In light of the tremendous costs associated with marketing biotechnology, successful competition in the industry requires designing licensing strategies to maximize income. Linking such strategies to corporate strategy is essential. In addition, because of the pressure and competition faced by large pharmaceutical companies to bring in promising new drugs from biotechnology companies, licensing deals must have financial and tactical advantages over other bidders. Table 1 shows examples of recent licensing transactions between biotechnology companies and large pharmaceutical companies.

Two useful in-licensing strategies for enhancing a competitive advantage are minimizing up-front payments and offering quid pro quo drugs. In quid pro quo transactions (or quids), a licensee offsets the cost of an alliance by offering a non-cash asset, such as trading one drug for the rights to another one. Quids often involve copromotion alliances (§). Large pharmaceutical companies generally trade only limited rights or less important products.

**UP-FRONT PAYMENTS**
Option or “right-to-negotiate” provisions and evaluation agreements involve up-front payments in exchange for an exclusive option to obtain a license, depending on the results of the evaluation. Such an agreement can defer the costs of a license when a product profile is still uncertain. A biotechnology company must, however, evaluate whether to have a prospective partner or to obtain an actual license at an earlier date.

Low-value/high-volume and high-value/low-volume strategies are useful if a technology can be easily designed around — and are especially lucrative for small biotech licensors. This strategy secures a royalty base and discourages competitors from developing competing technology.

Market foreclosure strategy offers a limited number of coexclusive licenses. This strategy is useful when a small biotech company is the licensor and a large entity is the licensee.

**THE SCOPE OF LICENSING**
Licenses and sublicenses can be negotiated according to field, geography, exclusivity, and patents and know-how. Field limitations pertain to indication and route of administration. Pharmaceutical companies prefer worldwide exclusive rights to geographic limitations, which pertain to continents (e.g., Asia or Europe) or specific country rights, such as for Mexico.

Similarly, most pharmaceutical companies seek exclusive rights; so exclusivity is more common than nonexclusivity in licensing agreements. This is particularly true when a licensed technology contributes to product differentiation. Exclusive licenses provide control over the risks of development and commercialization. Nonexclusive licenses are more common for patents on research tools and gene sequences than for genetic inventions that might result in a drug-based therapy. Nonexclusive licensing is useful when patents on (for example) delivery technology expire before those on the molecule.

Nonexclusivity can be based on a particular target or use of a compound. “Most-favored-nation” clauses are sometimes negotiated when licensing is nonexclusive. To protect themselves, licensees seek most-favored-nation status whereby any subsequent licenses will be no more favored than their own or will be modified to reflect the more favorable terms. Coexclusivity is covered through agreements that specify a licensor’s marketing rights and duties, such as for copromotion.
<table>
<thead>
<tr>
<th>Licensor/Licensee</th>
<th>Compound/Technology</th>
<th>Deal Terms</th>
</tr>
</thead>
<tbody>
<tr>
<td>Neurocrine/Pfizer</td>
<td>Indiplon, an insomnia agent</td>
<td>Pfizer gains exclusive worldwide development and marketing rights in exchange for upfront, milestone, and royalty payments.</td>
</tr>
<tr>
<td>Millennium/Ortho Biotech</td>
<td>Velcade, a first-in-class chemotherapeutic agent</td>
<td>Millennium retains all US commercialization rights to and profits; Ortho will commercialize outside the United States, and Millennium retains an option to co-promote the drug at a future date in certain European countries. Millennium will receive royalties from Ortho Biotech on sales outside the United States and receives an upfront payment of $15 million. Milestone payments for clinical development, regulatory development outside the United States, and sales milestones are included.</td>
</tr>
<tr>
<td>Avanir Pharmaceuticals/ Peregrine Pharmaceuticals</td>
<td>An anti-cancer antibody</td>
<td>In exchange for a license fee, milestone and royalty payments, or sales may be received for Avanir’s antibody.</td>
</tr>
<tr>
<td>Texas Biotechnology/ Revotar Biopharmaceuticals</td>
<td>Bimosiamose, a selectin antagonist for the treatment of asthma and other inflammatory indications</td>
<td>Through an exclusive license Revotar obtains exclusive worldwide rights to antiinflammatory indications as well as ex-North American rights for topical indications. Texas Biotechnology will have exclusive worldwide rights for use in organ transplantation as well as exclusive North American rights to all topical indications. Each party has certain revenue sharing and royalty obligations.</td>
</tr>
<tr>
<td>Vertex/Kassai Pharmaceuticals and Glaxo SmithKline</td>
<td>HIV protease inhibitor, Agenerase</td>
<td>An exclusive license agreement: Upon filing for approval in Japan, Vertex Pharmaceuticals and Glaxo SmithKline receive a $1 million milestone payment. In the United States, the drug is licensed to Vertex’s partner Glaxo for development outside the Far East.</td>
</tr>
<tr>
<td>Genentech/Serono</td>
<td>Raptiva, for psoriasis</td>
<td>Exclusive license for Serono to develop and market worldwide outside the United States and Japan. Development and marketing rights in the United States and Japan remain with Genentech. Additional emerging Asian markets were added to the license.</td>
</tr>
<tr>
<td>Enzon/Aventis</td>
<td>Oncaspan, for acute lymphoblastic leukemia</td>
<td>Reacquisition of marketing and distribution rights by Enzon for certain territories previously licensed to Aventis. Enzon to pay $15 million as well as 25% royalty on future net sales in the United States and Canada for a period of 12 years.</td>
</tr>
<tr>
<td>Neurobiological Technologies Inc./ Merz Pharmaceuticals</td>
<td>Memantine, for Alzheimer’s disease, neuropathic pain, AIDS-related dementia</td>
<td>Sharing of scientific, clinical, and regulatory information and revenue in certain geographic markets. Upon FDA approval, terms call for a milestone payment of $2.25 million, royalty payments, license fee payments from Merz, with substantially higher royalty rates for indications other than Alzheimer’s disease.</td>
</tr>
<tr>
<td>Nektar/GlaxoSmithKline</td>
<td>Advanced PEGylation technology</td>
<td>Nektar to receive milestone payments and manufacturing revenues during development and upon successful commercialization.</td>
</tr>
<tr>
<td>Cambridge Antibody Technology/Xoma</td>
<td>Antibody-related technologies</td>
<td>Cross-licensing by which CAT has rights to use the technology for developing products in exchange for license payments. XOMA receives the right to use the antibody libraries for its R&amp;D, with an option to develop antibodies into therapeutic agents in exchange for license payments.</td>
</tr>
<tr>
<td>CuraGen/Bayer</td>
<td>Genomic technologies</td>
<td>CuraGen will provide 80 drug targets. Bayer will use screening to develop small-molecule compounds against these targets, with co-commercialization of the resulting products.</td>
</tr>
</tbody>
</table>

The stage of development determines the breadth of a license. Additionally, generation of technology covered by the license must be clearly defined because differing rights could be granted in different patents. For example, one patent might be licensed exclusively and a second nonexclusively, or the licensed territories might be different. For one patent, the claimed use could be licensed exclusively and the compound per se nonexclusively, whereas for a second patent, the compound per se could be licensed exclusively (9).

Cross licenses to existing IP are typically used to prevent conflict or competing patent positions. The environment in which such agreements are negotiated is often one of actual or threatened litigation.

**Placing a Value on Research Tools**
Some strategies to capture the value of research tools include grant-backs, reach-through provisions, research collaboration/joint ventures, vertical integration into pharmaceutical drug discovery, and marketing.

**Grant-back provisions** license back to a licensor discoveries made using research tools. These provisions are often met with resistance within the pharmaceutical industry. Unless a licensor can exploit discoveries using research tools (e.g., selling drugs developed using a tool), the licensor will have a problem extracting value from the licensed IP.

**Reach-through provisions** provide royalties on drugs discovered using a given tool. In general, “reach through” claims attempt to capture the value of
companies alike must improve the pharmaceutical and biotechnology industry. Myriad issues confront the process through which they can achieve their corporate objectives. Licensing is playing an increasing role in the business model of pharmaceutical and biotechnology companies. Industry leaders now recognize licensing as a strategic mechanism through which they can achieve their corporate objectives. Myriad issues confront the process of licensing biotechnology, and pharmaceutical and biotechnology companies alike must improve the execution of licenses to reduce the current rate of attrition. Interests and goals of the parties to licensing agreement affect the negotiation process and define the terms of their agreement. Of importance is the need to balance the need for clarity in the license language with the need to avoid overcomplication, either of which can result in disagreements and litigation. Additionally, the various key elements of the licensing process must be adjusted if there is to be a successful outcome that meets each party’s needs.

**REFERENCES (PART 3)**


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**NEGOTIATED LICENSING TERMS**

- Confidentiality obligations
- Consideration
- Duration
- Indemnification and product liability responsibility
- Licensed property
- Obligations of the licensee
- Obligations of the licensor
- Ownership, right to use and improvements of intellectual property
- Recordkeeping requirements
- Reporting and recordkeeping requirements
- Scope of rights granted
- Termination and exit strategies
- Terms of the license
- Territory

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a discovery before it may be a full invention. That is, such provisions are designed to cover biotechnology products or their use before identification of the products themselves. One advantage of a reach-through provision is that a licensee shares a risk with a licensor of being unable to commercialize product. Additionally, the licensor can participate in the upside potential of downstream discoveries. Disadvantages of reach-through provisions include patent stacking, industry resistance, and difficulty determining which products were the result of using the research tool.

**Research Collaboration/Joint Ventures:** Academic research collaboration may take the form of material transfer agreements (MTAs). Such agreements are useful when a pharmaceutical company is negotiating with a biotech company to evaluate a potential product or when third-party researchers need to be given materials for specified research purposes. Under MTAs, compounds or technologies can be transferred for noncommercial research. Such agreements pose few limitations such as reach-through rights. The transfer may limit use to research. MTAs can be used as ancillary agreements separate from or as appendices to a main license agreement. They can detail confidentiality, product liability and indemnification, and use of trademarks, among other issues.

For further information on biotechnology licensing, readers are referred to the resources listed in the “Licensing Resources” box.

**REACHING FOR A SUCCESSFUL OUTCOME**

Licensing is playing an increasing role in the business model of pharmaceutical and biotechnology companies. Industry leaders now recognize licensing as a strategic mechanism through which they can achieve their corporate objectives. Myriad issues confront the process of licensing biotechnology, and pharmaceutical and biotechnology companies alike must improve the