

Value creation and sharing among universities, biotechnology and pharma

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An analysis of deal structures in biotechnology from the past 25 years reveals that universities often neglect important economic aspects in their licensing agreements.

The three decades since the first breakthroughs in biotechnology and the subsequent passage of the Bayh-Dole Act have seen an enormous rise in the direct participation of universities and academic scientists in the development of novel medicines, diagnostics and discovery techniques. Over this same period, biotechnology companies have made substantial strides, both as developers of novel products and as value-adding 'intermediaries' in the translation of university discoveries into commercial products. In fact, most of biotechnology's blockbuster drugs to date have emanated, at least partially, from university license agreements. Biotechnology companies have, in turn, after considerable development and investment of resources, licensed lead compounds or technologies, for at least some territories or certain applications, to large pharmaceutical partners.

Much can be learned from the 30-year history of the biotechnology industry if it is viewed as a series of licensing and collaborative relationships, first from universities to biotechnology enterprises, and then from biotechnology firms to large pharmaceutical companies. In this article, using a detailed database of licenses (<http://www.recap.com/>), we examine licensing agreements between these entities, analyze how deal structures have changed in the period from 1975 to 2000, and study the prevalence of particular deal characteristics between universities and their biotechnology licensees, such as sublicensing terms and milestone payments. For a subset of the deals, we also match the upstream and downstream license for a specific university technology and in doing so assess the way in which value is shared among the different parties.

Our analysis is based on the assembly of three data sets from the Alliances Database

(see Box 1). The first contains a sample of 119 distinct research institutions licensing patents and/or know-how to 122 distinct biotechnology companies; the second contains all known commercial alliances undertaken by these 122 biotech companies for which we know some or all the economic terms; and the last data set is a subset of the second, containing 36 instances for which we know both the full upstream and downstream economic terms. Results are helpful in clarifying the value that universities capture, and the value biotechnology companies retain in those instances when a university invention is ultimately sublicensed by a biotechnology firm to a pharmaceutical partner.

The rise of university licensing

Scientific institutions have always made a contribution to medical progress, but their traditional role was to educate and to publish advances in basic science—creating the intellectual foundation upon which others have built more commercial discoveries. In recent times, however, universities have become active participants in the commercialization of scientific ideas through patenting and the establishment of active technology licensing as a legitimate and increasingly important part of academic life.

This is especially true with respect to university and medical center patenting in biotechnology. For example, before 1989 the top recipient of biotechnology patents was Merck (Whitehouse Station, NJ, USA); however, a decade later, in 1999, the combined campuses of the University of California held that spot. In fact, twelve academic institutions were among the top 40 biotechnology patent-generating entities over this past decade, including Stanford University (Palo Alto, CA, USA), the Massachusetts Institute of Technology (MIT; Cambridge, MA, USA), the Massachusetts General Hospital (MGH; Boston, MA) and The Scripps Research Institute (La Jolla, CA, USA)¹.

Patenting, in turn, has led to unprecedented licensing activity, and with a growing portfolio of life science patents, universities have entered into numerous licensing

arrangements with big pharmaceutical firms and with startup biotechnology companies. A recent Association of University Technology Managers (AUTM; Northbrook, IL, USA) survey of licensing activity showed that the top 25 US hospitals and research institutions alone executed over 400 licenses in 2000 (with startups, small and large companies) and in the same year yielded running royalty income from active licenses in excess of \$110 million².

Many universities grant licenses to biotechnology companies, typically with a series of economic provisions, including upfront licensing fees, annual maintenance fees, milestone payments and royalties. However, really valuable licenses are rare: the larger AUTM survey across about 180 US and Canadian universities and medical centers showed that only 0.6% of almost 21,000 active licenses (of all types, not only biomedical) generated royalties in excess of \$1 million, although about 8,000 of these licenses brought in some gross licensing revenue². These top-performing university licenses to biotech firms include several well-known blockbusters—for example, the MGH license of Embrel to Immunex (Seattle, WA, USA; now Amgen) yielded MGH \$16 million in 2001, and Memorial Sloan Kettering's (New York, NY, USA) licensing revenues of \$46 million were largely derived from their license on Neupogen to Amgen (Thousand Oaks, CA, USA).

Biotech's deal-doing pedigree

Licensing and alliance formation have long held a prominent role in the founding, capitalization and commercial success of the biotechnology industry. The Alliances Database contains over 2,000 university–biotechnology company deals (including therapeutics, diagnostics, devices and other medical deals) for which there were public announcements, many of which were associated with the formation of particular biotechnology companies. Similarly, the Alliances Database contains more than 10,000 commercial alliances involving biotechnology companies and either major

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pharmaceutical firms or other biotechnology firms as partners.

While the biotechnology industry has raised approximately \$100 billion over the past decade from private and public investors, at least an additional \$40 billion has been made available to the industry through its licensing deals with its commercialization partners.

Indeed, among the most successful biotechnology drugs, licensing has been a factor both upstream, through university technology, and downstream, through commercialization partners. Table 1 shows the 2002 worldwide sales of the top ten biotechnology products, along with the principal university and pharmaceutical partners associated with each product's commercialization.

Written the university way

The typical university–biotechnology company therapeutic license has evolved from the first decade of the biotechnology industry to the most recent (see Fig. 1). From the initial flurry of deals in the late 1970s to the years since 1995, upfront licensing fees have more than tripled, from \$20,000 to over \$70,000. Sponsored research fees have doubled, from \$300,000 to \$600,000, and license maintenance fees have quadrupled, from \$40,000 over an assumed five-year period of payments, to \$180,000 over the same period. Clinical milestone payments appear more frequently in recent deals, typically ranging

up to \$1.6 million through the commercial launch of a therapeutic product. Going in the other direction, however, the percentage of pre-commercial sublicensing payments shared with the university licensor dropped by half—from 50% in the earliest period to 25% more recently.

With respect to post-commercialization payments, whereas the effective royalty rate on \$100 million in assumed annual sales has stayed constant at 4%, minimum annual royalties have increased fivefold, from \$10,000 to \$50,000 per year. Finally, as with pre-commercial sublicense payment sharing, the average post-commercial sublicense sharing has dropped from 40% to 25% of sublicensee payments received by the biotechnology firm in the more recent period.

Table 2 gives a more complete breakdown of the average economic terms in all university–biotech licenses (both therapeutic and others including devices, screens and diagnostics)—how these have changed over time as well as the relative frequency with which universities incorporate these terms into their licenses. For example, royalties are the most consistently present element of these licenses, followed by upfront fees, which appear in roughly half of the deals for each time period. Research payments arise in about one-third of these agreements, while annual license maintenance fees (which we assume for valuation purposes to be paid only for the first five years of the license) are

present in roughly one of five deals. Infrequent economic elements (particularly in the early years) are milestone payments, minimum annual royalties, and both pre- and post-commercialization sublicense revenue sharing payments. (Such sublicense revenue sharing implies that the licensee would remit a portion of the upfront, milestone, royalty and/or other payments, as defined in the university–biotech license, received by the biotech firm in the event that it entered into one or more sublicense agreements.) Overall, the trend has been toward higher payments to university licensors over time, but most of this increase has come in the categories of upfront, sponsored research and license maintenance fee payments.

Down the road to enrichment

Turning to biotechnology firms and their relationships with downstream partners, Figure 2 shows the average pre-commercial payments owed to biotechnology companies by their commercialization partners for our data set of 112 commercialization alliances for licensed university technologies. We've grouped these deals by stage at time of signing of the downstream deal. For 'early stage' deals (for example, for downstream deals signed at the discovery or lead-generation stage), average upfront licensing fees were \$3 million, plus \$11 million in sponsored R&D, plus \$5 million in equity investment, plus \$9 million in clinical milestone payments (see

Table 1 Principal university and pharmaceutical company partners associated with the top ten biotechnology products in 2002

Product (biotechnology company)	2002 sales (\$ billion)	University licensor	Pharmaceutical licensee(s)
Procrit (Amgen, Thousand Oaks, CA, USA)	\$4.3	University of Chicago (Chicago, IL, USA)	Johnson & Johnson (New Brunswick, NJ, USA)
Epogen (Amgen)	\$2.3	University of Chicago (Chicago, IL, USA)	Kirin (Tokyo, Japan)
Neupogen (Amgen)	\$1.4	Memorial Sloan Kettering (New York, NY, USA)	Kirin & Hoffmann-La Roche (Nutley, NJ, USA)
Remicade (Centocor, Malvern, PA, USA)	\$1.3	University of Munich (Munich, Germany)	Schering-Plough (Kenilworth, NJ, USA) & Tanabe (Osaka, Japan)
Rituxan (IDEC, San Diego, CA, USA)	\$1.2	Stanford University (Stanford, CA, USA)	Genentech and Zenyaku Kogyo (Tokyo, Japan)
Avonex (Biogen, Cambridge, MA, USA)	\$1.0	None	Schering-Plough (terminated)
Humulin (Genentech, S. San Francisco, CA, USA)	\$1.0	University of California (San Francisco, CA, USA)	Eli Lilly (Indianapolis, IN, USA)
Combivir (Biochem Pharma, now Shire Pharmaceuticals, Newport, KY, USA)	\$0.9	None	GlaxoSmithKline (Brentford, UK)
Betaseron (Chiron, Emeryville, CA, USA)	\$0.8	Stanford University	Schering AG (Berlin, Germany) and Berlex (Richmond, CA, USA)

Source: J. Van Brunt, Product sales soar, *Signals Magazine*, (2003).

Fig. 2). For ‘mid-stage’ deals (signed at the preclinical or phase I clinical stage of development), average upfront licensing fees were \$2.5 million, plus \$10 million in sponsored R&D, plus \$10 million in equity investment, plus \$17 million in clinical milestone payments. For ‘late-stage’ deals (downstream deals signed at the phase II or later clinical stage of development), average upfront licensing fees were \$17 million, plus \$16 million in sponsored R&D, plus \$61 million in equity investment, plus \$76 million in late clinical milestone payments.

Inasmuch as the average upfront payment for an early- or mid-stage deal is more than the aggregate pre-commercial payments of a typical university license, there is no doubt that biotechnology companies are at least covering their initial investment and garnering a high fraction of the overall value embodied in a technology, compound or program at the time of a downstream alliance. To obtain even an approximation of the relative sharing of such value between university and biotechnology company, however, it seems useful to begin by drawing key distinctions between the various major categories of commercialization alliance payments.

First, the R&D payments are generally cost-reimbursement only, and so we contend these should be disregarded (except insofar as they allow a biotechnology company to spread their overhead expenses over a wider range of activities). Second, we believe that equity investments by pharmaceutical partners should only be regarded as ‘enriching’ to the extent that such investments are made at a premium to the fair market value (FMV) of the biotechnology company’s securities. If there is such a premium, however, we contend it would be appropriate to reclassify such premium amount as an additional upfront fee, with the balance of the equity

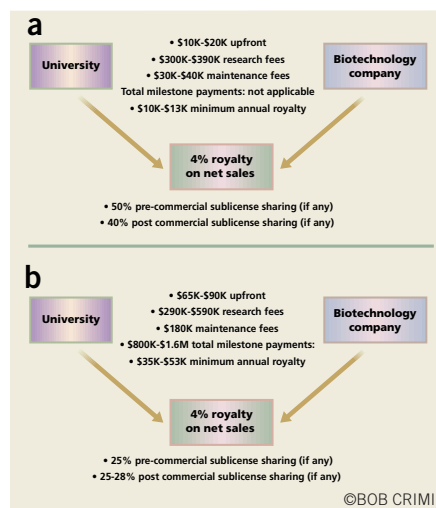


Figure 1 Evolution of the typical university–biotechnology company therapeutic deal. (a) Characteristics of deals in the period 1975–1986. (b) Characteristics of deals in the period 1995 to the present. Clinical milestone payments now appear more frequently than before.

investment attributed to purchasing the biotechnology company’s securities at FMV. Similarly, as the vast majority of biotechnology commercialization alliances involve milestone payments to be paid to the biotechnology firm that out-licenses after the licensee has both paid for a phase of clinical development and observed a favorable outcome, we believe that milestone payments are, in fact, delayed upfront fees, payable only in the event a particular milestone is reached, but clearly enriching once a commercialization partner determines to advance the program through the milestone event. Realistically, therefore, we contend it would be appropriate to reclassify all promised

milestones as upfront fees, after discounting such amounts for both the probability of a milestone’s achievement and the time value of money.

Assuming, therefore, no equity premiums and standard clinical attrition rates, we suggest that the average early-stage deal payments shown in Figure 2 equate to roughly \$4 million in enrichment value (\$3 million upfront, plus an additional \$1 million in discounted milestone payments) at the time of signing the downstream deal. Similarly, mid-stage deals would be worth \$6 million (\$2.5 million upfront, plus \$3.5 million in discounted milestone payments) on an equivalent basis, while late-stage deals would be worth \$55 million (\$17 million upfront, plus \$38 million in discounted milestone payments).

Of course, since universities are rarely in a position to take technologies or even compounds to the point of clinical development, it isn’t surprising that biotech companies would command substantially higher payments from their pharmaceutical partners for bringing university inventions forward to a mid-stage or late-stage commercialization alliance. In addition, biotech companies often bring to the table additional patents, other licenses and extensive further development and experimental evidence. With respect to early-stage downstream alliances, however, one might well ask whether the value added by the biotechnology company in these instances was indeed commensurate with the order of magnitude increase in the average downstream deal enrichment compared with the typical university–biotechnology company license.

The money value of time

Figure 3 shows the average passage of time (in months) from the signing of an upstream

Table 2 Average economic terms of university–biotechnology company deals				
Terms of agreement	Pre 1980–1986	1987–1990	1991–1994	1995–present
Post commercial payments				
Royalties	4% (n = 25)	5.1% (n = 43)	4.2% (n = 62)	3.9% (n = 24)
Minimum annual royalty	\$13,438 (n = 8)	\$33,212 (n = 22)	\$50,392 (n = 34)	\$53,479 (n = 11)
Sublicense revenue sharing	37.4% (n = 9)	34.3% (n = 17)	28.4% (n = 27)	28.4% (n = 14)
Pre-commercial payments				
Upfront fee	\$20,085 (n = 21)	\$40,655 (n = 35)	\$48,649 (n = 53)	\$87,942 (n = 24)
Research payments	\$409,321 (n = 14)	\$434,467 (n = 22)	\$1,159,941 (n = 31)	\$585,323 (n = 18)
Maintenance fees (5 years)	\$39,041 (n = 8)	\$53,333 (n = 15)	\$90,496 (n = 22)	\$183,909 (n = 11)
Milestone payments	\$16,250 (n = 2)	\$324,359 (n = 12)	\$445,017 (n = 25)	\$1,585,679 (n = 11)
Sublicense revenue sharing	46.6% (n = 8)	27% (n = 11)	23.4% (n = 21)	25.4% (n = 12)
Total number of deals	n = 40	n = 70	n = 110	n = 45

university license until the execution of its downstream alliance(s). Figure 3a suggests that whereas downstream early-stage deals have commenced within two years, late-stage deals required almost six years of effort by the biotechnology company licensee before the signing of a downstream alliance. This seems appropriate, given that drug discovery programs often require a year or more to generate compound leads, which in turn may require several years in lead and preclinical development, followed by 8–10 years in the clinic. More surprising is the trend line shown in Figure 3b, suggesting that university licenses commenced in the past decade have been sublicensed far more quickly than in earlier periods. (In fact, 11 of the 14 university licenses signed since 1995 were signed in 1995 or 1996, indicating that this time compression isn't simply a function of too little lapsed time since the university technology was licensed.)

Table 3 gives a more complete breakdown of the average time between commencement of a university license and its downstream commercialization alliance(s). For early-, mid- and late-stage downstream alliances, the average time from university license to downstream alliance has decreased (although only for late-stage alliances has this decrease been consistent) and has been quite dramatic across all time periods. Assuming that the stage of development of university technology licensed to biotechnology companies has remained relatively constant over time, Table 3 indicates a fairly consistent portion of incremental time and investment by a biotechnology licensee in achieving mid- or late-stage commercialization alliances, compared with partnering at the early stage.

Striking a balance

In Table 4, we look at the final data set—that being 36 'matched' instances for which we

The analysis

To enable a thorough analysis of biotechnology dealmaking over a 25-year period we assembled three data sets. First, we selected a sample of 265 'upstream' licenses from universities, medical centers and research institutes to biotechnology firms. This sample was drawn from over 2,000 university–biotechnology company deals available through the Alliances Database. These particular deals were selected because (i) the biotechnology company publicly filed the underlying licensing contracts with the US Securities and Exchange Commission (SEC) as material disclosures, (ii) the licensed technology appeared to be directed toward the development of therapeutic products, and (iii) the licenses themselves were unredacted (that is, none of the economic terms of the license were withheld from public disclosure). In all, our detailed data includes 119 distinct universities (or equivalent research institutions) licensing patents and/or know-how to 122 distinct biotechnology companies.

Next, we assembled a data set consisting of all known commercial alliances undertaken by these 122 biotech companies, initially without regard to whether any particular commercial alliance used the upstream university technology. Again using the Alliances Database, the first pass of this data set consisted of more than 1,500 commercial alliances. From this group, we then extracted a subset of 'downstream' commercial alliances that explicitly included the sublicensing of some or all of the specific university technology. In some cases, the upstream university technology was explicitly identified in the downstream contract. In other instances, we compared the patent applications and issued patents associated with both contracts to make this match. This effort yielded 160 instances in which a university technology licensed to a biotech firm in our first data set formed the basis of one or more subsequent sublicenses from the biotechnology firm to a commercial partner, typically a multinational pharmaceutical company. We then omitted those instances where the downstream contract was not filed with the SEC or where all of the economic terms had been redacted from the public filing. Our final data set thus contains 112 downstream commercialization alliances for which we know some or all of the economic terms.

Finally, we extracted from the second data set all those instances where the full economic terms of the downstream commercial alliance are known, again due to the public filing of the underlying alliance contracts with the SEC on a complete and unredacted basis. This yielded a third data set of 36 'matched' instances for which we know both the full upstream and downstream economic terms.

know the full economic terms of both the upstream university–biotechnology license and the downstream pharmaceutical–biotechnology commercialization alliance. With respect to pre-commercial payments, we inspected each university–biotechnology company contract to determine explicit pay-

ments owed to the university licensor. These included upfront fees, annual license maintenance fees and milestone payments. We disregarded sponsored research payments as being 'nonenriching' to the university (as we had done with biotechnology R&D payments above). We assumed that milestone payments were owed for a single commercialized therapeutic product, and that license maintenance fees (if contractually obligated) would be paid for ten years from signing. In the event a single university license resulted in two or more downstream alliances, we divided these explicit payments equally among the several downstream deals. Finally, in the instances where the biotechnology company was obligated to make pre-commercial revenue sharing payments, we calculated the payments owed based on the economic terms of the biotechnology company's downstream alliance. The results we obtained are shown in the column entitled 'Amount' under the 'Pre-commercial payment' heading. The adjoining column, entitled 'Percentage of

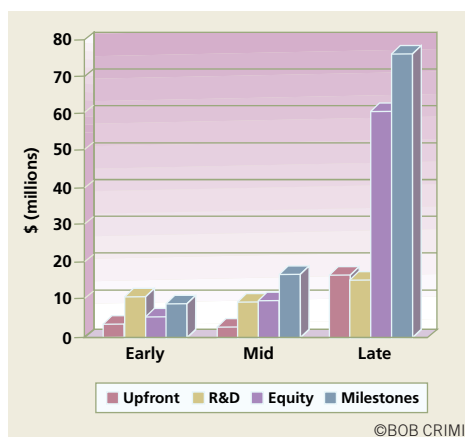


Figure 2 Average downstream economic terms in biotechnology deals. Early-stage deals encompass discovery and lead stage projects; mid-stage deals encompass preclinical and phase I studies; and late-stage deals encompass phase II, phase III, new drug applications and approvals. Of early-stage deals, 21 involved upfront payments, 24 R&D payments, 21 equity investment and 20 milestone payments; of mid-stage deals, 12 involved upfront payments, 8 R&D payments, 8 equity investment and 12 milestone payments; of late-stage deals, 24 involved upfront payments, 9 R&D payments, 21 equity investments and 23 milestone payments.

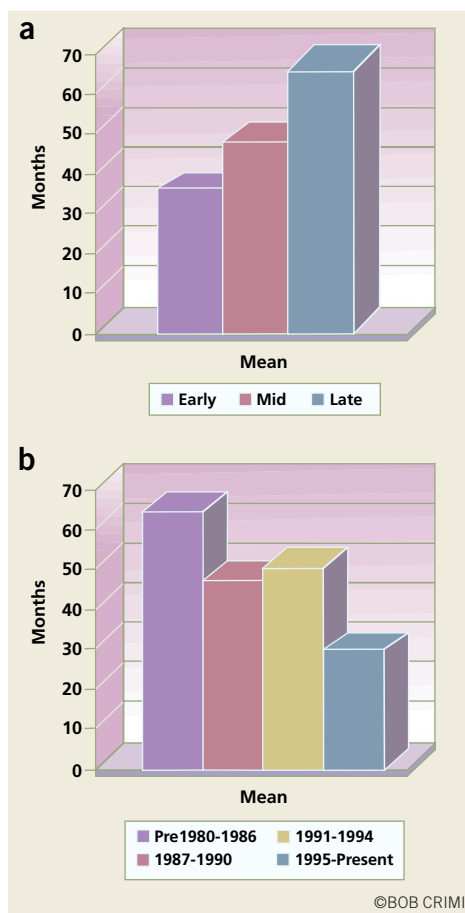


Figure 3 Time to sublicense. (a) The period between university license to biotechnology company and sublicense for stage of deal. Data shown for ($n = 44$) early-stage deals encompassing discovery and lead stage projects; ($n = 29$) mid-stage deals encompassing preclinical and phase I studies; and ($n = 39$) late-stage deals encompass phase II, phase III, new drug applications and approvals. (b) Historical speed of sublicensing, as measured from the date of the university license agreement. University licenses commenced in the past decade have been sublicensed far more quickly than in earlier periods. Data are shown for 17 deals in the period before 1986, 36 deals in the period 1987–1990, 45 deals in the period 1991–1994 and 14 deals in the period 1995. Full disclosure of terms tends to lag deal signing by 5–7 years.

total' shows this university pre-commercial payment amount as a percentage of the total enriching pre-commercialization payments (upfront plus milestones plus equity premium) owed to the biotechnology company by its commercialization partner.

With respect to post-commercialization payments, we have based our analysis of such royalty payments on an assumption of \$100 million in sales. Although this underestimates the value of a blockbuster, it also overestimates the risk-adjusted value of the royalty stream by ignoring the clinical attrition rate. Again, we inspected each university-biotech contract to determine both direct (that is, sales by the biotechnology company) and indirect (via sublicense) roy-

alty obligations. In the instances where the biotechnology company was obligated to make post-commercial revenue sharing payments, we calculated the payments owed based on the royalty or profit split terms of the biotechnology firm's downstream alliance. The results we obtained are shown in the column titled 'Amount' under the 'Royalty on \$100M sales' heading. The adjoining column, entitled 'Percentage of total', shows this university royalty payment amount as a percentage of the total post-commercialization royalty or profit split owed to the biotechnology company by its commercialization partner.

Assuming that the average partnered therapeutic product has profits before tax of 50%

of sales (while realizing that profitability varies widely), the royalty analysis taken alone suggests that the post-commercialization value split between university, biotechnology and big pharma is approximately 6:15:79 of the profits on \$100 million of sales (specifically \$2.9 million to the university, \$7.7 million to the biotechnology company, net of university obligations, and \$39.4 million of assumed profits retained by the commercialization partner).

But such an analysis would be incomplete, as the pre-commercial payments owed to university and downstream licensors are almost as large in amount as these parties' assumed royalties, are received earlier and are far less subject to the risks of clinical attrition. When these payments are factored in, we believe that the total value split between university, biotech and pharma is roughly 7:29:64 of the profits on \$100 million of sales (specifically \$2.9 million plus \$0.8 million to the university, \$7.7 million plus \$6.6 million to the biotechnology company, net of university obligations, and \$32 million of residual assumed profits retained by the commercialization partner). Somewhat simplified, this analysis suggests that pharmaceutical partners retain two-thirds of a product's value, while the remaining one-third is split between university licensors and biotechnology firms on a 20:80 basis.

Finally, we have added one additional dimension to Table 4 by grouping the matched alliances on the basis of whether the university-biotech license requires that the university receive a full and complete copy of each sublicense agreement (typically within 30 days of signing) plus any amendments. This grouping shows that those universities that require receipt of any downstream deal get a significantly larger share of the pre-commercial payments, though they share somewhat less on the royalty side of the value equation (using simple *t*-tests at 10% significance).

Where to go from here?

Universities are coming under increasing pressure to commercialize their scientific discoveries, nowhere more so than in the departments of biology, medicine and chemistry that have contributed to the biotechnology revolution. For academics and administrators alike the question remains: how much economic value can and should they expect to capture for their significant but nonetheless early-stage ideas? Moreover, how can they capture this economic value, particularly when it often comes in the form of ongoing R&D payments, in light of the

Table 3 Time in months between signing of university license and sublicense

Agreement type	Pre 1980–1986	1987–1990	1991–1994	1995–present
	Time in months (number of agreements)			
All	63 ($n = 17$)	46 ($n = 36$)	49 ($n = 45$)	27 ($n = 14$)
Early-stage	45 ($n = 7$)	27 ($n = 17$)	35 ($n = 15$)	21 ($n = 5$)
Mid-stage	72 ($n = 5$)	37 ($n = 7$)	45 ($n = 14$)	28 ($n = 3$)
Late-stage	81 ($n = 5$)	76 ($n = 12$)	36 ($n = 16$)	32 ($n = 6$)

Table 4. A list of 36 'matched' instances for which full economic terms of commercialization alliance are known.

University licensor/ biotechnology company (Date)	Sublicensee (Date)	Time to sublicense (months)	Pre-commercial payments Amount (\$M)	Percentage of total	Royalty on \$100M sales Amount (\$M)	Percentage of total	Copy of sublicense
University of Florida/Advanced Tissue Sciences (11/92)	Kirin Brewery (3/93)	4	\$4.9	20.0%	\$4.0	50.0%	Yes
MIT/Advanced Tissue Sciences (7/92)	Smith & Nephew (5/94)	22	\$0.7	7.0%	\$4.5	18.0%	Yes
Baylor College/Cephalon (4.89)	Schering-Plough (5/90)	13	\$0.1	0.4%	\$4.0	38.0%	Yes
Children's Hospital/EnzyTech (8/88)	Schering-Plough (2/92)	42	\$1.0	9.0%	\$2.0	25.0%	Yes
MIT/Immologic (4/87)	Merck (12/87)	8	\$0.6	31.0%	\$3.0	100.0%	Yes
Salk Institute/Ligand Pharmaceuticals (10/88)	Glaxo (9/92)	48	\$2.6	22.0%	\$3.0	25.0%	Yes
Penn State/Procept (3/98)	Access Oncology (10/00)	43	\$2.5	97.5%	\$1.8	22.5%	Yes
University of British Columbia/QLT (1/88)	Ciba-Geigy (7/94)	78	\$0.0	0.0%	\$0.5	2.0%	Yes
University of British Columbia/QLT (1/88)	Baxter (2/90)	25	\$0.0	0.0%	\$0.5	2.0%	Yes
Stanford University/Rigel Pharmaceuticals (10/96)	Janssen Pharmaceutica (12/98)	26	\$0.1	0.7%	\$0.5	8.0%	Yes
Stanford University/Rigel Pharmaceuticals (10/96)	Pfizer (1/99)	27	\$0.1	1.0%	\$0.5	25.0%	Yes
Stanford University/Rigel Pharmaceuticals (10/96)	Novartis (5/99)	31	\$0.1	0.4%	\$0.5	12.5%	Yes
Max Planck Institute/Sugen (8/91)	Amgen (1/93)	17	\$3.3	22.0%	\$3.0	20.0%	Yes
New York University/Sugen (9/91)	Amgen (1/93)	16	\$3.3	22.0%	\$3.0	20.0%	Yes
University of Florida/SunPharm (12/91)	Parke-Davis (5/93)	17	\$1.9	27.0%	\$2.8	28.0%	Yes
University of Florida/SunPharm (12/91)	Nippon Kayaku (2/94)	26	\$2.4	48.0%	\$2.8	28.0%	Yes
Walter Reed Army Institute/Univax Biologics (8/91)	Genentech (9/92)	13	\$0.0	0.0%	\$2.5	10.0%	Yes
<i>Average</i>		<i>26.8</i>	<i>\$1.4</i>	<i>18.1%</i>	<i>\$2.3</i>	<i>25.5%</i>	
Austin Research Institute/Alexion (1/94)	US Surgical (7/95)	16	\$0.3	2.0%	\$3.0	25.0%	No
University of Illinois/Alliance Pharmaceutical (1/85)	Boehringer Ingelheim (5/89)	52	\$1.1	4.0%	\$6.0	40.0%	No
Brigham & Women's Hospital/Athena Neurosciences (7/87)	Eli Lilly (10/88)	15	\$0.0	0.0%	\$4.0	40.0%	No
Ohio State University/AVI BioPharma (3/96)	SuperGen (4/00)	49	\$1.0	3.0%	\$5.0	20.0%	No
University of Medicine and Dentistry/ BioDelivery Sciences (9/95)	Wyeth (7/96)	11	\$0.6	15.0%	\$0.5	25.0%	No
State University of New York/Cortech (6/87)	Marion Merrell Dow (6/87)	0	\$0.0	0.1%	\$5.0	50.0%	No
NTIS/Genaera (6/89)	Colgate (6/90)	12	\$0.1	1.0%	\$1.2	40.0%	No
NTIS/Genaera (6/89)	Sandoz (now Novartis) (6/90)	12	\$0.1	1.0%	\$7.5	75.0%	No
NRDC/Genetic Therapy (1/92)	Genetics Institute (9/92)	8	\$0.7	37.0%	\$7.0	35.0%	No
University of California, San Diego/ ImClone Systems (4/93)	Bristol-Myers Squibb (9/01)	101	\$0.0	0.0%	\$0.8	2.0%	No
MIT/ImmuLogic (4/87)	Marion Merrell Dow (9/92)	59	\$2.3	6.0%	\$3.0	12.0%	No
University of North Carolina/ ImmuLogic (7/89)	Marion Merrell Dow (9/92)	31	\$0.0	0.0%	\$3.8	15.0%	No
Princess Margaret Hospital, Toronto/ ImmuLogic (7/90)	Marion Merrell Dow (9/92)	19	\$0.0	0.0%	\$6.3	25.0%	No
Brigham & Women's/NPS Pharmaceuticals (2/93)	SmithKline (11/93)	9	\$0.2	1.0%	\$1.0	10.0%	No
Dana-Farber Cancer Institute/Procept (2/87)	Bristol-Myers Squibb (2/90)	36	\$0.1	3.0%	\$0.7	20.0%	No
Southern Research Institute/US Bioscience (12/87)	SmithKline (5/92)	53	\$0.0	16.0%	\$4.0	50.0%	No

Southern Research Institute/US Bioscience (12/87)	Schering-Plough (2/92)	50	\$0.0	0.0%	\$6.0	50.0%	No
University of Wisconsin, Madison/ Viagene (12/91)	Bayer (12/92)	12	\$0.1	2.0%	\$0.4	10.0%	No
University of Wisconsin, Madison/ Viagene (12/91)	Chiron (11/93)	23	\$0.1	0.0%	\$0.3	5.0%	No
<i>Average</i>		29.9	\$0.3	4.8%	\$3.4	28.9%	
<i>Overall average</i>		28.4	\$0.8	11.1%	\$2.9	27.3%	

ongoing debate on conflicts of interest. Once an invention moves into the private sector, considerable capital, entrepreneurial energy and patience are needed to navigate the long journey to approval, but the expertise of the university and academic medical center remains critical on this journey.

Biotechnology firms are important intermediaries in this process, and by translating university technology they capture a considerable slice of the pie. However, our analysis raises a number of issues about the overall split of the pie. First, even in recent years, universities seem to neglect important economic aspects in the licensing agreements that they strike with biotechnology firms.

Only one license in five incorporates license maintenance fees, and milestone payments are even less frequently employed. While biotechnology firms may well be justified in diminishing their obligations when they negotiate the upfront fee, fees that accrue down the development path signal to the university that their technology is valuable and that the biotechnology firm is making diligent progress. Milestone payments and license maintenance fees help ensure that the university shares in (and confirms) such progress while minimizing upfront costs.

Second, it is clear that commercialization alliances across the development spectrum provide an important source of economic

revenue to biotechnology firms over and above their R&D costs. Universities have been slow to capture a meaningful share of such enriching downstream alliance payments to their detriment. At the very least, as we have shown, universities should require that biotechnology companies provide full and complete copies of the downstream alliances that leverage the university's technology.

1. Technology profile report: patenting examining technology center groups 1630–1660, biotechnology (United States Patent Office, Washington, DC, USA, 2003).
2. AUTM licensing survey, FY 2000, full report (The Association of University Technology Managers, Inc., Northbrook, IL, USA, 2000).