Big Picture Takeaways from ASCO 2014
Positives for Roche and AstraZeneca

June 2014

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Big Picture Takeaways from ASCO 2014

- **Immuno-oncology still the key focus.** We attended ASCO 2014, the largest scientific congress for cancer therapy. In this slide pack we set out our 8 key takeaways from the meeting. We conclude that investor excitement in the emerging field of immuno-oncology (I-O, using the body’s immune system to tackle cancer) remains justified. ASCO 2014 levelled the playing field, in our view, with Roche and MRK ‘catching up’ with BMY with data in bladder and head & neck cancer. Both companies also set out a more coherent strategy on biomarkers vs BMY. AZN remains the ‘fast follower’ with a broad portfolio of I-O agents. It is still too early to draw conclusions on winners, in our view, and the positive data in new tumour types raise the prospect of a much bigger overall I-O market. Key catalysts over the next year will provide further clarity. The key question of how we will pay remains unaddressed.

- **Small molecules still matter.** While I-O grabbed most of the headlines, impressive data on small molecules was presented on (among others) AZN’s AZD9291 and CLVS’ CO-1686 (lung cancer), AZN’s olaparib (ovarian cancer) and ROG/ABBV’s ABT-199 (lymphoma). All have significant commercial potential.

- **ROCHE (Outperform, TP SFR 300).** ASCO’14 was a clear positive for Roche, with clear signs of strength and depth in immuno-oncology addressing many of the bears’ concerns. The Diagnostics division may also strengthen the strategy in I-O biomarkers. Next catalysts: AAIC (Alzheimer’s) 12-17 July, ESMO (cancer) 26-30 Sept.

- **ASTRAZENECA (Neutral, TP £48).** AZN’s I-O portfolio is still early but showed signs of differentiation at ASCO and small molecules made significant advances. 2015 data will be critical. The conference provided sufficient excitement to maintain the stock price inflated by bid-speculation. Next catalyst: ADA (diabetes) 13-17 June, ESMO (cancer) 26-30 Sept, olaparib FDA decision 3 Oct.

- **BRISTOL MYERS (Outperform, TP $59).** While ASCO’14 brought some short-term disappointment, the portfolio is still robust with multiple clinical assets being investigated in multiple tumour types. Confidence in biomarkers and design of lung cancer trials will be key in 2H14. Next catalyst: 30 Oct-1Nov -readout of P2 lung, ESMO 26-30 Sept.

- **MERCK & CO (Restricted).** ASCO’14 was a clear positive for MRK, with impressive data in melanoma and head & neck cancer. Combination strategies are less clear but monotherapy with a coherent biomarker strategy has significant commercial potential. Next catalysts: ESMO (cancer) 26-30 Sept, pembro melanoma FDA decision 28 Oct.
## Comparative valuation

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<td>58.0</td>
<td>13.2</td>
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<td>17.7</td>
<td>14.5</td>
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<td>55.7</td>
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<td>19.7</td>
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<td>Bristol Myers Squibb Co.</td>
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<td>26.0</td>
<td>26.6</td>
<td>28.0</td>
<td>22.1</td>
<td>3.0%</td>
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<td>49.9</td>
<td>50.9</td>
<td>2.0%</td>
<td>10.3%</td>
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<td>Eli Lilly &amp; Co.</td>
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<td>61.0</td>
<td>17.6</td>
<td>14.4</td>
<td>21.8</td>
<td>20.0</td>
<td>15.9</td>
<td>3.3%</td>
<td>0.99</td>
<td>69.0</td>
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<td>Johnson &amp; Johnson</td>
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<td>20.2</td>
<td>18.7</td>
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<td>16.5</td>
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<td>1.09</td>
<td>86.3</td>
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<td>Pfizer</td>
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<td>13.3</td>
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<td>12.8</td>
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<td>3.5%</td>
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<td>28.2</td>
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<td><strong>US Sector average</strong></td>
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<td></td>
<td>20.5</td>
<td>20.2</td>
<td>20.4</td>
<td>18.9</td>
<td>16.0</td>
<td>2.7%</td>
<td>1.07</td>
<td></td>
<td></td>
<td>2.8%</td>
<td>8.1%</td>
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| AstraZeneca           | p 4,327| 4,800        | 11.7  | 14.5  | 18.2  | 19.6  | 19.7  | 3.9%            | 1.27   | 3762      | 3440             | -1.8%                 | -11.5%              |
| Bayer                 | € 105.0| 120         | 19.3  | 18.1  | 17.0  | 14.8  | 13.1  | 2.1%            | 1.11   | 125.7     | 99.4             | 5.4%                  | 11.3%               |
| GlaxoSmithKline plc   | p 1,599| 1,600       | 17.5  | 17.9  | 19.0  | 16.7  | 14.4  | 5.1%            | 1.36   | 1578      | 1099             | 2.4%                  | 9.1%                |
| Novartis              | SF 79.6| 87          | 17.9  | 18.7  | 17.8  | 15.7  | 14.1  | 3.7%            | 1.03   | 89.1      | 82.5             | 1.0%                  | 10.3%               |
| Novo Nordisk A/S      | DK 236.6| 230       | 30.9  | 25.4  | 23.6  | 21.0  | 18.6  | 2.1%            | 1.51   | 158.9     | 165              | 7.9%                  | 9.2%                |
| Roche                 | SF 267.2| 300       | 20.7  | 19.1  | 18.9  | 17.4  | 16.1  | 3.0%            | 1.11   | 265.0     | 250              | 3.1%                  | 6.6%                |
| Sanofi                | € 79.0 | 80          | 13.2  | 16.1  | 15.0  | 13.2  | 12.6  | 3.4%            | 1.04   | 90.9      | 79.6             | 3.2%                  | 6.9%                |
| **EU Majors average** |        |              | 18.7  | 18.6  | 18.5  | 16.9  | 15.5  | 3.3%            | 1.20   |            |                 | 3.0%                  | 6.0%                |

| Almirall              | € 11.7 | 16.00       | nr    | nr    | 22.0  | 12.2  | 8.7   | 1.3%            | 0.76   | 18.6      | 17.0             | 9.8%                  | 66.7%               |
| Ipsen                 | € 34.5 | 35.0        | 19.8  | 18.1  | 18.2  | 16.7  | 14.7  | 2.6%            | 0.86   | 45.5      | 44.5             | 5.3%                  | 8.9%                |
| Lonza                 | SF 98.7| 95          | 23.1  | 21.9  | 16.6  | 13.8  | 12.8  | 2.2%            | 4.96   | 16.7      | 17.1             |                      |                    |
| Lundbeck              | DK 141 | 140         | 16.9  | 18.6  | 34.8  | 40.5  | 21.2  | 0.5%            | 0.79   | 188       | 195              | -0.1%                 | 9.3%                |
| Meda (pre-amortisation)| SK 116.2| 80       | 12.8  | 13.6  | 11.8  | 10.4  | 9.3   | 2.3%            | 1.36   | 123       | 73               | 6.5%                  | 14.0%               |
| Meda (post-amortisation) | SK 116.2| 80       | 29.0  | 43.5  | 28.8  | 21.7  | 17.4  | 2.3%            | 1.36   | 123       | 73               | 6.5%                  | 33.8%               |
| Merck KGaA            | € 127.1| 143         | 16.6  | 14.5  | 13.6  | 12.5  | 12.4  | 1.6%            | 1.04   | 140       | 129              | 2.8%                  | 4.8%                |
| Orion                 | € 26.6 | 15.0        | 18.7  | 18.3  | 19.5  | 18.6  | 17.9  | 4.5%            | 1.62   | 15.4      | 15.0             | 0.6%                  | 1.6%                |
| Recordati             | € 13.5 | 11.0        | 18.9  | 16.7  | 15.2  | 14.1  | 13.7  | 3.1%            | 1.16   | 12.5      | 11.1             | 5.3%                  | 6.5%                |
| Shire Pharmaceuticals  | p 3886 | 3400        | 29.1  | 23.6  | 18.7  | 17.0  | 15.5  | 0.3%            | 1.44   | 2593      | 2404             | 9.3%                  | 14.1%               |
| UCB                   | € 57.1 | 53          | 34.5  | 32.2  | 28.8  | 23.0  | 19.0  | 2.0%            | 1.21   | 62.9      | 49.1             | 6.9%                  | 21.7%               |
| **EU Specialty average** |       |              | 22.0  | 19.7  | 19.9  | 17.9  | 14.5  | 2.0%            | 1.1    |            |                 | 5.1%                  | 16.5%               |

Source: Credit Suisse estimates as at 09/06/2014
Big Picture Takeaways from ASCO 2014

- Oncology & immuno-oncology background
- ASCO 2014 – levelling the playing field in I-O
- Lots more targets emerging
- I-O combinations – we’ve only just begun
- PD-L1 biomarkers a big clinical debate
- Not all I-O is created equal
- Small molecules still matter
- Doctors’ efficacy expectations have changed
- How will we pay for everything?
- Stock readacross from ASCO 2014
Oncology – a $91bn worldwide market in 2013

- 46% targeted therapy, 20% cytotoxic chemotherapy, 10% hormonal, 24% supportive care

Source: Credit Suisse PharmaValues estimates, IMS Health
Types of Cancer – worldwide incidence & mortality

Source: http://globocan.iarc.fr
Immuno-oncology emerging as novel treatment option

Source: adapted from AstraZeneca & Weinberg & Hanahan, Cell 2011
The immune system balance in cancer (the three Es)

Cancer transformation

Normal cells

Elimination

Equilibrium

Escape

LEGEND

- Normal cell
- Immunogenic tumour cell
- Immunoevasive tumour cell

Source: adapted from Schreiber, Science 2011 & Teng et al, 2013
Multiple targets in immuno-oncology

Source: adapted from Chen & Mellman, Immunity 2013
Duration of response – the hope for I-O

- Will early signs of long duration of response on I-O be sustainable?
- Will targeted therapy combinations improve the immunotherapy survival outcome?
- How will we afford it?
  - 500,000 patients @ $100,000 pa for 6 months = $25bn
  - 1m patients @ $100,000 pa for 2 years = $200bn

Source: Roche ASCO 2014 investor day
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BMY – mixed data in lung, positive melanoma

BMY PD-1 melanoma clear positive

- 41% 3yr survival, 6% Grade 3/4 AEs
- Positive efficacy in Yervoy combo

BMY PD-1 mono lung cancer (P1)

<table>
<thead>
<tr>
<th>Tumor response- RECIST</th>
<th>Total n = 20</th>
<th>PD-L1+ n = 10</th>
<th>PD-L1- n = 7</th>
</tr>
</thead>
<tbody>
<tr>
<td>ORR, n (%)</td>
<td>6 (30)</td>
<td>5 (50)</td>
<td>0</td>
</tr>
</tbody>
</table>

- ORR: 50% PD-L1 high, 0% PD-L1 low
- 10% Grade 3/4 adverse events

BMY PD-1+CTLA4 lung cancer (P1)

<table>
<thead>
<tr>
<th>Tumor response</th>
<th>Nivolumab 1 mg/kg + ipilimumab 3 mg/kg n=24</th>
<th>Nivolumab 3 mg/kg + ipilimumab 1 mg/kg n=25</th>
<th>PD-L1+ n=16</th>
<th>PD-L1- n=22</th>
</tr>
</thead>
<tbody>
<tr>
<td>ORR, n (%) - RECIST</td>
<td>3 (13)</td>
<td>5 (20)</td>
<td>3 (19)</td>
<td>3 (14)</td>
</tr>
</tbody>
</table>

- ORR: 19% PD-L1 high, 14% PD-L1 low
- 42% Grade 3/4, 6% drug-related deaths
- BMY already in P3 H&N, P1 bladder

Source: ASCO 2014, BMY company data
Roche and MRK impress in new indications

Roche PD-L1 bladder cancer (Phase 1)  MRK PD-1 H&N cancer (Phase 1)

- ORR: 43% PD-L1 high, 11% PD-L1 low
- 6% Grade 3/4 adverse events

- ORR: 46% PD-L1 high, 11% PD-L1 low
- 17% Grade 3/5 adverse events

Source: ASCO 2014, Roche company data, MRK company data
All-comers are competitive in mono-therapy

MRK PD-1 melanoma (Phase 1)

- ORR: 40% ipilimumab naïve, 28% ipi pre-treated, 69% overall survival at 1 year
- 12% Grade 3/4 adverse events

Source: ASCO 2014, MRK company data
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New targets emerging in Immuno-oncology

Roche anti-CSF1R (Phase 1) in pigmented villonodular synovitis (PVNS)

- Proof-of-concept of novel mode of action in I-O
- CSF1 is essential for survival of supressing macrophages in tumour environment

<table>
<thead>
<tr>
<th>Patients</th>
<th>%</th>
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<tbody>
<tr>
<td>Partial Response</td>
<td>15/18</td>
</tr>
<tr>
<td>Partial Metabolic Response</td>
<td>15/17</td>
</tr>
<tr>
<td>Clinically progression-free*</td>
<td>17/18</td>
</tr>
</tbody>
</table>

Source: ASCO 2014, Roche company data
The emergence of the ‘secret NME’!

2. LOTS MORE TARGETS ARE EMERGING

- **ROCHE**
- **ASTRAZENECA**
- **BMY**
- **MERCK**

** lots more targets are emerging **

**Infiltration of T cells into tumors**
- Anti-VEGF
- Neo-vascular activators

**Recognition of cancer cells by T cells**
- CARs
- T cell bispecifics
- ImmTACs

**Killing of cancer cells**
- Anti-PD-L1
- Anti-PD-1
- IDO inhibitors
  - Neg. Regulator (NME 1)
  - Anti-CSF1R (RG7156)
  - Anti-CEA IL2v (RG7813)
  - Anti-Cytokine (NME 2)

**Release of cancer cell antigens**
- Chemotherapy
- Radiation therapy
- Targeted therapy

**Cancer antigen presentation**
- Vaccines (IMA942 & INO-5150)
- Anti-CD137 (agonist)
- Anti-OX40 (agonist)
- TLR agonists
- IFN-α

**Priming and activation**
- Anti-CTLA4
- Anti-CD137 (agonist)
- Anti-CD27 (agonist)
- IL-2
- IL-12

**Immune checkpoint inhibitors**
- anti-GITR
- CD-137
- anti-KIR
- m-OX40

**4x NMEs**

**2x NMEs**

**Source:** adapted from Chen & Mellman, company data
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Combinations trials only just beginning

- **Safety & tolerability critical in combination market**
  - BMY Yervoy+PD-1 very significant toxicity burden
  - Mechanistic hope of lower toxicity with PD-L1 (Roche/AZN)
  - Mechanistic hope of lower toxicity with tremelimumab (AZN) vs Yervoy (BMY)

- **Can combos tap the potential of PD-L1 negative patients**
  - BMY Yervoy+PD-1 should equal efficacy in lung cancer in PD-L1+/-

- **Targeted therapy & radiation combos as important as I-O doublets**
  - BMY most advanced in I-O doublets (nivo + Yervoy, LAG-3, KIR)
  - Targeted therapy combos key: Avastin, Sprycel, Tarceva, AZD9291, Votrient
  - Radiation up-regulates PD-L1 expression and is synergistic

**Significant data to emerge from 2015**

*Source: Credit Suisse PharmaValues estimates*
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Biomarkers – a huge clinical debate at ASCO

Response clearly linked to PD-L1 status … but not a black/white answer

<table>
<thead>
<tr>
<th></th>
<th>PD-L1+</th>
<th>PD-L1-</th>
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<tbody>
<tr>
<td>BMY Lung nivo mono</td>
<td>50%</td>
<td>0%</td>
</tr>
<tr>
<td></td>
<td>nivo+ipi</td>
<td>19%</td>
</tr>
<tr>
<td>ROG Bladder PD-L1</td>
<td>43%</td>
<td>11%</td>
</tr>
<tr>
<td>MRK H&amp;N PD-1</td>
<td>46%</td>
<td>11%</td>
</tr>
<tr>
<td>Melanoma PD-1</td>
<td>37%</td>
<td>7%</td>
</tr>
<tr>
<td>Lung PD-1</td>
<td>37%</td>
<td>11%</td>
</tr>
<tr>
<td></td>
<td>39%</td>
<td>9%</td>
</tr>
</tbody>
</table>

- MRK PD-1 melanoma data (phase 1)
- Response rate by PD-L1 expression

Source: Credit Suisse analysis, MRK investor presentation, ASCO 2014
Biomarker debates at ASCO 2014

- Four competing PD-L1 tests
  - BMY (Dako), Roche, MRK and AZN

- What counts as PD-L1 positive?
  - Different cut-offs for each test
  - Level of cut-off being defined as we go

- What tissue matters for PD-L1 status?
  - Should we look at PD-L1 on tumour cells (BMY) ...
  - ... or on infiltrating immune cells (ROG)

- Doctors very clear that PD-L1- patients should still get therapy?
  - There are too many strong responders in PD-L1- to exclude
  - Response rates in PD-L1- still better than standard of care (bladder, lung)

Source: Credit Suisse estimates
Multiple biomarkers to be evaluated over time

Source: Bristol Myers investor presentation, ASCO 2014
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PD-1 versus PD-L1

5. NOT ALL I-O IS CREATED EQUAL

Source: adapted from www.biooncology.com

**PD-1**
- Blocking PD-1 (MRK, BMY) inhibits PD-L1 and PD-L2 interaction
- May lead to superior efficacy

**PD-L1**
- Blocking PD-L1 (ROG, AZN) leaves PD-L2 interaction intact
- May lead to improved tolerability

---

**Diagram:**
- T cell
  - TCR
  - MHC
- Dendritic cell
  - B7.1
  - PD-L1
  - PD-L2
- Tumour cell
  - T cell
Differences emerging in PD-L1s

**Uniquely engineered human IgG1κ mAb**
- Triple mutation in Fc domain removes ADCC activity
- No immunogenicity impacting PK-PD at Phase 3 dose (10mg/kg) to date
- 2/196 patients treated at 10 mg/kg showed anti-drug antibodies (ADA)
- 1/18 patients treated with doses other than 10 mg/kg showed ADA impacting PK-PD

**AstraZeneca PD-L1**
- No drug antibodies form against AZN’s PD-L1
- May lead to more reproducible efficacy
- But no sign that this is a problem for others

**Merck KGaA PD-L1**
- Very limited efficacy
- Only one partial response out of 28 patients
- Implied ORR = 4%

*Source: ASCO 2014, Merck KGaA & AZN company data*
Tremelimumab (AZN) vs ipilimumab (BMY)

- Both antibodies target CTLA4
- treme (AZN) reversibly inhibits CTLA4, ipi (BMY) permanently depletes CTLA4
- AZN data suggests treme+PD-L1 combo could be more tolerable vs ipi+PD-1 combo

### MEDI4736 + tremelimumab: Dose escalation

<table>
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<tr>
<th>Cohort</th>
<th>Anti-PDL1 (mg/kg)</th>
<th>Tremelimumab (mg/kg)</th>
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<td>1</td>
<td>3</td>
<td>1</td>
</tr>
<tr>
<td>2</td>
<td>10</td>
<td>1</td>
</tr>
<tr>
<td>3a</td>
<td>15</td>
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<td>3</td>
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<td>4</td>
<td>15</td>
<td>3</td>
</tr>
<tr>
<td><strong>5</strong></td>
<td><strong>15</strong></td>
<td><strong>10</strong></td>
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### Nivolumab + ipilimumab: Dose escalation

<table>
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<th>Cohort</th>
<th>Nivolumab (mg/kg)</th>
<th>Ipilimumab (mg/kg)</th>
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<td>1</td>
<td>0.3</td>
<td>3</td>
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<td><strong>2a</strong></td>
<td><strong>1</strong></td>
<td><strong>3</strong></td>
</tr>
<tr>
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<tr>
<td>4</td>
<td>10</td>
<td>3</td>
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- **Current Cohort**

**Differentiating features**

<table>
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<tr>
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<th>MEDI4736 (PD-L1) + tremelimumab</th>
<th>nivolumab (PD-1) + ipilimumab</th>
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<tbody>
<tr>
<td>Scheduling</td>
<td>Q4W for both agents</td>
<td>Q3W for nivolumab</td>
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<tr>
<td></td>
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<td>4 x Q3W ipilimumab</td>
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<tr>
<td>Combination dose</td>
<td>PD-L1 dose is higher in all cohorts</td>
<td>CTLA-4 higher at MTD</td>
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Source: AZN company data, ASCO 2014
Big Picture Takeaways from ASCO 2014

- Oncology & immuno-oncology background
- ASCO 2014 – levelling the playing field in I-O
- Lots more targets emerging
- I-O combinations – we’ve only just begun
- PD-L1 biomarkers a big clinical debate
- Not all I-O is created equal
- Small molecules still matter
- Doctors’ efficacy expectations have changed
- How will we pay for everything?
- Stock readacross from ASCO 2014
T790M mutant lung cancer emerges after c. 12mths treatment on Iressa/Tarceva

- Positive response data in line with Clovis CO-1686
- Different side effect profiles – AZN interstitial lung disease, CLVS hyperglycaemia & QTc
- Mature PFS outcomes data will be key to differentiate – expected 1H15
- First line opportunity unclear

Source: AZN company data, ASCO 2014
Olaparib + cediranib in ovarian

Platinum-sensitive ovarian cancer (Phase 1 data)

- Olaparib showed 6.9 mths improvement in median PFS in BRCAm ovarian cancer
- Cediranib is a previously-failed oral VEG-F inhibitor (old brand name Recentin)
- Combination showed 8.7 mths improvement in median PFS over olaparib alone
- High toxicity burden but manageable given unmet need (77% pts need dose reductions)

Source: AZN company data, ASCO 2014
ABT-199 in leukaemia

Bcl-2 inhibitor in CLL refractory to Rituxan (Phase 1 data)

- 84% overall response rate, 36% complete response rate
- Encouraging duration of response
- Previous severe side effect (tumour lysis syndrome, TLS) – now well managed by monitoring and dose titration, especially in mild-moderate patients.

![Graph showing best % change from baseline in Lymphocyte Count]

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<tr>
<th>Response</th>
<th>Evaluable** n=25</th>
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<tr>
<td>Response rate</td>
<td>21 (84%)</td>
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<tr>
<td>Complete response</td>
<td>9 (36%)</td>
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<tr>
<td>Partial response</td>
<td>12 (48%)</td>
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<td>Stable disease</td>
<td>1 (4%)</td>
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<tr>
<td>Disease progression</td>
<td>1 (4%)</td>
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<tr>
<td>Discontinued prior to assessment</td>
<td>2 (8%)</td>
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</table>

*Evaluable pts have reached the month 7 bone marrow assessment, discontinued, or progressed on therapy

Source: ASCO 2014, Roche company data
Big Picture Takeaways from ASCO 2014

- Oncology & immuno-oncology background
- ASCO 2014 – levelling the playing field in I-O
- Lots more targets emerging
- I-O combinations – we’ve only just begun
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- Not all I-O is created equal
- Small molecules still matter
- Doctors’ efficacy expectations have changed
- How will we pay for everything?
- Stock readacross from ASCO 2014
7. Changing Doctors’ Expectations

Source: ASCO 2014 company data
Big Picture Takeaways from ASCO 2014

- Oncology & immuno-oncology background
- ASCO 2014 – levelling the playing field in I-O
- Lots more targets emerging
- I-O combinations – we’ve only just begun
- PD-L1 biomarkers a big clinical debate
- Not all I-O is created equal
- Small molecules still matter
- Doctors’ efficacy expectations have changed

- How will we pay for everything?
- Stock readacross from ASCO 2014
How will we pay?

- Estimates of immuno-oncology potential are $30bn+
- ASCO 2014 highlights there is potential in many more tumours types
- Duration of response continues to be long
- New I-O modes of action could add further potential = COST

IMPLICATIONS

- In-house combinations will offer a clear advantage
- Could this accelerate adoption of generic biologics?
  - Oncologists have previously been reticent on biosimilar potential …
  - But they all want immuno-oncology, and do not want to limit to PD-L1+
- Could I-O substitute targeted drugs with relatively poor efficacy?

Source: Credit Suisse estimates
How will we pay?

Biosimilar risk – complex biologics as a % of total

Source: Credit Suisse estimates
How will we pay?

Biosimilar risk – complex biologics as a % of total

Source: Credit Suisse estimates
Big Picture Takeaways from ASCO 2014

- Oncology & immuno-oncology background
- ASCO 2014 – levelling the playing field in I-O
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- PD-L1 biomarkers a big clinical debate
- Not all I-O is created equal
- Small molecules still matter
- Doctors’ efficacy expectations have changed
- How will we pay for everything?

Stock readacross from ASCO 2014
ROCHE  Outperform  TP SFR 300
- Strength and depth in immuno-oncology addresses bear’s concerns
- Diagnostics division may strengthen strategy in I-O biomarkers
- Next catalyst: AAIC (Alzheimer’s) 12-17 July, ESMO (cancer) 26-30 Sept

ASTRAZENECA  Neutral  TP £48
- I-O portfolio still early but signs of differentiation, small molecules advances
- 2015 data will be critical. Sufficient excitement to maintain inflated stock price
- Next catalyst: ADA (diabetes) 13-17 June, ESMO (cancer) 26-30 Sept

BRISTOL MYERS  Outperform  TP $59
- Some short-term disappointment but portfolio robust with multiple assets in multiple tumours
- Confidence in biomarkers and lung cancer trial design will be key in 2H14
- Next catalyst: 30 Oct-1 Nov - readout of P2 lung, ESMO (cancer) 26-30 Sept

It’s still very early to draw conclusions – level playing field
Next oncology catalysts

**Merck**
- **pembrolizumab**, melanoma 65% prob, $1bn peak
  - 28 Oct (PDUFA)
- **pembrolizumab**, head&neck cancer 30% prob, $500m peak
- **pembrolizumab**, lung 50% prob, $2bn peak
  - 30 Oct – 1 Nov

**AZN**
- **olaparib**, ovarian cancer 80% prob, $500m peak
  - 3 Oct (PDUFA)
- **AZD9291**, lung cancer 30% prob, $500m peak
- **tremelimumab**, mesothelioma 60% prob, $200m peak
- **MEDI4736**, lung cancer 40% prob, $2bn peak
  - mono & combo
  - P2 mono PDL1+
  - P3 treme combo

**Roche**
- **RG7446**, lung cancer 60% prob, $2bn peak
- **RG7446**, bladder cancer 30% prob, $500mn peak

**BMY**
- **nivolumab**, lung cancer 70% prob, $4bn peak
  - P3 Yervoy combo
- **nivolumab**, melanoma 75% prob, $2.5bn peak
  - mono & combo
- **nivolumab**, renal and H&N 70% prob, $1bn peak
  - ???
## STOCK IMPLICATIONS

### P/E

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<td>12.8</td>
<td>12.2</td>
<td>3.5%</td>
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<td>28.8</td>
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<td>1.07</td>
<td>51.3</td>
<td>54.1</td>
<td>-1.0%</td>
<td>4.2%</td>
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### US Sector average

|                      | 20.5 | 20.2 | 20.4 | 18.9 | 16.0 | 2.7% | 1.07 | 2.8% | 8.1% |

### AstraZeneca

|                      | p    | 4,327| 4,800| 11.7 | 14.5 | 18.2 | 19.6 | 19.7 | 3.9% |

### Bayer

|                      | €     | 105.0| 120  | 19.3 | 18.1 | 17.0 | 14.8 | 13.1 | 2.1% |

### GlaxoSmithKline plc

|                      | p    | 1,599| 1,600| 17.5 | 17.9 | 19.0 | 16.7 | 14.4 | 5.1% |

### Novartis

|                      | SF   | 79.6 | 87   | 17.9 | 18.7 | 17.8 | 15.7 | 14.1 | 3.7% |

### Novo Nordisk A/S

|                      | DK   | 236.6| 230  | 30.9 | 25.4 | 23.6 | 21.0 | 18.6 | 2.1% |

### Roche

|                      | SF   | 267.2| 300  | 20.7 | 19.1 | 18.9 | 17.4 | 16.1 | 3.0% |

### Sanofi

|                      | €     | 79.0 | 80   | 13.2 | 16.1 | 15.0 | 13.2 | 12.6 | 3.4% |

### EU Majors average

|                      | 18.7 | 18.6 | 18.5 | 16.9 | 15.5 | 3.3% | 1.20 | 3.0% | 6.0% |

### Almirall

|                      | €     | 11.7 | 16.00| nr   | nr   | 22.0 | 12.2 | 8.7  | 1.3% |

### Ipsen

|                      | €     | 34.5 | 35.0 | 19.8 | 18.1 | 18.2 | 16.7 | 14.7 | 2.6% |

### Lonza

|                      | SF   | 98.7 | 95   | 23.1 | 21.9 | 16.6 | 13.8 | 12.8 | 2.2% |

### Lundbeck

|                      | DK   | 141  | 140  | 16.9 | 18.6 | 34.8 | 40.5 | 21.2 | 0.5% |

### Meda (pre-amortisation)

|                      | SK   | 116.2| 80   | 12.8 | 13.6 | 11.8 | 10.4 | 9.3  | 2.3% |

### Meda (post-amortisation)

|                      | SK   | 116.2| 80   | 29.0 | 43.5 | 28.8 | 21.7 | 17.4 | 2.3% |

### Merck KGaA

|                      | €     | 127.1| 143  | 16.6 | 14.5 | 13.6 | 12.5 | 12.4 | 1.6% |

### Orion

|                      | €     | 26.6 | 15.0 | 18.7 | 18.3 | 19.5 | 18.6 | 17.9 | 4.5% |

### Recordati

|                      | €     | 12.5 | 11.0 | 18.9 | 16.7 | 15.2 | 14.1 | 13.7 | 3.1% |

### Shire Pharmaceuticals

|                      | p    | 3586 | 3400 | 29.1 | 23.6 | 18.7 | 17.0 | 15.5 | 0.3% |

### UCB

|                      | €     | 57.1 | 53   | 34.5 | 32.2 | 28.8 | 23.0 | 19.0 | 2.0% |

### EU Specialty average

|                      | 22.0 | 19.7 | 19.9 | 17.9 | 14.5 | 2.0% | 1.1  | 5.1% | 16.5% |

Source: Credit Suisse estimates as at 09/06/2014
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**CS PLUS**
Quickly navigate and access the Bank’s global thought leadership

**Global industry team analytics**
We have extensive industry data and information at the sector level.
Disclosure Appendix

Important Global Disclosures

Vamir Divan, MD, Ari Jahja, Riccardo Lowi, Jo Walton and Matthew Weston PhD each certify, with respect to the companies or securities that the individual analyzes, that (1) the views expressed in this report accurately reflect his or her personal views about all of the subject companies and securities and that (2) no part of his or her compensation was, is or will be directly or indirectly related to the specific recommendations or views expressed in this report.

3-Year Price and Rating History for AstraZeneca (AZN.L)

<table>
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<th>Date</th>
<th>Closing Price</th>
<th>Target Price</th>
<th>Rating</th>
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<td>28-Apr-14</td>
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* Asterisk signifies initiation or assumption of coverage.

3-Year Price and Rating History for Bristol Myers Squibb Co. (BMY.N)

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* Asterisk signifies initiation or assumption of coverage.

As of December 10, 2012 Analysts’ stock rating are defined as follows:

**Outperform (O)**: The stock’s total return is expected to outperform the relevant benchmark over the next 12 months.

**Neutral (N)**: The stock’s total return is expected to be in line with the relevant benchmark over the next 12 months.

**Underperform (U)**: The stock’s total return is expected to underperform the relevant benchmark over the next 12 months.

Relevant benchmark by region: As of 15th December 2012, Japanese ratings are based on a stock’s total return relative to the analyst’s coverage universe which consists of all companies covered by the analyst within the relevant sector. Analysts’ sector weightings are distinct from analysts’ stock ratings and are based on the analyst’s expectations for the fund’s total return potential within an analyst’s stock rating definition. Prior to 10th December 2012, Japanese ratings were based on the stock’s total return relative to the relevant country or regional benchmark.

Volatility Indicator [V]: A stock is defined as volatile if the stock price has moved up or down by 20% or more in a month in at least 8 of the past 24 months or the analyst expects significant volatility going forward.

3-Year Price and Rating History for Merck & Co., Inc. (MRK.N)

<table>
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<th>Closing Price</th>
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<td>23-Jul-12</td>
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<td>10-Mar-13</td>
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<td>07-May-14</td>
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* Asterisk signifies initiation or assumption of coverage.

The analyst(s) responsible for preparing this research report received Compensation that is based upon various factors including Credit Suisse’s total revenues, a portion of which are generated by Credit Suisse’s investment banking activities.

Volatility Indicator [V]: A stock is defined as volatile if the stock price has moved up or down by 20% or more in a month in at least 8 of the past 24 months or the analyst expects significant volatility going forward.

Analysts’ sector weightings are distinct from analysts’ stock ratings and are based on the analyst’s expectations for the fund’s total return potential within an analyst’s stock rating definition. Volatility Indicator [V]: A stock is defined as volatile if the stock price has moved up or down by 20% or more in a month in at least 8 of the past 24 months or the analyst expects significant volatility going forward.

Market Weight: The analyst’s expectation for the sector’s fundamentals and/or valuation is neutral over the next 12 months.

Underweight: The analyst’s expectation for the sector’s fundamentals and/or valuation is cautious over the next 12 months.
Credit Suisse's distribution of stock ratings (and banking clients) is:

**Global Ratings Distribution**

<table>
<thead>
<tr>
<th>Rating</th>
<th>Versus universe (%)</th>
<th>Of which banking clients (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Outperform</td>
<td>44% (53% banking clients)</td>
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<tr>
<td>Neutral</td>
<td>40% (49% banking clients)</td>
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<tr>
<td>Underperform</td>
<td>3% (47% banking clients)</td>
<td></td>
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<tr>
<td>Restricted</td>
<td>3%</td>
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</tr>
</tbody>
</table>

*For purposes of the NYSE and NASD ratings distribution disclosure requirements, our stock ratings of Outperform, Neutral, and Underperform most closely correspond to Buy, Hold, and Sell, respectively; however, the meanings are not the same, as our stock ratings are determined on a relative basis. (Please refer to definitions above.) An investor's decision to buy or sell a security should be based on investment objectives, current holdings, and other individual factors.

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Price Target: (12 months) for AstraZeneca (AZN.L)

**Method:** Our target price of £48.00 reflects 1) approx. 35% bid premium to an unaffected AZN 3 month average price of £39.33 (35% = mean bid premium for historical major pharma M&A transactions) and 2) approx. 60% probability of a PFE/AZN merger occurring.

**Risk:** AZN acquisition by Pfizer fails to progress. Our AZN PharmaValues NPV/share is £39.

Price Target: (12 months) for Bristol Myers Squibb Co. (BMY.N)

**Method:** Our TP of $59 for BMY is based on 75/25 blend of DCF value ($50) and forward P/E ($53). We apply 7% WACC and perpetuity growth forecast of 1.5% for DCF valuation and 30.0 times 2014 EPS of $1.78 for P/E valuation.

**Risk:** Key risks to our target price of $59 are two fold: (1) Pipeline failures, particularly in the immuno-oncology space could cause estimates to come down, and (2) Underperformance of core franchises could bring longer-term estimates on these key franchises down.

Price Target: (12 months) for Roche (ROG.VX)

**Method:** We value Roche on a PE relative basis to the European markets modulated by our PharmaValues NPV methodology. Our European Major Pharma 2014 PE market relative assumption is 110% and our sector PE relative for Roche is 110%, giving a price target of SFr 300 per share. Roche’s 3 year historical average PE sector relative is 101%.

**Risk:** In the Pharma business the key risks centre on the high price structure of leading oncology drugs (Avastin, Herceptin and MabThera) and the outcome of future clinical trials that will be necessary to expand their clinical use. In Diagnostics intensifying pricing and competitive pressures may also pose a threat. For the business as a whole general market and sector risk is also important.

Please refer to the firm’s disclosure website at https://have.credit-suisse.com/disclosures for the definitions of abbreviations typically used in the target price method and risk sections.

See the Companies Mentioned section for full company names

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Credit Suisse provided non-investment banking services to the subject company (AZN.L, MRK.N, BMY.N, ROG.VX) within the past 12 months.

Credit Suisse has managed or co-managed a public offering of securities for the subject company (BMY.N) within the past 12 months.

Credit Suisse has received investment banking related compensation from the subject company (BMY.N) within the past 12 months.

Credit Suisse expects to receive or intends to seek investment banking related compensation from the subject company (AZN.L, MRK.N, BMY.N) within the next 3 months.

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Credit Suisse Securities (Europe) Limited---------------------------------------------Riccardo Lowi; Jo Walton; Matthew Weston PhD

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