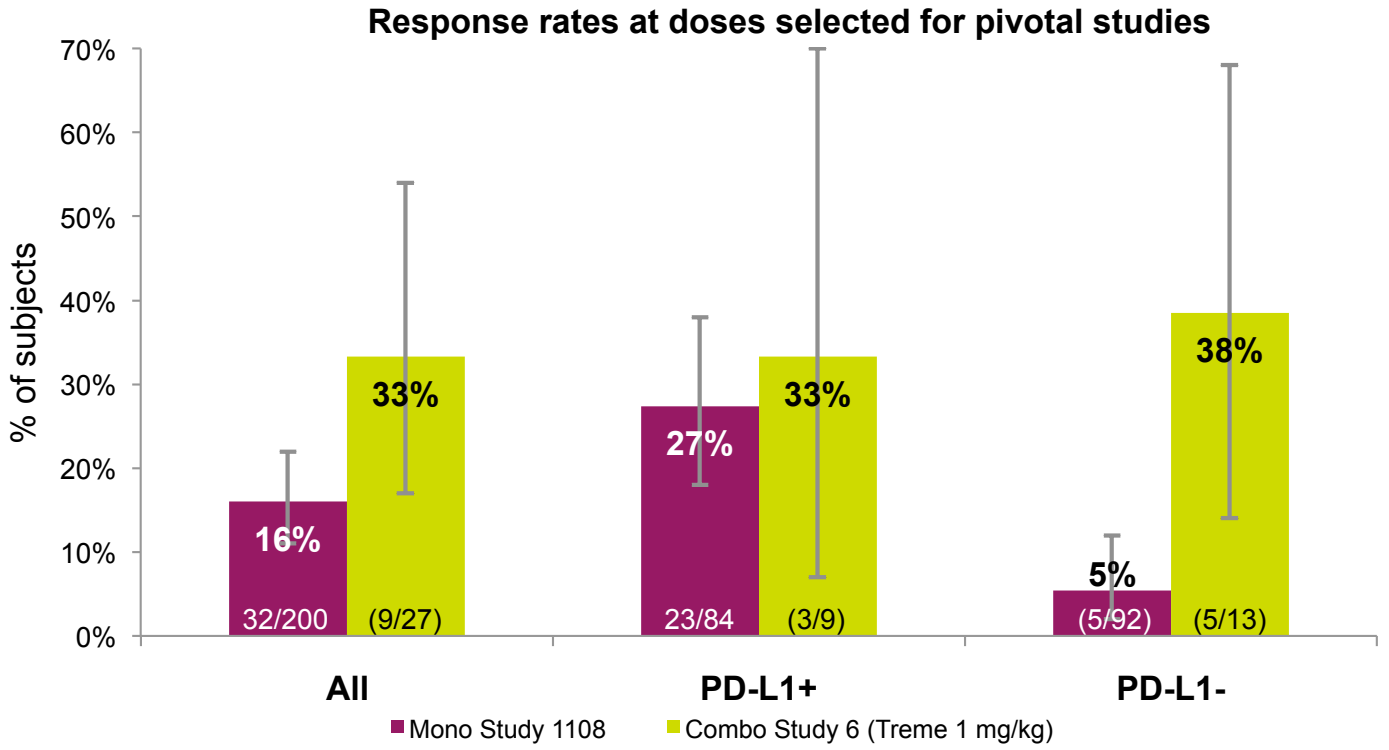
PD-L1 negative



M = MEDI4736; PD-L1 = programmed death-ligand 1; Q#W = every # weeks; SD = stable disease; T = tremelimumab

MEDI4736 + treme increases ORR over monotherapy

Important improvement in PD-L1 negative patients



Monotherapy = M10 mg/kg Q2W in NSCLC (all lines) in 1108 (data cut-off = 27 Feb 2015)
Combination therapy = M10-20/T1 in 006 (data cut-off =15 Apr 2015)
ORR = overall response rate

MEDI4736 + treme show promising activity

Large unmet medical need in PD-L1 negative NSCLC patients

PD-1/PD-L1 class monotherapy	Durable clinical benefit for a **subset** of patients
PD-1/PD-L1 + CTLA-4 MoA combination	Strongest **clinically-validated** IO-IO combination to date
MEDI4736 + treme	**Promising clinical activity** in NSCLC especially in PD-L1 neg. subset with **manageable safety profile**
IO-IO combination strategy	Develop novel IO combinations targeting patients who are less likely to respond to PD-1/PD-L1 monotherapy

MoA = mode of action

Clinical experience with MEDI4736 + treme

Scott Antonia
Department Chair and Program Leader, Thoracic Oncology and Program Leader of the Immunology Program at Moffitt Cancer Center, Tampa, FL, USA

Study overview

Study design

Key elements
Ph Ib zone-based dose escalation design with ability to expand selected cohorts for safety/PD/efficacy
Previously-treated patients with NSCLC

Key eligibility criteria

Key inclusion criteria	Key exclusion criteria
ECOG PS 0–1	Active or prior auto-immune disease
Adequate organ function	Prior severe or persistent adverse events (AE)
Immunotherapy-naïve: No prior immunotherapy* Any number of prior therapies	Current/prior immunosuppressive medication ≤14 days before first MEDI4736 and tremelimumab dose

Study endpoints

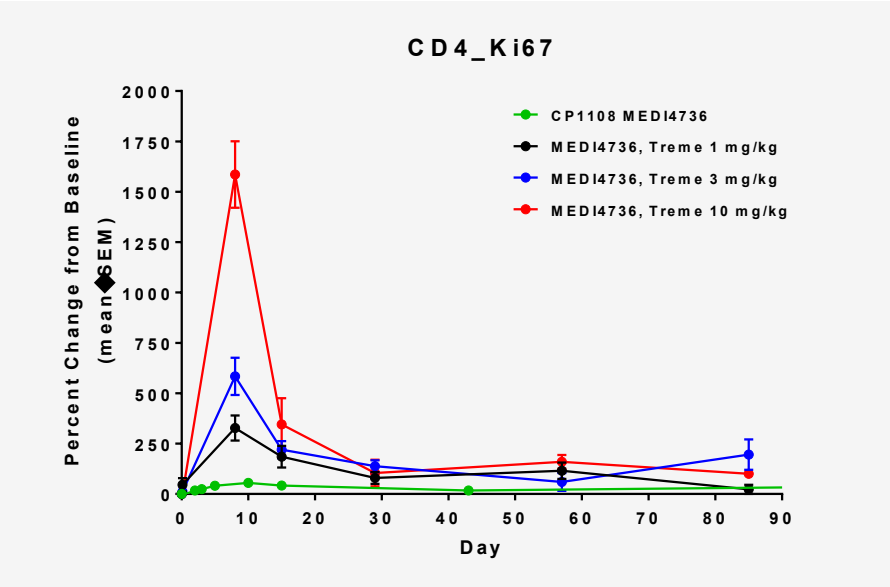
Primary	Secondary	Exploratory
Safety	PK	PD-L1 status*
Tolerability	Immunogenicity	Serum PD-L1
	Anti-tumor activity	

*PD-L1 immunohistochemical staining on automated BenchMark ULTRA® platform using the PD-L1 SP263 assay (see ASCO 2015 Poster 8033)

MOFFITT CANCER CENTER

MEDI4736 + tremelimumab: PK/PD summary

- PK exposure consistent with respective monotherapy studies; suggesting no PK interaction
- Dose as low as 1 mg/kg of tremelimumab in combination demonstrated log fold greater peripheral pharmacodynamic activity (T-cell proliferation/activation) compared to MEDI4736 monotherapy



MOFFITT CANCER CENTER

Treme 1 mg/kg Q4W well tolerated in combo with MEDI4736

- Related grade 3/4 AEs and discontinuations due to related AEs were lowest in the 1 mg/kg Q4W tremelimumab cohorts
- AEs did not appear related to dose or schedule of MEDI4736

	M10-20 Q4/2W T1 mg/kg n=56	M10-20 Q4/2W T3 mg/kg n=34	M15 Q4W T10 mg/kg n=9
Related AE	35 (63%)	30 (88%)	8 (89%)
Related G3/4 AE	16 (29%)	18 (53%)	7 (78%)
Related death	1 (2%)	1 (3%)	0
Related serious AE	10 (18%)	17 (50%)	7 (78%)
Related AE leading to discontinuation	4 (7%)	12 (35%)	4 (44%)

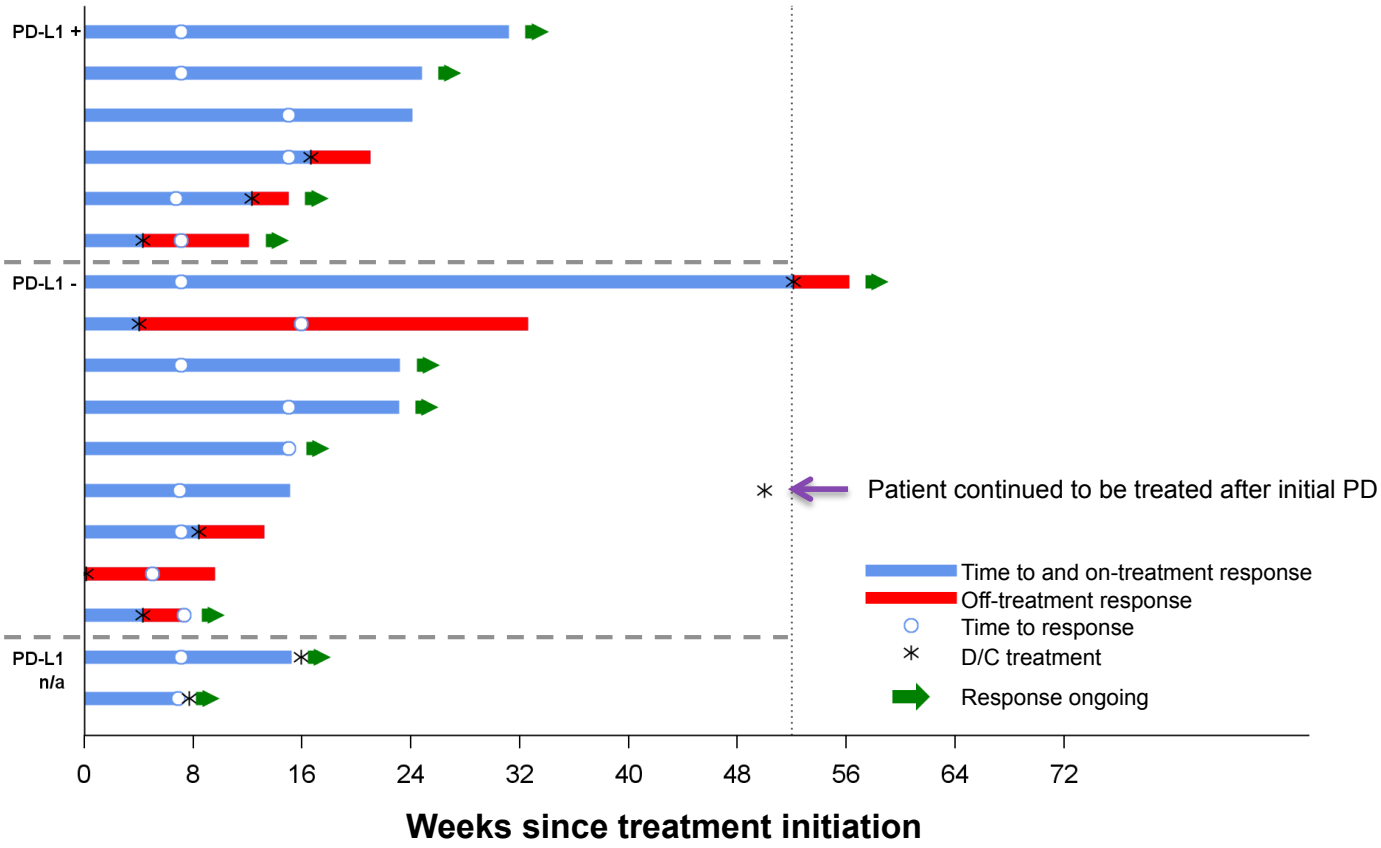
MOFFITT CANCER CENTER

Related grade 3/4 events of special interest

Comparison to MEDI4736 monotherapy

System organ class	Event	Mono (study 1108) n=228	M10-20 Q4/2W T1 mg/kg n=56
Any event		3%	13%
Gastrointestinal	Diarrhea Colitis	<1% 0%	5% 2%
Respiratory	Pneumonitis	0%	0%
Skin	Rash (maculopapular)	<1%	0%
Endocrine	Hyperthyroidism Hypothyroidism Thyroiditis	<1% 0% <1%	0% 2% 0%
Investigations	ALT increased AST increased Amylase increased Lipase increased	<1% 1% 0% 0%	4% 5% 2% 7%

Time to response and duration of response



MOFFITT CANCER CENTER

MEDI4736 + treme combination: High level of activity and manageable safety

- MEDI4736 20 mg Q4W and tremelimumab 1 mg/kg Q4W (M20T1 Q4W) has been selected for Phase III development
  - Maximizes PD-L1 inhibition
  - Demonstrates manageable safety
  - Incorporates biologically-active dose of tremelimumab associated with clinical activity

- Across all dose cohorts:
  - AEs were manageable and generally reversible using standard treatment guidelines
    - 31% of patients received corticosteroids for management of AEs

High level of clinical activity was seen in pre-treated NSCLC patients, especially in patients with PD-L1 negative tumors

MOFFITT CANCER CENTER

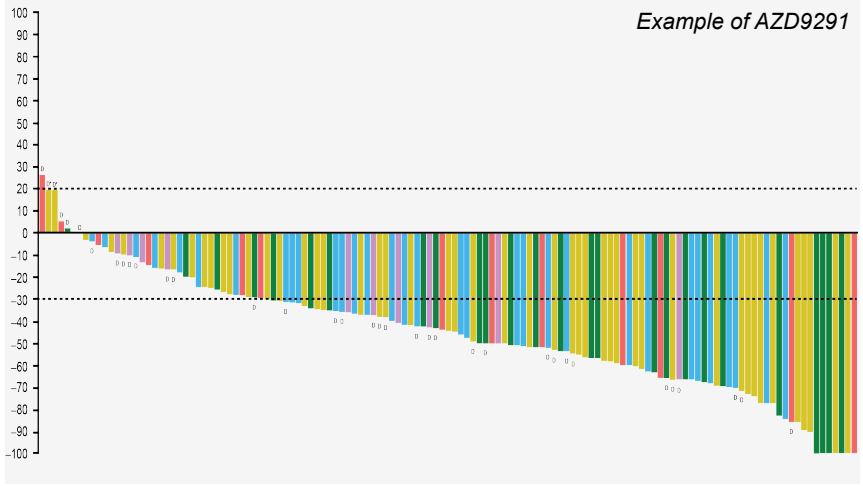
Small-molecule combinations

AstraZeneca
What science can do

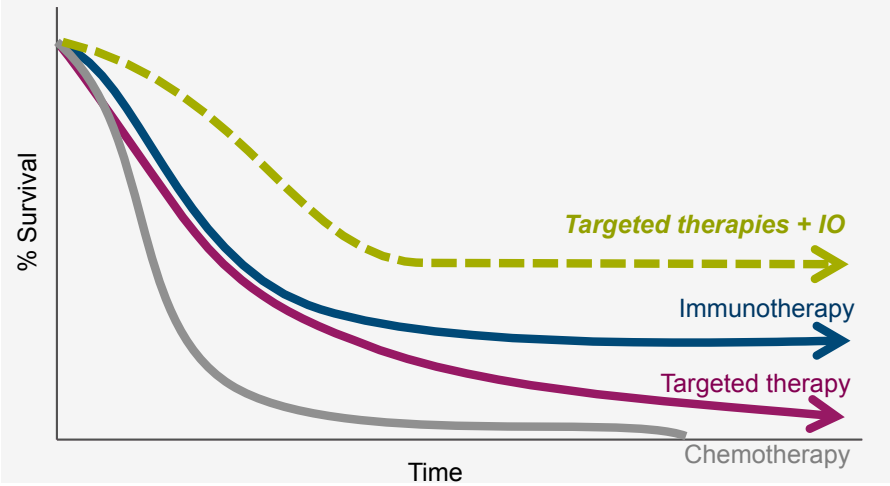
Susan Galbraith
Head of Oncology, Innovative Medicines Biotech Unit

Combination of targeted therapy and immune checkpoints

Targeted therapies: High response rate



IO: High duration of response



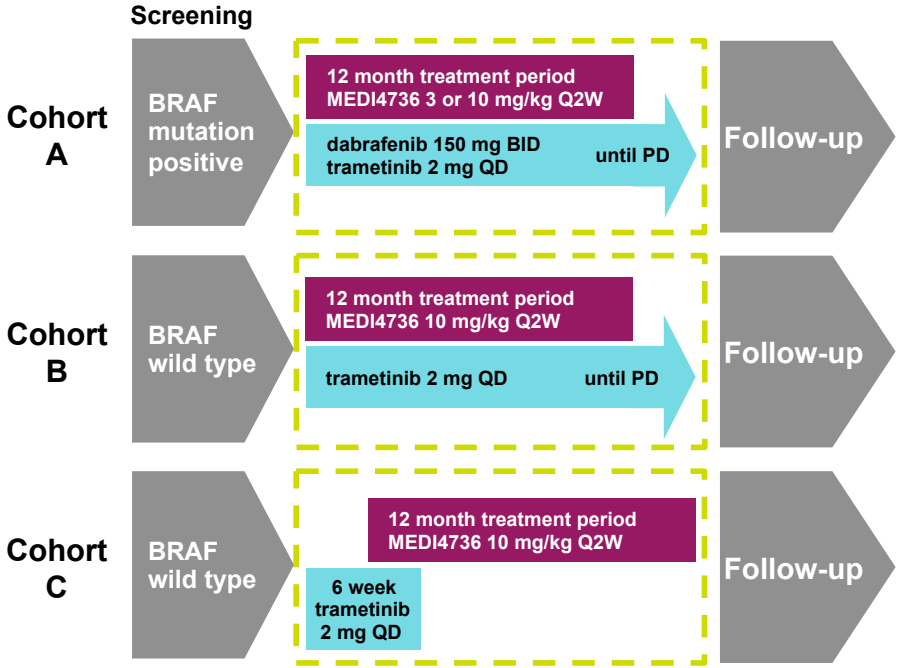
Potential synergistic effect

High RR and median PFS of targeted therapies with extended duration of response of IO

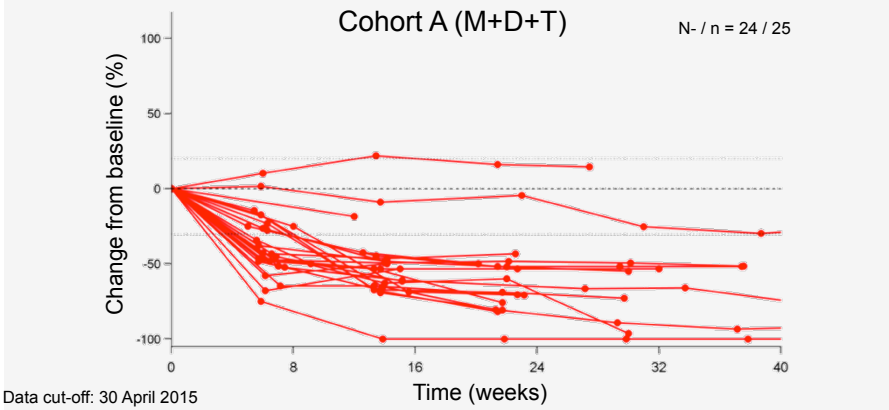
BRAFi + MEKi + MEDI4736

Unprecedented ORR (69%) and DCR (100%)

Potential for well-tolerated, durable benefit in BRAFm melanoma



Tumour size change from baseline: Cohort A



Data cut-off: 30 April 2015

Clinical activity, n (%)	Cohort A (n=26)	Cohort B (n=19)	Cohort C (n=18)
	M + D + T	M + T	T M (sequential)
ORR	18 (69)	4 (21)	2 (13)
DCR	26 (100)	15 (79)	12 (80)
DoR, wks (range)	(7.7+, 50.6+)	(7.9+, 24.7+)	(7.0+, 8.0+)

Lynparza + MEDI4736

DNA damage prone to immune response

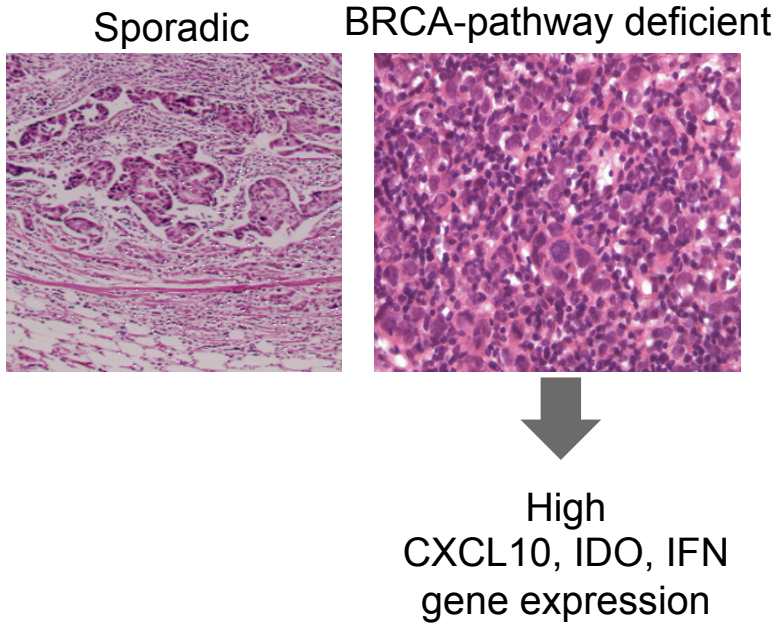
Rationale

- BRCA-mutant breast and ovarian cancers associated with a CXCR3+ T-cell lymphocytic infiltrate: Immune response associated with DNA damage[1,2]
- High CXCL10, IDO, IFN gene expression

Combination trials to start by Q3 2015

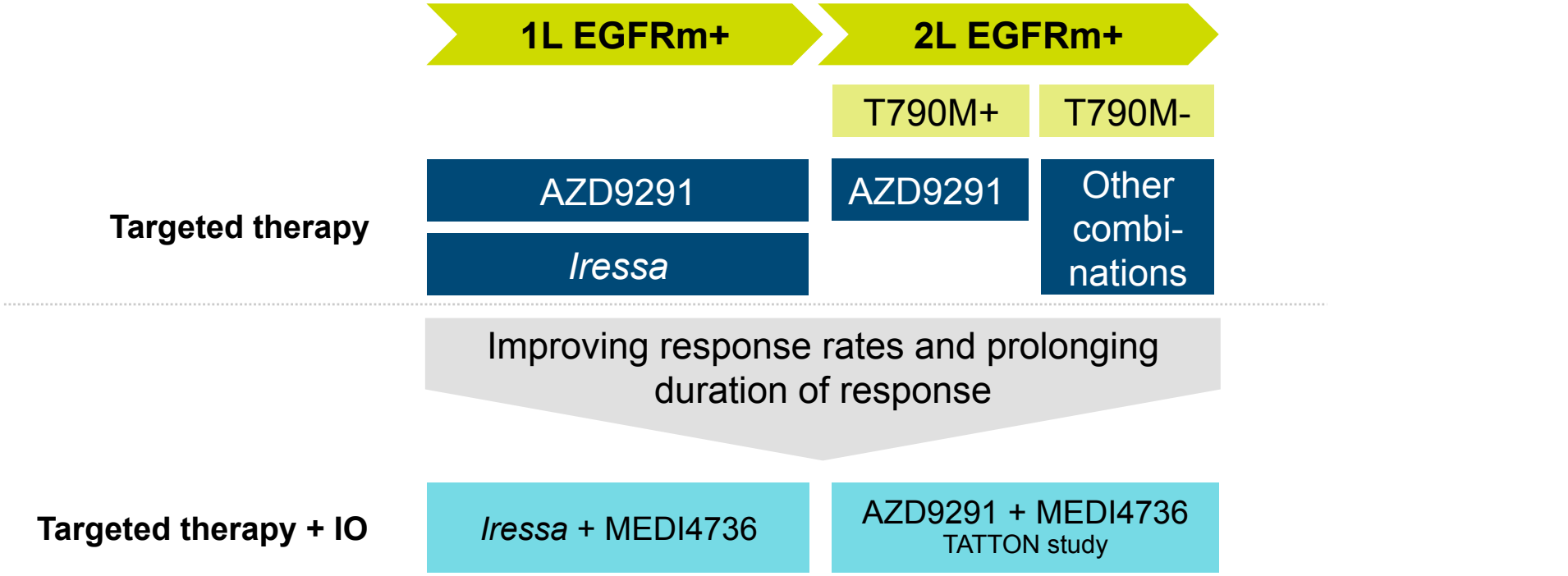
- DDR deficient ovarian cancer (BRCA, ATM etc.)
- DDR deficient SCLC, TNBC, bladder, gastric, NSCLC, H&N, cervical and pancreatic cancer
- Add tremelimumab if doublet combination well tolerated

T-cell infiltrates in BC



1 Lakhani et al Breast Cancer Res. 1999;1(1):31-5;
2 Fujiwara et al Am J Surg Pathol. 2012;36(8):1170-7; Images courtesy of Almac diagnostics

EGFRm+ NSCLC: SM-IO combination strategy



AZD9291 + MEDI4736: TATTON study

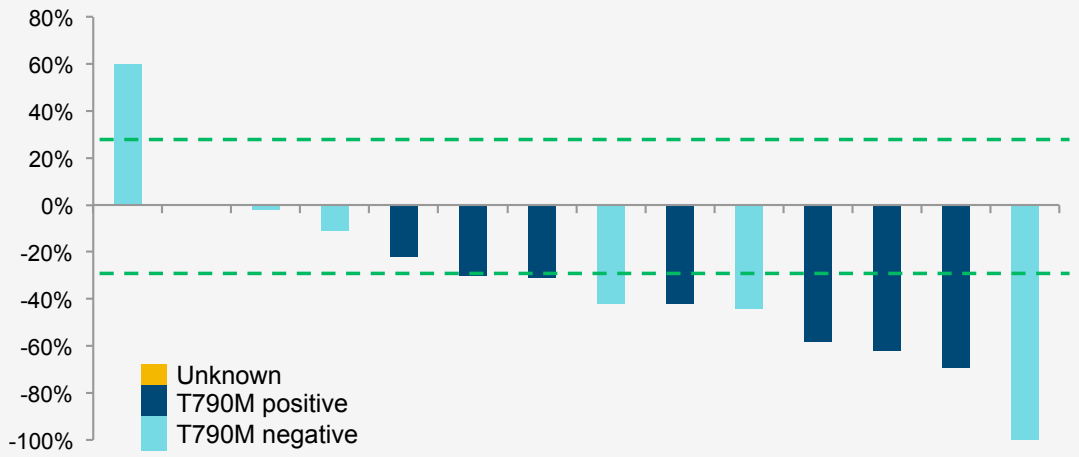
Potential for new SoC in EGFRm+ NSCLC

Basket study in EGFRm+ NSCLC after progression on prior EGFRi

AZD9291 + MEDI4736 arm

- Both drugs tolerated at full dose
- One grade 3 AE at this dose (WBC decrease)
- One complete response
- 9/14 (64%) PRs (four confirmed PRs)
  - 6/7 (85%) in T790M+
  - 3/7 (43%) in T790M-

Best percentage change from baseline in target lesion size



EGFR remains one of the major tumour drivers despite progression on EGFRi
Combination with MEDI4736 might increase RR and DoR in 2L EGFR+ NSCLC

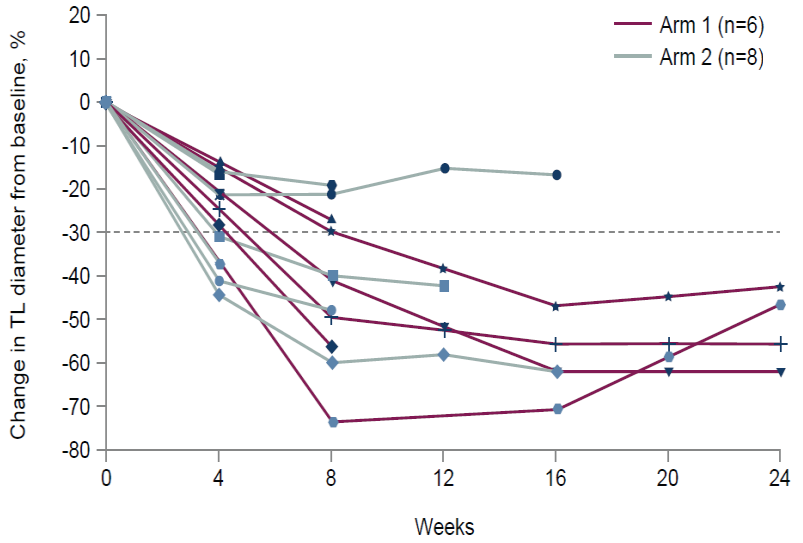
Iressa + MEDI4736 in EGFRm TKI-naïve NSCLC

Providing evidence of good combinability for MEDI4736

Initial clinical data

- Both drugs tolerated at full dose
- Two expansion cohorts at full doses:
  - Arm 1 concomitant (n=6 evaluable)
  - Arm 2 four weeks monotherapy *Iressa* then combination (n=8 evaluable)
- 9/14 (64%) partial responses
- AEs of interest: Grade 3 AST/ALT

Tumour assessment: Expansion phase



Iressa + MEDI4736 combination in 1L EGFR+ NSCLC to be tested in Phase III study

Additional small molecule + MEDI4736 combinations

Significant opportunities across multiple tumour types

Mechanism	Indication	Study start
IDO	Solid tumours	Dec 2014
BTK/ITK	DLBCL, FL, solid tumours	Mar 2015
STAT3	Solid tumours	Q3 2015
CXCR2	Solid tumours	Q3 2015
FGFR	Bladder cancer	Q3 2015
PI3Kβ/δ	Bladder cancer	Q3 2015
PI3Kδ	Haematological tumours	2015

Small-molecule combinations

SM + MEDI4736 potential tested in >2,700 patients

Tolerability	MEDI4736 is tolerated in combination at full dose with multiple SMs
Efficacy	Encouraging preliminary efficacy data. Update with larger patient numbers and duration of follow-up later this year
IO-targeted therapy combination strategy	Well-tolerated combination therapy delivering both high response rate and high durability of response leading to improved survival

IO: Maximising value across tumour types

AstraZeneca
What science can do

Robert Iannone
Head of Immuno-Oncology, Global Medicines Development

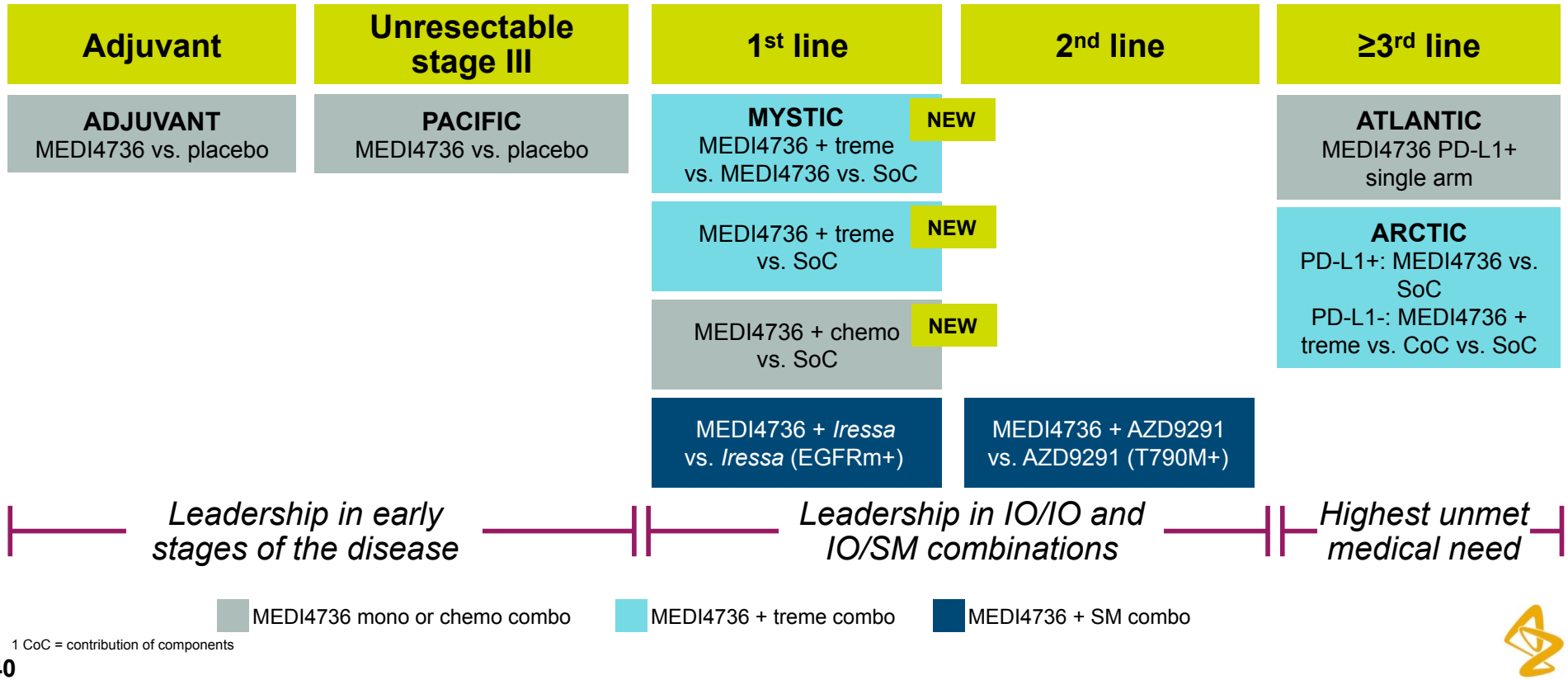
IO strategy

Focus on combination & first-mover indications

Speed	• Mono MEDI4736 in PD-L1 positive NSCLC 3L+ / Head & Neck (SCCHN) 2L • MEDI4736 + treme in PD-L1 negative SCCHN 2L
Differentiation	• Early-stage disease e.g. Adjuvant and stage III unresectable NSCLC • **Chemo-free** regimen e.g. MEDI4736 + treme
Leadership	• Novel combinations e.g. MEDI4736 + AZD9291 • New tumour types e.g. haematological malignancies

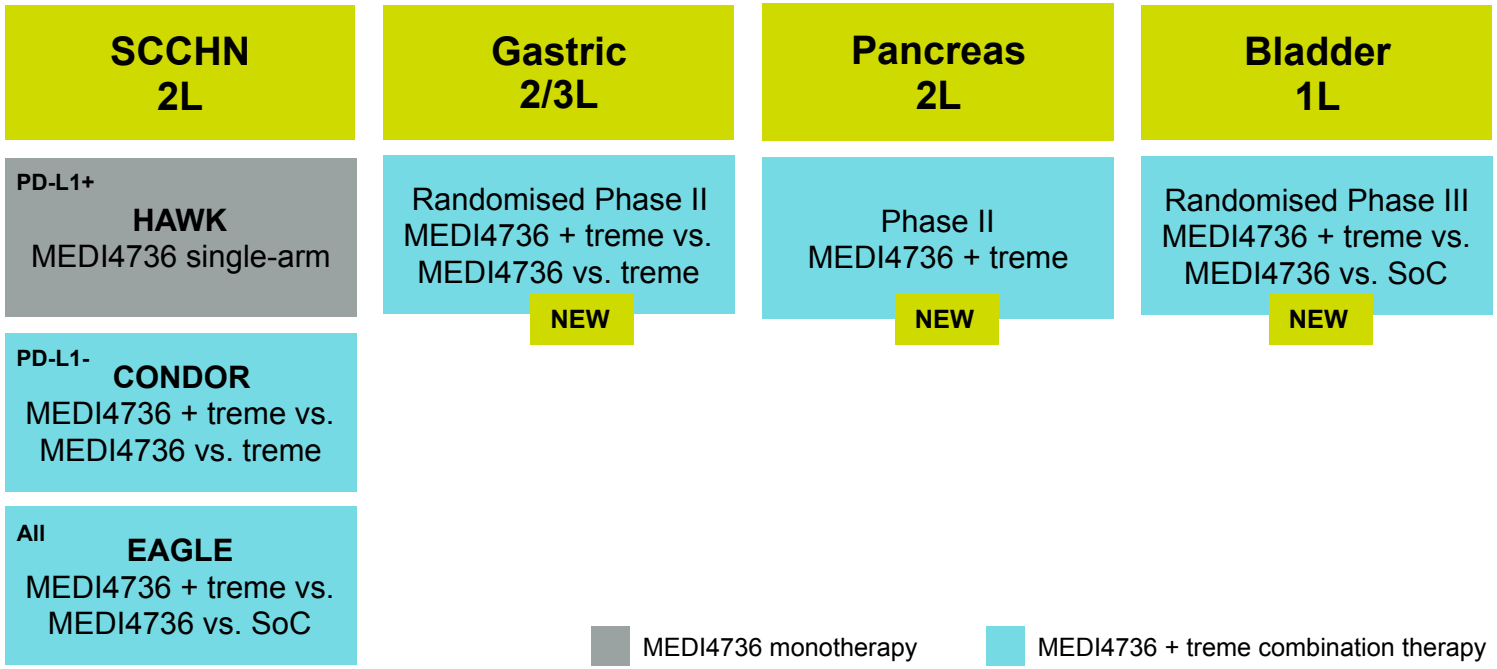
NSCLC: IO development programmes

Total now includes more than 5,600 patients



1 CoC = contribution of components

Additional tumour types: Exploring the benefit of MEDI4736 + treme combination



Change paradigm with chemo-free regimen

IO development summary

Pivotal Phase II & Phase III studies in >8,300 patients

	# of Phase II studies	# of Phase III studies
Lung	1	8
Mesothelioma	1	-
SCCHN	2	1
Gastric	1	-
Pancreas	1	-
Bladder	-	1
Total	**6**	**10**

IO: Maximising value across tumour types

Pioneer in IO combinations; registration studies well underway

- Well-tolerated MEDI4736 + treme combination dose has been selected for Phase III and studies have been initiated
- Comprehensive registration programme with MEDI4736 is underway across multiple tumour types, stages of disease, lines of therapy, and in combination with tremelimumab, small molecules and chemotherapy
- Clinical development of MEDI4736 has been accelerated in haematological malignancies in combination with effective therapies through the alliance with Celgene

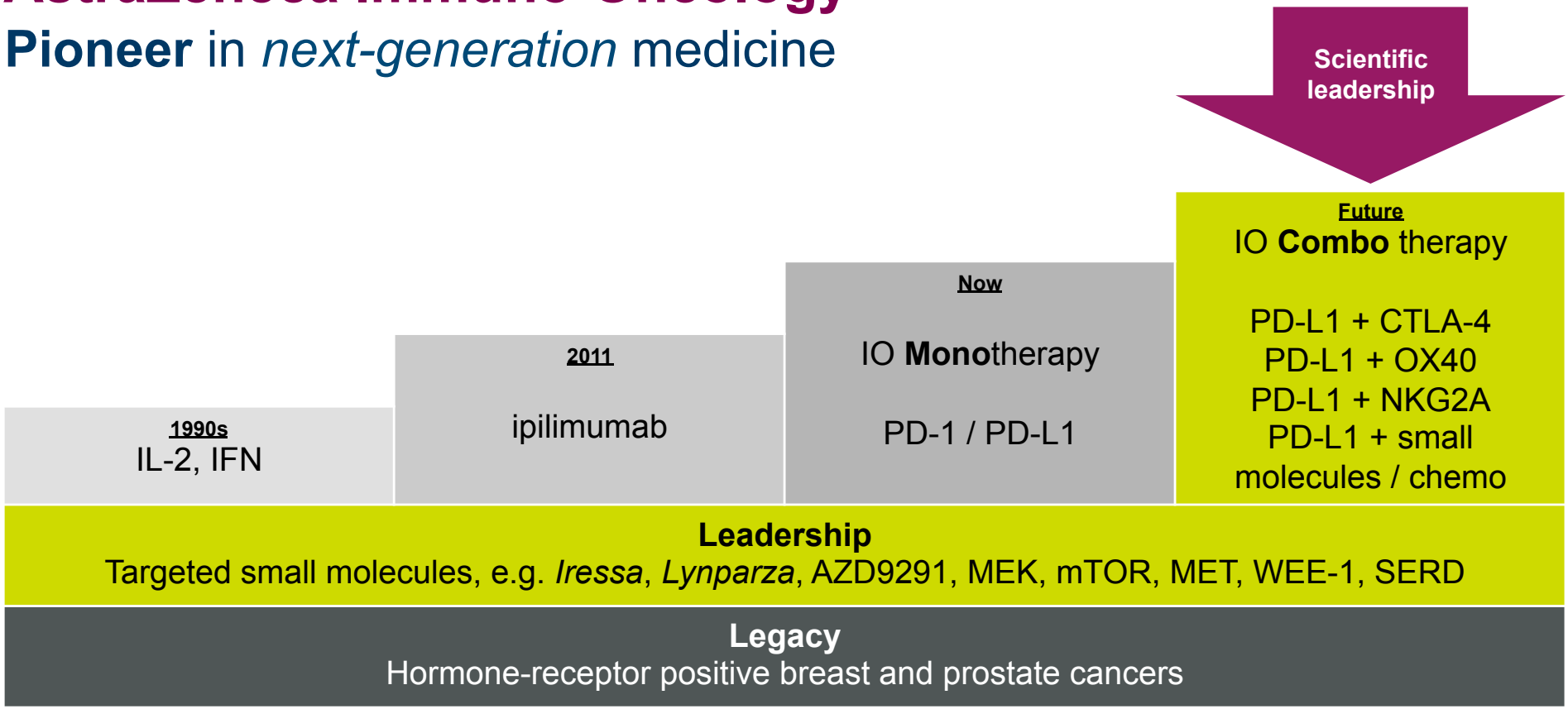
Closing and Q&A

AstraZeneca
What science can do

Pascal Soriot
Chief Executive Officer

AstraZeneca Immuno-Oncology

Pioneer in *next-generation* medicine



Q&A

Please press *1 on your phone if you wish to ask a question

- **Pascal Soriot, *moderator***
- Scott Antonia, Moffitt Cancer Center
- Mondher Mahjoubi
- Mohammed M. Dar
- Susan Galbraith
- Robert Iannone

Q&A expected to end at 10pm

Thank you for joining today's ASCO investor science event

Please join for drinks in Continental Room C

AstraZeneca
What science can do

ASCO 2015 investor science event

Chicago, IL, USA
01 June 2015