11

Financing Drug Development

Mark Kessel & Robert Masella

The biopharmaceutical industry is bifurcated—big pharmaceutical companies ("big pharma"), with anemic product pipelines but plenty of cash, and the biotech sector, which is often cash-constrained but with rich pipelines.

Big pharma's blockbuster drugs are losing patent protection and facing generic competition. The pharmaceutical companies are desperate for replacement drugs, which are not coming out of their own pipelines. Health care reform has placed additional pressure on prices, coupled with the imposition of pay for performance; and earnings pressure is causing big pharma to reduce its own research and development (R&D) efforts.

At the same time, biotech companies may face a major challenge in securing financing for drug discovery and development, jeopardizing the progress of the very drugs that big pharma desperately needs. Unlike product development in other technology-driven companies, biotech product development

is highly regulated and the development cycle for a drug can be as long as fifteen years, with cost estimates as much as $1 billion or more. Also, it is rare for a biotech company to be able to commercialize its own product due to the lack of a global sales force, among other things.

This chapter addresses how both kinds of companies are reacting to these challenges. It describes some historical patterns of financing, and some newer alternatives. It also discusses the collaborative efforts that stem from big pharma's increasing need to rely on the drugs being developed by the biotech companies, and the biotech companies' need to monetize their portfolios through a sale or licensure to big pharma.

Background

Q 11.1 How have companies addressed recent developments in the biopharmaceutical industry?

In response to current conditions, including the lack of new drugs being developed in house, big pharma has reacted in a number of ways:

- Buying earnings through acquisitions;
- Expanding in emerging markets like China, Brazil, India, and other underpenetrated markets, which are projected to increase more dramatically than the U.S. and European markets;

- Entering into the ever-growing generics market;
- Expanding into branded biologics which are likely to retain market share even after patent expirations;
- Increasing focus on orphan drugs, which, while targeting small indications, can be highly profitable;
- Investing in biosimilars or follow-on biologics which are less competitive due to barriers to entry and thus attractive investments; and
- Restructuring R&D activities to reduce overhead, a short-term solution to earnings improvement.

But for purposes of this chapter, the important change is big pharma's greater reliance on externally developed drugs, such as can be provided by the biotech companies.

The fact that big pharma is turning to externally developed drugs may be viewed as boding well for the biotech companies. But the transactions may carry lower multiples than were enjoyed in the past, be structured with contingent payments based on value creation milestones, or provide for a major portion of the purchase price to be contingent on the successful commercialization of the drug.

In turn, biotech companies seeking drug development financing are turning to big pharma partnerships as a funding source, licensing away promising drug candidates to fill big pharma's draining pipeline (see QQ 11.7–11.11). Additional financing alternatives are also available (see QQ 11.12–11.12.4).

Financing from Seed Capital to Initial Public Offering

Q 11.2 How has the industry financed drug development historically?

Historically, the biotech industry was able to fund its capital needs from multiple sources, depending on a company's stage of development. Seed capital was provided from various sources, such as

the inventor, "friends and family," angel investors, and governmental grants, in amounts aggregating generally under $5 million, which would typically carry the company through early stages of development.

Venture capitalists would provide the next stage of funding to the tune of $20–$30 million, for the next three to five years of early-stage clinical trials.

As the drugs continued to advance through the development cycle, the public markets would become receptive to an initial public offering (IPO), funding further drug development efforts.

Q 11.3 What is the current role of angel investors?

As a compound advances through the various stages of development, each milestone provides an opportunity for raising additional capital at potentially increased valuations. This financial life cycle starts with an initial funding of a scientific discovery—"seed capital."

An important source of seed capital is angel investors: high-net-worth individuals who constitute a major source of startup capital, until venture capital financing can be attracted. Historically, the amounts of funding were modest, but they have been increasing to replace later-stage funding, which can be significantly more dilutive to early investors than was previously the case.

Angel investors in biotech companies often are retired executives from the industry who have accumulated significant capital or are entrepreneurs. These investors provide business acumen to the founders of biotech companies, as well as relevant industry networking. In more recent periods, these investors have formed informal networks furthering the raising of capital in a more efficient manner.

Q 11.4 What is the current role of venture capital?

As drug development approaches human clinical trials, the capital requirements increase significantly beyond that made available by angel investors.

Venture capital, once scarce, has become more readily available for earlier-stage compounds. Global venture funding of private biotech companies reached $7.7 billion in 2007, a peak year, and climbed

to $10 billion in 2015.[1] During the meltdown in the financial markets, valuations were significantly lower, and the IPO market was closed. Whether the surge in venture capital funding will continue will depend upon continued advances in science and perceptions regarding the strength of the M&A market and the IPO market in the mid-term. Some of the big pharma players have set up their own venture capital divisions to give them a leg up in competing to in-license promising compounds that the biotechs in which they invest may develop, and this activity may place a floor under venture capital financing activity. In the event of a step-back by traditional venture capital players, these investment vehicles will have further opportunity to exert their financial capabilities.

Q 11.5 What is the current role of initial public offerings?

The critical issue for the biotech sector is whether the IPO market, which was strong in both 2013 and 2014, will rebound from declines in 2015 and a weak start in the beginning of 2016. Positive investor sentiment and the 2012 Jumpstart Our Business Startups Act (JOBS Act),[2] designed to reduce the burden on smaller companies, helped fuel the IPO pipeline in 2014 and early 2015. However, M&A activity and a slowdown in the IPO market during the second half of 2015 led to an overall decrease of approximately 10% in the number of global biotech IPOs in 2015.[3]

When the IPO window is open, investors have tended to favor health care–focused companies. Health care IPOs comprised one of the largest segments of the IPO market in 2015 as investors focused on companies that had the potential for significant growth and future exit opportunities through M&A. If the global markets remain unsettled, there is a question whether public equity investors will have an appetite for higher-risk equities such as early-stage biotech companies.

Post-IPO Financing for Public Biotech Companies

Q 11.6 What financing needs exist after the initial public offering?

Public biotech companies have a continual need for capital to advance their drugs through clinical trials. Aside from the large-cap companies with meaningful revenues and liquid markets for their securities at attractive pricing, biotech companies have come to rely on multiple sources of alternative capital, not all of which are available at any given point in time and some of which are extremely dilutive to existing shareholders.

Q 11.6.1 What is a follow-on offering?

A common way for a biotech company to raise equity after having completed an IPO is to do a follow-on offering—issuing additional shares of common stock to public investors—which can be underwritten by investment banks. The ability to access this form of capital is subject to the vicissitudes of the public markets and may entail significant discounts from the prevailing trading price, particularly for early-stage companies.

Q 11.6.2 What is a registered direct offering?

Another way to access equity is a registered direct offering (RDO), which is a public offering marketed by a placement agent on an agency basis to a limited number of institutional investors.

Q 11.6.3 What are private investments in public equity?

Private investments in public equity (PIPEs) are also done with institutional investors, including private equity, but are often done on more investor-friendly terms, such as additional discounts and preferences (for example, a convertible preferred security). However, PIPEs can be implemented more quickly and less expensively than underwritten offerings.

As an additional incentive to investors, typical PIPE transactions also include warrants to purchase additional shares at some premium to the purchase price of the PIPE shares and/or attractive conversion prices if a convertible security is involved, with significant antidilution protection. Health care represented one of the largest segments of the total PIPE market in 2015, as companies took advantage of relatively favorable pricing terms in the first nine months of the year. If the market continues to experience significant volatility, the terms afforded to companies will become less favorable and the PIPE market will slow.

Q 11.6.4 What are at-the-market offerings?

At-the-market offerings (ATMs), which have become more popular, comprise a registered offering of listed securities sold directly into the public markets through a broker-dealer over a period of time. They usually involve a small number of shares being sold at the company's discretion on any given day at prevailing market prices, allowing the company to average its cost of capital over time at lower commissions than the other types of financings discussed in this chapter.

Unlike PIPEs, ATMs do not include warrants and there are no discounts to the investors.

Q 11.6.5 What are committed equity financing facilities?

A committed equity financing facility (CEFF) allows a biotech company to sell a specific dollar amount of equity securities to an investor over a period of time. The company can determine in its discretion the timing, dollar amount, and floor price for any draw under the facility, based upon a contractual formula tied to a volume-weighted average price of the common stock over a multiday pricing period.

Q 11.6.6 What other forms of equity financings are used to raise capital?

Preferred stock and convertible debt securities offer investors the opportunity to be senior to common stock and contain tailored terms and conditions depending on the requirements of investors and the financial strength of the biotech company.

Licensing and Other Collaborations Between Pharmaceutical and Biotech Companies

Q 11.7 Why is licensing becoming more attractive to big pharma?

Historically, big pharma's licensing was limited for several reasons: reluctance to partner outside of internal competencies; a bias to exploit internally developed drugs; and earnings constraints that tempered a desire to fund external programs.

With big pharma's declining internal R&D productivity, the ever-increasing cost of developing drugs, and the pressure on earnings, big pharma has increasingly turned to licensing drugs from biotech companies. This is especially the case for companies that have decided to restructure their internal R&D resources to reduce overhead costs.

For big pharma, collaborating with biotech via licensing provides an opportunity to replenish pipelines at a time when many blockbuster drugs are coming off patent and beginning to face generic competition.

Q 11.8 What can big pharma and biotech companies each contribute in a collaboration?

A collaboration can provide an opportunity to tap the strengths of both big pharma and biotech companies. Biotech companies are known for their entrepreneurial business model and agility in developing drugs. Big pharma's prowess lies in its global scope for the commercialization of drugs, ability to provide significant amounts of capital, experience in running worldwide clinical trials, and broad expertise—scientific, medical, and regulatory. A collaboration also allows biotech companies to finance drug development without incurring excessive dilution through equity offerings.

Q 11.9 At what stage of drug development does a collaboration take place?

Licensing of the intellectual property associated with a potential drug takes place at all stages of the drug development continuum:

- Research;
- Preclinical (animal testing);

- Phase 1 (testing the drug in healthy volunteers for safety);
- Phase 2 (testing the drug in patients for efficacy); and
- Phase 3 (large efficacy trials for registration purposes).

The licensing of later-stage drugs is associated with improved economics for the biotech companies as the risk of potential failure of the drug continues to diminish. Accordingly, the most coveted drugs are those in the latest stage of development—phase 3—with blockbuster potential (sales in excess of $1 billion annually).

Q 11.10 What terms can be expected in a licensing transaction?

The basic components of a licensing transaction between a biotech company and big pharma may include:

- An up-front payment upon the grant of the license;
- Funding of further development of the drug;
- Milestone payments tied to further development of the drug, such as filing for regulatory approval, receipt of such approval, and commercial launch of the drug;
- Milestones and/or royalties tied to sales;
- Investments in equity or debt of the biotech company; and
- More rarely, co-promotion or co-marketing rights.

Q 11.11 When are contingent value rights used?

At times, it is more advantageous to big pharma and biotech companies to enter into a business combination rather than a licensing transaction. To avoid over-paying in such circumstances or to share the risk of further development of the drugs owned by the biotech company, big pharma may pay part of the acquisition consideration in the form of contingent value rights (CVRs). Like licenses, CVRs provide future cash payments to the selling shareholders as milestones, typically regulatory approvals, are reached.[4]

CVRs can be used in acquisitions of both public and private companies as a mechanism to avoid stalemates over the inherent value of the pipeline of the company to be acquired. They can also be used as a form of earnout when tied to sales milestones or other financial metrics.

More Financing Alternatives

Q 11.12 What are some alternatives to dilutive equity financing of drug development?

As securing adequate funding for drug development is always a challenge for biotech companies, the sector has continued to seek alternatives to dilutive equity financings. In response to their needs, various alternative financing sources have become available, such as venture lending, royalty-based financing, clinical research organization financing, and structured drug development financing.

Q 11.12.1 What is venture lending?

Large biopharmaceutical companies have the ability to raise capital through the issuance of debt securities, often convertible notes or debentures sold in public offerings. For the small biotech companies, including those in the venture-backed stage and micro-cap or small-cap publicly traded companies, venture debt financings may be an attractive alternative to the issuance of equity.

These private loans, extended by a few banks and other financial institutions, are generally amortizable over three years. They are designed to correlate to the development pipeline, so that as the company progresses to the next value inflection point, additional capital in the form of equity or a licensing opportunity provides money to meet the debt obligations. The loans are generally secured by the intellectual property and contain financial and other covenants to protect the lender.

Q 11.12.2 What are royalty-based financings?

For companies that (1) have revenues from the sale of drugs that are on the market, (2) are receiving royalties on licensed drugs, or (3) have low-risk, late-stage drugs in development (such as drugs already approved in one jurisdiction but not in another), the sale of revenues on future product sales or royalties can provide an attractive source of capital. The uncertain future revenues are exchanged for up-front capital. These financings are very flexible and can be used to fund further development of other drugs, for acquisitions, or for other purposes and can be meshed with secured debt in the same

transaction. The discount to expected sales is based on an assessment of the risks associated with the product in question—product failure, delay, underperformance, competition, and other factors that may materially impact the value of the royalty stream.

Q 11.12.3 What are financings linked to clinical research organizations?

Clinical research organizations (CROs) are engaged by the biopharmaceutical industry to further the development of and manage clinical trials. Their contribution has thus been value-added clinical development resources. Either directly or through affiliates, CROs may partner with biotech companies to provide capital, or other forms of consideration in the form of reduced service fees, to further clinical development. These financings can be based on milestone payments, royalties on future product sales, equity interests in the company, or a combination of these.

Q 11.12.4 What are structured drug development financings?

Structured drug development financings are designed to provide both capital and drug development expertise to biotech companies with products in early- or mid-stage development.

Under the typical structure, a biotech company licenses drugs to a newly created drug development company (DDC) that is funded by investors for the sole purpose of furthering the development of the licensed drugs. In turn, the biotech company receives the exclusive option to acquire the DDC at a prenegotiated purchase price. This option would obviously be exercised at a time when the drugs have shown sufficient safety and efficacy to warrant the exercise price, thereby allowing the biotech company to capture the value of the drugs above the purchase price for its shareholders. Development agreements between the DDC and the biotech company may be used to achieve a similar result.

In this form of financing, if the trials fail to achieve the intended results, the investors in the DDC bear the loss of their capital used to further development of the drugs. If the option is not exercised, the investors retain all rights to the drug and can license it to third parties.

Notes to Chapter 11

1. Huggett, *Biotech's Wellspring—A Survey of the Health of the Private Sector in 2014*, NATURE BIOTECHNOLOGY 33, 470–77 (2015).
2. Jumpstart Our Business Startups Act, Pub. L. No. 112-106, 126 Stat. 306 (2012).
3. Bloomberg L.P., Bloomberg Professional Service, Feb. 4, 2016.
4. CVRs are discussed in more detail in chapter 2.