Roche Pharma Day 2015

Cancer Immunotherapy

Daniel S. Chen | Cancer Immunotherapy Franchise Head
Product Development, Genentech/Roche
Immunotherapy is changing the face of cancer treatment

Understanding of the biology has reached an inflection point

...translating into remarkable benefit for patients

Response in NSCLC to atezolizumab monotherapy

Anti-CTLA4 (ipilimumab)
Melanoma

Pooled OS (1861 patients)
Median OS, months (95% CI): 11.4 (10.7–12.1)
3-year OS rate, % (95% CI): 22 (20–24)

Schadendorf et al (2015) JCO
Intense industry effort resulted in demonstrated benefit in a large number of tumor types

>20 companies

>30 CIT targets

>400 studies

~$4bn in R&D*

Internal estimates
CIT=cancer immunotherapy; *Annual spend
Significant complexity remains

<table>
<thead>
<tr>
<th>Scientific</th>
<th>Clinical</th>
<th>Commercial</th>
</tr>
</thead>
</table>
| • Each tumor with distinct immune biology | • New endpoints needed to detect benefit of CIT agents  
• Patients with the same tumor type respond differently  
• Pre-clinical models poorly predict efficacy in humans | • Market becoming more competitive  
• New pricing models needed for combination regimens  
• Treatment paradigm changes requires continuous education for physicians |

Achieve synergies through combination regiments  
Combination toxicity not predictable
Traditional drug development

Linear development approach is not suited to address these challenges
Cancer immunotherapy committee (CITC)
Focused on knowledge exchange, speed and efficiency

Research
Better understand the underlying immune response to tumor cells

Clinical
Design studies demonstrating program activity and informing immune system biology

Biomarker Data / Biological Insights

Targets, Drugs and Combinations

Development Strategy
Biomarkers
Market Insights
Scientific Understanding
CITC contributing to advancement of the field

- Selecting patients
- Improving outcomes
- Improving SoC

**NSCLC (TC3 or IC3)**

<table>
<thead>
<tr>
<th>HR²</th>
<th>P value</th>
<th>Median Survival</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.49 (0.22, 1.07)</td>
<td>0.068</td>
<td>11.1 mo (6.7, 14.4)</td>
</tr>
</tbody>
</table>

**Bladder cancer**

Median follow up: 7 mo (range, 0–11 mo), 142 events

- **Overall Survival**
  - IC2/3
  - IC0/1
  - Censored

**Median Survival**

- Median 15.5 mo (9.8, NE)
- Median 11.1 mo (6.7, 14.4)
Leveraging basic science to identify and prioritize innovative therapies

**Patient subgroups**
- RCC: 59% (IC>1%), 2% (TC>1%)
- UBC: 68% (IC>1%), 1% (TC>1%)
- NSCLC: 57% (IC>1%), 11% (TC>1%)
- TNBC: 58% (IC>1%), 3.5% (TC>1%)

**Novel targets**
- Antigen Presenting Cell
- Effector T cell
- OX40
- OX40L
- IFN-
- aCSF-1R
- aCEA-IL2v FP
- aCEA/CD3 TCB

**Combinations**
- anti-OX40
- aPD-L1
- Chemo
- combo
**POPLAR: Overall survival by PD-L1 subgroups**

**Efficacy increasing with higher PD-L1 expression**

<table>
<thead>
<tr>
<th>Subgroup (% of enrolled patients)</th>
<th>Hazard Ratio</th>
<th>Median OS (95% CI), mo</th>
</tr>
</thead>
<tbody>
<tr>
<td>TC3 or IC3 (16%)</td>
<td>0.49</td>
<td>Atezolizumab n = 144: 15.5 (9.8, NE)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Docetaxel n = 143: 11.1 (6.7, 14.4)</td>
</tr>
<tr>
<td>TC2/3 or IC2/3 (37%)</td>
<td>0.54</td>
<td>Atezolizumab: 15.1 (8.4, NE)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Docetaxel: 7.4 (6.0, 12.5)</td>
</tr>
<tr>
<td>TC1/2/3 or IC1/2/3 (68%)</td>
<td>0.59</td>
<td>Atezolizumab: 15.5 (11.0, NE)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Docetaxel: 9.2 (7.3, 12.8)</td>
</tr>
<tr>
<td>TC0 and IC0 (32%)</td>
<td>1.04</td>
<td>Atezolizumab: 9.7 (6.7, 12.0)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Docetaxel: 9.7 (8.6, 12.0)</td>
</tr>
<tr>
<td>ITT (N = 287)</td>
<td>0.73</td>
<td>Atezolizumab: 12.6 (9.7, 16.4)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Docetaxel: 9.7 (8.6, 12.0)</td>
</tr>
</tbody>
</table>

**Atezolizumab: Doubled likelihood of survival in PD-L1-high tumors (IC2/3 or TC2/3)**

ECC 2015
POPLAR: PD-L1/PD-1 ligand and receptor family members predict clinical benefit in NSCLC

**PD-L1**

- **OS HR: 0.46**  
  (95% CI: 0.27 – 0.78)

- **PD-L1 high**
- **PD-L1 low**

**B7.1**

- **OS HR: 0.44**  
  (95% CI: 0.26 – 0.77)

- **B7.1 high**
- **B7.1 low**

**PD-1**

- **OS HR: 0.43**  
  (95% CI: 0.24 – 0.76)

- **PD-1 high**
- **PD-1 low**

**PD-L2**

- **OS HR: 0.39**  
  (95% CI: 0.22 – 0.69)

- **PD-L2 high**
- **PD-L2 low**

ECC 2015
Comprehensive biomarker effort
Cornerstone of our R&D strategy

DNA-mutation & CNVs
Ex: EGFR, BRAF
DNA sequencing

mRNA-expression
Cell signatures, targets
RNA sequencing

Protein-expression
PDL1, other CI targets
Multiplex IHC

Cell free tumor DNA
Ex: EGFR, BRAF
Blood DNA sequencing

Imaging
Ex: ImmunoPET
Imaging

To advance science

To aid development

To improve patient care
Unlocking full value of immunotherapy through combinations

**Broadest industry portfolio in oncology**

**Antigen presentation**
- T-Vec oncolytic viruses* (Amgen)
- INFα
- anti-CD40
- CMB305 vaccine* (Immune Design)

**Antigen release**
- EGFRi (Tarceva)
- ALKi (Alectinib)
- BRAFi (Zelboraf)
- MEKi (Cotellic)
- anti-CD20 (Gazyva)
- anti-HER2 (Herceptin; Kadcyla; Perjeta)
- various chemotherapies
- lenalidomide*
- rociletinib* (Clovis)

**Priming & activation**
- anti-CEA-IL2v FP
- anti-OX40
- anti-CD27* (Celldex)
- entinostat* (Syndax)

**T cell Trafficking**

**T cell infiltration**
- anti-VEGF (Avastin)
- anti-Ang2/VEGF (vanucizumab)

**Cancer T cell recognition**
- anti-CEA/CD3 TCB
- anti-CD20/CD3 TCB
- anti-HER2/CD3 TCB
- ImmTAC* (Immunocore)

**T cell killing**
- anti-PDL1 (atezolizumab)
- anti-CSF-1R (emactuzumab)
- IDOi (NewLink)
- IDOi* (Incyte)
- CPI-444* (Corvus)
- anti-TIGIT
- IDO1/TDOI* (Curadev)

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Chen and Mellman. Immunity 2013
Chemotherapy combinations
Creation of the favourable immune profile

Pre-clinical data

**Tumor CD8+ (T cells)**

Platinum doublet 1

Platinum doublet 2

On-treatment biopsy

**Pre-treatment**

**Post FOLFOX**

CD8

CD8
Chemotherapy combination in NSCLC

Atezolizumab and a standard of care

1L NSCLC

\[ n = 37 \]

**4–6 cycles**

Atezolizumab 15mg/kg IV q3w +
Carboplatin q3w + Paclitaxel q3w

**Maintenance**

Atezolizumab

Treat to PD or loss of clinical benefit

**Treat to PD or loss of clinical benefit**

**Treat to PD or loss of clinical benefit**

**cb/pac (N=8)**

PR/CR (n=4)

Stable disease (n=4)

Discontinued

New lesion

**cb/pem (N=17)**

PD (n=2)

PR/CR (n=13)

Stable disease (n=1)

Discontinued

New lesion

**cb/nab (N=16)**

PD (n=2)

PR/CR (n=9)

Stable disease (n=4)

Discontinued

New lesion

**ORR = 50.0% (4/8)**

**ORR = 76.5% (13/17)**

**ORR = 56.3% (9/16)**
Combination with Avastin

Aiding T-cell infiltration results in encouraging activity in RCC

Combination regimen benefits most patients irrespective of PD-L1 status

Change in sum of largest diameters from baseline (%)

Time on study (days)

AACR 2015
Combinations with targeted agents
Potential for enhanced efficacy

T cell Trafficking

Cancer T cell recognition

Antigen release

BRAFi (Zelboraf)
EGFRi (Tarceva)
ALKi (Alectinib)
MEKi (Cotellic)
anti-CD20 (Gazyva)
various chemotherapies
lenalidomide
rociletinib* (Clovis)

Cohort

1 (N=3) Concurrent Zelboraf+atezolizumab 33%
2 (N=8) 56 day run-in Zelboraf run-in (56 days) followed by Zelboraf+atezolizumab 75%
3 (N=6) 28 day run-in Zelboraf run-in (28 days) followed by Zelboraf+atezolizumab 100%
All (N=17) 76%

- mPFS=12.2mo, DoR=20.9mo
- Staggered dosing was better tolerated
- AEs were manageable and generally reversible

Full data including biomarkers at SMR 2015

Chen and Mellman, Immunity 2013
Enhancing atezolizumab efficacy through immunotherapy combinations

Priming & activation
- anti-CEA-IL2v FP
- anti-OX40
- anti-CD27* (Cellnex)
- entinostat* (Syndax)

Antigen presentation
- T-Vac oncolytic viruses* (Amgen)
- anti-CD40
- CMB305 vaccine* (Immune Design)

Antigen release

T cell trafficking
- anti-VEGF (Avastin)
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T cell infiltration

Cancer T cell recognition
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T cell killing
- anti-CSF-1R (emactuzumab)
- IDOi (NewLink)
- IDOi* (Incyte)
- CPI-444* (Corvus)
- anti-TIGIT
- IDO1/TDOi* (Curadev)

Clinical development
- Preclinical development
- Established therapies
  * Partnered or external

Seven immune doublets in clinic
**Personalized Cancer Immunotherapy**

**Evaluate tumor:**
*is the tumor inflamed?*

1. **Y** Inflamed
   - Strong PD-L1
     - Are suppressive myeloid cells present?
       - Anti-PDL1/PD1 plus Anti-CSF1R
     - IDO/kyneurinin expressed?
       - Anti-PDL1/PD1 plusIDO inhibitor

2. **2** Weak PD-L1

3. **3** No PD-L1

4. **4** No identifiable immune targets
   - Are T cells at tumor periphery?
     - MHC loss?
       - No T cells?
         - No identifiable immune targets
     - Tumor antigen expression?
       - Antigen experienced?
         - No T cells?
           - No identifiable immune targets

5. **N** Non-inflamed
   - No identifiable immune targets

*Possible hypothetical algorithm*
Leverage two businesses to deliver all tools for better patient care

**Tools to characterize individual’s disease**

<table>
<thead>
<tr>
<th>DNA-Mutation &amp; CNVs</th>
<th>mRNA-Expression</th>
<th>Protein-Expression</th>
<th>Cell free Tumor DNA</th>
<th>Imaging</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ex: EGFR, BRAF</td>
<td></td>
<td></td>
<td>Ex: EGFR, BRAF</td>
<td>Ex: ImmunoPET</td>
</tr>
<tr>
<td>DNA Sequencing</td>
<td>mRNA Expression</td>
<td>Cell signatures, targets</td>
<td>RNA Sequencing</td>
<td>Multiplex IHC</td>
</tr>
<tr>
<td></td>
<td></td>
<td>PDL1, other CI targets</td>
<td></td>
<td>Blood DNA Sequencing</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Multiplex IHC</td>
<td></td>
<td>Imaging</td>
</tr>
</tbody>
</table>

**Personalized treatment options**

1. T cell Trafficking
2. T cell infiltration
3. T cell recognition
4. Cancer T cell killing

*Evaluate tumor: Is the tumor inflamed?*

- High PDL1 expression
- Low/No PDL1 expression

- T Cells at Periphery
- No detected target

- No Effectors
- MHC Low

- No identified target

- Assay + Other CIT (target, MHC, TCR)
- Assay + Chemo / SOC
- Assay + Nurtin + MHC
- Assay + IDA49 (or other, matched)
- Assay + TCRs (or IDA49)
Roche Pharma Day 2015

Cathi Ahearn | Lifecycle Leader Atezolizumab, Lung and GU Genentech/Roche
## Roche cancer immunotherapy beginning 2015

**Status as at December 31, 2014**

### Phase I

<table>
<thead>
<tr>
<th>Study</th>
<th>Tumor Type</th>
</tr>
</thead>
<tbody>
<tr>
<td>atezolizumab</td>
<td>Solid tumors</td>
</tr>
<tr>
<td>atezolizumab + IFN-alfa</td>
<td>Solid tumors</td>
</tr>
<tr>
<td>atezolizumab + aCD40</td>
<td>Solid tumors</td>
</tr>
<tr>
<td>atezolizumab + Tarceva</td>
<td>NSCLC</td>
</tr>
<tr>
<td>atezolizumab + Zelboraf</td>
<td>Melanoma</td>
</tr>
<tr>
<td>atezolizumab + Cotellic</td>
<td>Solid tumors</td>
</tr>
<tr>
<td>atezolizumab + Avastin</td>
<td>Solid tumors</td>
</tr>
<tr>
<td>atezolizumab + Gazyva</td>
<td>R/R FL / aNHL</td>
</tr>
<tr>
<td>atezolizumab + Avastin + chemo</td>
<td>Solid tumors</td>
</tr>
<tr>
<td>aCSF-1R</td>
<td>Solid tumors</td>
</tr>
<tr>
<td>aCEA-IL2v FP</td>
<td>Solid tumors</td>
</tr>
<tr>
<td>aOX40</td>
<td>Solid tumors</td>
</tr>
<tr>
<td>aCEA/CD3 TCB</td>
<td>Solid tumors</td>
</tr>
<tr>
<td>IDO</td>
<td>Solid tumors</td>
</tr>
<tr>
<td>atezolizumab + ipilimumab</td>
<td>Solid tumors</td>
</tr>
</tbody>
</table>

### Phase II

<table>
<thead>
<tr>
<th>Study</th>
<th>Tumor Type</th>
</tr>
</thead>
<tbody>
<tr>
<td>atezolizumab</td>
<td>NSCLC (Dx+)</td>
</tr>
<tr>
<td>atezolizumab 2/3L</td>
<td>NSCLC</td>
</tr>
<tr>
<td>atezolizumab + Avastin</td>
<td>1L Renal</td>
</tr>
<tr>
<td>atezolizumab 1/2L</td>
<td>Bladder</td>
</tr>
</tbody>
</table>

### Phase III

<table>
<thead>
<tr>
<th>Study</th>
<th>Tumor Type</th>
</tr>
</thead>
<tbody>
<tr>
<td>atezolizumab</td>
<td>Solid tumors</td>
</tr>
<tr>
<td>atezolizumab 2/3L</td>
<td>NSCLC</td>
</tr>
</tbody>
</table>

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**Legend**

- **Blue**: atezolizumab trials
- **Green**: NMEs monotherapy
- **Orange**: Immune doublets
Roche cancer immunotherapy today

**Phase I**
- **atezo**
  - Solid tumors
- **atezo + chemo**
  - Solid tumors
- **atezo + Tarceva**
  - NSCLC
- **atezo + Zelboraf**
  - Melanoma
- **atezo + Cotelic**
  - Solid tumors
- **atezo + Avastin**
  - Solid tumors
- **atezo + Gazyva**
  - R/R FL / aNHL
- **atezo + Avastin + chemo**
  - Solid tumors
- **atezo + lenalidomide**
  - MM
- **atezo + Zelboraf + Cotelic**
  - Melanoma
- **atezo + alectinib**
  - ALK+ NSCLC
- **atezo +/- azacitidine**
  - MDS
- **atezo + Gazyva + chemo**
  - R/R FL/aNHL
- **atezo + Gazyva + lenalidomide**
  - R/R FL/aNHL
- **atezo + Herceptin + Perjeta**
  - HER2+ eBC/mBC

**Phase II**
- **atezo**
  - NSCLC (Dx+)
- **atezo**
  - 2/3L NSCLC
- **atezo + Avastin**
  - 1L Renal
- **atezo**
  - 1/2L Bladder
- **atezo + iplisimumab**
  - Solid tumors
- **atezo + IFN-alfa**
  - Solid tumors
- **atezo + aCD40**
  - Solid tumors
- **atezo + aOX40**
  - Solid tumors
- **atezo + aCSF-1R**
  - Solid tumors
- **atezo + aCSF-1R**
  - Solid tumors
- **atezo + Gazyva + chemotherapeutic agents**
  - R/R FL / aNHL
- **atezo + Avastin + chemotherapeutic agents**
  - Solid tumors
- **atezo + Kadcyla**
  - HER2+ eBC/mBC
- **aCD20/CD3 TCB**
  - Lymphoid tumors
- **aCSF-1R**
  - Solid tumors
- **aOX40**
  - Solid tumors

**Phase III**
- **atezo**
  - 2/3L NSCLC
- **atezo**
  - 2/3L Bladder
- **atezo + Avastin + chemotherapeutic agents**
  - 1L non sq NSCLC
- **atezo + chemo**
  - 1L non sq NSCLC
- **atezo + chemo**
  - 1L sq NSCLC
- **atezo**
  - 1L non sq NSCLC (Dx+)
- **atezo**
  - 1L sq NSCLC
- **atezo + Avastin**
  - 1L TNBC
- **atezo**
  - Adjuvant MIBC (Dx+)
- **atezo**
  - Adjuvant NSCLC (Dx+)

**Immune doublets**
- **atezo + aCD20/CD3 TCB**
  - Lymphoid tumors
- **atezo + aOX40**
  - Solid tumors
- **atezo + aCEA**
  - CD3 TCB
- **atezo + aOX40**
  - Solid tumors
- **atezo + aCSF-1R**
  - Solid tumors

**Additions in 2015**
- **atezo + Zelboraf**
  - Melanoma
- **atezo + aCD20/CD3 TCB**
  - Lymphoid tumors
- **atezo + aOX40**
  - Solid tumors
- **atezo + aCSF-1R**
  - Solid tumors
- **atezo + Avastin + chemotherapeutic agents**
  - Solid tumors
- **atezo + Gazyva + chemotherapeutic agents**
  - R/R FL / aNHL
- **atezo + Avastin**
  - Solid tumors
- **atezo + Kadcyla**
  - HER2+ eBC/mBC
- **aCD20/CD3 TCB**
  - Lymphoid tumors
- **atezo + Herceptin + Perjeta**
  - HER2+ eBC/mBC

Status as of Nov 5, 2015
Non-small cell lung cancer

*Cause of the highest number of cancer related deaths*

- 433,800 patients diagnosed each year

- One of the highest incidence rates
- Highly heterogeneous disease
- Treatment becoming increasingly personalized based on molecular profile of each cancer
- Significant unmet need exist for therapies that extend lives

**Atezolizumab Phase III studies**

- **Adjuvant**: Stage IB-IIIA
- **1L metastatic**: Stage IV
- **2L+ metastatic**: Stage IV
## Atezolizumab NSCLC programme

**Studies addressing all patient subgroups**

<table>
<thead>
<tr>
<th>Adjuvant</th>
<th>Phase I</th>
<th>Phase II</th>
<th>Phase III</th>
<th>Filing</th>
<th>Data</th>
</tr>
</thead>
<tbody>
<tr>
<td>Atezo Monotherapy</td>
<td><strong>IMpower010</strong></td>
<td></td>
<td></td>
<td></td>
<td>post 2018</td>
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</tbody>
</table>

### 1L

<table>
<thead>
<tr>
<th>Adjuvant</th>
<th>Phase II</th>
<th>Phase III</th>
<th>Filing</th>
<th>Data</th>
</tr>
</thead>
<tbody>
<tr>
<td>Atezo + carbo/pac +/- bev</td>
<td><strong>IMpower 150</strong></td>
<td></td>
<td></td>
<td>2017</td>
</tr>
<tr>
<td>Atezo + carbo + nab-pac</td>
<td><strong>IMpower 130</strong></td>
<td></td>
<td></td>
<td>2017</td>
</tr>
<tr>
<td>Atezo + carbo + pac/nab-pac</td>
<td><strong>IMpower 131</strong></td>
<td></td>
<td></td>
<td>2017</td>
</tr>
<tr>
<td>Atezo + cis/carbo + pem</td>
<td>[Not yet listed]</td>
<td></td>
<td></td>
<td>2018</td>
</tr>
<tr>
<td>Atezo NSq Monotherapy</td>
<td><strong>IMpower 110</strong></td>
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<td>2017</td>
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<td>Atezo Sq Monotherapy</td>
<td><strong>IMpower 111</strong></td>
<td></td>
<td></td>
<td>2017</td>
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</table>

### 2L+

<table>
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<th>Phase III</th>
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<th>Data</th>
</tr>
</thead>
<tbody>
<tr>
<td>Atezo NSq/Sq Monotherapy Randomized Ph3</td>
<td><strong>OAK</strong></td>
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<tr>
<td>Atezo NSq/Sq Monotherapy Randomized Ph2</td>
<td><strong>POPLAR</strong></td>
<td>✓</td>
<td></td>
<td>✓</td>
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<tr>
<td>Atezo NSq/Sq Monotherapy Single Arm Ph2</td>
<td><strong>BIRCH</strong></td>
<td>✓</td>
<td></td>
<td>✓</td>
</tr>
<tr>
<td>Atezo NSq/Sq Monotherapy Single Arm Ph2</td>
<td><strong>FIR</strong></td>
<td></td>
<td></td>
<td>✓</td>
</tr>
<tr>
<td>Various combinations</td>
<td>targeted, CI and chemo</td>
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</table>
Bladder cancer treatment flow today

Incident NMIBC (~70%, 127K)

Incident MIBC (~20%, 28K)

Incident mUBC (~10%, 13K)

MIBC (~15%)

Neoadj + surg (~40%)

Surg only (~30%)

Surg+Adj (~30%)

mUBC (~35K, de novo and relapsed)

1L prior-platinum (~30%)

1L platinum-naïve (~70%)

2L/3L (~60%)

NMIBC=non-muscle invasive bladder cancer; MIBC=muscle invasive bladder cancer; Roche internal estimates (Mar 2014)
# Atezolizumab bladder programme

**Monotherapy and combination studies**

<table>
<thead>
<tr>
<th>Phase</th>
<th>Study</th>
<th>Filing</th>
<th>Data</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>MIBC adj.</strong></td>
<td>Atezo Monotherapy</td>
<td>2019</td>
<td></td>
</tr>
<tr>
<td></td>
<td>IMvigor 010</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>1L cis-ineligible</strong></td>
<td>Atezo Monotherapy Single-Arm Ph2</td>
<td>2016</td>
<td></td>
</tr>
<tr>
<td></td>
<td>IMvigor 210 Cohort 1</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>2L+</strong></td>
<td>Atezo monotherapy Randomized Ph3</td>
<td>2017</td>
<td></td>
</tr>
<tr>
<td></td>
<td>IMvigor211</td>
<td></td>
<td></td>
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<td>Atezo monotherapy Single-Arm Ph2</td>
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<td>IMvigor210 Cohort 2</td>
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<td></td>
<td>Various combinations</td>
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<tr>
<td></td>
<td>CI</td>
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</tbody>
</table>

- **PD-L1-selected**
- **all-comers**
- **first-to-market**
- **rolling filing**

MIBC=muscle invasive bladder cancer
Renal cell carcinoma (RCC)

Increasing market with need for agents that improve survival

- ~15% of RCC patients are diagnosed with metastatic disease
- mRCC population is expected to grow due to population ageing
- There is a need for well tolerated, efficacious treatments in 1L
- Atezolizumab + Avastin combination demonstrated high diseases control rate (PR=40%, SD=50%)*
Triple negative breast cancer (TNBC)
Disease with high unmet medical need

- Accounts for 10-20% of breast cancer
- Defined by lack of expression of ER, PR and HER2
- Median OS ~12 months
- No standard of care, no unique targeted therapies
- Atezolizumab demonstrated single-agent activity in phase I (ORR=19%)*

Emens, AACR 2015; ER=estrogen receptor; PR=progesterone receptor
### Atezolizumab RCC and TNBC programmes

**Monotherapy and combination studies**

#### Renal cell carcinoma (RCC)

<table>
<thead>
<tr>
<th>Phase</th>
<th>Study 1</th>
<th>Study 2</th>
<th>Filing</th>
<th>Data</th>
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</thead>
<tbody>
<tr>
<td>1L</td>
<td>Atezo+Avastin IMmotion151</td>
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<td>Atezo+Avastin / Atezo Monotherapy Randomized Ph2 IMmotion150</td>
<td>-</td>
<td>2016</td>
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<td>2L+</td>
<td>Various combinations</td>
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</table>

#### Triple negative breast cancer (TNBC)

<table>
<thead>
<tr>
<th>Phase</th>
<th>Study 1</th>
<th>Study 2</th>
<th>Filing</th>
<th>Data</th>
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<td>1L</td>
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<td>-</td>
<td>2018</td>
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<td>2L+</td>
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</tbody>
</table>

**Legend**
- **PD-L1-Selected**
- **all-comers**
- **first-to-market**

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Increasing value of cancer immunotherapy
Earlier lines, new indications, combinations

2016

Launch

2L NSCLC Dx+
2L bladder Dx+

Expand & Lead

1L NSCLC allcomers
1L TNBC allcomers
1L RCC allcomers

Transform

Adjuvant NSCLC
Adjuvant bladder
New indications
CI combinations
Setting new standards, developing combinations
Driven by the breadth of our in-house portfolio

Launched portfolio

Targeted combinations approved
Chemotherapy combinations approved
Roche combinations in trials
Chemotherapy combinations in trials
NMEs filed/to be filed soon
## Cancer immunotherapy newsflow in 2015

<table>
<thead>
<tr>
<th>Event</th>
<th>Presentation</th>
<th>Location</th>
<th>Dates</th>
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</thead>
<tbody>
<tr>
<td><strong>atezolizumab + Zelboraf</strong> - mM: Phase I</td>
<td>Society for Melanoma Research (SMR) 2015 Congress</td>
<td>San Francisco</td>
<td>18-21 Nov</td>
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<tr>
<td><strong>atezolizumab</strong> - GBM: Phase I</td>
<td>Society for NeuroOncology (SNO)</td>
<td>San Antonio</td>
<td>19-22 Nov</td>
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<tr>
<td><strong>atezolizumab + abraxane</strong> - TNBC: Phase Ib</td>
<td>San Antonio Breast Cancer Symposium</td>
<td>San Antonio</td>
<td>8-12 Dec</td>
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<tr>
<td><strong>atezolizumab</strong> - mUC: IMvigor 210</td>
<td>2016 Genitourinary Cancers Symposium</td>
<td>San Francisco</td>
<td>7-9 Jan</td>
</tr>
</tbody>
</table>

Planned presentations