Partnering with Big Pharma: Is it changing or still the same?

European Business Development Conference for Pharma and Biotech

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22-23 Nov 2015, Antwerp, Belgium
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The Bio-Pharma landscape today and its future
Challenges Ahead
PWC: Pharma 2020 – From Vision to Decision

There’s arguably a bigger hurdle facing pharma: namely, the rising healthcare bill.

Healthcare expenditure as a percentage of gross domestic product (GDP) is climbing in countries in every income bracket, and it’s climbing most steeply in the mature markets where the industry has historically made most of its money.

Maximising the Molecule
“A thing is worth only as much as it can be sold for”

- Affordable care!
- Outcomes lever!
- The value dilemma: What is it worth?
- Collect real-world evidence
- Measure the feel factor
- Develop companion diagnostics
- Reinforce the power of the pill
  - Ingestible microchips
  - Mobile health applications
  - Remote monitoring devices and apps
  - Gamification of healthcare

But if the industry is to prosper in the future, it must first make sure it has a future.

Major scientific and technological advances, coupled with socio-demographic changes, increasing demand for medicines and trade liberalisation, will revive pharma’s fortunes and deliver dramatic improvements in patient care.
The changing big picture for Healthcare companies

- Change corporate culture
  - Create more value for patients, care providers, payers!
  - Ethical behavior at all times – be an organizations other want to associate with

- Increase R&D productivity
  - Early and bold pipeline decisions; decide and stick with rules; know when it’s time to quit
  - Build disease expertise and category leadership
  - Collaborate broadly with academia, government, non-government organizations, patient organizations, etc - access to best innovation

- Real-world data on outcomes
  - Payers want more value for their money and they establish performance measure
  - Value/ outcome based reimbursement

- Invest in growth markets
  - But it comes with its own challenges: Value vs. Volume?
  - How to serve the broad low income population and still make a profit?
Key challenges to Big Pharma’s R&D portfolio

Implications for partnering with Big Pharma

Pharma’s Challenges
- Ever increasing R&D costs
- Need to improve productivity, ROI, margins
- Out-come, value based prescription, pricing
- Personalized medicine, patient segmentation; orphan indications
- Limited health care budgets
  - Compulsory licensing
- Make health care affordable in emerging markets
- “Patent cliff”
- Shorter exclusivity due to stronger generics/ bio-similars pressures

Biotech’s Challenges & Opportunities
- Pharma not anymore the party that can easily fund phase III
- Need more risk- and cost-sharing approaches to collaboration
- Cannot rely anymore on quick exit after PoC
  - Need to be strong on science and development capabilities
  - No “quick and dirty” PoC studies but define best target patients and product profile ("right drug to right patient at right time")
- Regulatory approval is not the goal anymore but only a step on the path to commercialization
  - Consider market access, pricing, HEOR
  - Consider development outside US and EU
- Challenges but also opportunities in areas of non-traditional Pharma spaces
  - eHealth, devices, diagnostic, biomarkers (screening, monitoring)
The R&D challenge: high attrition - low productivity

“The great tragedy of science – the slaying of a beautiful hypothesis by an ugly fact.”
Thomas Huxley

Eroom’s Law

<table>
<thead>
<tr>
<th>NMEs per $B</th>
</tr>
</thead>
<tbody>
<tr>
<td>100</td>
</tr>
<tr>
<td>10</td>
</tr>
<tr>
<td>1</td>
</tr>
<tr>
<td>0.1</td>
</tr>
</tbody>
</table>

Attrition

<table>
<thead>
<tr>
<th></th>
<th>PC</th>
<th>Ph.I</th>
<th>Ph.II</th>
<th>Ph.III</th>
</tr>
</thead>
<tbody>
<tr>
<td>1990-94</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>2004-08</td>
<td>∆15%</td>
<td>∆68%</td>
<td>∆69%</td>
<td>∆165%</td>
</tr>
</tbody>
</table>

Source: Bernstein Research “The Long View – R&D Productivity” (September 30, 2010), and Pammoli et. al, “The productivity crisis in pharmaceutical R&D” NRDD, June 2011
How to increase R&D efficiency:

*NOT size (small or big) matters but...*

...it is factors such as great science and an organization tuned to rewarding the right behaviors - not structural factors such as company size - that will ultimately drive renewed R&D productivity.


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**Reduce rate of failure**

- %

**Reduce spend per failure**

- $

**Better decision-making**

**Scientific acumen:** capability and information

**Judgment behavior:** collective intelligence, cooperation and energy

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**Indicators of scientific acumen**
- Scientific track record (prior years)
- Publication per $R&D$
- Patents per $R&D$
- Citations per publication
- R&D in a science hub

**Indicators of good judgment**
- R&D tenure (prior years)
- Frequent mention of ROI
- Frequent mention of ‘decision-making’
- Early termination of projects

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**Factors correlated with success or failure in drug development.** These factors (laid out as in FIG. 1) have a statistically significant relationship with success or failure in our data set of 842 molecules. For details of the data set and analysis, see Supplementary information S1 (box). R&D, research and development; ROI, return on investment.
What matters in successful collaborations/ deal making?

What do "sell-side" partners value most?

<table>
<thead>
<tr>
<th>Attribute</th>
<th>Average</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ability to add value to your compound/TA of interest</td>
<td></td>
</tr>
<tr>
<td>Allows partners to develop and prosper</td>
<td></td>
</tr>
<tr>
<td>Creativity and flexibility on deal terms</td>
<td></td>
</tr>
<tr>
<td>Executive leadership committed to partnering</td>
<td></td>
</tr>
<tr>
<td>Clinical capability</td>
<td></td>
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<tr>
<td>Responsiveness during the deal negotiations</td>
<td></td>
</tr>
<tr>
<td>Global / international reach</td>
<td></td>
</tr>
<tr>
<td>Regulatory capability</td>
<td></td>
</tr>
<tr>
<td>BD/licensing group easy to access</td>
<td></td>
</tr>
<tr>
<td>Willingness to pay the highest price</td>
<td></td>
</tr>
<tr>
<td>Sales / marketing capability</td>
<td></td>
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<tr>
<td>Fit with corporate culture</td>
<td></td>
</tr>
<tr>
<td>Pricing, access and reimbursement capability</td>
<td></td>
</tr>
<tr>
<td>Alliance management</td>
<td></td>
</tr>
<tr>
<td>Allows partners to retain control in dev</td>
<td></td>
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<tr>
<td>Medical affairs capability</td>
<td></td>
</tr>
<tr>
<td>Research capability</td>
<td></td>
</tr>
<tr>
<td>HEOR capability</td>
<td></td>
</tr>
<tr>
<td>Manufacturing capability</td>
<td></td>
</tr>
</tbody>
</table>

Implications for "buy side"

Value creation expertise ranked first, yet partnering skills increasingly sought for
- Commercial, Regulatory, Pricing / access capabilities are table stakes
- Allowing partners to develop and prosper and to maintain control is important

Perceptions of partnering skills can be impacted (positively or negatively) even in the short term

Complacency not an option as partnering market becomes ever more competitive

Managing negative perceptions is key, especially among those companies that you actually engage with!

Source: BCG survey of Biotech CEOs and Licensing Executives, 2014; BCG analysis
Changing trends in Bio-Pharma deal making
Take aways of BCG 2014 partnering survey

• Partnering today is highly competitive, reflected in declining deal volumes at high valuations
  • Partnership deals have declined ~41% since 2010, driven in part by the favorable IPO market
  • Deal valuations have increased by ~$100M (57%) including upfronts which have more than doubled
  • Heavy concentration in a small number of specialty TAs, including oncology and inflammation

• The sell-side continues to focus on partnering skills in selecting a partner
  • Sell-side looking for a partner who can add value to their product
    • Has partnering skills to close the deal
    • Has dependable clinical development capabilities
    • Can deliver internationally
  • Sell-side looking less for a partner who can bring certain capabilities (commercial, regulatory, access / reimbursement) that are seen as "table stakes"
Continued strong trend of global deal activity

*besides strong M&A, strategic business alliances and JV*

Deal value and volume continued to be strong in Q2/3 2015
Still strongest focus in US but trend is global: ~½ of deals in US; >¼ in Asia-Pacific; ~1/5 in Europe & others

The following trends were noted among deals in the industry:

- **Generics – lines continue to blur:** As generics morph into specialty services, traditional generic companies are shifting their strategic focus and restructuring their product portfolios to include patent-protected products.

- **Consolidation:** Consolidation continued to be a trend in Q2 and Q3, 2015 across all sectors and geographies within the PLS industry, and most prominently in specialty pharmaceuticals, generics and biotechs.

- **Divestitures:** During this quarter, companies focused on their core competencies and engaged in divestitures to unlock shareholder value. This is expected to be a consistent theme; companies will continue to evaluate their newly combined businesses and product portfolios and seek to maximize the value of these assets through selective divestitures, thus creating additional acquisition opportunities.

- **Collaboration spins:** As companies re-evaluate their portfolios, many sellers are retaining rights to future products via collaboration agreements. These deal structures may continue as companies seek to reduce risk while preserving potential upside in their portfolios.

- **Contingent consideration:** The industry continued to structure deals with significant payments and earn-outs. Companies protect themselves from uncertain events tied to pre-commercial products and bridge value gaps between buyers and sellers.

*Data from PWC, PLS Deals Insights, Q2 and Q3 2015*
Shift in terms of deal structures

Licensing deal volume down 41% while IPO on the rise

Source: BCG survey of Biotech CEOs and Licensing Executives, 2014; BCG analysis

1. Biotech public offerings that are closed, effective, expired. Does not include announced but not yet closed IPOs
Deal focus shifting from development to either early/discovery stage or marketed products

**Distribution of licensing deals by development stage**

- **Filed/Marketed**
  - 2010: 14
  - 2011: 10
  - 2012: 7
  - 2013: 12
  - 2014: 16

- **Development**
  - 2010: 52
  - 2011: 53
  - 2012: 60
  - 2013: 49
  - 2014: 40

- **Discovery**
  - 2010: 34
  - 2011: 36
  - 2012: 33
  - 2013: 39
  - 2014: 44

Source: BCG survey of Biotech CEOs and Licensing Executives, 2014; BCG analysis
Licensing deal values increased >$ 100m since 2010

Upfronts make up growing portion of total deal value

Breakdown of average deal value into upfront vs. milestone

Note: Deal value includes upfront and milestone payments
Source: EvaluatePharma as of December 2014

Source: BCG survey of Biotech CEOs and Licensing Executives, 2014; BCG analysis
Increase in purchases of marketed products

Paying big to take the lead

Out-right product purchases lead the pack of high-value, big up-front deals:

- 11 of the 64 big-up-front deals were cash buyouts of specific assets
- 10 were for marketed drugs
- 9 were paid fully up front (royalties aside), mostly in cash
- 3 made the top 10 list by deal value for the big-up-front class.

Source: A.Mancini, In Vivo, BioPharma Strategies, November 18 2015
Biopharma Up-Fronts Hit A High

**Top 10 Deal with Up-Front Values ≥ $100m, 2013-Sep 2015**

<table>
<thead>
<tr>
<th>Date</th>
<th>Deal</th>
<th>Total Value ($m)</th>
<th>Up-Front Value ($m)</th>
<th>Latest Dvlpt. Phase</th>
<th>Therapeutic Area</th>
</tr>
</thead>
<tbody>
<tr>
<td>Feb. 2013</td>
<td>Biogen Idec buys Elan's share of Tysabri</td>
<td>3,250</td>
<td>3,250</td>
<td>Marketed</td>
<td>Immune disorders</td>
</tr>
<tr>
<td>July 2015</td>
<td>Regeneron and Sanofi in new antibody deal</td>
<td>1,015</td>
<td>640</td>
<td>Phase I</td>
<td>Cancer</td>
</tr>
<tr>
<td>April 2014</td>
<td>Celgene buys Nogra's Crohn's disease candidate</td>
<td>2,575</td>
<td>710</td>
<td>Phase II</td>
<td>Gastrointestinal</td>
</tr>
<tr>
<td>May 2014</td>
<td>Valeant sells five dermatology assets to Nestle's Galderma</td>
<td>1,400</td>
<td>1,400</td>
<td>Marketed</td>
<td>Dermatology</td>
</tr>
<tr>
<td>June 2015</td>
<td>Celgene and Juno partner in CART/TCR deal</td>
<td>1,100</td>
<td>1,000</td>
<td>Phase I</td>
<td>Cancer</td>
</tr>
<tr>
<td>Jan. 2015</td>
<td>Depomed gets US rights to Janssen's Nucynta</td>
<td>1,050</td>
<td>1,050</td>
<td>Marketed</td>
<td>Neurology</td>
</tr>
<tr>
<td>Aug. 2015</td>
<td>Novartis buys remaining atumumab interest from GSK</td>
<td>1,034</td>
<td>300</td>
<td>Phase II</td>
<td>Immune disorders</td>
</tr>
<tr>
<td>June 2013</td>
<td>Aspen licensed Glaxo’s Arixtra, Fraxiparine</td>
<td>1,100</td>
<td>1,000</td>
<td>Marketed</td>
<td>Blood and Coagulation Disorders</td>
</tr>
<tr>
<td>May 2014</td>
<td>Bayer, Merck co-develop cardiovascular sGC modulators</td>
<td>2,100</td>
<td>1,000</td>
<td>Marketed</td>
<td>Cardiovascular</td>
</tr>
<tr>
<td>May 2015</td>
<td>Baxter buys Oncaspar portfolio from Sigma-Tau</td>
<td>900</td>
<td>900</td>
<td>Marketed</td>
<td>Cancer</td>
</tr>
</tbody>
</table>

Source: A. Mancini, In Vivo, BioPharma Strategies, *November 18 2015*
High deal activity in specialty therapeutic areas

Distribution of licensing deals by TA

Source: BCG survey of Biotech CEOs and Licensing Executives, 2014; BCG analysis
Novartis – a Healthcare company in change

So how does Novartis fare in this changing landscape?
Leading the trend of innovative deals and collaborations
Novartis is a world-leading healthcare company

**Leading market position**

One of **25 largest** companies by market capitalization

Among **most respected** companies globally

### Key figures

<table>
<thead>
<tr>
<th>Year</th>
<th>USD billion</th>
</tr>
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<tbody>
<tr>
<td>2014</td>
<td></td>
</tr>
<tr>
<td>Net sales:</td>
<td>58.0</td>
</tr>
<tr>
<td>Net income:</td>
<td>10.3</td>
</tr>
<tr>
<td>R&amp;D investment:</td>
<td>9.9</td>
</tr>
</tbody>
</table>

### Sales by region 2014

- **Europe**: 37%
- **US**: 32%
- **Asia/Africa/Australasia**: 21%
- **Canada/Latin America**: 10%
Powerful demographic trends are changing healthcare and raising the bar for innovation

**Growing populations**
Almost 1 billion more people are expected to inhabit the planet by 2025, driving up demand for healthcare worldwide.

**Aging**
By 2025 there will be 500 million more people aged over 50+, posing a challenge for governments and health insurers as they try to keep spending in check.

**Rise of chronic diseases**
Chronic illnesses such as cancer and heart disease are on the rise. By 2025 they will account for 70% of all illnesses as the population ages and standards of living improve.

**Increasing demand for healthcare**
These factors and the accelerating pace of innovation will contribute to increasing demand for healthcare. By 2025 global healthcare spending is expected to more than double to over USD 15 trillion.
Our strategy is to lead through science-based innovation, driving better patient outcomes in growing areas of healthcare.

Science-based innovation

To deliver better patient outcomes

In growing areas of healthcare
Innovation overview 2014

**9.9 USD billion** invested in research and development of new drugs and medical devices

More than **200** R&D projects underway, 135 of them in the Pharmaceuticals Division

The Novartis Institutes for BioMedical Research (NIBR) is the research engine of Novartis, with more than **6,000** scientists

Focus on **molecular pathways** shared by several diseases

Research-to-Development transition determined by **fast and rigorous** “proof-of-concept” trials

Strategic alliances with academia and other companies **strengthen** our preclinical pipeline
We have an industry-leading pipeline

FDA breakthrough therapy designation for two drug candidates in 2014, making 5 in total

Studying 25 biological pathways associated with cancer progression

20 compounds in development for a range of disorders in dermatology and rheumatology

6 Sandoz biosimilars in Phase III trials or undergoing registration

13 major approvals in US, EU, Japan in 2014
Transactions focus Novartis on three leading divisions

Acquisition of **GlaxoSmithKline** (GSK) oncology products

Merger of **OTC** unit with GSK’s OTC business to form a joint venture

Sale of **Vaccines Division**, excluding influenza, to GSK (deals closed March 2015)

Sale of **Animal Health** to Eli Lilly (deal closed January 2015)

Sale of **influenza vaccines business** to CSL Limited (deal closed August 2015)
Expanding our presence in emerging markets

Fast-growing demand for healthcare

Asia

Africa

Latin America
Novartis active in a variety of deals
Examples of deals announced for 2014-2015 (1/2)

Strengthen therapeutic area

Novartis broadens immuno-oncology pipeline with acquisition of Admune Therapeutics and licensing agreements with XOMA and Palobiofarma
Oct 21, 2015 07:15

Novartis accelerates cancer immunotherapy efforts with Aduro Biotech alliance and launch of new immuno-oncology research group
Mar 30, 2015 07:15

Novartis announces clinical collaboration to evaluate Bristol-Myers Squibb’s novel immunotherapy in combination treatments for NSCLC
Oct 06, 2014 07:15CET

Novartis acquires all remaining rights to GSK’s Ofatumumab to develop treatments for MS and other autoimmune indications
Aug 21, 2015 07:25

Novartis expands cancer immunotherapy research program with acquisition of CoStim
Feb 17, 2014 07:15CET

Novartis deepens its industry leading pipeline with acquisition of Spinifex Pharmaceuticals, Inc.
Jun 29, 2015 07:00

Transformational portfolio refocus

Novartis completes divestment of Animal Health business to Eli Lilly for USD 5.4 billion
Jan 01, 2015 07:00CET

Novartis announces completion of transactions with GSK
Mar 02, 2015 06:59

Novartis completes divestiture of influenza vaccines business to CSL Limited for USD 275 million
Aug 03, 2015 00:30
Novartis active in a variety of deals

Examples of deals announced for 2014-2015 (2/2)

Digital/ eHealth

- Novartis Pharmaceuticals announces a joint investment company with Qualcomm leading innovation in digital medicines for physicians and patients
  - Jan 12, 2015 03:00 CET
- Novartis to license Google "smart lens" technology
  - Jun 27, 2014 12:40 CET

Research & Option Deals

- Novartis collaborates with Intellia Therapeutics and Caribou Biosciences to explore making medicines and drug discovery tools with CRISPR genome editing technology
  - Jan 07, 2015 07:15 CET

Development Portfolio Partnering

- Novartis partners with Phase 4 Partners and institutional investors to help create Mereo BioPharma Group Ltd
  - Jul 29, 2015 07:15
- Novartis announces global partnership with Amgen to develop and commercialize pioneering neuroscience treatments
  - Sep 01, 2015 22:30

Watch the Space others to come!
The new Novartis Pharma BD&L structure

3 business area; 5 franchises, 2 specialty areas, divestment/partnering

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GenMed

- I&D
  - S&E
- NS
  - S&E
- CV
  - S&E
- Retina & Resp
  - S&E
- SPT
  - S&E
- Digital
  - S&E
- Divest, Outlicense
  - Partnering
  - Partnering
  - Partnering
  - AM

Onc (Cell&Gene Tx)

CGTU

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knut.sturmhoefel@novartis.com
Basel, Switzerland

31 | EBDC 2015, Antwerp | Knut Sturmhoefel | 24 Nov 2015 | Changes in BioPharma partnering
Summary:
So what is changing for Bio-Pharma Partnering?

• The deal environment is active
• However, deals will be more selective
  • Risk adjusted
  • Specialty TAs
  • Partner quality counts as the collaborations are there to last
• More deals in early stage (preclinical, pre-PoC) or late stage, on market products
• Larger variety of deals/ deal structures
• For Biotechs:
  • Fewer “quick exits”; more risk sharing
  • Strong science and R&D capabilities matter
  • Risk sharing; take on more development activities
  • Advance beyond early PoC
  • Regulatory approval is not the goal but only a milestone towards successful commercialization
  • Early focus on value generation; consider HEOR during clinical development