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Promotion and Development Collaborations Between Established Players

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Pharma and Biotech In-Licensing, Co-Development
and Co-Promotion Agreements

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Morgan Lewis
C O U N S E L O R S A T L A W

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Morgan Lewis: Life Sciences Focus

- **Founded in 1873, today 1,100 lawyers in 13 offices worldwide**
- **175 Life Sciences professionals, including 90 with advanced degrees ranging from biochemistry to molecular genetics to immunology**
- **Interdisciplinary coordination of transactions, IP, litigation, FDA and antitrust expertise to meet our clients' strategic objectives**
- **Recently ranked as the 5th leading transactional law firm in the nation by *The American Lawyer* "Corporate Scorecard"**
- **Named by many *Fortune* 250 companies as one of their primary law firms**
- **Recognized by corporate counsel for exceptional client service in a survey of *Fortune* 1000 companies**
- **Featured prominently in the annual *National Law Journal* survey of "Who Defends Corporate America"**

Morgan Lewis: Recent Life Sciences Deals

- **Aventis - Genta** collaboration for co-development and commercialization of Genasense™
- **Enzon - Elan** acquisition of Abelcet® product rights and manufacturing assets
- **Quintiles - Eli Lilly** co-promotion and marketing collaboration for Cymbalta™
- **Adolor - GlaxoSmithKline** development and commercialization collaboration for Alvimopan™
- **Arena Pharmaceuticals - Merck** drug discovery collaboration
- **Cephalon - Anesta** stock-for-stock public company acquisition
- **Aventis - Millennium** alliance for drug discovery and development and bioinformatics technology transfer
- **Barrier Therapeutics - Johnson & Johnson** spin-out, venture financing and license agreements
- **Principia - Human Genome Sciences** stock-for-stock acquisition
- **3-Dimensional Pharmaceuticals - Bristol-Myers Squibb** drug discovery alliance
- **Pharmacia - Novo Nordisk - Wyeth** license agreement and related patent dispute settlement
- **Eos Biotechnology - ICOS** drug discovery collaboration

Promotion and Development Collaborations Between Established Players: Current Deal Trends and Special Deal Factors

- **Pharmaceutical and biotech drivers toward partnering**
 - Access to technologies and expertise
- **Interdependent relationship of collaboration partners**
 - “Lead partner” status vs. “niches” of control
- **Maintaining alignment of interests among partners**
 - Non-competes, exclusivity and ex-program activities
- **Current industry environment of pipeline “gaps” and company consolidations**
 - Demand and supply for late-stage products
- **Special deal factors and terms driven by current environment**
 - Low valuations, shedding of low-performing assets and aversion to risk
- **Surprises - Good and Bad**
 - There’s no such thing as a “typical” deal

Life Sciences Industry: Current Environment

- **Pharmaceutical industry reliance on “life cycle management” of existing products**
 - Prevalence of “me-too” drugs
 - 2/3 of prescription drugs approved by FDA between 1989 and 2000 were identical to existing drugs or modified versions of them*
- **Big pharma and big biotech looking for late-stage products**
 - Innovation gap
 - Patent expirations
- **R&D payoff slower than expected**
 - FDA appears to be tougher
- **Big pharma and big biotech strive for double-digit growth**
- **Wave of consolidation in industry “raises the bar”**
 - Pfizer - Pharmacia
 - Amgen - Immunex
- **Independence requires a promising pipeline**

Current Deal Trend: Biotech Shift “Downstream”

- **Move from research focus (platform technology and FTEs) to drug development and commercialization and booking sales**
- **Biotech negotiating leverage over big pharma and big biotech due to need for late-stage products (supply and demand)**
- **Need to demonstrate drug discovery ability and “product promise” to investors**
- **Willingness and ability to do more early clinical development before partnering**
- **Looking to partner for late-stage development risk-sharing, expertise in regulatory and/or manufacturing supply chain and/or marketing, and to maximize opportunity for potential blockbuster**
- **Demonstration of value of contribution translates into profit split (and expense and detail sharing)**

Current Deal Trend: More Demanding Partners

- **Biotech values depressed by ImClone-effect and other recent product development disappointments**
 - E.g., FDA advisory panel recommendation against approval of ViroPharma's lead product Picovir led to termination of collaboration, restructuring and RIF
 - Similar recent events for Geron, BioCryst, Corixa, Oxford GlycoSciences and many others
- **Increased due diligence**
 - FDA due diligence on filings, correspondence, clinical study protocols, meetings and approval strategy
 - Late-stage partnering drives need for increased due diligence on clinical development, manufacturing supply chain and pricing/reimbursement
 - IP due diligence and equity investment-related due diligence
 - Current economic environment may require "financial ability" due diligence
- **Insistence on deal term flexibility**
 - Risk aversion (or at least containment)

Risk Reduction: Economic Terms

- **Reduced “buy-in” fees**
 - Smaller up-front payments
 - Deficit made up by additional deferred milestones
 - Can be same net value, but spread out in more stages
- **More, but smaller, milestones**
 - Single milestone events split into multiple events
 - E.g., Phase IIa and IIb separate milestones
 - Milestones keyed to product achievement + 3P action
 - E.g., NDA or BLA *acceptance for filing*
- **Loans to fund biotech partner development activities**
 - Instead of funding FTEs, especially in deal with downstream participation
 - Instead of equity investment
 - Repayable from collaboration products or in equity
 - Forgiven if product is successful
 - In overall economics, in lieu of milestones or royalties

Risk Reduction: Economic Protections

- **Reimbursement of up-front payments**
 - Negative clinical trial developments
 - E.g., failure to meet endpoints
 - Negative regulatory event
 - E.g., failure to achieve target labeling
 - Negative marketing environment
 - E.g., failure to meet sales levels
 - Used to adjust economics, with termination or stand-alone
- **Cap on further investment in product development**
 - Agreed-to development budgets, with limits on unilateral increase
 - Separate funding responsibility for different indications
 - Halt further investment upon negative development or regulatory events, or failure to meet timelines or target dates
 - Adjust decision-making powers

Risk Reduction: Diligence Requirements

- **Biotech demand for partner's diligence**
 - Demand for continued focus and activity
 - Especially in view of reduced economic terms and greater protections
 - Leverage to make demands in late-stage product deals
- **More than “Commercially Reasonable Efforts”**
 - “CRE” can be modified to take into account many extraneous factors
- **Specific diligence requirements**
 - Timelines for clinical development, regulatory and marketing events
 - Can be date-specific, or keyed-off of prior accomplishments
- **Ramifications if not met**
 - Loss of specific rights to indication or product
 - Dispute resolution process, but carve-out from big pharma decision-power
- **“CRE” Boomerang**
 - In return, biotech may be held to “CRE” on its R&D activities
 - In addition to economic rewards being specific milestone-bases

Risk Reduction: Termination Events

- **Failure to meet Phase IIb or Phase III clinical trial endpoints**
 - Investing partner wants to cut losses and further efforts
 - Innovator may not need partner's detailing
- **Delays beyond date-certain or timeline**
 - NDA acceptance
 - Marketing approval
 - First commercial sale
- **Failure to meet TPP**
 - Approval but with different labeling
 - Can impact managed-care reimbursement and sales projections
- **Negative FDA advisory panel recommendation**
 - But innovator wants partner's continued input and investment
- **Receipt of non-approval letter**
- **Big pharma partner failure to meet specific diligence requirements**

Risk Reduction: Termination Effects

- **Effective date of termination**
 - Notice date vs. end of notice period
- **Partial vs. whole termination**
 - Termination in response to specific breach or problem
 - E.g., terminate research phase only
 - E.g., terminate specific indication or formulation
- **Reversion of product rights on termination**
 - Pre-collaboration technology
 - Collaboration-generated inventions, data, materials and filings
- **Post-termination compensation**
 - Reimbursement for studies where data remains useful
 - Royalties on future products derived from collaboration activities
 - Transition detailing or other services
 - Sales force training and marketing materials

Risk Reduction: Product Rights

- **Ownership of pre-existing technologies**
- **License grant: exclusive? scope?**
- **Ownership of collaboration-based technologies and discoveries**
 - Sole or joint as per inventorship
 - Ownership by collaboration partner whose existing technology it “solely” or “primarily” relates to, or who is funding program
- **Selection and qualification of targets or compounds for collaboration**
- **Criteria and decision-making process to select collaboration candidates for progression through development**
- **Back-ups dedicated or available to collaboration**
 - Distinction between back-ups and second generation technologies
- **Residual pool of collaboration candidates**
 - Picking mechanisms for sharing exploitation opportunities

“Ex-Program” Activities

- **Uses of targets, technologies and compounds outside of collaboration**
 - Different treatment for inventing partner
 - Sharing of information between collaboration and “ex-program”
 - Economic terms for sharing “ex-program” exploitation
 - Royalties, or buy-in rights
- **Deal carve-outs for specific indications or combination products**
 - Non-alignment if same or similar molecule or mechanism-of-action
 - Cannibalization monitoring mechanisms
 - Relative pricing provisions
- **Non-competition and exclusivity provisions**
 - May contract if collaboration scope changes
 - New competing technologies brought to collaboration for first look

Duration of Promotion and Development Collaboration

- **Sufficient term for innovator partner to become able to successfully promote product independently**
 - Ultimate goal to develop “downstream” capabilities
- **Sufficient term for development/promotion partner to obtain a positive return on investment**
 - Buy-in fee and milestones
 - Partners’ split of
 - Development funding
 - Launch advertising & promotion spend
 - Detail requirements
 - Profits and losses
- **Products with large launch year and near term advertising & promotion can take several years to become profitable**
- **Peak year sales and profits may be several years out**

Residual “Tail” Payments

- **Payments after cessation of active detailing of collaboration product and spending on advertising & promotion**
 - Payment period can be from one to several years
- **Incentive for promotion partner to continue diligent efforts for full term to build product franchise for the future**
 - Also can be a buy-out at end of promotion term
- **Tail period sales formula**
 - Can be based on sales in last year of promotion partner’s term
 - Or can be based on sales in following year or years
 - Deciding factor may be whether peak sales year has occurred
- **Payment can be a royalty on “net sales” or a split of “profits”**
 - Usually lower than profit split in active collaboration years
- **Percentages sometimes scale down over a multi-year tail**
 - Promotion partner avoids “cliff”
- **Transition services for successful product turn-back**

“Quid” Products

- **Additional compensation to collaboration innovator partner**
 - Can enable biotech partner to develop “downstream” capabilities
- **Opportunity to promote a marketed or future product**
 - Can be designated, left open or selected in future from list of potential quid products
 - Can be sole or co-promotion
 - Use of CMOs
- **Opportunity to ramp-up a sales force**
 - Usually in same timeframe as collaboration product
 - Earlier marketing of quid can create disalignment if collaboration product is later abandoned
 - Usually detailed to same physician audience
- **Compensation Mechanism**
 - Profit split above historical baseline
 - Fee per detail
- **Term**
 - Can be co-terminous with collaboration
 - Can be independent and arms’ length
- **Impact of termination on “quid”**

Collaboration Surprises

- **Partner change-in-control**
 - Acquisition by competing third party
 - Stage of collaboration
- **O-T-C switch of Rx product**
 - Forced
 - Voluntary
- **Manufacture and supply**
 - Biotech capability for clinical vs. commercial supply
 - Use and management of CMOs
 - Big pharma preference to control manufacturing
 - Supply chain from API to finished packaged product, and “cost-plus”
- **Intellectual property**
 - IP litigation
 - Generics
- **Additional products**
 - New opportunities for the collaboration