LICENSING DEALS FORECASTS

The next five years and future deal values

Sharon Finch, CEO
Outline

- Current deal landscape
- Deal values and trends
- Conclusions

Deal Watch: Current Trends in Deals
www.medius-associates.com/deal-watch/

Based on Medius monthly review of pharma deals which captures the top deals by value.
20 years of progress: volume of deals

- 10 x more deals, 3 x more big pharma deals
- NGOs now high number of reported valued deals
- Big pharma becoming more shy? 1994: 50% of deals valued vs 27% today

Volume has increased, what about values?
20 years of progress: price of deals

Average deal values
- Big Pharma 8-10 x higher
- Other pharma 6-7 x higher
### Major Pharma pays more upfront

<table>
<thead>
<tr>
<th></th>
<th>Case study Feb 1994</th>
<th>Case study Feb 2014</th>
</tr>
</thead>
<tbody>
<tr>
<td>Licensor/Licensee</td>
<td>Onyx/Bayer</td>
<td>Ablynx/Merck</td>
</tr>
<tr>
<td>Headline deal value</td>
<td>$40m</td>
<td>$2.3bn</td>
</tr>
<tr>
<td>Financials</td>
<td>Equity $13.5m</td>
<td></td>
</tr>
<tr>
<td></td>
<td>R&amp;D $25m</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Upfront $27m</td>
</tr>
<tr>
<td></td>
<td></td>
<td>R&amp;D $14m</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Multiple products</td>
</tr>
<tr>
<td></td>
<td></td>
<td>milestones $2.3 bn</td>
</tr>
<tr>
<td>Product / technology</td>
<td>Raf kinase inhibitors</td>
<td>Nanobodies</td>
</tr>
<tr>
<td>Development status</td>
<td>Research</td>
<td>Research</td>
</tr>
<tr>
<td>2013 product sales</td>
<td>Nexavar $1bn</td>
<td></td>
</tr>
</tbody>
</table>

- Big pharma **entry price** for Ablynx deal 2 x Onyx deal
- But, **overall deal cost** to get to proof of concept similar

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Volume and value of deals has increased, have deal terms changed?
Deal Terms: issues remain the same

<table>
<thead>
<tr>
<th>Terms</th>
<th>Onyx - Bayer</th>
</tr>
</thead>
<tbody>
<tr>
<td>Initial term</td>
<td>5 year research 1994-99 Amendment - 96, 99 (co-devt), 06 (co-pro)</td>
</tr>
<tr>
<td>Clinical development</td>
<td>Co-development excl. Japan (100% Bayer) Cost split 50/50 Managed by Joint Development Committee</td>
</tr>
<tr>
<td>Onyx option to co-promote in US if Onyx shares development costs</td>
<td>94: Based on profit/(loss) share (Recognition given to Bayer’s investment in S&amp;M infrastructure) 06: Managed by Committee who determine strategy and budget Equal numbers of sales reps, Bayer marketing services shared, Bayer distributes and receives a fixed % of sales</td>
</tr>
</tbody>
</table>

Deal terms appear not to have changed much, so what has?
Pharma Environment: impact on deals

**INTERNAL**
- Productivity down
- Cost up
- Competition 3rd party assets
- Early stage deals, higher values
- Co-promotion

**EXTERNAL**
- VC and IPO funding dries up
- Risk aversion greater
- Options, mainly early stage deals
- Regulatory hurdles higher
- Rx prices down, market access
- Financial regulations tougher
- Orphan drugs, medical devices, supply and technical agreements
- Health economics, market entry
- Revenue recognition, tax and transfer pricing

**Co-development deals**
- Acquisition one prod/tech companies
- Big pharma collaborations (+ Govt)

**Acquisition of brands**
- Generic settlements, exclusive distributor
- Emerging market collaborations

**Emerging markets**
- Pharma competition tougher
- Generics growth
- OTC growth, POM to P

**Funding by NGOs, pharma VCs**
- Acquisition deals resemble licences
- Royalty monetisation
Current trends

**THERAPEUTIC FIELDS**
- Oncology the next generation antibodies: ADCs
- Other areas: CNS e.g. MS, Parkinson’s, Alzheimer’s

**RISK MANAGEMENT**
- Options or first right of refusal
  - to buy company or product
  - to co-development or co-commercialise
  - to license leads (e.g. platform deals)

**EQUITY**
- Buying into TAs or technologies, product portfolios/turnover
- Consolidating businesses
- Building geographic outreach
- As a means of risk management

**HEADLINE VALUES**
- Values around $1bn include multiple candidates or targets
- Additional indications
- Upfronts are not always quoted
- Focus on Bio$ being as large as possible can be misleading
## RNA based therapeutics: back in vogue?

<table>
<thead>
<tr>
<th>Year</th>
<th>Event</th>
</tr>
</thead>
<tbody>
<tr>
<td>2006</td>
<td>Merck &amp; Co buys Sirna for $1.1bn</td>
</tr>
<tr>
<td>2010</td>
<td>Alnylam reports ALN-PCS P1 data</td>
</tr>
<tr>
<td>2011</td>
<td>ISIS/Genzyme Kynamro approved</td>
</tr>
<tr>
<td>2012</td>
<td>ISIS signs multiple partners</td>
</tr>
<tr>
<td>2013</td>
<td>Moderna/AZ and Alexion</td>
</tr>
<tr>
<td>2014</td>
<td>Dicerna IPO</td>
</tr>
</tbody>
</table>

**Buying IN**
- Merck & Co buys Sirna for $1.1bn
- Alnylam reports ALN-PCS P1 data
- ISIS/Genzyme Kynamro approved
- ISIS signs multiple partners
- Moderna/AZ and Alexion
- Dicerna IPO

**EXITING**
- Roche exits RNAi
- Merck & Co closes Sirna/RNAi
- Pfizer exits RNAi
- Novartis exits RNAi

**NB:** Only selected company deals shown
## Hepatitis C strategic deals

<table>
<thead>
<tr>
<th>Date</th>
<th>Licensor/Target</th>
<th>Licensee/Acquiror</th>
<th>Product</th>
<th>Status</th>
<th>Approach</th>
<th>Headline value $</th>
</tr>
</thead>
<tbody>
<tr>
<td>June 14</td>
<td>Idenix</td>
<td>Merck &amp; Co</td>
<td>Samtasvir NS5A inhibitor</td>
<td>P2</td>
<td>Acquisition bid</td>
<td>3.9 bn</td>
</tr>
<tr>
<td>June 14</td>
<td>OraSure</td>
<td>AbbVie</td>
<td>Diagnostic for hepatitis C</td>
<td></td>
<td>Co-promotion point of care testing</td>
<td>Up to $75m</td>
</tr>
<tr>
<td>April 13</td>
<td>BMS</td>
<td>Merck</td>
<td>Daclatasvir and MK 51722</td>
<td>P2</td>
<td>Non exclusive co-development</td>
<td>ND</td>
</tr>
<tr>
<td>April 13</td>
<td>Ascletis</td>
<td>Roche</td>
<td>Danoprevir</td>
<td>P2</td>
<td>Partner in China</td>
<td>ND</td>
</tr>
<tr>
<td>April 13</td>
<td>BMS</td>
<td>Vertex</td>
<td>Daclatasvir and VX 135</td>
<td>P2</td>
<td>Co-development</td>
<td>ND</td>
</tr>
<tr>
<td>Jan 13</td>
<td>Idenix</td>
<td>J&amp;J</td>
<td>IDX 719 Simeprevir TMC 647055</td>
<td>P2</td>
<td>Non exclusive collaboration</td>
<td>ND</td>
</tr>
<tr>
<td>Nov. 12</td>
<td>Vertex</td>
<td>GSK</td>
<td>GSK 2336805 / VX135</td>
<td>P2</td>
<td>Non exclusive co-development</td>
<td>ND</td>
</tr>
<tr>
<td>Nov. 12</td>
<td>Vertex</td>
<td>J&amp;J</td>
<td>Simeprevir / VX135</td>
<td>P2</td>
<td>Non exclusive co-development</td>
<td>ND</td>
</tr>
<tr>
<td>April 12</td>
<td>BMS</td>
<td>J&amp;J / Medivir</td>
<td>Daclatasvir / TMC 435 plus BMS 986094</td>
<td>P2</td>
<td>Co-development extension of earlier agt.</td>
<td>ND</td>
</tr>
<tr>
<td>Feb 12</td>
<td>Enanta</td>
<td>Novartis</td>
<td>EDP 239 NS5A</td>
<td>PC</td>
<td>Exclusive global licence, US copromotion</td>
<td>440m</td>
</tr>
<tr>
<td>Jan 12</td>
<td>Inhibitex</td>
<td>BMS</td>
<td>INX 189 / BMS 986094</td>
<td>P2</td>
<td>Acquisition</td>
<td>2.5 bn</td>
</tr>
<tr>
<td>Dec 11</td>
<td>J&amp;J Tibotec</td>
<td>BMS</td>
<td>TMC 435</td>
<td>P2</td>
<td>Collaboration</td>
<td>ND</td>
</tr>
<tr>
<td>Nov 11</td>
<td>Pharmasset</td>
<td>Gilead</td>
<td>Solvadi / PSI 7977</td>
<td>P3</td>
<td>Acquisition; $137 per share</td>
<td>10.8 bn</td>
</tr>
<tr>
<td>June 11</td>
<td>Vertex</td>
<td>Alios BioPharma</td>
<td>ALS 2200/ALS 2158 polymerase inhibitors</td>
<td>Approved</td>
<td>Global licence</td>
<td>1.525 bn 60m upfront</td>
</tr>
</tbody>
</table>
## Oncology: recent deals

<table>
<thead>
<tr>
<th>Licensor/Target</th>
<th>Licensee/Acquiror</th>
<th>Deal type</th>
<th>Product / technology</th>
<th>Headline $</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ablynx</td>
<td>Merck</td>
<td>Collaboration</td>
<td>Nanobody candidates to target “immune checkpoint modulators”</td>
<td>2,331</td>
</tr>
<tr>
<td>Cellectis</td>
<td>Sevier</td>
<td>Licence</td>
<td>Product candidates for solid tumours, UCART19 (allogenic CAR-T) for leukaemia and lymphomas (6 candidates in total)</td>
<td>850</td>
</tr>
<tr>
<td>Amplimmune</td>
<td>AZ</td>
<td>Acquisition</td>
<td>Novel immuno cancer therapeutics</td>
<td>500</td>
</tr>
<tr>
<td>Five Prime Therapeutics</td>
<td>BMS</td>
<td>Collaboration, licence</td>
<td>Drug discovery against 2 undisclosed targets in immune checkpoint pathways</td>
<td>350.5</td>
</tr>
<tr>
<td>GSK</td>
<td>Adaptimmune</td>
<td>Collaboration and licensing agreement</td>
<td>TCR engineered T cells which target NY ESO 1 and other targets in oncology</td>
<td>350</td>
</tr>
<tr>
<td>AnaptysBio</td>
<td>Tesaro</td>
<td>Collaboration, licence</td>
<td>mAbs to activate immune system response &quot;checkpoints&quot; - 3 targets: TIM-3, LAG-3 and PD-1 (preclinical)</td>
<td>341</td>
</tr>
<tr>
<td>Immunocore</td>
<td>AZ Medimmune</td>
<td>Collaboration and licence</td>
<td>Immune mobilising monoclonal T-Cell receptor against cancer (ImmTAC) therapies</td>
<td>320</td>
</tr>
<tr>
<td>Cellectis</td>
<td>Pfizer</td>
<td>Collaboration</td>
<td>Chimeric Antigen Receptor T-cell (CAR-T) immunotherapies directed at select oncology targets</td>
<td>265</td>
</tr>
<tr>
<td>Agios</td>
<td>Celgene</td>
<td>Option to exclusive licence</td>
<td>AG 221 first in class mutant IDH2 protein inhibitor</td>
<td>120+</td>
</tr>
<tr>
<td>Agenus</td>
<td>Merck</td>
<td>Collaboration</td>
<td>Therapeutic antibodies to immune checkpoint modulators</td>
<td>100+</td>
</tr>
<tr>
<td>Licensor/Target</td>
<td>Licensee/Acquiror</td>
<td>Deal type</td>
<td>Product / technology</td>
<td>Headline value $</td>
</tr>
<tr>
<td>----------------</td>
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<td>-----------------</td>
</tr>
<tr>
<td>Novo Nordisk</td>
<td>Innate Pharma</td>
<td>Licence with equity partial payment</td>
<td>P2 ready Anti-NKG2A antibody “immune checkpoint inhibitor”</td>
<td>30</td>
</tr>
<tr>
<td>CoStim</td>
<td>Novartis</td>
<td>Acquisition</td>
<td>Novel immuno modulating targets</td>
<td>Not disclosed</td>
</tr>
<tr>
<td>Aurigene</td>
<td>Pierre Fabre</td>
<td>Collaboration</td>
<td>AUNP – 12 immune checkpoint modulator</td>
<td>Not disclosed</td>
</tr>
<tr>
<td>Morphosys</td>
<td>Merck Serono</td>
<td>Collaboration</td>
<td>Immune checkpoints developed from the Morphosys Ylanthia platform</td>
<td>Not disclosed</td>
</tr>
<tr>
<td>Juno</td>
<td>Novartis</td>
<td>Collaboration</td>
<td>Study of chimeric antigen receptor (CAR) technology for the treatment of cancer including CART 13</td>
<td>Not disclosed</td>
</tr>
</tbody>
</table>
## Risk management: options for everything, building flexibility

### Licensee Perspective

- To license lead development candidates for development/commercialisation:
  - Resolve/Takeda collaboration for SLE; option to license lead and all other compounds from platform on completion of P1b/2a
  - To extend term of research alliance [Ablynx/Merck Serono extend 4 yr alliance with option to extend by 2.5 yr]
- To license technology for specific candidates (e.g. drug delivery)
- To acquire company [Acetylon/ Celgene collaboration on oral, selective HDAC inhibitors in oncology; option to acquire with independent valuation, min upfront $500m]

### Licensor Perspective

- Options to enable biotech to take an increased stake in downstream value i.e. to co-commercialise
- To co-promote typically in the US:
  - Prothena/ Roche collaboration on PRX002 for Parkinson’s disease; co-promotion in US
- To co-develop/ cost and profit share or convert to license global rights with milestones and royalties:
  - Ablynx/Merck Serono collaboration on Nanobodies for osteoarthritis
Options pros and cons

**Licensor**
- Validation of platform and value in PR
- Some income – potentially big headline
- Ties up targets or programmes without long term commitment (strategic poison pills)
- Importance of tight/narrow fields
- Managing option timelines and decision process – danger of “option period creep”
- Ownership of new IP, results etc
- Reversion of rights if option not exercised
- Co-commercialisation potential downstream

**Licensee**
- Caters for the risk averse – manage/share the development risk
- Ring fences specific discovery targets or programmes/protects from competition
- Buys time to evaluate platform and data, consider overall strategic objectives/how a field develops
- May be relatively small upfront + R&D funding to cover initial option period
- Keep “toe in the water” don’t need to commit until later

As broad options will (most likely) have pre-negotiated terms for a licence why not enter into a licence that the Licensee has an ability to terminate at will?
Shifts in strategic direction

- Novartis acquires GSK’s oncology with an option to the future pipeline for $14.5bn [+$1.5bn m/s]
- GSK acquires Novartis’ vaccines excluding ‘flu for $7.1bn
- Lilly acquires Novartis animal health franchise for $5.4bn
- Novartis and GSK Consumer form a JV with t/o of $10.9bn
- Bayer acquires Merck & Co’s OTC for $14.2bn
  - High price paid, 6.5x sales; 21x EBITDA
  - Bayer targets global leadership following acquisitions in Germany and China
- Divestments
  - GSK planned divestment of mature products
  - Merck moving out of ophthalmology
  - AbbVie move into orphans via Shire? Bid made of $46bn
Novartis
2013 sales $57.9bn

Prescription Drugs
$32.2bn

Eyecare
$10.5bn

Generics
$9.2bn

Consumer Health
$2.9bn [Animal Health $1.1bn]

Vaccines
$1.4bn

Novartis acquires GSK’s oncology products for $14.5bn + $1.5bn contingent on milestones

GSK acquires Novartis’ vaccine franchise (excl. flu) for $5.25bn upfront + $1.8bn milestones + royalties

Eli Lilly acquires Novartis’ Animal Health franchise for $5.4bn cash

GlaxoSmithKline
2013 sales $44.5bn

Prescription Drugs
$30.1bn
Cancer Drugs $1.63bn

Consumer Health
$8.7bn

Vaccines
$5.7bn

Consumer Health JV [63.5% GSK owned] $11bn*

2013 sales by divisions provided/ *based on 2013 pro forma revenues
Headline values

• Early stage deals are typically multiple programme deals for drug discovery against specific (but often undisclosed) targets
• What is behind the headlines? Multiple elements:
  – Upfront / access fee; R&D funding; milestones per programme for reaching development/ clinical/ regulatory hurdles
  – Options to license drug candidates for development and commercialisation
  – Equity stake [occasionally] tiered royalties in xx digit range
• May include additional options:
  – For licensor to co-promote, to co-fund and co-develop
  – For licensee to acquire company/ IP/ product, extend option period, + further targets

<table>
<thead>
<tr>
<th></th>
<th>2014 Q1</th>
<th>2013</th>
<th>2012</th>
<th>2011</th>
</tr>
</thead>
<tbody>
<tr>
<td>Quoted headline figure ($m)</td>
<td>88 – 2,330</td>
<td>100 – 1,182</td>
<td>186 – 1,463</td>
<td>178 - 888</td>
</tr>
<tr>
<td>Value per programme ($m)</td>
<td>108 - 320</td>
<td>97 - 320</td>
<td>30 - 350</td>
<td>61 - 236</td>
</tr>
<tr>
<td>Upfront as % headline</td>
<td>1 – 7</td>
<td>1 – 13*</td>
<td>1 – 8</td>
<td>1 – 9</td>
</tr>
</tbody>
</table>

• Selected data for 1997-9 shows discovery deals of headline ranges $25-64m
Summary and Conclusions
Where next?

Over the last 20 years there have been more deals, higher prices, changes in deal structure and content essentially driven by:

- Higher regulatory hurdles
- Pressure on Govt. budgets
- Increased generic competition
- Risk aversion

• Looking out for the next 5+ years: more of the same plus
  - More partnership deals between pharma companies
  - More Govt. funded programmes in ‘uneconomic’ therapeutic areas
  - Increasing NGO funding of early stage companies
  - Big pharma moving away from conglomerate structure
  - Larger generic companies diversifying out of commodity business
  - Biosimilars forcing big pharma to compete with big pharma
  - The demise of the GP salesforce in Western Europe
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