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Successful Partnering in Drug Development

I. Threshold Considerations

Different Approaches to Partnership

- A wide range of possibilities exist:
  - Funding in exchange for an option to acquire rights in the future
  - Sponsored research agreements
  - Research collaboration
  - Pure out-license of global rights
  - Co-development allocating rights and responsibilities
  - Joint venture with each party contributing assets and resources to a new entity
- Each approach involves varying degrees of commitment and collaboration between the parties which lead to different issues and considerations, both practical and legal.
- What approach makes sense in a given situation will be driven by a number of considerations, including:
  - What stage of development the compound or product is in when the deal is struck
  - The parties' ultimate objectives
  - The parties' relative resources
  - The parties' relative need for / willingness to give up control

Benefits and Challenges of Licensing and Collaboration Transactions

- Collaboration combines resources and mitigates risk
  - Over the past decade, 80% of biotech products were launched through a collaborative effort
  - Products developed through collaborative efforts are four times more likely to reach market
- Collaboration comes with its unique set of challenges, including:
  - Challenges associated with a long-term relationship
  - Issues associated with sharing responsibilities and control with unfamiliar party
  - Potential for misaligned and evolving interests

Considerations Based on the Stage of Development

- Collaborations in the early stages
  - Firm commitments are more difficult to impose given extent of uncertainties.
  - Governance and/or accountability terms and dispute resolution provisions become more important.
  - Concepts allowing flexibility, such as opt-out and opt-in rights, are more common.
  - More careful attention to rights to innovations is warranted.
- Collaborations in the later stages
  - Easier to agree on firm commitments for completion of development and commercialization given greater visibility into commercial potential (prospects and timing of approval; competitive landscape, etc.).
  - Valuation likely easier as well, leading to greater weighting of consideration toward upfront payments and near-term milestones.
  - Significant innovations become less likely, reducing focus on allocation of new IP rights.

II. IP Due Diligence

Types of Assets

- Technology – physical and intangibles assets
  - processes, know-how, data, manufacturing
- Intellectual Property – the method to protect the technology and research plan
  - patents, trademarks, trade secrets, copyrights
- Defining terms separately allows for cleaner agreements
  - Allows party to clearly define rights transferred, e.g., ownership of technology or IP, right to use technology or IP
  - Allows more precise representations and warranties

Background IP Ownership Issues

- Ownership of intellectual property
  - Existing employees
    - Confirm that employment agreements act as an assignment rather than a promise to assign
    - Bona fide purchaser for value (35 U.S.C. § 261)
  - Consultants, Contractors or Professors
    - Make sure that no other entity, e.g., university, has rights to the inventions
  - Government Funded Research
    - Bayh-Dole Act – permits certain organizations to elect to pursue ownership of an invention in preference to the government
      - Confirm compliance with Act to ensure ownership vests in the company
        - Inform government about invention, provide written election to retain and identify government's rights: 35 U.S.C. § 202(c)(1), (2) & (6)
      - Will governmental rights affect the financial returns?
        - Government obtains a paid-up non-exclusive license 35 U.S.C. § 202(c)(4)
      - March-in rights

Joint Ownership Concerns

- When performing due diligence remember that if a patent is jointly owned:
  - A contributor to any part of claim has an undivided interest in the entire patent (35 U.S.C. § 116)
  - Each party has the right to exploit or license to a 3rd party without permission or accounting (35 U.S.C. § 262)
  - Ownership rights in other countries may be different than the U.S.
  - All owners will need to be involved in enforcement of U.S. patent

Defining the IP Assets Required for a Successful Collaboration – Considerations When Reviewing IP

- Understanding the nature of the technology involved in the collaboration
  - Work with scientists to understand the type of IP that will be necessary to protect the technology from competition
    - Is new chemical entity protection on active available and sufficient?
      - Can a competitor make a similar compound and compete?
    - If compound is old, will indication of use protection suffice?
    - If technology encompasses a process, can IP protect the competitive advantage that the process provides?
    - Will competitors be able to design their own process?
    - If technology encompasses assays, diagnostics or DNA sequences, consider recent jurisprudence on patentability

Where Will the IP Come From?

- What are the entities' IP positions relative to the proposed collaboration?
  - Background IP of Each Entity
    - Constraints on the Background IP
      - Existing rights
      - Field of use limitations
      - Worldwide versus local rights
    - In-licensed IP – Is it transferrable?
- What type of IP can the collaboration expect to generate?
  - Foreground IP – How will the parties divide the rights?

III. Key Terms for Agreement

Scope of Collaboration and Licensed Rights

- Key parameters:
  - Licensed technology and IP rights
  - Compounds, antibodies, targets, active ingredients, etc. that are the focus of the collaboration or license
  - Field
  - Territory
- Challenges of dividing rights to the same compound, antibody or product.
- Exclusivity – consider any upstream limitations on what rights licensor can convey.
- Considerations for rights of first offer.
- Role of and challenges with non-competition provisions.

Scope of Collaboration and Licensed Rights

- Sublicensing
  - Whether or not to require consent to sublicensing
  - Prerequisites for sublicensees if consent is not required (e.g., exclude competitors, minimum financial criteria, etc.)
  - Importance of clarity re: how agreement terms apply to sublicensees
- Retained rights and grant backs
  - Grant back may be preferred to retained rights for standing purposes
  - Grant back necessary where licensee will solely own improvements or other developed IP
  - Especially important in the context of platform technology – be careful with confidentiality/non-use provisions
  - Grant back of right of reference under regulatory approvals may also be necessary
- Importance of coordination among all stakeholders

Roles and Responsibilities

- Who is doing what and the extent to which parties will collaborate will drive many aspects of an agreement.
- Will roles be static or could they change?
  - Possibility of opt-out / opt-in rights – particularly useful in early-stage collaborations.
  - In that construct, it's important to consider and provide for transition.
  - What are the financial consequences of opt-out / opt-in? Penalty for opting out? Change in future cost-sharing, revenue-sharing or payment terms? Cost of opting-in – fixed or determined based on metrics at the time?
- Governance and reporting provisions
  - Approach and function varies based on nature of collaboration.
  - Committee and reporting structures serve an important accountability function in any partnership.
  - Extensive collaborations may involve a single steering committee or a number of committees with different functional roles: Development; Manufacturing; IP; Regulatory; Commercialization; etc.; or a combination of both.

Roles and Responsibilities

- Governance and reporting provisions (continued)
  - Having capable, consistent and authoritative representation on committees is critical.
  - Authority given to committees can vary, although typically no committee will have the power to amend the primary agreement.
  - Decision making can be by one party, unanimous or unanimous with casting votes or escalation requirements.
  - Ultimately, negotiation of governance terms comes down to who can ultimately decide what and how much process is required before they can do so.
  - Less collaborative arrangements tend to focus more on reporting commitments. Where they are included, committees tend to serve an information-sharing purpose.

Roles and Responsibilities – Co-Promotion

- Co-Promotion Basics
  - Parties agree to divide detailing and other promotional activities in respect of a product, either among or within countries.
  - Co-promotion within a country often involves allocating based on indication, target healthcare professionals or regions.
  - Typically one party is the commercial lead and responsible for booking sales, order fulfillment and distribution.
  - Arrangement may be built into the primary agreement for a broader collaboration or a stand-alone agreement.

Roles and Responsibilities – Co-Promotion

- Commitments
  - Often set out in an annual plan that the parties develop together within parameters linked to forecasts, prior year's performance, competitors' efforts, minimums, etc.
  - Focus on number and type of details, often with weighting of secondary or tertiary details to come up with "primary detail equivalents" or similar concept.
  - Subcontracting often permitted, sometimes up to a maximum number of details.
  - Parties often commit to minimum bonus arrangements for sales force to ensure they're incentivized.

Roles and Responsibilities – Co-Promotion

- Coordination
  - Arrangement often overseen by its own committee.
  - Typically each party's reps participate in the same training program that one party is responsible for administering.
  - One party is responsible for providing samples and sales literature.
  - Adverse event reporting will often be covered by a separate SDEA.

Roles and Responsibilities – Co-Promotion

- Financial terms
  - May be a simple “pay per detail” arrangement.
  - More complexity when co-promotion economics are factored into broader expense and profit-sharing arrangement.
    - Often parties will establish tracking accounts for promotion-related expenses that are charged for purposes of true-up mechanism and profit allocation.
    - More focus on budgeting and other controls on expenses that can be taken into account, subject to true-up mechanism.
    - Profit share may be credited based on value of details or a partner’s share may be reduced based on a formula if they don’t achieve their detail quota.

Consideration Structures

- True collaborations are likely to focus more on cost-sharing and revenue sharing whereas less collaborative structures focus more on consideration for licensed rights.
- Upfront payment – cash or equity investment – likely to be higher in later stages of development (often thought of as compensation for past efforts)
- Milestone payments
    - Tie to any number of developmental and/or commercial events: designation of Investigational New Drug; filing of NDA or BLA; fast track designation; approval; commercial launch; ex-US approvals; net sales thresholds, etc.
    - Important to ensure that milestones are as objective as possible. Avoid ambiguous standards, e.g., who determines “success”?

Consideration Structures

- Royalties
  - Tiered approach is most common
  - Duration commonly for later of a number of years post-launch and life of patents with licensing becoming fully-paid thereafter
  - Calculation methodologies
    - Net Sales is most common. Significant focus on deducts, approach to combination or bundled products
    - Net Profit calculations – all the fun of negotiating Net Sales deducts and a COGS definition
  - Royalty step-downs
    - Commonly seen in licensing transactions for patent expiration and sometimes generic competition
    - Patent misuse considerations (but maybe not for long – pending U.S. Supreme Court Spiderman case). Especially complicated in blended licenses involving multiple patents and know-how

Consideration Structures

- Royalties (continued)
  - Royalty-Stacking clauses
    - If the parties are aware of third party IP that may be relevant at the outset (e.g., a particular delivery technology), consider addressing at the outset
    - Who decides what third party IP counts?
    - Should there be a floor?
- Other considerations
  - How sublicensing proceeds are treated – does licensor share in upfronts or milestones or just royalties?
  - Auditing provisions – limits; third party auditor only?

Licensee's Diligence Obligations

- Exclusive licensor seeks to ensure that licensee remains committed to project
- Specific Diligence obligations
  - Objective, measurable requirements are ideal, but often difficult to agree upon, particularly at early stages
  - Can be focused on development-related requirements (e.g., obligation to begin clinical trials) or commercial requirements (e.g., a minimum marketing spend or minimum number of details)
- Commercially Reasonable Efforts
  - Most common approach
  - Typically defined – either licensee-focused (e.g., efforts consistent with those that licensee uses in relation to other products) or industry-focused (efforts that a similarly-situated industry participant would use). Latter is more typical
  - Undefined commercially reasonable, reasonable best, or other efforts standards are very difficult to interpret and apply in practice

Licensee's Diligence Obligations

- Commercially Reasonable Efforts (continued)
  - Example:

    "Commercially Reasonable Efforts" means efforts that are consistent with the type and scope of efforts that a similarly-situated company within the pharmaceutical industry would devote to a product of similar risk profile and profit potential, but in no event less than the type and scope of efforts that the applicable Party would devote to any of its other products of similar risk profile and profit potential. Without limiting the foregoing, Commercially Reasonable Efforts require that such Party: (i) assign responsibility for the relevant activities to specific employees who are responsible for progress and monitor such progress on a regular basis; (ii) set and consistently seek to achieve specific and meaningful objectives and timelines for carrying out such activities; and (iii) consistently make and implement decisions and allocate resources consistent with the efforts described above.

  - Many factors can be taken into account – patent protection; market conditions; party's resources; party's other products (likely disregarded); anticipated regulatory pathway; etc. – all of which can serve as bases on which licensor can test licensee's performance and on which licensee can demonstrate that appropriate efforts have been used.

Licensee's Diligence Obligations

- Commercially Reasonable Efforts (continued)
  - Additional clarity can come from coupling the standard with specific obligations to, e.g.,
    - Complete development tasks outlined in a mutually-agreed development plan within a timeline set out in the plan (although providing for sufficient flexibility in the plan can be challenging)
    - Commence clinical trials by a specified date
    - File for approval within a specified period of time after pivotal clinical trials are completed
    - Commercially launch within a specified period of time after approval
  - Licensor would ideally link diligence commitments to anything that's linked to a milestone
- Minimum Annual Payments – License "Maintenance" Fees
  - Alternative to having diligence requirements
  - Difficult for licensee to agree to given uncertainty of regulatory process

Licensee's Diligence Obligations

- What happens if licensee is acquired?
  - Ideally licensor would like the ability to terminate if they're not happy with the new partner.
    - More often seen in extensive, early-stage collaborations where identity of counterparty is more critical.
    - In later stage transactions, very difficult for licensee to have that kind of impediment to a future transaction.
  - Compromise could be a right for licensor to consent or terminate if certain conditions are or are not present (e.g., financial characteristics of acquiror; specified competitors; acquiror has competing products).
  - Parties may also provide that acquiror must provide specific assurances of their commitment to the collaboration or product(s).

Ownership of IP from the Collaboration

- Joint Ownership
  - Benefits
    - Prevent blocking patents
      - Both parties can exploit so neither can prevent the other from practicing the invention
  - Challenges
    - Loss of control of licensing and exploitation
    - Complicates assertion of rights
      - All joint-owners must participate in enforcement of U.S. patent
    - Rights of joint owners may vary from country to country
    - Not ideal in relation to improvements to a party's preexisting IP

Alternatives to Joint Ownership

- One party owns all IP and the other party is licensed under the IP
  - License should limit owner's ability to license to third parties and should allow licensee some rights to sublicense
- Divide IP between parties and cross-license
  - One party may hold the NCE while other holds methods of use or manufacture
    - Can depend on what technology each party brings to the partnership
- Creation of special purpose vehicle to hold IP and each party has ownership rights within that entity

Obligations to Manage IP Prosecution, Maintenance & Enforcement

- Party that owns the rights to the patent will have the obligation to prosecute, maintain and enforce patents
  - Addressing expenses – sharing of costs or deduction from future payments
  - Option to take over if party does not want to continue
    - If a party decides to discontinue prosecution, maintenance or undertake enforcement, ensure that other party has the right to take control
- Structure obligations based upon inventors
  - If one party's employees are inventors, then that party should control prosecution and enforcement
  - Patent applications with inventors from each entity can be the responsibility of both parties through a committee
    - Much more complicated arrangement to develop a prosecution strategy

Obligations to Manage IP Prosecution, Maintenance & Enforcement

- Obligations to cooperate with prosecution
  - Provide reasonable access to inventors
    - Will need inventors when drafting specification and claims
    - Will need inventors when responding to office actions or submitting declarations
    - Will need inventors to execute documents
- Key to define enforcement rights and obligations
  - Defining the party that has control, e.g., right to bring suit, selection of counsel, right to resolve
    - Payment obligations of party not controlling lawsuit, rights to relief, ability to enforce IP if controlling party decides not to bring suit
  - Obligation of non-controlling party
    - Will join suit if necessary for standing or indispensible party
    - Preserve evidence and participate in discovery

Dispute Resolution Provisions

- Be clear as to what is and is not subject to dispute resolution provisions
  - Matters over which one party is meant to have a casting vote at a committee level.
  - Matters where injunctive relief may be necessary.
- Escalation provisions, e.g.,
  - From an operating committee to an overall committee or to relationship managers.
  - To more senior officers at the respective parties.
  - Consider timeframes and procedures.
- Alternatives to litigation – mediation & arbitration
  - Resolution by industry experts
    - Many differences do not lend themselves to resolution by an industry expert

Termination and Transition Provisions

- Critically important to consider the end at the beginning – like a prenuptial agreement.
- Different implications depending on basis of termination – considerations include:
  - Whether or not license remains in effect and on what terms (e.g., lower ongoing royalty?).
  - Ongoing commitments and coordination with respect to IP can be tricky.
  - What kinds of transition efforts are required and at what cost?
  - What happens to sublicensees – do they have step-in rights?
- Termination for material breach
  - Licensor's biggest "hammer".
  - Licensee will focus on the process and cure provisions of a material breach termination provision to avoid hair trigger.
  - Consider whether a breach that affects only one part of the territory should support a breach of the whole agreement.
- Termination for bankruptcy often won't be effective.

Termination and Transition Provisions

- Transition considerations include:
  - Transfer of IP or shifting of license terms (e.g., license back becomes exclusive)
  - Tech transfer
  - Transition of any ongoing clinical trials
  - Data privacy issues
  - Transfer of regulatory filings or approvals
  - Assignment of manufacturing and other third party agreements
  - Right to sell-off inventory
  - Return of materials to licensor
  - Safety reporting obligations

III. Potential Disputes

Disputes with Partner

- Common Sources of Disputes
  - Differing expectations
  - Differences over the best way to proceed at different points
  - What commercially reasonable efforts entails
  - Bad faith “hold up” disputes
- Drafting to Reduce Likelihood of Disputes
  - Spend time thinking about and discussing the possible sources of disputes during the contract drafting process.
  - In general, more specificity in the agreement is better.
  - Objective, specific and measurable requirements limit bases for dispute.
  - Define Commercially Reasonable Efforts thoughtfully.
  - Focus on governance structures and reporting obligations that will effectively identify and resolve disagreements are they arise and before they become irreconcilable.
  - If one party is meant to have the final say on something, ensure that is ironclad and can’t be challenged under some other aspect of the agreement.

Disputes with Partner

- Being Prepared for and Managing Disputes
  - Document important decisions and rationale.
  - Consider actions in context of commercially reasonable efforts definition and other contractual terms (e.g., is this consistent with how we're approaching other projects?). Ideally, reflect those kinds of considerations in the record.
  - Get sign-off from partner on meeting minutes.
  - Ensure that team members appreciate the importance of the record so as to reduce the risk of emails and other evidence that cast doubt on motives or challenges stated positions.
  - Be mindful of the ongoing relationship. A full-blown arbitration or litigation could be devastating to future collaborative efforts.
  - At the same time, be mindful of formalities of the agreement's dispute resolution provisions – time frames for escalation steps, etc.
  - As licensee, be careful about profit projections and other forward-looking statements that might later become evidence.