Overview of Trends in Dealmaking

MEDIUS ASSOCIATES : DEAL WATCH TEAM
Overview of Trends in Dealmaking

- Top licensing and acquisition deals
- Emerging Markets
- Biosimilars
- Options and Terminations
- Leading dealmakers
  - NGOs
- Alliances
  - Big pharma : big pharma collaborations
  - Industry/academia
- Conclusions
Deal Watch

- Review of pharma deals published each month on the Medius web site
- Based on information in the public domain
- Captures top deals by value each month plus other deals of note
- Each author provides insight, analysis and commentary
<table>
<thead>
<tr>
<th>Licensor</th>
<th>Partner</th>
<th>Product / Technology</th>
<th>Headline $m</th>
<th>Upfront ( $m)</th>
<th>% of headline</th>
</tr>
</thead>
<tbody>
<tr>
<td>Molecular Partners</td>
<td>Allergan</td>
<td>MP0260 preclinical dual anti VEGF-A/PDGF-B DARPin for wet AMD; discovery alliance/options against selected targets in serious eye disease</td>
<td>1,463</td>
<td>62.5</td>
<td>4.3%</td>
</tr>
<tr>
<td>Galapagos</td>
<td>Abbott</td>
<td>Collaboration for oral JAK1 inhibitor (GLPG0634) in RA and other autoimmune diseases (phase 2)</td>
<td>1,350</td>
<td>150</td>
<td>11.1%</td>
</tr>
<tr>
<td>Five Prime Therapeutics</td>
<td>GSK</td>
<td>Discovery collaboration with options for asthma and COPD targets</td>
<td>1,191</td>
<td>30 over 4 yrs</td>
<td>2.5%</td>
</tr>
<tr>
<td>Genmab</td>
<td>J&amp;J</td>
<td>Licence to daratumumab, oncology (phase 1/2)</td>
<td>1,100</td>
<td>135</td>
<td>12.3% (55 cash; 80 equity)</td>
</tr>
<tr>
<td>MacroGenics</td>
<td>Servier</td>
<td>Discovery alliance with options for Dual-Affinity Re-Targeting (DART™) platform technology for 3 cancer targets</td>
<td>1,100</td>
<td>20</td>
<td>1.8%</td>
</tr>
<tr>
<td>Endocyte</td>
<td>Merck</td>
<td>Licence to vintafolide (EC 145) for ovarian cancer, NSCLC and other solid tumours (phase 3)</td>
<td>1,000</td>
<td>120</td>
<td>12%</td>
</tr>
<tr>
<td>Astellas</td>
<td>J&amp;J</td>
<td>Exclusive rights outside Japan to ASP015K, an oral JAK inhibitor for RA and psoriasis (phase 2)</td>
<td>945</td>
<td>65</td>
<td>6.9%</td>
</tr>
<tr>
<td>Selecta</td>
<td>Sanofi</td>
<td>Discovery collaboration for antigen-specific immuno-therapies for life threatening allergies based on Synthetic Vaccine Particle (SVP™) platform</td>
<td>900</td>
<td>ND</td>
<td></td>
</tr>
<tr>
<td>Forma Therapeutics</td>
<td>Boehringer &amp; Ingelheim</td>
<td>Discovery of small molecule therapeutics against oncology-relevant protein-protein interactions</td>
<td>815</td>
<td>65</td>
<td>8%</td>
</tr>
<tr>
<td>Evotec</td>
<td>Bayer</td>
<td>5 year multi-target collaboration to develop 3 candidates for endometriosis</td>
<td>765</td>
<td>15</td>
<td>2%</td>
</tr>
</tbody>
</table>
## Top Licensing Deals 2012 by Value

<table>
<thead>
<tr>
<th>Licensor</th>
<th>Partner</th>
<th>Product / Technology</th>
<th>Headline $m</th>
<th>Upfront ( $m) % of headline</th>
</tr>
</thead>
<tbody>
<tr>
<td>Forma Therapeutics</td>
<td>J&amp;J</td>
<td><strong>Discovery</strong> and development of novel small molecule drug candidates that target tumour metabolism</td>
<td>700</td>
<td>ND</td>
</tr>
<tr>
<td>Xenon Pharma</td>
<td>Genentech</td>
<td><strong>Strategic alliance</strong> to discover, develop compounds and companion diagnostics for pain</td>
<td>646</td>
<td>ND</td>
</tr>
<tr>
<td>Symphogen KgaA</td>
<td>Merck</td>
<td>Licence to Sym004, an antibody targeting EGFR in advanced metastatic colorectal cancer (phase 1/2) and squamous cell carcinoma head and neck (phase 2)</td>
<td>638</td>
<td>26 4.1%</td>
</tr>
<tr>
<td>Isis Pharma</td>
<td>Biogen Idec</td>
<td>Licence with options to discover /develop antisense drugs against 3 targets (undisclosed) to treat neurological disorders</td>
<td>630</td>
<td>30 4.8%</td>
</tr>
<tr>
<td>Ablynx</td>
<td>Merck</td>
<td>Licence with options for discovery of Nanobodies against a voltage gated ion channel target</td>
<td>587</td>
<td>8 1.4%</td>
</tr>
<tr>
<td>AiCuris</td>
<td>Merck</td>
<td>Licence to leterminovir (AIC246), orphan anti-CMV (phase 2)</td>
<td>572</td>
<td>142 24.8%</td>
</tr>
<tr>
<td>Onconova</td>
<td>Baxter</td>
<td>Licence to Estybon® (rigosertif) for Myelodysplastic Syndromes (phase 3) / pancreatic cancer (phase 2/3)</td>
<td>565</td>
<td>50 8.9%</td>
</tr>
<tr>
<td>Threshold</td>
<td>Merck</td>
<td>Licence to TH302 for soft tissue sarcoma (phase 3) and pancreatic cancer (phase 2)</td>
<td>550</td>
<td>25 4.6%</td>
</tr>
<tr>
<td>Halozyme Therapeutics</td>
<td>Pfizer</td>
<td>Collaboration / licence for Enhanze™ drug delivery technology for up to 6 Pfizer biologics</td>
<td>515</td>
<td>8 1.6%</td>
</tr>
<tr>
<td>Sutro Biopharma</td>
<td>Celgene</td>
<td>Collaboration to design novel antibody drug conjugates / bi-specific antibodies for 2 targets (undisclosed)</td>
<td>500</td>
<td>ND</td>
</tr>
</tbody>
</table>
Top Licensing Deals

Values of top 20 licensing deals in 2012 down 15%
- Aggregate value $16.5bn cf. $19.4bn in 2011
- Average deal value $827m cf. $969m in 2011
- 6 deals with headline value ≥$1bn in both years

Trends of note in the Top 20:
- Nearly 60% of the big headline deals were platform/discovery transactions with multiple targets
- Slight bias towards small molecules vs. biologics (55%)
- Majority of deals in
  - oncology (8)
  - CNS (3)
  - autoimmune diseases (2)
- Amongst other therapeutic areas, women’s health and respiratory also featured

Jill Ogden
Top licensing deals cont’d.

- **Upfronts as % of headline value not always correlated with stage:**
  - Phase 3 assets: approx. 5 - 12%
  - Phase 1/2 assets: approx. 4 - 12%
  - Majority of platform / discovery deals: 1.4% - 2.5%

- **But there are outliers:**
  - AiCuris received 25% value ($142m/€110m) upfront from Merck for access to its HCMV portfolio including letermovir, an oral phase 2b CMV orphan drug with fast track status
  - Thrombogenics received 20% value ($98m/€75m) upfront from Alcon for ex-US rights to ophthalmology drug ocriplasmin (MAA stage in Europe; FDA approved) in symptomatic vitreomacular adhesion
  - Novartis paid Enanta 8% value ($34m) upfront for EDP-239 an IND stage small molecule from a hepatitis C inhibitor programme [targeting NS5A]

- **Royalties – reading the codes/how many digits?**
  - Double digit royalties – low double digit or high double digit?
  - Tiered and up to double digits
  - Single digits – or just royalties!

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**Jill Ogden**
## Top Acquisitions 2012 by Value

<table>
<thead>
<tr>
<th>Company Acquired</th>
<th>Acquiring Company</th>
<th>Product / Technology</th>
<th>Headline value $m</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pfizer Nutrition</td>
<td>Nestlé</td>
<td>Childrens’ nutritional business</td>
<td>11,850</td>
</tr>
<tr>
<td>Amylin</td>
<td>BMS/AZ</td>
<td>Diabetes product portfolio</td>
<td>7,000</td>
</tr>
<tr>
<td>Actavis</td>
<td>Watson</td>
<td>Acquisition of generics business adding geographic outreach – creates 3rd largest generics business</td>
<td>5,927</td>
</tr>
<tr>
<td>Gambro</td>
<td>Baxter</td>
<td>Medical equipment - haemodialysis</td>
<td>4,000</td>
</tr>
<tr>
<td>HGS</td>
<td>GSK</td>
<td>Acquisition secured access to Benlysta, a novel monoclonal antibody to treat SLE and other pipeline products</td>
<td>3,600</td>
</tr>
<tr>
<td>Boston Biomedical</td>
<td>Dainippon</td>
<td>Access to cancer stem cell technology</td>
<td>2,600</td>
</tr>
<tr>
<td>Medicis</td>
<td>Valeant</td>
<td>Acquisition of dermatology and aesthetics business</td>
<td>2,600</td>
</tr>
<tr>
<td>Inhibitex</td>
<td>BMS</td>
<td>Acquires portfolio of anti-infectives including lead INX 189 an oral nucleotide polymerase inhibitor against hepatitis C (phase 2)</td>
<td>2,500</td>
</tr>
<tr>
<td>Dako</td>
<td>Agilent Technologies</td>
<td>Cancer diagnostic tools business</td>
<td>2,200</td>
</tr>
<tr>
<td>Par</td>
<td>TPG</td>
<td>TPG (private investment company) acquires the US generic company</td>
<td>1,900</td>
</tr>
</tbody>
</table>

*Jill Ogden*
# Top Acquisitions 2012 by Value

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<th>Company Acquired</th>
<th>Acquiring Company</th>
<th>Product / Technology</th>
<th>Headline value $m</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fougera Pharmaceuticals</td>
<td>Sandoz (Novartis)</td>
<td>Fougera, a generic dermatology business previously owned by Nycomed</td>
<td>1,525</td>
</tr>
<tr>
<td>Ardea Biosciences</td>
<td>AZ</td>
<td>Clinical stage development programmes in gout and cancer</td>
<td>1,260</td>
</tr>
<tr>
<td>Schiff Nutrition International</td>
<td>Bayer</td>
<td>US-based nutritional supplement company</td>
<td>1,200</td>
</tr>
<tr>
<td>Fenwal</td>
<td>Fresenius</td>
<td>Acquisition of a complementary US company with separation technologies for blood and cell collection and therapy</td>
<td>1,100</td>
</tr>
<tr>
<td>Enobia Pharma</td>
<td>Alexion</td>
<td>ENB 0040 enzyme replacement therapy for patients with hypophosphatasia, orphan indication (phase 2)</td>
<td>1,080</td>
</tr>
<tr>
<td>Micromet</td>
<td>Amgen</td>
<td>Oncology portfolio - lead product Bispecific T cell Engager (BiTE) antibody for acute lymphoblastic leukemia (ALL) (phase 2) and BiTE antibody platform</td>
<td>1,000</td>
</tr>
<tr>
<td>Avila Therapeutics</td>
<td>Celgene</td>
<td>Lead product AVL-292, Bruton’s tyrosine kinase (Btk) inhibitor for B-cell cancers (phase 1) and discovery platform, Avilomics™, for developing targeted covalent drugs that treat diseases through protein silencing</td>
<td>925</td>
</tr>
<tr>
<td>Pronova BioPharma</td>
<td>BASF</td>
<td>Portfolio of lipid therapies including omega-3 fatty acid for preventive care and treatments</td>
<td>844</td>
</tr>
<tr>
<td>URL Pharma</td>
<td>Takeda</td>
<td>Lead product Colcrys (colchicine) used to treat and prevent gout flares and generics products</td>
<td>800 + earn-outs</td>
</tr>
<tr>
<td>Mercury Pharma</td>
<td>Cinven</td>
<td>Portfolio of niche off-patent prescription pharmaceuticals</td>
<td>738</td>
</tr>
</tbody>
</table>
Top Acquisition Deals

- 16 company acquisitions with headlines ≥$1bn in 2012 with an average price of $3.2bn (range $1bn – $11.85bn)
- cf. 7 ≥ $1bn corporate acquisitions in 2011 with an average price of $11.2bn (range $1.2bn – $21.3bn)
- The rationale for corporate M&A is consistent with previous trends:
  - For Buyers:
    - Strengthening an existing business area
    - Entering into a new therapeutic or technology area
    - Buying into a clinical development pipeline
    - Extending geographical outreach
  - For Sellers:
    - Focus / alignment of the business
    - Cutting the cost base
    - Possibly in trouble!
Acquisitions with Licensing Terms

- Private investors in companies with:
  - One clinical lead product and others in preclinical
  - May be seeking an exit rather than a licence
- The Acquirer agrees to buy company but because effectively only wants a licence, the Acquirer will not pay the full value and so the company is sold with a high proportion of contingent value rights [CVRs]
- Example:
  - Biogen Idec acquisition of Stromedix (a privately owned company) with a Portfolio of:
    - a phase 1 complete monoclonal antibody, STX-100, for treatment of fibrosis
    - a second compound in preclinical development.
  - So, what is a reasonable valuation of the company?
  - According to the press release, “STX-100 has potential in several additional fibrotic indications”. This is reflected in the acquisition price where Biogen Idec paid $75m (maybe less than the equity?) to buy the company plus up to $487.5m in contingent value depending on development and approval milestones across multiple indications
  - The upfront is only 13% of the potential total value of the company which is normally the type of structure that would be seen as a licensing deal

Roger Davies
<table>
<thead>
<tr>
<th>Target / Acquirer</th>
<th>Comments</th>
<th>Headline $m</th>
</tr>
</thead>
<tbody>
<tr>
<td>Actavis / Watson</td>
<td>Acquisition of generics business adding geographic outreach - creates 3rd largest generics business</td>
<td>5,927 (5,600 upfront, + 327 milestones)</td>
</tr>
<tr>
<td>Mustafa Nevzat Pharmaceuticals / Amgen</td>
<td>Acquires 95.6% of Turkish company to strengthen Amgen’s presence in Turkey and surrounding area</td>
<td>700</td>
</tr>
<tr>
<td>Multilab / Takeda</td>
<td>Acquisition of Brazilian OTC company</td>
<td>266</td>
</tr>
<tr>
<td>Cipla Medpro / Cipla</td>
<td>Acquisition of 51% of South Africa’s third largest drug company</td>
<td>215</td>
</tr>
<tr>
<td>Natur Produkt International/ Valeant</td>
<td>Acquisition of OTC company in Russia</td>
<td>185 (180 upfront + 5 potential milestones)</td>
</tr>
<tr>
<td>Gerot Lannach/ Valeant</td>
<td>Acquisition of branded generics with approximately 90% of sales in Russia and CIS countries</td>
<td>ca. 185 (up to 20 milestones)</td>
</tr>
<tr>
<td>Lundbeck / Recordati</td>
<td>Acquisition of non-core Lundbeck product portfolio primarily related to the US</td>
<td>100</td>
</tr>
<tr>
<td>Akvion Group/ Recordati</td>
<td>Acquisition of 5 product lines on the Russian and CIS market</td>
<td>87</td>
</tr>
<tr>
<td>Atlantis Pharma/ Valeant</td>
<td>Acquisition of certain assets in Mexico</td>
<td>71</td>
</tr>
<tr>
<td>Welichem Biotech / Stiefel GSK</td>
<td>Product acquisition WBI-1001 for psoriasis and atopic dermatitis (phase 2). Global rights acquired excluding China, Taiwan, Macao and Hong Kong with conditional right to acquire rights to the remaining markets for an additional payment of $14.5m</td>
<td>34+</td>
</tr>
</tbody>
</table>
Acquisitions for Emerging Markets

- Extending geographical outreach into fast growing markets remains a continuing trend
  - Key territories include: Russia, Eastern Europe, Brazil, India, China
- Generics players remain very active at tapping into these territories
  - Watson’s $5.9bn acquisition of Actavis brings a deeper presence in high growth markets, such as Eastern Europe and Russia
  - Valeant’s acquisition of Natur Produkt and Austrian generics player Gerot Lannach focuses on Russia and CIS
- Takeda and UCB both bought into Brazil
- Amgen’s $700m acquisition of Turkey’s Mustafa Nevzat (MN) Pharmaceuticals - an unusual move for a US biotech?
  - MN Pharmaceuticals is leading hospital supplier with major focus in injectables in Turkey
  - Fast growth in the Turkish and surrounding territories’ economies
  - Fits with Amgen’s international expansion plans

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<table>
<thead>
<tr>
<th>Licensor / Licensee</th>
<th>Comments</th>
<th>Territories</th>
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</thead>
<tbody>
<tr>
<td>MacroGenics / Servier</td>
<td>Discovery alliance with options for Dual-affinity Re-Targeting (DART™) platform technology for 3 cancer targets</td>
<td>Excluding US, Canada, Mexico, Japan, Korea and India</td>
<td>1,100</td>
</tr>
<tr>
<td>Astellas / Janssen</td>
<td>ASP015K for RA, psoriasis (phase 2)</td>
<td>WW excluding Japan</td>
<td>945</td>
</tr>
<tr>
<td>Onconova / Baxter</td>
<td>Estybon® (rigosertif) for Myelodysplastic Syndromes (phase 3) / pancreatic cancer (phase 2/3)</td>
<td>Europe</td>
<td>565</td>
</tr>
<tr>
<td>Thrombogenics / Alcon (Novartis)</td>
<td>Ocriplasmin for symptomatic vitreomacular adhesion (VMA) and additional vitreoretinal conditions (FDA-approved)</td>
<td>WW excluding US</td>
<td>490</td>
</tr>
<tr>
<td>Ironwood / AZ</td>
<td>Linaclotide, IBS with constipation (FDA approved)</td>
<td>China co-develop &amp; co-commercialise</td>
<td>150 (profit share)</td>
</tr>
<tr>
<td>AZ/ Impax Pharmaceuticals</td>
<td>Licences to rights to three versions of Zomig</td>
<td>US</td>
<td>130</td>
</tr>
<tr>
<td>Optimer Pharmaceuticals / Astellas</td>
<td>Collaboration / licence for antibiotic fidaxomicin for Clostridium difficile Infection (CDI) (approved US and EU)</td>
<td>Japan</td>
<td>90</td>
</tr>
<tr>
<td>Furiex Pharma / Menarini</td>
<td>Priligy® for premature ejaculation (launched/ phase 3)</td>
<td>Europe, most of Asia, Africa, Latin America and Middle East</td>
<td>75</td>
</tr>
<tr>
<td>Evotec / Zhejiang CONBA Pharmal</td>
<td>EVT401 for inflammatory diseases (phase 1)</td>
<td>China</td>
<td>75</td>
</tr>
<tr>
<td>Theravance / Alfa Wasserman</td>
<td>Velusetrag for gastroparesis (phase 2a)</td>
<td>EU, Russia, China, Mexico and other countries</td>
<td>64</td>
</tr>
<tr>
<td>Kamada / Chiesi</td>
<td>Distribution agreement for phase 2/3 stage Glassia, inhaled alpha-1 antitrypsin for cystic fibrosis</td>
<td>Europe, Turkey and former CIS countries</td>
<td>60</td>
</tr>
<tr>
<td>Ethical Oncology Science / Servier</td>
<td>E-3810, novel kinase inhibitor for breast cancer (phase 1/2)</td>
<td>WW excluding US, JP, China</td>
<td>58 (upfront)</td>
</tr>
<tr>
<td>Veloxis Pharma / Chiesi</td>
<td>LCP-Tacro™ (tacrolimus) immunosuppressant for kidney transplantation (phase 3)</td>
<td>Europe, Turkey and CIS countries</td>
<td>48</td>
</tr>
<tr>
<td>Newron / Zambon</td>
<td>Safinamide for Parkinson’s Disease (phase 3)</td>
<td>WW excluding Japan and key Asian territories</td>
<td>25</td>
</tr>
<tr>
<td>ProMetic Life Sciences / Hematech Biotherapeutics</td>
<td>Plasma-derived orphan drug - 50:50 co-development &amp; profit share</td>
<td>WW excluding China</td>
<td>10</td>
</tr>
</tbody>
</table>
Regional Licensing Deals

- Frequently the arena for the European mid-caps, deploying their marketing strengths
  - Servier, Chiesi, Menarini and Alfa Wassermann all completed regional deals for their key territories in 2012
- Single territory deals for later stage products, e.g.
  - Astellas took JP rights to Optimer’s *C. difficile* antibiotic fidaxomicin (US / EU approved) for $90m
  - In contrast, Astellas out-licensed ex-JP rights to phase 2 RA/ psoriasis drug to Janssen for $945m (of which $65m upfront)
  - AZ paid $25m upfront to license Ironwood’s FDA-approved linaclotide for China (phase 3) for IBS-C
- US (and other) biotechs with growth aspirations still focus on retention of US rights or US co-promotion rights, e.g.
  - Onconova granted Baxter a European licence for rigosertib, phase 3 anticancer compound in myelodysplastic syndromes for $565m ($50m upfront)
  - Thrombogenics (Belgium) granted Alcon ex-US rights to FDA-approved ophthalmic drug Ocriplasmin for $490m
  - This model will continue to provide attractive opportunities for the regional deal players such as Servier

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Biosimilars

- In 2012 US & EU regulators set the bar high, namely that a biosimilar has to follow the same basic principles of development as the original product and demonstrate there are no clinically meaningful differences in terms of safety, purity and potency.
- As a consequence, lengthy and high cost development blocks will mean mostly only the bigger companies will develop biosimilars, in collaboration with biological manufacturers and generic companies for commercialisation.
- So potentially Big Pharma will be competing with Big Pharma in biosimilars!

2012 Deals

<table>
<thead>
<tr>
<th>Company 1</th>
<th>Company 2</th>
<th>Development Details</th>
<th>Cost/Investment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Merck Serono</td>
<td>Dr Reddy’s</td>
<td>Co-development oncology Mabs</td>
<td>ND</td>
</tr>
<tr>
<td>Amgen / Watson</td>
<td>Synthon</td>
<td>Co-development Herceptin</td>
<td>ND</td>
</tr>
<tr>
<td>Pfizer</td>
<td>Biocon</td>
<td>Commercialisation alliance for insulin</td>
<td>$200m paid</td>
</tr>
</tbody>
</table>
## Option Agreements

<table>
<thead>
<tr>
<th>Licensor / Licensee</th>
<th>Subject</th>
<th>Headline (Upfront) $m</th>
</tr>
</thead>
<tbody>
<tr>
<td>MacroGenics/Servier</td>
<td>Option to 3 Dual-Affinity Re-Targeting (DART™) platform Technology for cancer targets</td>
<td>1,100</td>
</tr>
<tr>
<td>Selexys/Novartis</td>
<td>Option to acquire Selexys SelG1, humanised anti-P-selectin antibody to treat vaso-occlusive crisis in sickle cell disease</td>
<td>665</td>
</tr>
<tr>
<td>Isis/Biogen Idec</td>
<td>Option to licence antisense oligonucleotide ISIS-SMNRx, rare diseases spinal muscular atrophy</td>
<td>299 (29)</td>
</tr>
<tr>
<td>Isis/Biogen Idec</td>
<td>Option to a novel antisense drug for the treatment of myotonic dystrophy type 1</td>
<td>271 (12)</td>
</tr>
<tr>
<td>Epizyme/Celgene</td>
<td>Option to histone methyl transferase</td>
<td>250</td>
</tr>
<tr>
<td>Warp Drive Bio/Sanofi</td>
<td>Option to acquire as part of discovery deal for early drugs found in microbial genomes</td>
<td>125</td>
</tr>
<tr>
<td>BMS/The Medicines Company</td>
<td>A two year licence and option plus royalties to market a device to control bleeding during surgery</td>
<td>115</td>
</tr>
<tr>
<td>Constellation/Genentech</td>
<td>Option to acquire company with early stage epigenetic drug programmes</td>
<td>95</td>
</tr>
<tr>
<td>MAK scientific/Biogen Idec</td>
<td>Option to licence drug candidates modulating cannabinoid pathways in MS</td>
<td>34</td>
</tr>
<tr>
<td>Altacor/NicOx</td>
<td>Option to acquire UK ophthalmic business</td>
<td>30.9 (3.17)</td>
</tr>
<tr>
<td>Newron/Zambon</td>
<td>Option to the dual action MAO-B/ dopamine uptake inhibitor safinamide, targeting PD</td>
<td>26</td>
</tr>
<tr>
<td>Prosidion/AZ</td>
<td>Option to the Oral GPR119 receptor agonists PSN821 and PSN842 for type 2 diabetes</td>
<td>N/D</td>
</tr>
<tr>
<td>Biocon/BMS</td>
<td>Option to Biocon’s oral insulin IN 105</td>
<td>N/D</td>
</tr>
</tbody>
</table>
Options

- Companies are seeking risk averse approaches to protect their deal investments
- There has been an increase in the use of options for both licences and also acquisitions across the industry
- Clearly less attractive to the Licensor than a fully signed up deal
  - but other than the headline – does it differ from a licence if the Licensee has an ability to terminate at will?
# Agreement Terminations

<table>
<thead>
<tr>
<th>Originator</th>
<th>Partner</th>
<th>Agreement</th>
</tr>
</thead>
<tbody>
<tr>
<td>Anacor</td>
<td>GSK</td>
<td>GSK 2251052 agreement terminated following microbial resistance in patients in a phase 2b study in complicated UTI</td>
</tr>
<tr>
<td>Biocon</td>
<td>Pfizer</td>
<td>Development of biosimilar insulin and insulin analogues</td>
</tr>
<tr>
<td>BiolInvent / Thrombogenics</td>
<td>Roche</td>
<td>Licensing deal for TB-403 (antiplacental growth factor) terminated due to portfolio prioritisation</td>
</tr>
<tr>
<td>Cardiome</td>
<td>Merck</td>
<td>Development discontinuation of oral vernakalant for long term prevention of recurrence of atrial fibrillation</td>
</tr>
<tr>
<td>Medivation</td>
<td>Pfizer</td>
<td>Mediation’s dimebon failed to reach endpoints in its phase 3 trials for mild to moderate Alzheimer’s</td>
</tr>
<tr>
<td>Crucell</td>
<td>Royal DSM</td>
<td>Joint venture combining Crucell’s development technology with manufacturing know-how from Royal DSM</td>
</tr>
<tr>
<td>Jubilant</td>
<td>Lilly</td>
<td>Joint venture bought out by Jubilant</td>
</tr>
<tr>
<td>Auxilium</td>
<td>Pfizer</td>
<td>European marketing rights for Xiapex Dupuytren’s contracture closed</td>
</tr>
<tr>
<td>Pfizer</td>
<td>Amgen</td>
<td>Co-promotion of Enbrel in North America; Amgen to promote in US but not Canada</td>
</tr>
<tr>
<td>XenoPort</td>
<td>GSK</td>
<td>Commercialisation collaboration on Horizant (gabapentin enacarbil) extended release tablets for treatment of restless legs syndrome</td>
</tr>
<tr>
<td>Therabance</td>
<td>Astellas</td>
<td>Termination of World Wide license to co-market Telavancin (VIBATIV) once daily antibacterial</td>
</tr>
</tbody>
</table>
Terminations

- With the need to enforce performance throughout the life of an agreement, in the case that an asset is unlikely to reach its anticipated potential, companies are electing to hand back their rights.
- Occurring across a range of deals – commercialisation, joint ventures and licences.
- Varied rationales: strategic, portfolio prioritisation, lack of commercial prospects, poor scientific outcomes.
Leading Dealmakers

- The major movers and shakers in 2012 did a total of 81 deals as captured by Deal Watch between them:
  - AZ
  - GSK
  - J&J
  - Merck & Co
  - Pfizer
  - Roche

- The next tranche of activity came from a mix of “biotech wannabes”, “big pharma” and the new “Generics R us” namely; Amgen, Biogen Idec, BMS, Sanofi, Takeda, Watson Pharmaceuticals and Valeant
Roche through Genentech started the year with a collaboration and future option to acquire Constellation Pharmaceuticals and a patent settlement with Regeneron.

Roche’s biggest headlines though have been around the unsuccessful bid for Illumina ($5.7bn increased to $6.5bn).

Other deals struck in the year have focused on pipeline consolidation in Alzheimer’s Disease, anti-infectives and oncology.

Examples of Roche Deal Activity:
- In-licensing
  - Antibodies targeting FGF2 from Galaxy Biotech for oncology indications
- Drug discovery collaborations -
  - Constellation Pharmaceuticals epigenetic programmes
  - AC Immune in Alzheimer’s disease
  - Savira for anti-infectives
- Patent settlement
  - Regeneron
Merck

- Merck has been busy gaining access to platform technologies for novel drug discovery and development, as well consolidating its position in key therapeutic areas via in-licensing; antivirals, CNS, cardiovascular disease, while doing some out-licensing in oncology.

- Examples of Merck Deal Activity
  - In-licensing -
    - AiCuris for HCMV therapeutics
    - Chimerix’s CMX 157 for HIV
  - Drug discovery collaborations –
    - Ablynx for Nanobodies
    - Ambrx for site specific conjugation chemistry
    - Theravance therapeutics hypertension & heart failure
  - Out-licensing -
    - PARP Inhibitor MK-4827 for oncology indications to Tesaro Pharma

Bridget Lacey
J&J

- J&J has been busy gaining access to platform technologies for novel drug discovery and development, as well consolidating its position in key therapeutic areas via in-licensing; in antivirals, CNS, oncology and autoimmune disease
- Examples of J&J Deal Activity
  - In-licensing
    - Evotec for NMDA antagonists for depression
    - Genmab Daratumumab in multiple myeloma
    - Astellas’ oral JAK inhibitor for RA and psoriasis
  - Drug discovery collaborations –
    - Evotec/ Harvard for regeneration of insulin producing beta cells
    - Genmab for bispecific antibodies
    - Immunext for novel cancer therapeutics
  - Development collaborations –
    - BMS in combination HCV antivirals

Bridget Lacey
GSK

- Besides the acquisition of HGS, GSK has been forging and extending collaborations in the drug discovery area, including deals in the orphan diseases and in respiratory diseases.

- Examples of GSK Deal Activity
  - **Acquisitions**: HGS
  - **Drug discovery collaborations**
    - Angiochem for lysosomal storage diseases
    - FivePrime Therapeutics in refractory asthma & COPD
  - **Joint Venture**: Daiichi Sankyo for vaccines in Japan – aiming to be the leading vaccine company in Japan
  - **Divestment**: Non-core OTC brands to Aspen – the last of a series with total proceeds exceeding $1.5bn
  - **Terminations**
    - Anacor for UTI
    - Xenoport for Horizant

Bridget Lacey
Pfizer’s activities in the first half of the year focused on the **divestiture of its infant nutrition business to Nestlé** and the terminations with Biocon for biosimilars and with Amgen for US marketing of Enbrel. Later in the year, Pfizer embarked on a series of acquisitions. It finished the year in a series of creative funding for early stage research.

**Examples of Pfizer Deal Activity**

- **Acquisitions** -
  - Nexium OTC rights from AZ
  - NextWave for Quillivant XR for ADHD

- **Drug discovery collaborations** -
  - Halozyrne for biologics delivery

- **Terminations** - Biocon for biosimilars
  - Amgen for US marketing of Enbrel

- **Early stage research partnerships** -
  - Neomed Institute
  - AZ/Cystic Fibrosis Foundation

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**Bridget Lacey**
Astra Zeneca

- AZ has been hit hard by generic competition and is facing rapidly declining sales on 3 blockbusters (amounting to $15bn in US sales alone in the next 3 to 4 years)
- As a result AZ has begun to, and will continue to undertake a series of bolt on acquisitions, in-licensing, collaborations and other transactions
- Examples of AZ Deal Activity
  - Acquisition
    - Ardea Biosciences
  - In-licensing
    - Rigel’s R256, inhaled JAK inhibitor
  - Collaborations
    - Amgen for anti-inflammatory mAbs
    - BMS for diabetes post Amylin acquisition
    - Isis Pharmaceuticals for antisense drug discovery
  - Divestment/out-licensing
    - Nexium OTC rights sold to Pfizer
    - Product tail portfolio to Alliance

Bridget Lacey
Alliances: Big pharma / big pharma collaborations

A sign of the times: large pharma increasingly prepared to work with competitors to rescue compromised assets, enable deal execution and for straightforward commercial advantage

- AstraZeneca – a case history
  - The $7bn BMS acquisition of Amylin made possible by AZ entering the fray with $3.4bn.
    - The prize: 2 GLP-1 receptor agonists; Byetta and its long acting stable-mate Bydureon; the leptin analogue Metreleptin currently under FDA review; Symlin
- AZ / Amgen – a match made in heaven – Amgen’s pipeline overflows into AZ’s empty bowl!
  - The prize: Amgen secures the resources and respiratory / inflammation expertise to advance 5 mAB including the Phase 3 Brodalumab; AZ breaths life into its barren coffers!
- AZ / Pfizer - $250m upfront plus milestones and royalties for exclusive global rights to the OTC version of Nexium
  - The prize: Pfizer boosts its consumer health business; AZ maximises revenues upon patent expiry

Margaret Beer
### Alliances: Industry/academia

<table>
<thead>
<tr>
<th>Industry / Academic partner</th>
<th>Areas covered</th>
<th>Headline $m</th>
</tr>
</thead>
<tbody>
<tr>
<td>GSK University of Texas MD Anderson Cancer Center</td>
<td>New therapeutic antibodies to promote an immune attack against cancer. WW rights to develop antibodies which activate OX40 on the surface of T cells</td>
<td>335 + royalties</td>
</tr>
<tr>
<td>Novartis University of Pennsylvania</td>
<td>A multi-year collaboration to study chimeric antigen receptor (CAR) technology and develop personalised T-cell therapy for cancer, novel cancer immunotherapies</td>
<td>20</td>
</tr>
<tr>
<td>UCB Oxford University</td>
<td>5-10 Immunology / neurology projects over 3 years</td>
<td>£3.6m over 3 years</td>
</tr>
<tr>
<td>UCSF</td>
<td>Type 1 and Type 2 diabetes</td>
<td>3.1</td>
</tr>
<tr>
<td>J&amp;J Queensland University</td>
<td>Spider venom peptides, ion channel pathway inhibitors for the treatment of chronic pain</td>
<td>N/D</td>
</tr>
<tr>
<td>Novo Nordisk Oxford University, Kennedy Inst Rheumatology</td>
<td>Drug candidates and novel biomarkers and targets for RA and other autoimmune inflammatory diseases</td>
<td>N/D</td>
</tr>
<tr>
<td>Novo NordiskJuvenile Diabetes Research Foundation (JDRF)</td>
<td>Autoimmune disorder - focus on T1DM</td>
<td>N/D</td>
</tr>
<tr>
<td>BMS Vanderbilt University</td>
<td>mGluR4 glutamate receptor PAMs – PD</td>
<td>N/D up front research funding, milestones royalties</td>
</tr>
<tr>
<td>Sanofi Brigham &amp; Women’s Hospital / Harvard</td>
<td>Immunomodulatory therapies for T1DM</td>
<td>N/D</td>
</tr>
<tr>
<td>GSK Yale</td>
<td>PROTACs - proteolysis targeting chimeric molecules to target disease-causing proteins in cancer, inflammation, infectious disease</td>
<td>N/D milestone s royalties</td>
</tr>
<tr>
<td>AZ The Broad Institute</td>
<td>NCEs - anti-bacterials, anti-virals2 year collaboration</td>
<td>N/D</td>
</tr>
<tr>
<td>AZ, Weill Cornell Medical College, Washington University School of Medicine, Feinstein Institute, University of British Columbia</td>
<td>The A5 alliance - Apolipoprotein E4 genotype (ApoE) targeting Alzheimer’s disease</td>
<td>N/D</td>
</tr>
<tr>
<td>Accuray University Heidelberg</td>
<td>Radiation oncology research to provide tools to treat patients</td>
<td>N/D</td>
</tr>
<tr>
<td>Daiichi Sankyo Japanese National Cancer Centre</td>
<td>To create anticancer agents using research capabilities of both organisations</td>
<td>N/D</td>
</tr>
</tbody>
</table>
Alliances: Industry/academia

Cutting out the middle man: big pharma increasingly directly engaging with academics. Oncology, autoimmune diseases and neuroscience being areas favoured in 2012

- Of particular note, the $335 plus royalties GSK / MD Anderson Cancer Center deal to develop novel immune promoting ABs for the treatment of cancer
  - Large pharma finding not only do they have to pay big but also share potential future spoils
  - Exemplified also with the BMS / Vanderbilt PD collaboration based on mGluR4 glutamate receptor PAMs; the GSK/Yale collaboration utilising proteolysis targeting chimeric molecules (PROTACs)

- An evolving trend in industry / academic alliances is the formation of consortia giving pharma access to governmental and not-for-profit organisation funding.
  - “European Autism Interventions” - King’s College London, Roche, Eli Lilly, Servier, Janssen, Pfizer accessed $38.7m from the EU's Seventh Framework Programme
  - “TB Drug Accelerator” - Texas A&M University, Weill Cornell Medical College, Abbott, AZ, Bayer, Eli Lilly, GSK, Merck, Sanofi - part funded by a $20m grant from the Bill & Melinda Gates Foundation

- Will these industry/academic strategic alliances capitalising on each other’s strengths offer a lifeline to the beleaguered industry?
  - the expertise and free-thinking commitment of academia
  - the drug discovery know-how, discipline, regulatory experience and marketing acumen of industry.

- Only time will tell!
Conclusions

- 2012 saw a down turn in overall values
- With the continuing difficult global economic circumstances, more risk averse approaches were being taken with an increase in the use of options and terminations
- New money from PE and NGOs has been coming in to replace the lower investments from VCs
- So, will the trends we have seen continue?
And so into January...

- Licensing continues but still risk averse
  - MacroGenics/Gilead $1bn for access to 4 undisclosed targets from the DART platform; following the pack: Servier, BI and Pfizer!
- And yet more acquisitions!
  - Map/Allergan $958m securing Levadex in migraine - building the portfolio
  - Uteron/Watson $305m extending its women’s health franchise
- Emerging Markets / Options
  - Celsion/Zhejiang Hisun an exclusive option to Thermodox (phase 3) in liver cancer in China; headline value $125+
- Terminations
  - Novartis discontinues the development of Cytos’ NIC 002 in smoking cessation
- Continued NGO involvement
  - Wellcome Trust invest $200m in Syncona Partners
- Early stage alliances / rare diseases
  - Baylor Research Institute / Ultragenyx - in licensing of triheptanoin for long-chain fatty acid oxidation disorders
Deal Watch Team

With thanks to the Deal Watch reporting team!

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Roger Davies

Bridget Lacey

Jill Ogden

http://www.medius-associates.com/deal-watch/