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# **ESMO IO Congress 2017, Geneva**

*Roche Analyst Call*

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# **Introduction**

**Karl Mahler**

*Head of Investor Relations*

# Agenda

## Welcome

Karl Mahler, Head of Investor Relations

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## **IMpower150: Phase 3 results of carboplatin + paclitaxel +/- Avastin, with or without Tecentriq in 1L non-squamous metastatic NSCLC**

Alan Sandler, M.D., Global Development Team Leader Tecentriq Lung

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## **Tecentriq program overview: Focusing on novel combination approaches**

Sushil Patel, Ph.D., Global Product Strategy Tecentriq, Lifecycle Leader

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## Q&A

Karl Mahler, Head of Investor Relations

# Emerging insights from IMpower150

## IMpower150 Phase 3

## Open questions for the industry

- ✓ First Ph3 using CIT chemo combo ± Avastin to show statistically significant and clinically meaningful PFS benefit in 1L non-sq NSCLC
- ✓ Tecentriq + Avastin + chemo combo shows benefit in all patients, regardless of :
  - PD-L1 expression / Teff signature
  - EGFR or ALK genetic alterations
  - Liver metastases
- ✓ Tecentriq + Avastin + chemo combo well tolerated, consistent with known safety risks

Translatability of data from small studies to outcomes of definitive Ph3 studies

Efficacy of CIT agents across histologies (non-sq, sq, SCLC)

Efficacy of CIT agents dependent on chemo backbones

**Tecentriq + Avastin + chemo combo has the potential to set a new standard of care**

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**IMpower150: Phase 3 results of carboplatin +  
paclitaxel +/- Avastin, with or without Tecentriq  
in 1L non-squamous metastatic NSCLC**

**Alan Sandler, M.D.**

*Global Development Team Leader Tecentriq Lung*

See Dr. Martin Reck presentation, ESMO IO 2017

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# **Tecentriq program overview: Focusing on novel combination approaches**

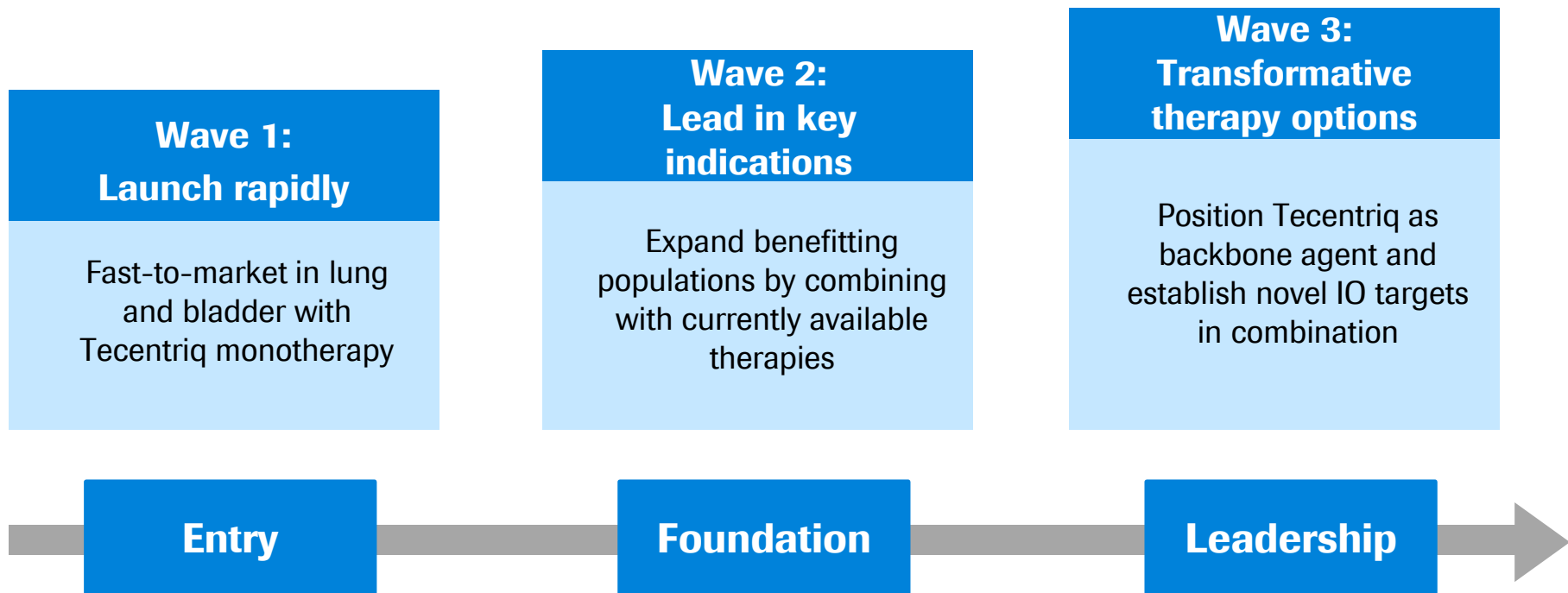
**Sushil Patel**

*Global Product Strategy Tecentriq, Lifecycle Leader*



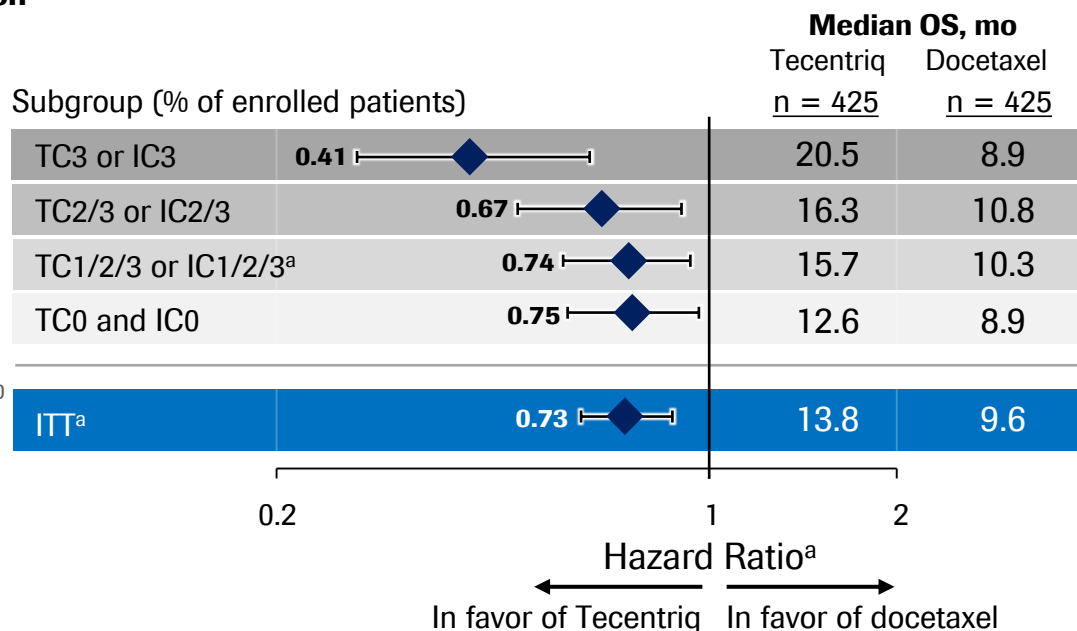
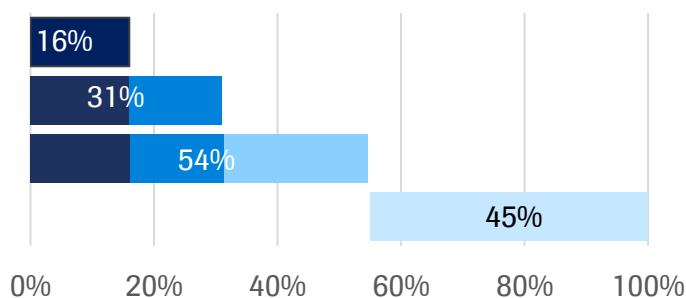
# Tecentriq: Vision & strategy

## *Shaping the treatment landscape long term*



# Wave 1: Ph3 OAK study shows OS benefit of Tecentriq monotherapy in all 2L+ NSCLC patients<sup>1</sup>

## On-study prevalence: OS by PD-L1 expression



## Ph3 OAK data:

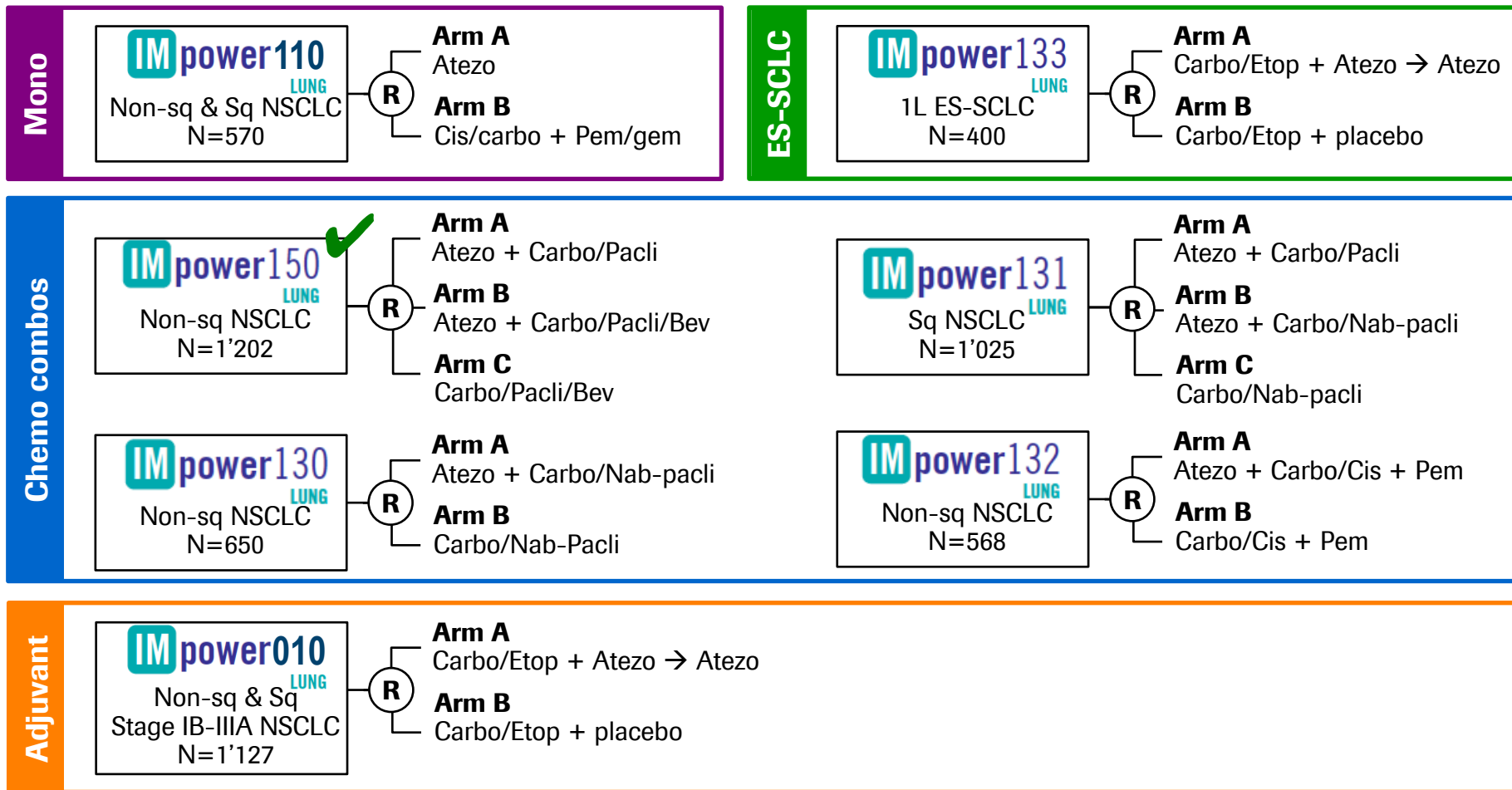
- Approved for all-comers
- First CIT agent to be efficacious irrespective of PD-L1 status, including low/no PD-L1 expression
- Efficacy in important sub-groups, such as never smokers and patients with brain metastases
- Active in squamous and non-squamous histologies

<sup>1</sup>Barlesi et al., ESMO 2016

<sup>a</sup>Stratified HR for ITT and TC1/2/3 or IC1/2/3. Unstratified HR for subgroups.

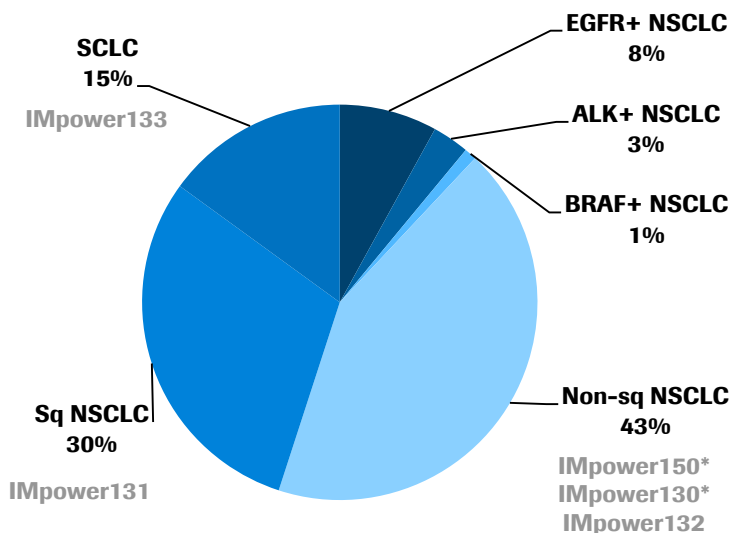
# Tecentriq Ph3 program in 1L & early lung cancer

## Wave 2 combo studies to read out

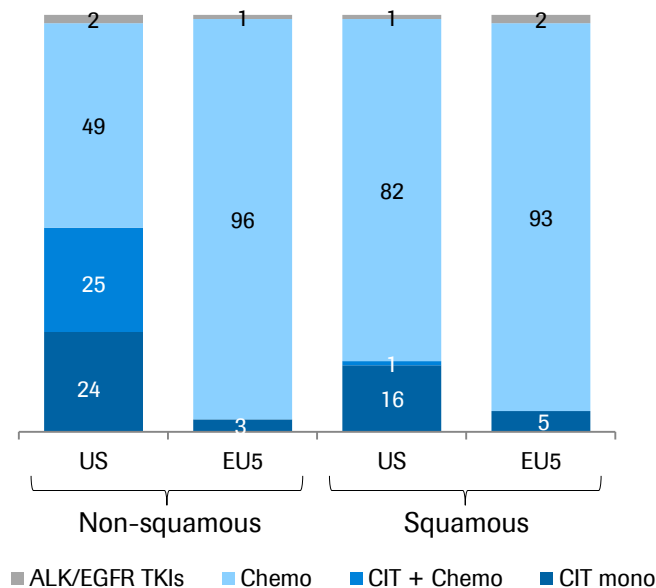


# 1L NSCLC: Not one disease

**Histology-based subtypes**



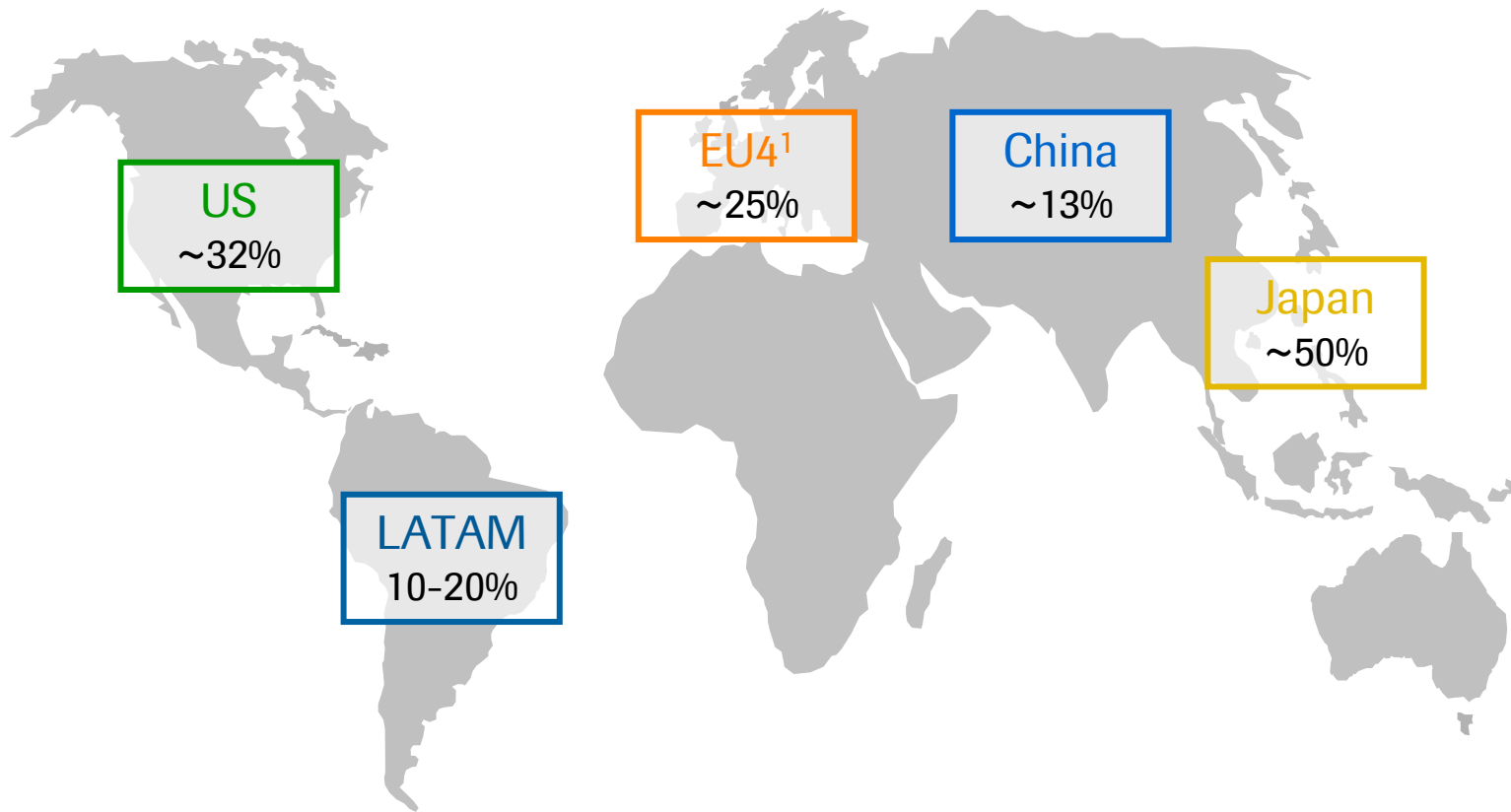
**Current market share of treatment options\*\***



**Tecentriq's Ph3 program in 1L lung cancer addresses all market segments and chemo backbones**

\*Primary analysis population excludes patients with tumors harboring actionable mutations, EGFR and ALK, (=ITT-WT). Secondary endpoints include PFS and OS in ITT, regardless EGFR/ALK status. \*\*1L EGFR mut- / Alk mut- NSCLC (all PD-L1 expressions) by histology. NSCLC=non-small cell lung cancer; SCLC=small cell lung cancer; Non-sq=non-squamous; Sq=squamous; TKI=tyrosine kinase inhibitor; CIT=cancer immunotherapies

# Avastin: A standard of care in non-sq 1L NSCLC



**Global Avastin shares remain significant, including key markets like US and Germany**

EGFR-/ALK- platinum treated 1L NSCLC; <sup>1</sup>Avastin not reimbursed in UK  
 NSCLC=non-small cell lung cancer; Non-sq=non-squamous

# IMpower150: PFS statistically significant & clinically meaningful in both ITT-WT and Teff-WT

	E4599 <sup>1</sup>	IMpower150 <sup>2</sup>	
Regimen	Avastin+CP vs. CP	Arm B vs C (Tecentriq+Avastin+CP vs. Avastin+CP)	
Population	1L AC	1L ITT-WT	1L T <sub>eff</sub> -high WT
Phase	Phase 3 N=878	Phase 3 N=692	Phase 3 N=284
ORR	35% vs. 15%	64% vs 48%	69% vs 54%
mOS (mos)	12.3 vs. 10.3 HR 0.79, p=0.003	19.2 vs 14.4 HR 0.775*, p=0.0262	--
mPFS (mos)	6.2 vs. 4.5 HR 0.66, p<0.001	8.3 vs 6.8 HR 0.617, p<0.0001	11.3 vs 6.8 HR 0.505, p<0.0001
Landmark PFS @ 1yr	18% vs 8.5%**	37% vs 18%	46% vs 18%

**Tecentriq adds additional benefit to Avastin + chemo backbone, preliminary OS shows numerical improvement**

<sup>1</sup>Sandler A, et al., NEJM 2006, 355(24):2542-50; <sup>2</sup>Reck M, et al. ESMO IO 2017

\*OS data are preliminary. Mature OS expected in H1 2018. \*\*taken from KM curve

IMpower150: Investigator-assessed, data cutoff: September 15, 2017; CP=carboplatin and paclitaxel



# IMpower150: Some preliminary assessments on Arm A vs C

	ITT-WT
Regimen	Arm A vs C (Tecentriq+CP vs. Avastin+CP)
PFS HR <sup>a</sup>	0.936
ORR, <sup>b</sup> %	49% vs 48%
OS HR <sup>a</sup>	0.884

- Neither PFS nor OS formally tested (only when B vs C shows significant OS improvement in ITT-WT)
- Tecentriq in combination with chemotherapy well tolerated and consistent with known risks
- Preliminary data suggest that Tecentriq plus chemo look at least as good as the control (E4599); while PFS benefit of Tecentriq over the control (Avastin) is unlikely to change in IMpower150, preliminary OS data indicate the possibility of OS benefit in final data read out
- Formal assessment only in 1H 2018 post final look



# Tecentriq key read outs through 2019

## Potentially first-to-market in 1L SCLC and sq NSCLC





	2017	2018	2019
<b>NSCLC</b>	<b>IMpower150</b> 1L Non-sq NSCLC PFS ✓	<b>IMpower150</b> 1L Non-sq NSCLC OS	<b>KEYNOTE-189</b> 1L Non-sq NSCLC PFS/OS
	<b>MYSTIC</b> 1L NSCLC Dx+ PFS ✗	<b>IMpower130</b> 1L Non-sq NSCLC PFS/OS	<b>KEYNOTE-407</b> 1L Sq NSCLC PFS
	<b>CheckMate 227</b> 1L NSCLC PFS	<b>IMpower131</b> 1L Sq NSCLC PFS/OS	<b>KEYNOTE-042</b> 1L NSCLC Dx+ OS
	<b>PACIFIC</b> STAGE III UNRES NSCLC ✓	<b>IMpower132</b> 1L Non-sq NSCLC PFS/OS	<b>CheckMate 227</b> 1L NSCLC OS
		<b>MYSTIC</b> 1L NSCLC OS	<b>CheckMate 568</b> 1L NSCLC OS
		<b>KEYNOTE-407</b> 1L Sq NSCLC PFS	<b>CheckMate 9LA</b> 1L NSCLC OS
		<b>KEYNOTE-042</b> 1L NSCLC Dx+ OS	<b>POSEIDON</b> 1L NSCLC PFS
<b>SCLC</b>		<b>IMpower133</b> 1L ES-SCLC PFS/OS	<b>CheckMate 451</b> 1L SCLC (Maintenance only)
			<b>CheckMate 331</b> 2L SCLC OS

■ Roche combo  
■ Chemo combo  
■ CTLA4 combo

Note: Outcome studies are event driven, timelines may change. Timelines based on publicly available disclosures.  
 NSCLC=non-small cell lung cancer; SCLC=small cell lung cancer; Non-sq=non-squamous; Sq=squamous

# Going beyond lung cancer: Multiple Wave 2 Tecentriq read outs to come

## Readouts until Q2 2018

	Potential	Indication	Study
 <b>Lung</b>	Most comprehensive lung cancer program addressing all common backbones and histologies	1L non-sq NSCL, sq NSCLC, SCLC	IMpower130 IMpower131 IMpower132
 <b>GU</b>	Among the leaders in renal cancer	1L RCC	IMmotion151
 <b>Breast</b>	First-in-class in triple negative breast cancer	1L TNBC	IMpassion130
 <b>CRC</b>	First-in-class in colorectal cancer	2/3L CRC	IMblaze370

### New insights on fundamental questions:

Indications, combos ( $\pm$ chemo,  $\pm$ targeted therapy), biomarkers, endpoints (OS, PFS)

Note: Outcome studies are event driven, timelines may change.

NSCLC=non-small cell lung cancer; SCLC=small cell lung cancer; Non-sq=non-squamous; Sq=squamous; RCC=renal cancer; TNBC=triple negative breast cancer; CRC=colorectal cancer

# Wave 3: Adding novel CIT targets to Tecentriq

## *Improving clinical outcomes through combinations*

Agent	Target	Phase	Indication	Data
CD20 TDB + Tecentriq	CD20/CD3	Ph 1b	r/r FL, DLBCL, MCL	2018
CEA-TCB + Tecentriq	CEA/CD3	Ph 1b	Solid tumors	2018
emactuzumab + Tecentriq	CSF-R1	Ph 1b	Solid tumors	2018
selicrelumab + Tecentriq	CD40	Ph 1b	Solid tumors	2018
aTIGIT + Tecentriq	TIGIT	Ph 1b	Solid tumors	2018
aCEA-IL2v + Tecentriq	CEA	Ph 1b	Solid tumors	2018/2019
aFAP-IL2v + Tecentriq	FAP	Ph 1b	1L RCC	2019
Personalized cancer vaccine + Tecentriq	Personalized	FPI expected Q1 2018	Solid tumors	TBD

# Conclusions from IMpower150

## *Providing a potential new standard of care*

- First Ph3 immunotherapy-based chemo combo study to demonstrate statistically significant and clinically meaningful improvement in PFS in all-comer 1L non-sq NSCLC
- PFS per IRF is consistent with PFS per INV
- PFS benefit in Arm B vs C was observed in key subgroups, including patients with
  - Sensitizing *EGFR* or *ALK* genetic alterations
  - Teff-low tumors
  - PD-L1-negative tumors
  - Liver metastases
- Tecentriq in combination with chemotherapy and Avastin was well tolerated and its safety profile is consistent with known safety risks
- OS has numerical improvement in Arm B vs C, but data are not fully matured; next interim analysis for all arms is anticipated in 1H 2018

*Doing now what patients need next*