Trends in the Japanese pharma R&D industry: from clinical trials to market

Ian Lloyd, Senior Director, Pharmaprojects/Pipeline & Data Integration
Tokyo, Tuesday 28th May, 2013
Agenda: Trends in the Japanese pharma R&D industry

- Overall number of pipeline drugs, globally and in Japan
- New Active Substance (NAS) launches 2012
- The R&D pipeline by phase and by leading companies, both worldwide and in Japan
- Drugs by therapy area, indication and target
- Deal activity in Japan
- Trends in clinical trials in Japan
- Case study: new drugs for hepatitis-C
Total pipeline size in 2013
Growth in global pipeline size levels off

Source: Pharmaprojects/Pipeline
Total global pipeline size – key facts

• Number of active drugs stands at 10,479

• 0.3% increase, in contrast to 7.6% seen in 2012

• Increases from 2011-2012 sustained

• ~10,500 the new norm?

Source: Pharmaprojects/Pipeline
Growth in Japan-originated pipeline

Source: Pharmaprojects/Pipeline
Japan’s share of global R&D

Source: Pharmaprojects/Pipeline
New active substance launches 2012
Global new active substance launches 2012 - key facts

- 39 NAS launches in 2012 (up from 35 in 2011)
- Twelve (31% are first-in-class)
- Fourteen for orphan indications
- Ten biologicals (up from 7 in 2011)
- 20 (51%) had US as debut market; 5 (13%) in Japan
- Pfizer the top company

Source: Pharmaprojects/Pipeline
NAS launches per year

Source: Pharmaprojects/Pipeline
Breakdown of NASs by Therapy & Country

By Therapy Area:
- Anticancer: 14
- Alimentary/Metabolic: 6
- Anti-infective: 1
- Neurological: 1
- Musculoskeletal: 2
- Respiratory: 2
- Blood/Clotting: 3
- Dermatological: 6
- Genitourinary: 3
- Hormonal: 1

By Country:
- USA: 21
- Europe: 7
- Japan: 4
- RoW: 7

Source: Pharmaprojects/Pipeline
First-in-class NAS launches 2012 - 1

CANCER:

- T-cell lymphoma: Kyowa Hakko/OncoTherapy Science’s mogamulizumab (Poteligeo)
  - *CC chemokine receptor 4 antagonist*

- Metastatic basal cell carcinoma: Roche’s vismodegib (Erivedge)
  - *Hedgehog pathway inhibitor*

- Effects of toxic methotrexate concentrations during chemotherapy: HPA Porton Down/BTG’s glucarpidase (Voraxaze)
  - *Serine carboxypeptidase inhibitor*

Source: Pharmaprojects/Pipeline
First-in-class NAS launches 2012 - 2

ANTI-INFECTION:

- Prevention of hepatitis-E: Xiamen Innovax Biotech’s hepatitis-E vaccine (Hecolin)

- Prevention of anthrax infection: AstraZeneca/HGS’ raxibacumab (ABthrax)
  - B anthracis protective antigen inhibitor

- Malaria: Ranbaxy’s arterolane maleate component of Synriam (with piperaquine phosphate)
  - Ca2+ ATPase inhibitor

Source: Pharmaprojects/Pipeline
First-in-class NAS launches 2012 - 3

RESPIRATORY:
• Cystic fibrosis: Vertex’ ivacaftor (Kalydeco)
  • CF transmembrane conductance regulator agonist

NEUROLOGICAL:
• Transthyretin familial amyloid polyneuropathy: Pfizer’s tafamidis meglumine (Vyndaqel)
  • Transthyretin stabilizer

• Epilepsy: Eisai’s perampanel (Fycompa)
  • AMPA receptor antagonist

Source: Pharmaprojects/Pipeline
First-in-class NAS launches 2012 - 4

ALIMENTARY/METABOLIC:
• Mucogingival conditions: Organogenesis’ Gintuit
  • Allogeneic cultured keratinocytes and fibroblasts in bovine collagen

IMMUNOLOGICAL:
• Rheumatoid arthritis: Pfizer’s tofacitinib (Xeljanz)
  • Janus kinase 1 and 3 inhibitor

DERMATOLOGICAL:
• Actinic keratosis: Leo Pharma’s ingenol mebutate (Picato)
  • Protein kinase C delta stimulant

Source: Pharmaprojects/Pipeline
Other 2012 NASs first launched in Japan

- Type 2 diabetes: Sanwa Kagaku Kenkyusho/Kowa’s anagliptin (Suiny/Beskoa)
  - Dipeptidyl peptidase IV (DPP IV) inhibitor

- Type 2 diabetes: Mitsubishi Tanabe Pharma/ Daiichi Sankyo’s teneligliptin (Tenelia)
  - Dipeptidyl peptidase IV (DPP IV) inhibitor

- Hyperphosphataemia: Astellas/ Sanwa Kagaku Kenkyusho’s bixalomer (Kiklin capsules)
  - Phosphate antagonist

Source: Pharmaprojects/Pipeline
Dissecting the 2013 R&D pipeline

- by phase, worldwide and Japan
- by company, worldwide and Japan
Global Pipeline by phase – a subtle shift

Figure 2: Pipeline by development phase

Source: Pharmaprojects/Pipeline
Phase I fall first ever at a clinical phase

Figure 3: Clinical phase trends 2007-2013

Source: Pharmaprojects/Pipeline
The Japanese-originated pipeline by Phase

Source: Pharmaprojects/Pipeline
Japanese status of pipeline drugs

Source: Pharmaprojects/Pipeline
## Top 10 pharma companies by pipeline size

<table>
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<tr>
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<tbody>
<tr>
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<td>GlaxoSmithKline</td>
<td>269 (257)</td>
<td>157</td>
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<td>2 (5)</td>
<td>Hoffmann-La Roche</td>
<td>227 (198)</td>
<td>166</td>
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<tr>
<td>3 (4)</td>
<td>Novartis</td>
<td>215 (218)</td>
<td>148</td>
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<tr>
<td>4 (3)</td>
<td>Merck &amp; Co</td>
<td>207 (223)</td>
<td>135</td>
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<td>5 (2)</td>
<td>Pfizer</td>
<td>202 (225)</td>
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<td>6 (6)</td>
<td>Sanofi</td>
<td>183 (178)</td>
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<td>7 (10)</td>
<td>Johnson &amp; Johnson</td>
<td>157 (142)</td>
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<td>8 (9)</td>
<td>AstraZeneca</td>
<td>157 (144)</td>
<td>82</td>
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<td>9 (8)</td>
<td>Bristol-Myers Squibb</td>
<td>141 (146)</td>
<td>108</td>
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<tr>
<td>10 (7)</td>
<td>Takeda</td>
<td>141 (149)</td>
<td>75</td>
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Source: Pharmaprojects/Pipeline
## Top pharma companies – 11-25

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<tr>
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<td>Eli Lilly</td>
<td>117 (125)</td>
<td>100</td>
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<td>12 (13)</td>
<td>Abbott</td>
<td>114 (96)</td>
<td>81</td>
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<td>13 (14)</td>
<td>Amgen</td>
<td>95 (91)</td>
<td>81</td>
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<tr>
<td>14 (12)</td>
<td>Astellas</td>
<td>93 (104)</td>
<td>55</td>
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<tr>
<td>15 (16)</td>
<td>Daiichi Sankyo</td>
<td>91 (89)</td>
<td>48</td>
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<tr>
<td>16 (15)</td>
<td>Bayer</td>
<td>87 (91)</td>
<td>57</td>
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<td>17 (17)</td>
<td>Eisai</td>
<td>81 (79)</td>
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<tr>
<td>18 (18)</td>
<td>Teva</td>
<td>75 (78)</td>
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<td>19 (19)</td>
<td>Boehringer Ingelheim</td>
<td>68 (69)</td>
<td>46</td>
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<tr>
<td>20 (20)</td>
<td>Merck KGaA</td>
<td>56 (58)</td>
<td>20</td>
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<tr>
<td>21 (-)</td>
<td>Dainippon Sumitomo Pharma</td>
<td>54 (-)</td>
<td>36</td>
</tr>
<tr>
<td>22 (22)</td>
<td>Kyowa Hakko Kirin</td>
<td>51 (48)</td>
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</tr>
<tr>
<td>23 (25)</td>
<td>Shionogi</td>
<td>49 (45)</td>
<td>24</td>
</tr>
<tr>
<td>24 (23)</td>
<td>Gilead Sciences</td>
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<td>36</td>
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<tr>
<td>25 (21)</td>
<td>Celgene</td>
<td>47 (45)</td>
<td>29</td>
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# Top 10 Japanese pharma companies

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<tbody>
<tr>
<td>1 (1)</td>
<td>Takeda</td>
<td>141 (149)</td>
<td>75</td>
</tr>
<tr>
<td>2 (2)</td>
<td>Astellas</td>
<td>93 (104)</td>
<td>55</td>
</tr>
<tr>
<td>3 (3)</td>
<td>Daiichi Sankyo</td>
<td>91 (89)</td>
<td>48</td>
</tr>
<tr>
<td>4 (4)</td>
<td>Eisai</td>
<td>81 (79)</td>
<td>46</td>
</tr>
<tr>
<td>5 (8)</td>
<td>Dainippon Sumitomo Pharma</td>
<td>54 (43)</td>
<td>36</td>
</tr>
<tr>
<td>6 (5)</td>
<td>Kyowa Hakko Kirin</td>
<td>51 (48)</td>
<td>22</td>
</tr>
<tr>
<td>7 (7)</td>
<td>Shionogi</td>
<td>49 (45)</td>
<td>24</td>
</tr>
<tr>
<td>8 (6)</td>
<td>Mitsubishi Tanabe Pharma</td>
<td>46 (47)</td>
<td>25</td>
</tr>
<tr>
<td>9 (-)</td>
<td>Otsuka</td>
<td>40 (32)</td>
<td>21</td>
</tr>
<tr>
<td>10 (9)</td>
<td>Ono</td>
<td>40 (39)</td>
<td>18</td>
</tr>
</tbody>
</table>

Source: Pharmaprojects/Pipeline
More global companies, but more leaving R&D

Figure 4: Total number of companies with active pipelines 2000-2013

Source: Pharmaprojects/Pipeline
Europe gains share at the expense of the US

Figure 5: Distribution of R&D companies by country/region 2012 and 2013

Source: Pharmaprojects/Pipeline
The R&D pipeline by therapy, disease and target
Pipeline by therapy – it’s still all about cancer

Figure 6: Pipeline by therapy group

Source: Pharmaprojects/Pipeline

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Pipeline by therapeutic area – key facts

• Oncology pipeline growth outperforms overall pipeline by factor of ten

• Breaks 30% barrier for first time

• CNS, Anti-infectives flat
  • Affective disorders down

• Biotech falls back to 26.2%
  • Monoclonals take bigger share

Source: Pharmaprojects/Pipeline
## Top 10 Indications

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<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>1 (1)</td>
<td>Cancer, breast</td>
<td>437 (434)</td>
<td>↔</td>
</tr>
<tr>
<td>2 (4)</td>
<td>Cancer, colorectal</td>
<td>347 (332)</td>
<td>↑</td>
</tr>
<tr>
<td>3 (3)</td>
<td>Cancer, prostate</td>
<td>340 (355)</td>
<td>↓</td>
</tr>
<tr>
<td>4 (2)</td>
<td>Diabetes, Type 2</td>
<td>336 (355)</td>
<td>↓</td>
</tr>
<tr>
<td>5 (6)</td>
<td>Alzheimer’s disease</td>
<td>331 (312)</td>
<td>↑</td>
</tr>
<tr>
<td>6 (7)</td>
<td>Cancer, lung, non-small cell</td>
<td>314 (308)</td>
<td>↔</td>
</tr>
<tr>
<td>7 (5)</td>
<td>Arthritis, rheumatoid</td>
<td>313 (316)</td>
<td>↔</td>
</tr>
<tr>
<td>8 (9)</td>
<td>Cancer, pancreatic</td>
<td>303 (289)</td>
<td>↑</td>
</tr>
<tr>
<td>9 (8)</td>
<td>Pain, general</td>
<td>292 (295)</td>
<td>↔</td>
</tr>
<tr>
<td>10 (10)</td>
<td>Cancer, ovarian</td>
<td>273 (263)</td>
<td>↑</td>
</tr>
</tbody>
</table>

Source: Pharmaprojects/Pipeline
## Top 10 Drug protein targets

<table>
<thead>
<tr>
<th>Position</th>
<th>Target (official EntrezGene name [except where italicized, added for clarity])</th>
<th>No. of R&amp;D products 2013 (2012)</th>
</tr>
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<tbody>
<tr>
<td>1 (1)</td>
<td>opioid receptor, mu 1</td>
<td>131 (142)</td>
</tr>
<tr>
<td>2 (5)</td>
<td>nuclear receptor subfamily 3, group C, member 1 (glucocorticoid receptor)</td>
<td>98 (95)</td>
</tr>
<tr>
<td>3 (2)</td>
<td>prostaglandin-endoperoxide synthase 2 (prostaglandin G/H synthase and cyclooxygenase) [COX-2]</td>
<td>94 (103)</td>
</tr>
<tr>
<td>4 (3)</td>
<td>polyprotein, hepatitis-C virus</td>
<td>90 (102)</td>
</tr>
<tr>
<td>5 (4)</td>
<td>prostaglandin-endoperoxide synthase 1 (prostaglandin G/H synthase and cyclooxygenase) [COX-1]</td>
<td>85 (97)</td>
</tr>
<tr>
<td>6 (8)</td>
<td>v-erb-b2 erythroblastic leukaemia viral oncogene homologue 2, neuro/glioblastoma derived oncogene homologue (avian) [erbB2]</td>
<td>83 (66)</td>
</tr>
<tr>
<td>7 (7)</td>
<td>opioid receptor, kappa 1</td>
<td>72 (74)</td>
</tr>
<tr>
<td>8 (12)</td>
<td>insulin receptor</td>
<td>70 (60)</td>
</tr>
<tr>
<td>9 (9)</td>
<td>tumour necrosis factor (TNF superfamily, member 2)</td>
<td>69 (65)</td>
</tr>
<tr>
<td>10 (6)</td>
<td>gag-pol, HIV-1</td>
<td>68 (74)</td>
</tr>
</tbody>
</table>

Source: Pharmaprojects/Pipeline
Drug protein targets – key facts

• 26% increase in drugs targeting HER2 (breast cancer)

• 89 novel targets identified during past 8 months, to bring total to 2,473

• 11 novel targets per month, vs 15 in 2011-12

• Total number of targets under active investigation 1,416, up from 1,404

Source: Pharmaprojects/Pipeline
Trends in drug pipelines – key facts

• 2012’s gains sustained – which way will things head in 2013?

• Fall in Phase I a concern

• Fewer novel targets being identified – will this trend continue?

• Will Oncology continue getting bigger and bigger?

• Ultimately, it’s all about the NASs

Source: Pharmaproductions/Pipeline
Pharma deals/finance in Japan
Japanese Pharmaceutical & Biotechnology Partnership Deals

Note that $ amount raised may not be disclosed in various instances

Source: Medtrack®
Japanese Pharmaceutical & Biotechnology Partnership Deals – Average Deal Value by Year

$'s in mm

<table>
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<tr>
<th>Year</th>
<th>Value</th>
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<tr>
<td>2008</td>
<td>$231.4</td>
</tr>
<tr>
<td>2009</td>
<td>$105.0</td>
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<tr>
<td>2010</td>
<td>$260.0</td>
</tr>
<tr>
<td>2011</td>
<td>$226.4</td>
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<tr>
<td>2012</td>
<td>$104.8</td>
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<tr>
<td>Q 1 2013</td>
<td>$239.5</td>
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</table>

Source: Medtrack®
Japanese Pharmaceutical & Biotechnology Partnership Deals – Average Deal Value by Trial Phase

Source: Medtrack®
Japanese Pharmaceutical & Biotechnology M&A Deals

*Note that $ amount raised may not be disclosed in various instances

Source: Medtrack®
Top 10 Japanese Pharmaceutical/Biotechnology Companies by Total R&D Spend

R&D Spending (m)

$'s in mm

R&D Spending (m)

Source: Medtrack®
Top 10 Japanese Pharmaceutical / Biotechnology by Total R&D Spend – R&D Intensity and R&D Spend by Employee

![Graph showing R&D Intensity and R&D Spend per Employee for top 10 Japanese companies.]

- R&D Intensity* (%)
- R&D Spending per Employee (000)**

*R&D Intensity defined as R&D spending/Sales (expressed as %)

Source: Medtrack®
The clinical trial landscape in Japan
Active trials by Phase: World vs Japan

Source: Trialtrove
Planned trials by Phase: World vs Japan

Source: Trialtrove
Trial starts in 2012 by company

Figure 4. Top 20 Sponsors of Trials with an Unapproved Drug Started in 2012


Source: Trialtrove
Accrual, sites and countries for trials with unapproved drugs started in 2012

<table>
<thead>
<tr>
<th>SPONSOR</th>
<th>NO OF TRIALS</th>
<th>AVG TARGET ACCRUAL PER TRIAL</th>
<th>AVG SITES PER TRIAL</th>
<th>AVG COUNTRIES PER TRIAL</th>
<th>AVERAGE PATIENTS PER SITE</th>
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<tbody>
<tr>
<td>Overall Avg</td>
<td>241.6</td>
<td>21.6</td>
<td>3.6</td>
<td>11.4</td>
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<tr>
<td>Novartis</td>
<td>118</td>
<td>195.8</td>
<td>27.7</td>
<td>3.6</td>
<td>7.1</td>
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<tr>
<td>Roche</td>
<td>103</td>
<td>403.4</td>
<td>50.1</td>
<td>6.1</td>
<td>8.1</td>
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<tr>
<td>GSK</td>
<td>94</td>
<td>292.3</td>
<td>16.3</td>
<td>5.8</td>
<td>17.9</td>
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<tr>
<td>Pfizer</td>
<td>84</td>
<td>208.3</td>
<td>26.0</td>
<td>3.2</td>
<td>8.0</td>
</tr>
<tr>
<td>AstraZeneca</td>
<td>74</td>
<td>200.6</td>
<td>13.9</td>
<td>4.9</td>
<td>14.4</td>
</tr>
<tr>
<td>Eli Lilly</td>
<td>74</td>
<td>411.1</td>
<td>34.2</td>
<td>4.7</td>
<td>12.0</td>
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<td>Sanofi</td>
<td>68</td>
<td>589.7</td>
<td>19.7</td>
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<td>Boehringer Ingelheim</td>
<td>63</td>
<td>194.5</td>
<td>27.8</td>
<td>5.0</td>
<td>7.0</td>
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<td>Merck &amp; Co</td>
<td>61</td>
<td>208.7</td>
<td>27.0</td>
<td>5.3</td>
<td>7.7</td>
</tr>
<tr>
<td>Johnson &amp; Johnson</td>
<td>61</td>
<td>395.1</td>
<td>13.7</td>
<td>4.6</td>
<td>28.8</td>
</tr>
</tbody>
</table>

Ex-US locations for trials started in 2012

Figure 8. Top 20 Locations of Industry-Sponsored Trials with Unapproved Drugs Started in 2012 (Excluding US)

Source: Citeline’s Trialtrove.
Data accessed January 31, 2013

Source: Trialtrove
Leading diseases by active trials in Japan

Source: Trialtrove
Top drugs under clinical trial in Japan

Source: Trialtrove
Detail on Japanese trials involving TS-1

**Primary Drugs**
- TS-1: 301
- cisplatin: 55
- gemcitabinehydrochloride: 47
- irinotecan (IV): 38
- bevacizumab: 24

**Sponsor**
- Other Hospital/Academic/IM: 173
- Other Cooperative Group: 65
- Japanese Ministry of Health: 22
- Otsuka: 18
- Taiho: 18

**Disease Type**
- Colorectal: 77
- Gastric: 76
- Lung, Non-Small Cell: 67
- Pancreas: 51
- Liver: 28
- Breast: 2

**Location**
- Japan: 323
- Asia: 2
- China: 1
- Hong Kong: 1
- Singapore: 1
- South Korea: 1

**Trial Status**
- Open: 275
- Closed: 46
- Temporarily Closed: 2

**Trial Phase**
- III: 220
- II: 37
- I: 35
- IV: 28
- Other: 1
# Top 10 trial sites in Japan

<table>
<thead>
<tr>
<th>Trial Site</th>
<th>No of Investigators</th>
<th>No of Active Trials</th>
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<tbody>
<tr>
<td>Osaka University Graduate School of Medicine - Faculty of Medicine</td>
<td>64</td>
<td>118</td>
</tr>
<tr>
<td>National Cancer Center (NCC) Hospital - Tsukiji Campus</td>
<td>47</td>
<td>111</td>
</tr>
<tr>
<td>Keio University School of Medicine - Shinanomachi Campus</td>
<td>49</td>
<td>106</td>
</tr>
<tr>
<td>Aichi Cancer Center Hospital and Research Institute</td>
<td>24</td>
<td>89</td>
</tr>
<tr>
<td>Kyoto University - Kyoto University Hospital</td>
<td>36</td>
<td>84</td>
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<tr>
<td>National Cancer Center Hospital East (NCCHE) - Kashiwa Campus</td>
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<td>79</td>
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<tr>
<td>Nagoya University - Graduate School of Medicine (NUGSM) - Tsurumai</td>
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<tr>
<td>Tohoku University Hospital (TUH)</td>
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<tr>
<td>National Hospital Organization - National Kyushu Cancer Center</td>
<td>17</td>
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<tr>
<td>Tokyo Metropolitan Cancer and Infectious Diseases Center Komagome Hospital</td>
<td>15</td>
<td>72</td>
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</table>

Source: Sitetrove
## Top 10 trial sites in Tokyo

<table>
<thead>
<tr>
<th>Trial Site</th>
<th>Investigators</th>
<th>Matching Trials</th>
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<tbody>
<tr>
<td>National Cancer Center (NCC) Hospital - Tsukiji Campus</td>
<td>47</td>
<td>111</td>
</tr>
<tr>
<td>Keio University School of Medicine - Shinanomachi Campus</td>
<td>49</td>
<td>106</td>
</tr>
<tr>
<td>Tokyo Metropolitan Cancer and Infectious Diseases Center Komagome Hospital</td>
<td>15</td>
<td>72</td>
</tr>
<tr>
<td>The University of Tokyo Hospital</td>
<td>59</td>
<td>72</td>
</tr>
<tr>
<td>Juntendo University School of Medicine</td>
<td>37</td>
<td>65</td>
</tr>
<tr>
<td>Japanese Foundation for Cancer Research (JFCR) - The Cancer Institute Hospital</td>
<td>24</td>
<td>64</td>
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<tr>
<td>Keio University Hospital</td>
<td>38</td>
<td>59</td>
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<tr>
<td>The University of Tokyo - Graduate School of Medicine and Faculty of Medicine</td>
<td>32</td>
<td>49</td>
</tr>
<tr>
<td>The Jikei University School of Medicine</td>
<td>17</td>
<td>41</td>
</tr>
<tr>
<td>Tokyo Medical University Hospital</td>
<td>12</td>
<td>41</td>
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</tbody>
</table>

Source: Sitetrove
Case study: hepatitis-C therapeutics
HCV therapy – the landscape

• Treatment of hepatitis-C is undergoing a paradigm shift

• Established treatment of PEG-interferon + ribavirin has limitations
  • 50-70% cure rates
  • Serious side-effects and poor compliance

• New generation of small molecule therapeutics
  • Ultimate goals: remove PEG-interferon; increase cure/compliance

• So what is the current landscape, in terms of:
  • Leading drugs and new mechanisms of action
  • Companies and deals
  • Trials and trial locations
  • Investigator utilization?
The current pipeline for HCV therapeutics

Source: Pharmaprojects/Pipeline
# Deals in the HCV area in the past 12 months

<table>
<thead>
<tr>
<th>Deal Date</th>
<th>Deal Type</th>
<th>Deal Subtype</th>
<th>Company 1</th>
<th>Company 2</th>
<th>Deal headline</th>
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</thead>
<tbody>
<tr>
<td>28 Jan '13</td>
<td>Partnership</td>
<td>Development</td>
<td>Idenix</td>
<td>Johnson &amp; Johnson</td>
<td>Idenix signs agreement with Janssen for antiviral (DAA) HCV combination therapies</td>
</tr>
<tr>
<td>2 Jan '13</td>
<td>Partnership</td>
<td>Acquisition of Rights</td>
<td>Merck</td>
<td>MicroBiotiX</td>
<td>Microbiotix signs agreement with Merck for MBX-700 and MBX-701</td>
</tr>
<tr>
<td>1 Nov '12</td>
<td>Partnership</td>
<td>R&amp;D</td>
<td>Vertex</td>
<td>GlaxoSmithKline</td>
<td>Vertex Pharmaceuticals signs agreement with GlaxoSmithKline for VX-135 and GSK2336805</td>
</tr>
<tr>
<td>1 Nov '12</td>
<td>Partnership</td>
<td>R&amp;D</td>
<td>Vertex</td>
<td>Johnson &amp; Johnson</td>
<td>Vertex Pharmaceuticals signs agreement with Janssen for VX-135 and simeprevir (TMC435)</td>
</tr>
<tr>
<td>5 Sep '12</td>
<td>M&amp;A</td>
<td>Asset Purchase</td>
<td>Novadex</td>
<td>Medivir</td>
<td>Medivir acquires preclinical research stage assets from Novadex Pharmaceuticals</td>
</tr>
<tr>
<td>20 Jun '12</td>
<td>Partnership</td>
<td>Service/support</td>
<td>BMS</td>
<td>Emory University</td>
<td>Bristol-Myers Squibb signs agreement with Emory University</td>
</tr>
<tr>
<td>18 Jun '12</td>
<td>Partnership</td>
<td>Commercialization</td>
<td>Merck &amp; Co</td>
<td>R-Pharm</td>
<td>R-Pharm signs agreement with Merck &amp; Co (MSD) for narlaprevir</td>
</tr>
</tbody>
</table>

Source: Medtrack®
HCV dominated by Top 10 companies

Figure 1. Distribution of clinical trials conducted by top 10 companies vs. other companies

Top 10 Companies 83%
- Bristol-Myers Squibb (37)
- Gilead (35)
- Merck & Co. (18)
- AbbVie (16)
- Boehringer Ingelheim (15)

Other Companies 17%
- Johnson & Johnson (14)
- Roche (14)
- Vertex (9)
- Achillion (8)
- Novartis (6)

Source: Citeline’s Trialtrove® (data accessed 03/01/2013)
Top 10 trial sponsors shown by Phase

Figure 2. Top 10 sponsors, trials by phase

Source: Citeline’s Trialtrove® (data accessed 03/01/2013)

Source: Trialtrove
# Top clinical trial locations for HCV drugs

## Table 2. Top 5 clinical trial locations

<table>
<thead>
<tr>
<th>BY COUNTRY</th>
<th>TOTAL</th>
<th>BMS</th>
<th>GILEAD</th>
<th>MERCK</th>
<th>ABBVIE</th>
<th>BI</th>
<th>J&amp;J</th>
<th>ROCHE</th>
<th>VERTEX</th>
<th>ACHILLION</th>
<th>NOVARTIS</th>
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<tbody>
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<td>Total*</td>
<td>144</td>
<td>35</td>
<td>31</td>
<td>18</td>
<td>14</td>
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<td>3</td>
<td>5</td>
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<td>United States</td>
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<td>27</td>
<td>9</td>
<td>13</td>
<td>7</td>
<td>5</td>
<td>9</td>
<td>5</td>
<td>3</td>
<td>4</td>
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<td>14</td>
<td>12</td>
<td>7</td>
<td>3</td>
<td>12</td>
<td>6</td>
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<td>0</td>
<td>2</td>
</tr>
<tr>
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<td>61</td>
<td>20</td>
<td>11</td>
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<td>4</td>
<td>7</td>
<td>5</td>
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<td>0</td>
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<tr>
<td>Puerto Rico</td>
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<td>4</td>
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</tr>
<tr>
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<td>8</td>
<td>3</td>
<td>6</td>
<td>7</td>
<td>4</td>
<td>4</td>
<td>0</td>
<td>0</td>
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</tr>
</tbody>
</table>

* Number of trials with disclosed locations

Source: Citeline’s Trialtrove® (data accessed 03/01/2013)
Completion dates for IFN-free Phase III trials

Figure 4. Projected primary completion dates for Phase III trials of IFN free regiments by sponsor

Source: Citeline’s Trialtrove®, Trialpredict® (data accessed 03/01/2013)

Source: Trialtrove
Country and Investigator utilization

• Looked at industry-sponsored completed Phase III trials in HCV from 1999

• Trials where start and end dates of recruitment reported

• Analysed 87 trials and 1,223 clinical investigators

• Compared overall data set with the subset of trials with enrolment periods lower than the mean ("outperformers")

• Examined countries and no. of investigators used over three time periods
Country utilization in Asia-PAC HCV Phase III

Figure 2c. Country Utilization in Asia PAC as Percent Share

Source: Citeline, Inc., Trialtrove. Data accessed 10 March 2013

Source: Trialtrove
Investigator utilization by region in HCV Phase III

Figure 3. Average Investigators by Region Overall Versus Outperformers

Source: Sitetrove

Source: Citeline, Inc., Trialtrove. Data accessed 10 March 2013
Trends in the Japanese pharma R&D industry: from clinical trials to market - Summary

• Japanese drug pipelines growing after years of stagnation

• Only 4% of companies are Japanese, but 7 of Top 25 are

• Japan is a leading centre for clinical trials, although % of planned trials is comparatively low

• More trials for non-small cell lung cancer in Japan than any other disease (cf breast cancer worldwide)

• Citeline databases can be used to forensically look at the competitive landscape by drugs, companies, deals, trials, sites and investigators
Thanks for your attention

Q & A

Tuesday May 28th, 2013

Ian Lloyd, Senior Director

Please send any additional questions to: info@citeline.com