

# **Working Together in the Pharmaceutical, Biotech and Medical Device Industries: Contractual Terms and Conditions**

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## **I. Background**

Collaboration between companies is essential for success in the Pharmaceutical, Biotechnology and Medical Device (PB&MD) industries. The efforts required in bringing a therapy from discovery through development, regulatory approval, manufacturing and marketing are rarely the result of one company's efforts. Instead, there is typically joint activity at one or more stages along the product development timeline. For the calendar quarter ended March 31, 2004, earned alliance revenues by biotech companies from pharma companies increased by 26% versus the first quarter of 2003, totaling \$756 million.<sup>1</sup> Technology platform firms, including genomics companies such as Affymetrix, Millennium and Incyte, were the beneficiaries of 62% of these earned revenues through license agreements with large pharma companies. Disease-oriented companies accounted for 31% of the revenues recorded, with drug delivery companies receiving the remaining 7%.<sup>2</sup>

Even companies previously known for conducting all research and development activities in-house, such as Amgen and Merck, have been behaving more like perennial networker, Eli Lilly. Amgen is currently co-developing a monoclonal antibody used to treat colorectal cancer with Abgenix and collaborated with Immunex and Tularik prior to acquiring both companies. Merck made headlines earlier this year when it agreed to partner with Lundbeck to develop and commercialize a Phase III product for sleep disorders.<sup>3</sup>

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<sup>1</sup> Signals Magazine, "First Quarter 2004 Alliance Scorecard – Chemistry, Cancer Coming On Strong," July 30, 2004, available at <http://www.signalsmag.com/signalsmag.nsf/0/AC6574BAF77819ED88256EE100711FBA>.

<sup>2</sup> Ibid.

<sup>3</sup> Contract Pharma, "Top 20 Pharma" and "Top 20 BioPharma," July/August 2004, available at <http://www.contractpharma.com/>.

The pace of alliances continues unabated. According to the brochure for Allicense 2004, this year's version of Recombinant Capital's premier alliance and license program, the industry struck \$8.8 billion in new alliances in 2003, surpassing all previous years.<sup>4</sup> Traditionally, many of these collaborations involved biotech companies relying on big pharma to gain funding, expertise, credibility and strategic positioning in return for technologies that enable target identification and validation.<sup>5</sup> Recently, however, there have been an increasing number of biotech/biotech, pharma/pharma and biotech or pharma/medical device collaborations as well. With the continued skyrocketing costs to develop and commercialize a compound, device or drug, the trend towards increased collaboration is expected to continue. Pharma companies will continue to seek partnerships in an effort to replenish their famously dry pipelines with a steady flow of specialty and medium-sized drugs and, with a few notable exceptions like Amgen and Genentech, biotech companies still rely on the strength of big pharma for funding and critical mass in sales and marketing.<sup>6</sup> As Ligand's CEO David Robinson's articulated in his well-known "10/50/40 formula" several years ago, financing provided by pharma to biotech companies struggling during periods of dry capital markets continues to be relevant.<sup>7 8</sup>

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<sup>4</sup> Brochure for "Allicense 2004: Creating and Sharing Value Through Alliances" available at [www.recap.com/sitehome.nsf/alliance](http://www.recap.com/sitehome.nsf/alliance).

<sup>5</sup> Nature Reviews, "The Evolution of Biotech," Volume 1, November 2002 available at [www.nature.com/nrd](http://www.nature.com/nrd).

<sup>6</sup> Contract Pharma, "Pharma – Biotech Alliances: Jockeying for Position in the Race to Become 'Partner of Choice,'" September 2003 available at <http://www.contractpharma.com/Sep031.htm>.

<sup>7</sup> Signals Magazine, "10 Deals That Changed Biotechnology," November 1998, available at <http://www.signalsmag.com/signalsmag.nsf/0/BB43E11A1620473F882566BB00762E28>.

<sup>8</sup> The 10/50/40 Formula refers to the expected percentages of the several hundred million dollars in capital required by a typical biotech company over its first decade from venture capital firms, big pharma strategic investments and alliances, and public equity markets, respectively.

This paper examines the various types of collaborative efforts commonly undertaken by companies in the pharma, biotech and medical device industries. It analyzes real-world examples of each type, from the much-litigated agreements whereby Amgen granted a global product and technology license for erythropoietin to Johnson & Johnson for all uses except dialysis in the United States in exchange for a few million dollars when the biotech industry was in its infancy to the recent early-stage research and development collaboration blockbuster between Bayer and CuraGen for metabolic disorders. As a group, biotech companies have been able to obtain much more favorable deals in the last few years than was the case in the prior decade. Since the strengths and weaknesses and negotiating leverage of each party will vary from deal to deal, the specific terms and conditions contained in each agreement will be varied and distinct. Nevertheless, since many companies face similar challenges in bringing new therapies to market, there is value in identifying commonalities and classifying common types of collaborations into categories. This categorization will allow for the identification and study of those issues commonly raised by each type of agreement. Excerpts from the agreements governing the real-world examples mentioned throughout the study to demonstrate how the parties address these issues in the context of the legal documents.

## **II. Types of Collaborations**

First, it is useful to start with a basic definition of collaborations. I have defined it very broadly to mean any agreement between two or more separate companies (but excluding simple customer / supplier relationships) in an effort to bring a product or therapy to market. The relative involvement of the parties in that joint effort can

obviously vary greatly depending on the needs and capabilities of each party, as will become apparent below.

Although relationships between collaborators often include more than one of the following elements, most agreements can be grouped as follows: (i) traditional product or technology licenses, (ii) full collaborations involving research, development and commercialization phases, (iii) contract manufacturing arrangements, and (iv) co-marketing and co-promotion agreements.

#### **A. Traditional Licensing Deals**

##### ***Basic Structure of Licensing***

In the traditional product or technology license model, the buyer of the license receives product or technology rights from the seller in exchange for an up-front fee and royalties on milestones. In addition, the buyer is typically responsible for all development and commercialization expenses and may have an obligation to make milestone payments to the seller upon reaching or completing various stages in the U.S. Food and Drug Administration's (FDA) approval process.<sup>9</sup> The main purpose of a license agreement is the grant of intellectual property rights. In that broad sense, a licensing component is present in the majority of collaborations in the industry. In fact, one study identified a licensing arrangement in about two-thirds of all alliances tracked between 1993 and 2001 by the database created by Recombinant Capital (ReCap).<sup>10 11</sup>

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<sup>9</sup> Signals Magazine, "The New Deal Drivers," June 2001, available at <http://www.signalsmag.com/signalsmag.nsf/0/A40FB8300B07C17188256A62007A4AB2>.

<sup>10</sup> Rasmussen, Bruce, "The Role of Pharmaceutical Alliances," June 2002, available at [www.cfses.com/pharma/documents/02-Role\\_of\\_Alliances.pdf](http://www.cfses.com/pharma/documents/02-Role_of_Alliances.pdf).

<sup>11</sup> The ReCap database contains comprehensive worldwide alliance information that it garners from public sources, such as press releases and filings with the U.S. Securities and Exchange Commission (SEC), and from companies themselves. It is available for a subscription-fee at [www.recap.com](http://www.recap.com).

## *Reasons for Licensing*

There are a number of reasons a company might out-license a technology or product. It may be a technology that the company owns but does not intend to use or does not have the resources or expertise to exploit the technology to its full potential. This latter instance is a primary reason behind biotech companies licensing late-stage drug and protein candidates to large pharma companies that have a large-scale sales and marketing program already in place. It is also common to develop a product or technology in a particular field or territory and license it to a third party to develop it for different applications or in other locations in exchange for an upfront payment.<sup>12</sup> This is what Amgen did with EPO back in 1985 when it was strapped for cash and granted a license to Ortho, a subsidiary of Johnson & Johnson (J&J), to sell and market the product for all indications outside the field of kidney dialysis in the United States. Even though Amgen has realized nearly \$7 billion in revenues from EPO in the last three years alone, J&J's sales have been in the billions of dollars each year as well for sales in the cancer market and abroad.<sup>13</sup> For this, J&J made an upfront payment to Amgen attributable to EPO of just \$1 million, milestone payments aggregating \$6 million paid upon the commencement of clinical studies and approval of the product, and a 10% ongoing royalty on product sales. Finally, many technology platform companies use licensing revenue as a central part of their business plan. Affymetrix is an example of a company that created a library of genetic information that it licenses to third parties for a substantial fee. In fact, in January 2003, Affymetrix signed a licensing deal with Roche

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<sup>12</sup> Bio-Science Law Review, "Collaborations and Licensing – Key Legal Issues," August 2001, available at [http://pharmalicensing.com/features/disp/999169964\\_3b8e1facbc8a1](http://pharmalicensing.com/features/disp/999169964_3b8e1facbc8a1).

<sup>13</sup> Amgen's Annual Report on Form 10-K for the year ended December 31, 2004, available at [www.sec.gov](http://www.sec.gov).

for access to its GeneChip platform in exchange for an upfront payment of \$70 million.<sup>14</sup>

Language from the contracts for both the Amgen / Ortho and the Affymetrix / Roche deals will be reviewed in more detail below.

Obtaining license rights is desirable for companies who wish to expand their portfolio of drug candidates quickly while reducing the time, risk and expense associated with internal research and development programs. This was the driving force behind Merck's recent license of a late-stage sleep disorder drug from Lundbeck.<sup>15</sup> Having invested significant resources in a powerful sales force, Merck needed to fill its pipeline quickly with products so that sales force can continue to sell, even as many of its internally developed blockbuster drugs lose patent protection in the short-term.

Licensing may also assist a company in its own internal R&D efforts by allowing for access to platform technologies and software products that assist in its internal research and drug development. Finally, licensing is often necessary to avoid an infringement action by a third party who owns prior intellectual property rights that would make it difficult or impossible to move forward without it.<sup>16</sup>

### ***Key Issues in License Agreements***

#### **Subject Matter and Scope**

The most important provision in any license agreement concerns the subject matter and scope of the license grant. This includes a careful description of exactly what rights are being licensed (patents, trademarks, know-how, etc.), the field of use for which the rights are being granted, the territory in which the rights are being granted and

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<sup>14</sup> Affymetrix, Inc.'s Annual Report on Form 10-K for the year ended December 31, 2003, available at [www.sec.gov](http://www.sec.gov).

<sup>15</sup> Biotech Infowire, "Merck Licenses Late-Stage Sleep Drug From Lundbeck," February 11, 2004, available at <http://www.biotechinfowire.com/news.asp?nid=722&ntid=113&pg=1>.

<sup>16</sup> Bio-Science Law Review, *supra*, note 12.

whether or not the license is to be exclusive, non-exclusive or sole. Also important is to delineate what rights, if any, the parties will have in any improvements to the licensed subject matter.

The license grant in the Amgen – Ortho product license agreement provides that:

***“Amgen hereby grants to Ortho, but not to its Affiliates, except as hereinafter provided, an exclusive license to make in one location, have made and use Licensed Know-How, Licensed Patents and Licensed Products in the Licensed Territory in the Licensed Field and to sell Licensed Product in the Licensed Territory.”***

And:

***“Amgen, having received the consent of Kirin Brewing Co., Ltd., hereby grants to Ortho but not affiliates, an exclusive license, except as against Amgen’s rights under this Agreement in the Licensed Territory, to make EPO in one location in the United States for use and sale outside the Licensed Territory but not including China and Japan.”***

The key defined terms in this clause include the Licensed Territory, which is the United States, including Puerto Rico, and the Licensed Field, which is all indications for human use except dialysis and diagnostics. This means that, by way of these provisions, Amgen granted an exclusive license for EPO to J&J for all indications except dialysis in the United States and for all indications outside the United States. Since the license grant is exclusive (only J&J has the right to use and sell the product in certain cases), as opposed to sole (Amgen would retain rights to use and sell in addition to J&J but would not grant rights to other third parties), or non-exclusive (J&J would have rights, but so could anyone else to whom Amgen wished to grant a similar license), the only way that Amgen benefits economically from the license grant in the future is if J&J successfully exploits the technology or product. Therefore, it is common to include a provision regarding the licensee’s efforts, as Amgen did, as follows:

***“Ortho agrees to use reasonable efforts to market and sell Licensed Products in the Licensed Territory.”***

In the case of EPO, however, subsequent litigation around the license grant did not arise as a result of the licensee failing to use reasonable efforts to exploit the product, but rather its zealously in doing so. In an arbitration brought by Amgen and decided in October 2002, Amgen sought termination of the license on the grounds that Ortho had breached the agreement by selling into the dialysis market. Although the arbitrator did, indeed, find that Ortho had sold into the Amgen’s retained market, he decided that this activity did not warrant the extraordinary remedy of terminating the agreement, but rather Amgen could be adequately compensated with monetary damages. Amgen was awarded \$150 million in damages plus its reasonable costs and attorney’s fees.<sup>17</sup>

The right to use improvements in the subject matter will be important from both the perspective of the licensee having access to improvements made by the licensor and the licensor having access to improvements made by the licensee. These issues can be dealt with in any number of ways from allowing the other party access to use the improvements without requiring additional royalties to giving the non-inventing party a right of first option to the improvements. Amgen and Ortho chose the common method of allowing the other royalty-free access to the improvements on a reciprocal basis:

***“If Amgen, on the one hand, or Ortho and/or its Affiliates and sublicensee(s), on the other hand, improve the Product Organisms, and/or the Licensed Know-How, or make Licensed Products or process improvements, all such improvements shall become part of the Licensed Know-How and shall be promptly transferred and/or communicated to the other party in order to maintain parity among Amgen, Ortho and its Affiliates and sublicensees and by the provisions hereof shall be deemed to be a part of the Licensed Patents or Licensed Know-How as the case may be and licensed to Amgen or Ortho, as the case may be, on a royalty-free basis.”***

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<sup>17</sup> Johnson & Johnson’s Annual Report on Form 10-K for the year ended December 31, 2003, available at [www.sec.gov](http://www.sec.gov).

The agreement does provide, however, that any technology or improvements developed by either party shall be and remains the property of the developing party, which becomes very important if and when the license is terminated.

### **Economic Terms**

License payments in the license agreement can be structured in an infinite number of ways. The most common are: (i) lump sum licenses, where the licensor pays a fixed sum up-front for continuing access to the licensed technology, (ii) pure royalty licenses, which are usually based on a percentage of sales, (iii) down payment license with royalty fees, which are basically a combination of (i) and (ii) and ensure some level of commitment by the licensee but allow for the licensor to share in the ‘upside’, (iv) royalty licenses that include a ‘kicker’ or scaled on level of sales, which could include higher or lower royalty percentages as sales increase or maybe even include a maximum royalty amount.<sup>18</sup>

Affymetrix structured its royalty payment mechanism to ensure Roche would use diligence in creating array-based diagnostic products based on Affymetrix’s proprietary GeneChip platform. In addition to an access fee of \$70 million, Roche agreed to pay minimum royalty amounts as follows:

***“Roche and its Affiliates shall pay Affymetrix quarterly royalties of [\*\*\*]% of Net Sales (the “Base Sales Royalty”); provided, however, that the Base Sales Royalty associated with any particular Diagnostic Product may be reduced to no less than [\*\*\*]% of Net Sales associated with that Diagnostic Product sold by Roche or its Affiliates (the “Minimum Sales Royalty”)....”***

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<sup>18</sup> Razgaitis, Richard, “Structure of Licensing Payments,” appearing as Chapter 11 in Valuation and Pricing of Technology-Based Intellectual Property, 2002 ed.

### **Maintenance and Enforcement of Patents**

The license agreement must also address which party will be responsible for maintaining and enforcing the patents and for paying the expenses associated therewith. This can be a significant issue, especially in instances involving a large number of patents in many jurisdictions. Typically, the patent owner will bear this responsibility. In some grants of exclusive licenses, this obligation is transferred to the licensee. In either case, an exclusive licensee will want the power to enforce the patent against infringing third parties.<sup>19</sup> In the Amgen / Ortho agreement, Amgen has the obligation to maintain the patents and the right but not the obligation to defend them against infringement and to cooperate with Ortho in the defense of same. In the event Amgen elects to not exercise its rights, or fails to meet its obligations, Ortho has the right but not the obligation to do so instead. Affymetrix did not extend the same courtesy to Roche:

***“No Roche Right to Enforce the Licensed Patents. It is expressly understood that nothing contained herein shall in any way grant or be construed to grant to Roche the right to enforce the Licensed Patents or any other Affymetrix Technology. Affymetrix shall have the sole right to bring legal action to enforce the Licensed Patents against any alleged infringement by any Third Party.”***

### **Term and Termination**

The term of the license will depend on the subject matter being licensed and will typically be limited to the last to expire patent involved in the license grant. The agreement will specify certain events that will lead to early termination of the license. These vary from a typical clause involving material breach of contract and insolvency of either party to heavily negotiated provisions involving termination for change of control or failure to meet certain minimum product sales levels or a minimum level of royalty payments. Given the ever-changing nature of the pharma and biotech industries, some

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<sup>19</sup> Bio-Science Law Review, supra note 12.

agreements will allow for unilateral termination with a period of notice and, often, the payment of a fee. For example, Roche has the right to terminate its agreement with Affymetrix upon one year's notice at certain specific time periods and payment of the next installment payment due on the license:

***“Early Termination without Cause. Roche shall have the option of terminating this Agreement in its entirety effective on December 31, 2007, June 2, 2013 or any date after June 2, 2013 but prior to the Termination Date by written notice to Affymetrix (“Early Termination Notice”) as provided herein. An Early Termination Notice must be provided at least one year prior to early termination. If Roche terminates effective as of June 2, 2013, Roche shall pay to Affymetrix the License Installment Payment deemed earned January 1, 2013 and payable June 1, 2013 but shall have no obligation to pay any further License Installment Payment required hereunder (but shall continue to pay royalties on Diagnostic Product sales through the final termination date of this Agreement in accordance with the terms hereof).”***

#### **Other**

Each license agreement will also contain standard terms and conditions governing such things as prohibitions on assignments and sublicensing, confidentiality, dispute resolution, representations and warranties, limitations of liability and indemnities.

### **B. Research, Development and Commercialization Collaborations**

#### ***Basic Structure of Collaborations***

A comprehensive collaboration agreement addresses all aspects of the product development process from identifying a therapeutic candidate through basic research, developing the candidate and shepherding it through clinical trials and the FDA approval process, to setting forth a plan for manufacturing and commercializing the resulting product in the marketplace. Typically, each party to the collaboration brings existing intellectual property rights (known as background rights) that has relevance to the area in which the parties intend to join efforts and the agreement would contemplate working

together on a research project creating new intellectual property rights (known as foreground rights) for which ownership would be governed by the terms of the contract. These relationships tend to include a funding element, including both up-front payments as well as additional payments based on the achievement of specified milestones. The agreement will also address how the parties divide revenues generated by the resulting product.

### ***Reasons for Collaborations***

Collaborations arise for a variety of reasons. In some cases, two companies will realize that they have complementary intellectual property rights and/or expertise that require them to cooperate in order to make further advancement in their chosen field.<sup>20</sup> Collaborations with larger, more established companies are often sought after by nascent companies with a desire to fund its research and development expenses. Collaboration is often doubly beneficial to these smaller players because the larger partner often provides direct financing and the mere existence of the collaboration serves as to enhance the start-up's reputation and provide validation for the subject technology in the scientific and financial realms, which often leads to additional outside funding from venture capitalists or public capital markets. The more established partner has its own reasons for collaborating in those instances, including access to new technologies and platforms without making as large an investment as would be required to acquire its partner or duplicate its efforts internally. In that way, the major players can diversify research dollars across more projects and programs.

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<sup>20</sup> Bio-Science Law Review, *supra*, note 12.

A number of these factors were involved when Bayer and CuraGen announced their astonishing \$1.3 billion joint development deal for drug discovery and development in the metabolic disorder area in 2001. In that deal, both parties contribute toward development costs (Bayer 56% to CuraGen's 44%) and share in the profits in the same proportion. CuraGen is responsible for identifying a number of gene and protein targets for which Bayer will then apply its massive drug discovery efforts to find small molecule compounds that work on those targets.<sup>21</sup>

Earlier this year, NitroMed, Inc., an emerging pharmaceutical company that specializes in therapies based on the naturally occurring molecule nitric oxide, extended its exclusive worldwide research collaboration, licensing and commercialization agreement with The Boston Scientific Corporation.<sup>22</sup> Boston Scientific agreed to provide additional funding to continue the joint development effort to bring nitric oxide coated stents to the cardiology marketplace.

ImClone Systems also benefited enormously from funding by its development and commercialization partner, Bristol-Myers Squibb, who agreed to pay ImClone upfront and near-term royalty payments in excess of \$1 billion to join ImClone's effort to develop, promote, manufacture and distribute Erbitux, ImClone's monoclonal antibody treatment used to target and block cancerous cells, especially in the colon. In addition, Bristol-Myers invested another \$1 billion in ImClone by purchasing 20% of its stock. This late-stage deal was signed on the eve of ImClone's filing of its fast-tracked Biologics License Application with FDA and what most expected to be a swift and

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<sup>21</sup> The Motley Fool, "CuraGen, Bayer in Historic Biotech Drug Deal," January 19, 2001, available at <http://www.fool.com/news/foolplate/2001/foolplate010119.htm>.

<sup>22</sup> Forbes.com, "NitroMed, Boston Scientific Extend Licensing Pact," January 8, 2004, available at <http://www.forbes.com/home/newswire/2004/01/08/rtr1203184.html>.

certain approval process. Unfortunately, faulty trial design led to the FDA sending a letter of refusal to file just a few months later, which sent ImClone's stock into its now-famous tailspin, causing Bristol-Myers Squibb to try to renegotiate its deal and landing Martha Stewart a jail sentence.<sup>23</sup> Language from each of the Bayer / CuraGen, NitroMed / Boston Scientific and the ImClone / BMS deals appears below.

### ***Key Issues in Collaborations***

#### **Objectives and Governance**

An important issue in any research and development collaboration is defining the objective and creating a research plan that is specific enough so that the parties know exactly what is expected of them, but also flexible enough to adjust for unforeseen situations and complications that will inevitably arise. The roles and responsibilities of each party should be clearly defined at all stages of the collaboration. The Bayer / CuraGen agreement provides a good example of this by breaking the overall collaboration into several separate but related phases, including the Qualified Target Production Phase, the Target Screening Phase, the Strategic Project Phase, the Pre-Clinical Development Phase, the Clinical Development Phase and the Commercialization Phase, each with several pages of specific obligations of each party. The NitroMed / Boston Scientific agreement provided the following with respect to the R&D program:

***“Pursuant to the terms of this Agreement, the Parties have agreed to collaborate on the research and development of Royalty-Bearing Products. The objective of the R&D Program will be for NitroMed to identify and deliver to BSC two (2) NitroMed Delivered Compounds meeting the criteria set forth in the R&D Plan and for BSC to develop and commercialize Royalty-Bearing Products based on such NitroMed Delivered Compounds. Both Parties will be engaged in, and responsible for, the***

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<sup>23</sup> Burrill, G. Steven, American Technology Laboratory, BioBusiness, “ImClone: The Drama Comes Full Circle ... but What Did We Learn?” April 2004, available at <http://www.iscpubs.com/articles/agpt/g0404bur.pdf>.

***conduct of the R&D Program. BSC will be responsible for the commercialization of Royalty-Bearing Products.”***

All three agreements use one or more committees to allow for flexibility; the ImClone / BMS agreements is very formal in this regard, setting up a Joint Commercialization Committee, a Joint Executive Committee and a Joint Manufacturing Committee, as well as appointing Alliance Managers from each company:

***“Alliance Managers. Each of the Company, on the one hand, and BMS and ERS collectively, on the other hand, shall appoint one senior representative who possesses a general understanding of clinical, regulatory, manufacturing and marketing issues to act as its respective alliance manager for this relationship (each, an "Alliance Manager"). The initial Alliance Managers are set forth on Exhibit 2.1. Each of the Company, on the one hand, and BMS and ERS collectively, on the other hand, may replace its respective Alliance Manager at any time upon written notice to the other in accordance with Section 16.5 of this Agreement. Any Alliance Manager may designate a substitute to temporarily perform the functions of that Alliance Manager. Each Alliance Manager shall be charged with creating and maintaining a collaborative work environment within and among the Committees. Each Alliance Manager will also be responsible for:***

***(a) Coordinating the relevant functional representatives of the Parties, in developing and executing strategies and plans for the Products in an effort to ensure consistency and efficiency within the Territory;***

***(b) providing a single point of communication for seeking consensus both internally within the respective Party's organizations and together regarding key strategy and plan issues;***

***(c) identifying and raising cross-country, cross-Party and/or cross-functions disputes to the appropriate Committee in a timely manner; and***

***(d) planning and coordinating: (i) cooperative efforts in the Territory; and (ii) internal and external communications.***

***The Alliance Managers shall be entitled to attend meetings of any of the Committees, but shall not have, or be deemed to have, any rights or responsibilities of a member of any Committee. Each Alliance Manager may bring any matter to the attention of any Committee where such Alliance Manager reasonably believes that such matter requires such attention.”***

### **Intellectual Property Rights**

It is standard for the parties to acknowledge that background intellectual property remains the property of the original owner:

***“Bayer acknowledges and agrees that CuraGen is and shall remain the sole owner of the CuraGen Know How and the CuraGen Patent Rights and that CuraGen shall be and remain the sole owner of the CuraGen Improvements and the CuraGen Improvement Rights. Bayer further acknowledges and agrees that neither Bayer nor any of its Affiliates shall have any rights in or to the CuraGen Patent Rights, the CuraGen Know-How, the CuraGen Improvements, or the CuraGen Improvement Rights, other than the rights specifically granted herein. CuraGen acknowledges and agrees that Bayer is and shall remain the sole owner of the Bayer Know How and the Bayer Patent Rights and that Bayer shall be and remain the sole owner of the Bayer Improvements and the Bayer Improvement Rights. CuraGen further acknowledges and agrees that neither CuraGen nor any of its Affiliates shall have any rights in or to the Bayer Patent Rights, the Bayer Know-How, the Bayer Improvements, or the Bayer Improvement Rights, other than the rights specifically granted herein.”***

It is also standard to grant the other party a license to such rights to the extent necessary to further the objectives of the collaboration:

***“Subject to the terms and conditions of this Agreement, NitroMed hereby grants to BSC a non-exclusive, non-royalty-bearing right and license in the Territory, without the right to grant sublicenses, under NitroMed's rights in 9 NitroMed Intellectual Property, to make and use NitroMed Nitric Oxide Releasing Compounds in the course of the R&D Program to develop Royalty-Bearing Products.”***

Inventions made in the course of the joint research and development efforts is either vested in one party (usually, but not always, with a royalty-free, perpetual license granted to the other party) or in both parties (joint ownership). NitroMed and Boston Scientific took a tailored approach as their primary areas of interest in nitric oxide releasing compound and medical devices, respectively, do not overlap, except where there is overlap in the technologies themselves:

***“Compound Inventions. NitroMed shall exclusively own all inventions made by either Party, their employees, agents and consultants, or jointly by any of the foregoing, in the course of, and while engaged in, the R&D Program that relate solely to the composition of Nitric Oxide Releasing Compounds ("Compound Inventions").***

***Device Inventions. BSC shall exclusively own all inventions made by either Party, their employees, agents and consultants, or jointly by any of the foregoing, in the course of, and while engaged in, the R&D Program that relate solely to medical devices, coatings for medical devices or the use of medical devices ("Device Inventions").***

***Compound / Device Inventions. BSC and NitroMed shall jointly own all inventions made by either Party, their employees, agents and consultants, or jointly by any of the foregoing, in the course of, and while engaged in, the R&D Program that relate to both the composition or use of Nitric Oxide Releasing Compounds, on the one hand, and medical devices, coatings for medical devices or the use of medical devices, on the other ("Compound/Device Inventions").***

In the ImClone / Bristol-Myers Squibb deal, ImClone owns all intellectual property developed jointly and even that which is developed solely by BMS, except where the rights have general utility outside the subject matter of the agreement:

***“Ownership. All Inventions developed by any Party or jointly by the Company, ERS, and/or BMS shall be owned by the Company, except for Inventions developed solely by ERS and/or BMS which have general utility in connection with other products and/or compounds in addition to the Compounds and/or Products, in which case ERS shall own such Inventions ("ERS Inventions"). To the extent necessary to effectuate the foregoing, ERS shall take any action reasonably necessary to effectuate the Company's ownership pursuant to the foregoing. The Company shall have all right, title and interest in and to the Patents, Know-How, and Trademarks, whether in existence on the Effective Date or developed during the term of this Agreement, subject to the rights granted to ERS and BMS pursuant to this Agreement.”***

### **Economics**

The economic provisions of collaboration agreements tend to be a cross-between the provisions found in license agreements (such as upfront, milestone and royalty payments) discussed above and those found in co-promotion agreements (such as profit sharing provisions) discussed below. Since late-stage therapeutic candidates pose less risk than more speculative early-stage compounds, the payments to the innovator are typically much higher as is the sharing of the revenues. Some agreements may be so early-stage that the parties simply agree to agree at a later point in time on an appropriate royalty amount or set parameters between which the negotiations will take place.

Although it is usually better to avoid creating unrealistic expectations by agreeing on the economic terms at the point of signing (even if they are to be re-negotiated later), it is

sometimes impossible to do so because the final product has yet to be conceptualized and the resulting product margins are unknown. In this instance, it is useful to set up in advance how any disagreement will be resolved and what factors should be relevant to that resolution in the event the parties cannot reach agreement at the appropriate time.<sup>24</sup>

It is also very common to have an equity investment made as part of the funding program, either in a separate agreement or within the collaboration agreement as NitroMed and Boston Scientific provided:

***“On or prior to the Effective Date, NitroMed and BSC are entering into a Stock Purchase Agreement (the "Stock Purchase Agreement") pursuant to which, subject to the terms and conditions contained therein, BSC shall purchase Series F convertible preferred stock of NitroMed for an aggregate purchase price of Three Million Five Hundred Thousand U.S. Dollars (US\$3,500,000) at a per share price of Fourteen U.S. Dollars (US\$14).”***

#### **Term, Termination and Exclusivity**

The term of collaboration agreements tends to be quite long given the length of time required to develop and commercialize therapies in the PB&MD industries.

Grounds for termination are generally narrow, indicating that, with respect to the subject matter of the agreement, companies tend to treat collaboration more like a marriage than an engagement. To continue that analogy, each usually expects exclusivity on the part of its partner relative to the subject matter:

***“ERS wishes to: (i) obtain the exclusive right to distribute, and the co-exclusive right to develop and promote (together with the Company), the Products in North America; (ii) obtain the co-exclusive right to develop, distribute and promote (together with the Company and the Merck Entities), the Products in Japan; and (iii) use the Company's registered trademarks for the Products in the Territory in connection with the foregoing, and the Company desires to grant such rights to ERS, on the terms and conditions set forth in this Agreement.”***

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<sup>24</sup> Structure of Licensing Payments, supra, note 18.

And it is not uncommon to ask for option rights or rights to negotiate for products not included in the current subject matter:

***“Right of First Negotiation of ERS Regarding Partnering Transactions. At any time during the Restricted Period, ERS shall have, and the Company hereby grants to ERS, a right of first negotiation to enter into a partnering arrangement with the Company (including, without limitation, any co-development, co-promotion, research and development, commercialization or intellectual property license agreement, joint venture, partnership, or other partnering relationship) involving compounds or products not directly relating to the Other Compound, to the extent involving the out-licensing of any of intellectual property or know-how owned by the Company or to which the Company has an exclusive license ("Partnering Relationship").”***

#### **Other**

Collaboration agreements also contain general provisions regarding confidentiality, representations and warranties, indemnification, and dispute resolution. In the latter case, an escalation provision followed by binding arbitration is the preferred method for resolving disputes because of the necessity that the parties reach a quick and inexpensive resolution of disputes so that the collaboration can continue. The NitroMed / Boston Scientific agreement contains a typical arbitration provision that allows for recovery of attorneys’ fees for the prevailing party in an effort to discourage speculative claims:

***“Alternative Dispute Resolution. Any controversy, claim or dispute arising out of or relating to this Agreement that has not been resolved by the Executive Officers within thirty (30) days of referral in accordance with Section 2.3 shall be resolved through binding arbitration as follows: a. All disputes arising out of this Agreement and referred to arbitration pursuant to this Section 9.1 shall be finally resolved by arbitration conducted in the English language in Boston, Massachusetts, in accordance with the American Arbitration Association ("AAA") Arbitration Rules and Supplementary Procedures for Large, Complex Disputes. b. The arbitrator shall rule on each disputed issue within ninety (90) days after he or she has accepted the appointment to serve as an arbitrator, provided that if the arbitrator is unable to render a decision within such ninety (90) day period, he or she shall render such decision as soon thereafter as is practicable. The arbitrator shall issue a written decision in order to explain the basis of the ruling. The arbitrator shall not have the authority to award punitive damages. c. The arbitrator shall be paid reasonable fees plus expenses. These***

*fees and expenses, along with the reasonable legal fees and expenses of the prevailing Party (including all expert witness fees and expenses), the fees and expenses of a court reporter, and any expenses for a hearing room, shall be paid as follows: i. If the arbitrator rules in favor of one Party on all disputed issues in the arbitration, the losing Party shall pay 100% of such fees and expenses. ii. If the arbitrator rules in favor of one Party on some issues and the other Party on other issues, the arbitrator shall issue with the ruling a written determination as to how such fees and expenses shall be allocated between the Parties. The arbitrator shall allocate fees and expenses in a way that bears a reasonable relationship to the outcome of the arbitration, with the Party prevailing on more issues, or on issues of greater value or gravity, recovering a relatively larger share of its legal fees and expenses. d. Any decision or award of the arbitrator shall be final, conclusive, and binding on the Parties to the dispute, and judgment may be entered on any award in any court of competent jurisdiction. To the extent lawful, the Parties exclude any right of application or appeal to the Massachusetts, United States or other courts in connection with any question of law arising in the arbitration or in connection with any award or decision made by the arbitrator, except as is necessary to recognize or enforce such award or decision.”*

### **C. Contract Manufacturing Arrangements**

#### ***Basic Structure of Contract Manufacturing Arrangements***

In a contract manufacturing arrangement, one party (the client) engages another party (the contractor) to manufacture product to agreed-upon specifications in exchange for a negotiated fee. These can be as basic as an agreement to manufacture a simple medical device or an active pharmaceutical ingredient and/or the drug’s final dosage form, to a complex biomanufacturing partnership involving cell culture and protein expression on a batch manufacturing basis. Demand for contract manufacturing in this latter category may get a further boost if the FDA allows for generic versions of biologics without full-scale clinical trials by showing bio-equivalence, much like generics in the pharma arena.<sup>25</sup> Manufacturing outsourcing can be done for the production of pre-

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<sup>25</sup> Contract Pharma, “Bio-Outsourcing Report – Will Bio-Generics Create a New CMO Business Model?” June 2004 available at <http://www.contractpharma.com/pdfs/060401.pdf>.

clinical, clinical product or commercial product, depending on the needs of the client and the manufacturing capacity of the contractor.

### ***Reasons for Contract Manufacturing Arrangements***

A client will engage a contract manufacturer when it does not have the capacity to manufacture its own product, such as when ImClone engaged Lonza Biologics to manufacture Erbitux, which was finally approved in February 2004 as a chemotherapy-partnered therapeutic to treat metastatic colorectal cancer.<sup>26</sup> In other instances, a contract manufacturer may be used to free-up capacity in the client's own manufacturing facilities such as when Genentech recently outsourced the production of Rituxin to Lonza, previously been manufactured in-house, presumably to clear its own capacity for the newly-approved drug Avastin (which will compete with Erbitux).<sup>27</sup> Another reason for outsourcing is to avoid capital expenditures and/or reduce time to market, as it can be a long, expensive undertaking to build and scale-up an FDA-approved manufacturing facility. In pharmaceuticals, a new business model of specialty pharma "virtual" companies has emerged, which by definition have no manufacturing capacity of their own and, therefore, rely on contract manufacturers for production. Finally, a client will engage a contractor when it lacks the in-house expertise and experience in complicated processes such as biomanufacturing.<sup>28</sup>

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<sup>26</sup> Ibid.

<sup>27</sup> Ibid.

<sup>28</sup> Contract Pharma, "Maximizing Outsourced BioPharma Production," June 2004, available at <http://www.contractpharma.com/pdfs/060402.pdf>.

## ***Key Issues in Contract Manufacturing Arrangements***

### **Responsibilities of Contractor**

It is essential in any contract manufacturing arrangement to clearly delineate the responsibilities of the contractor in the agreement. In the agreement between The Dow Chemical Company and GelTex Pharmaceuticals, Inc., a subsidiary of GenZyme, Dow makes RenaGel, a polymeric phosphate absorber for kidney dialysis patients, on behalf of GelTex.<sup>29</sup> In so doing, Dow undertakes to do the following:

***“Dow's manufacturing responsibilities are: (a) unloading, handling and storing raw materials and packaging materials at the Dow Facility; (b) manufacturing Product; (c) collecting and retaining for three (3) years lot samples of the Product; (d) packaging Product; (e) handling and storing bulk and packaged Product; (f) preparing Product for shipment; (g) making the Product available to a common carrier; (h) keeping records and reporting to GelTex and applicable governmental agencies; (i) handling, storing, treating, and disposing of Wastes generated by Dow in Dow's performance of this Agreement; and (j) compliance with all applicable laws and regulations regarding the manufacture of the Product, including, but limited to, current GMPs.”***

### **Economics**

Pricing for the manufactured product is typically based on volume and can be fixed or may vary depending on the costs of important raw materials costs. In addition, agreements often contain an inflation index for price changes beyond some fixed term. In the Dow / GelTex agreement, pricing is fixed for two years but such fixed price may be adjusted for changes in anticipated volumes or significant variations in price of a key ingredient.

### **Termination**

Early termination is a heavily negotiated option due to the tension between flexibility for both the client and the contractor and the need for the contractor to have a

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<sup>29</sup> Chemical & Engineering News, “Serving Emerging Pharma,” April 23, 2003, available at <http://pubs.acs.org/cen/coverstory/8116/8116pharma.html>.

commitment from the client prior to expending the up-front investment necessary to manufacture the product. Both parties also need time to make alternate arrangements in the event of termination. In Dow / GelTex, this is addressed by fixing a date prior to which termination is not allowed, and by adding a long-term notice provision as follows:

***“Dow shall have the right to terminate this Agreement by providing written notice of its desire to do so to GelTex. However, any such notice of termination provided by Dow to GelTex (i) shall not have an effective date of termination prior to December 31, 2003, and (ii) shall not have an effective date of termination that is less than twelve (12) months from the date such notice is delivered to GelTex.”***

### **Product Quality**

Important terms relating to product quality place limits on the ability of the contractor to make changes to the manufacturing process and assign responsibility for designing the product specifications depending on the nature of the relationship.

Regardless of which party designed and owns the product specifications, the contractor is responsible for manufacturing the product in accordance with the specifications and allowing for inspection prior to acceptance by the client. In the Dow / GelTex agreement, GelTex is responsible for the accuracy and completeness of the specifications:

***“Dow shall test or cause to be tested each batch of Product as specified in the Specifications before shipment to GelTex or its designee for compliance with the Specifications. The completeness and accuracy of the Specifications are solely GelTex's responsibility”***

### **Forecasting**

Each contract manufacturing agreement is likely to have several provisions relating to forecasting product needs and the ramifications of failing to purchase forecasted levels. The client will wish to maintain maximum flexibility, but the contractor will usually insist upon strict provisions because predictability is essential to a smooth and cost-efficient manufacturing process. Shortfalls often lead to liquidated

damages that are typically a fixed percentage intended to make the contractor whole from a margin perspective. The harshest provision from the client's perspective is known as a 'take or pay' provision which essentially requires the client to pay the full value of the product whether it needs it or not. Although these provisions are generally enforceable, the contractor is required by law to take steps to mitigate its damages and if no steps have been taken to begin manufacturing, a 'take or pay' provision may prove unenforceable as a penalty and the contractor may be limited to recovering out-of-pocket costs plus lost profits. The Dow / GelTex agreement has such a provision:

***“If GelTex, either itself or through its Affiliates, does not place purchase orders for the quantities it is required to purchase during any Calendar Year, then GelTex shall be obligated to pay to Dow an amount as if GelTex had purchased from Dow the full quantity it is required to purchase for that Calendar Year.”***

#### **Other**

Other important provisions in contract manufacturing agreements include force majeure (the circumstances under which performance may be excused), limitation of liability (often limited to refund of purchase price), confidentiality, insurance and audit and plant inspection rights.

#### **D. Co-Promotion Relationships**

##### ***Basic Structure of Co-Promotion Relationships***

Co-promotion relationships are also effective ways of outsourcing to others with excess capacity, but in this instance it is not manufacturing capacity the client is seeking. Rather, it is the marketing expertise and sales force of the contract provider. Although this is not a new phenomenon within the industry (pharma and biotech inked over 300 such agreements in the 1980s and 1990s), companies like Pfizer have taken it to a new

level in recent years by making co-promotion an important part of its business strategy.<sup>30</sup> Co-promotion has become big business, and not just in biotech and pharma. The battle to capture the booming drug-coated stent market has featured no less than three major collaborations, from Boston Scientific's partnership with Angiotech Pharmaceuticals to develop its Taxus stent to Medtronic's collaboration with Abbott Laboratories to develop a competing drug-coated stent. The threat and initial success of Boston Scientific's launch of Taxus earlier this year (prior to its well-publicized recall this summer) gave market-leader Johnson & Johnson a scare, causing J&J to announce a deal with Guidant to co-promote its Cypher stent. Event though Guidant has plans to enter the market in 2006 with its own product, currently in development, this deal gives Guidant immediate access to the market and a boost to short-term earnings. J&J benefits by doubling the size of the field sales force promoting the Cypher stent as well as access to Guidant's proprietary 'bioabsorbable' polymer technology, which could make for an improved J&J product in years to come.<sup>31</sup>

Although there is some distinction between co-marketing arrangements (two companies promoting the same product under two different names, which tend to be more common in Europe) and co-promotion agreements (two companies promoting the same product side-by-side, which is typically the method used in the United States), the terms are used interchangeably here to describe any relationship where one party engages the services of another to help sell a product that it has already developed and shares profits on sales of the product (as opposed to earning a commission on sales as in a sales

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<sup>30</sup> The Boston Globe, "Joint Marketing Reward Pharma Industry," September 8, 2002, available at <http://www.mult-sclerosis.org/news/Sep2002/BiogenSeronoPfizerJointMarketingAgreements.html>.

<sup>31</sup> The Motley Fool, "J&J, Guidant Join Forces," February 24, 2004, available at <http://www.fool.com/news/mft/2004/mft04022410.htm>.

representation agreement, or purchases and resales of the product, as in a distribution agreement).

### ***Reasons for Co-Promotion Relationships***

As evident from the maneuvering described above in the drug-coated stent market, companies enter into these relationships to increase their breadth and reach in promoting products. Co-promotion can be used to increase sheer numbers of sales reps or to access sales reps who have contact with physicians and expertise in a therapeutic area when one's in-house sales force does not. This may have been the case in Sankyo Pharma's decision to select Forest Laboratories for co-promoting its newly-launched Benicar angiotensin receptor blocker (ARB) anti-hypertension class in 2002, as Forest Laboratories had ready access to the cardiologists that would be essential in the success of the launch.<sup>32</sup> Companies that have an internally-developed late-stage product nearly ready for market but lack the selling force necessary for a successful launch will also look for the ideal pharma partner to provide access to the market. This is the situation Immunex (now a subsidiary of Amgen) faced when it engaged Wyeth-Ayerst to co-promote Immunex's rheumatoid arthritis drug Enbrel in the United States, a mere eight months before filing for its biologics license application.<sup>33</sup> Pharmaceutical companies look for these deals because problems of promotional overcapacity have become exacerbated by dry pipelines and lost patent protection among big pharma. Co-promotion gives the sales force more products to sell and provides the co-promoter with increased

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<sup>32</sup> Press Release, "Sankyo Pharma Selects Forest Laboratories For U.S. Co-Promotion of BENICAR™ (Olmesartan Medoxomil)," December 12, 2001, available at [http://www.sankyopharma.com/headlines/index.cfm?article\\_ID=31](http://www.sankyopharma.com/headlines/index.cfm?article_ID=31).

<sup>33</sup> Signals Magazine, "Co-Co Deals: Recipe for Sweet Success," August 2001, available at <http://signalsmag.com/signalsmag.nsf/0/BE48EAA28220B9D888256A9D0055A8DE>.

revenues and profits during periods when their own drug discovery and development efforts have been disappointing.

### ***Key Issues in Co-Promotion Relationships***

#### **Responsibility and Economics**

The primary aspect of co-promotion agreements is the flow of funds, including up-front payments for securing the rights to co-promote, profit sharing on sales of the product and payments for marketing expenses. Although the percentages vary and nearly always given confidential treatment in the publicly-disclosed agreements, the general idea is the same: both parties engage in cooperative behavior to increase sales of the product that is the subject of the agreement. In the Forest / Sankyo agreement, the provisions are simple and written in plain-English:

***“Co-Promotion. Sankyo and Forest hereby agree to co-promote the Product effective as of the Commencement Date, subject to the terms and conditions hereof.”***

While the Immunex / Wyeth-Ayerst agreement is a bit more descriptive on most points, including the basic premise of the agreement:

***“Joint Responsibilities. The Parties undertake equal responsibility for Promotion and Detailing of Enbrel in the Territory under the terms and conditions set forth herein except that Immunex shall have exclusive responsibility for Promotion and Detailing of Enbrel in the Territory for any and all oncology indications for Enbrel, except as provided in Section 5.2 hereof. The Parties shall have equal responsibility for all tactical marketing and selling activities relating to Enbrel in the Territory and for any other activities approved from time to time by the EMC.”***

In both agreements, the parties will share profits according to a predetermined percentage division, which in neither case has been publicly-disclosed. In the Forest / Sankyo agreement, it is clear that Forest paid an up-front amount to acquire the rights to market the product and share in the profits:

***“Payment for Co-Promotion Rights. In consideration for the rights granted to Forest hereby, Forest agrees to make the following payments ("Milestone Payments") to Sankyo:***

***Agreement Signing. [Confidential Treatment] within five business days following execution and delivery of this Agreement; and***  
***Product Approval. [Confidential Treatment] within the later of (i) twenty five (25) days following FDA approval of the NDA, including FDA approval of Product labeling and package inserts or (ii) five business days following the date Sankyo has notified Forest that launch quantities of Product, as set forth in the Marketing Plan, are ready for shipment to customers. The payment shall be deferred until the satisfaction of the second condition (with such deferral not to be in limitation of Forest's rights pursuant to Section 7.3.3); and***  
***Combination Product Approval. [Confidential Treatment] within five business days following FDA approval of the NDA for the Combination Product, including FDA approval of Product labeling and package inserts.”***

The Immunex / Wyeth agreement does not contemplate up-front or milestone payments, but presumably these were addressed in an earlier co-development agreement between the parties with respect to the product that ultimately became Enbrel.

#### **Detailing Requirements**

A well-written co-promotion agreement also requires a specific level of product detailing (face-to-face communications with physicians) to be done by the co-promoting party. This is done to avoid “free-riding” or obtaining benefits without doing the work required to produce the favorable outcome from which the benefits are achieved. The Immunex / Wyeth agreement contains a very specific definition of detailing and draws the typical distinction between primary and second-level details:

***““Detail” and “Detailing” shall mean, with respect to Enbrel, an interactive face-to-face visit by a Party's sales representative with a physician within the Physician Audience (as defined herein) at his or her office, at hospitals or at other locations (excluding exhibits, displays and other forms of communication not involving face-to-face contact by such sales representative), during which the FDA, or HPB (as applicable) approved indicated uses, safety, effectiveness, contraindications, side effects, warnings and/or other relevant characteristics of Enbrel are described in a fair and balanced manner consistent with the FD&C Act (as defined herein) or the CF&D Act, as applicable, including, but not limited to, the regulations at 21 CFR Part 202 and using, as necessary or desirable, the Enbrel Labeling (as defined herein) or the***

***Enbrel Promotional Materials (as defined herein), in an effort to increase physician prescribing preferences of Enbrel for its FDA or HPB (as applicable) approved indicated uses. Primary Details (as defined herein) and Secondary Details (as defined herein) shall qualify as Details, while reminder details, mentions and incidental contacts shall not qualify as Details under this Agreement.”***

Failure to meet the prescribed level of primary and secondary details may result in a downward adjustment to the profit sharing amount or, in extreme cases, termination of the relationship:

***“This Agreement may be terminated by Immunex upon at least one hundred twenty (120) days' prior written notice to Wyeth-Ayerst if Wyeth-Ayerst's Details or Primary Details in any Calendar Year on an aggregate basis in the Territory are less than [ \* ] of the Annual Target Number of Details or Annual Target Number of Primary Details applicable for such Calendar Year in the Territory, provided that Wyeth-Ayerst shall have the opportunity to cure within the first [ \* ] of the subsequent Calendar Year (such [ \* ] to commence upon receipt of notice from Immunex of a default which if uncured, would give rise to a right to terminate under this Section 19.4(e)) by conducting the Annual Shortfall Details in addition to its other required Details during such [ \* ] period.”***

#### **Governance and Regulatory**

Co-Promotion agreements usually provide for the formation of a joint marketing committee comprised of individuals from both companies to agree upon the desirable level of marketing spending and the form the promotion should take. The committee is usually an even number of people from each company with a dispute resolution provision that provides a timely and inexpensive method for breaking deadlocks.

Another important area of these contracts are the provisions governing regulatory aspects, including obligations for obtaining approvals and additional indications from FDA, procedures for dealing with product complaints and recalls, and mechanisms for ensuring that all promotional materials are reviewed and approved by both parties prior to use.

## **Exclusivity**

No company wants its product to be detailed by a sales rep that is also promoting a competing product. To avoid the co-promoting company from offering its own or another's competing product, these agreements contain exclusivity provisions. Of course, there will be tension between the parties as to how broad this provision should be. In the Forest / Sankyo agreement, Sankyo succeeded in defining competitive products broadly to include all angiotensin receptor blockers and ACE inhibitors. Forest, on the other hand, was able to carve out the ability to promote certain combination products after a certain period of time, but only after meeting strict conditions, including setting up a separate, dedicated sales force for the new product. Obviously, much negotiation went into the following:

***“Exclusivity. During the Co-Promotion Period, neither party shall market, promote, distribute or sell in the Territory any pharmaceutical product indicated for the treatment of hypertension and which contains an angiotensin receptor blocker, other than the Product pursuant to this Agreement, ("ARB") or an ACE inhibitor (a "Competitive Product"). Notwithstanding the preceding, Forest may market, promote, distribute and sell a Competitive Product in the Territory after the third Co-Promotion Year if (i) such Competitive Product is a combination product comprised of lercanidipine and an ARB or an ACE inhibitor or (ii) Forest has offered co-promotion rights in such Competitive Product to Sankyo on commercially reasonable terms and Sankyo has declined to copromote such product, provided that Forest may only market and promote any such Competitive Product through separate, dedicated sales forces (including sales representatives and management for primary care, specialty, hospital and managed care sales forces) and separate, dedicated marketing groups.”***

Since both companies will have employees doing similar jobs, it may be advisable to include a no-hire clause to avoid poaching:

***Restrictions on Hiring. During the Co-Promotion Period and for a period of twelve months thereafter, neither party shall hire any sales representative, sales force manager or employee principally having marketing responsibilities (including, without limitation, managed care, governmental and other institutional marketing personnel) employed by the other party or who had been employed by such other party within the previous six months. Isolated violations of this provision shall not be deemed a material breach of this Agreement for purposes of Section 7.2 hereof.***

**Other**

Other provisions contained in co-promotion agreements include a mechanism for making residual payments to the co-promoter after the agreement is terminated (since a certain level of future sales will be a result of earlier efforts), indemnification, change of control (especially important because of the concerns around promoting competing products), confidentiality, trademarks, and representations and warranties. These agreements often have a very long term – they may even extend for the length of the remaining patent protection on the product being promoted. In some cases, this can be fifteen years or more.

### **III. Conclusion**

Collaboration between companies in the pharma, biotech and medical device industries is essential to continue the pace of development of new products and technologies. This has always been true, but is even more so today in light of the advancements in discovery platforms in biotech and the dearth of solid drug candidates in pharmaceutical company pipelines. A therapy discovered, developed and marketed by a single company is a rarity in this arena and the reasons for collaborating are expected to remain compelling for the foreseeable future. Collaboration is a broad concept, however, and can be better understood by examining the specifics of the agreements into which companies have entered. They range from traditional product and technology licenses that allow one company access (whether exclusive or not) to another's intellectual property, to full-scale research and development and eventually, commercialization agreements. Although each deal is unique, the collaborations can be categorized into several basic structures for further analysis. By examining the agreements that companies have created before, it is possible to gain insight and ideas for solutions to the issues posed anew.

#### **IV. Appendix**

##### **A. Traditional License Agreements**

- a. Product License Agreement dated September 30, 1985, between Amgen and Ortho Pharmaceutical Company
- b. Technology License Agreement dated September 30, 1985, between Amgen and Ortho Pharmaceutical Company
- c. License Agreement dated January 29, 2003, between F. Hoffmann-LaRoche Ltd. and Affymetrix, Inc.

##### **B. Research, Development and Commercialization Collaborations**

- a. Metabolic Disorder Collaboration Agreement dated January 16, 2001, between Bayer Corporation and CuraGen Corporation
- b. Development and License Agreement dated November 20, 2001, between NitroMed, Inc. and Boston Scientific Corporation
- c. Development, Promotion, Distribution and Supply Agreement dated September 19, 2001, among E.R. Squibb & Sons, LLC, Bristol-Myers Squibb Company, and ImClone Systems Incorporated

##### **C. Contract Manufacturing Arrangements**

- a. Contract Manufacturing Agreement dated September 14, 2001, between The Dow Chemical Company and Geltex Pharmaceuticals, Inc.

##### **D. Co-Marketing and Co-Promotion Arrangements**

- a. Co-Promotion Agreement dated December 10, 2001, between Sankyo Pharma Inc. and Forest Laboratories, Inc.

- b. Amended and Restated Promotion Agreement dated December 16, 2001, among Immunex Corporation, American Home Products Corporation and Amgen Inc.