The best biotech collaborations are prepared for the worst

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AUGUST 29, 2023

Research and development (R&D) collaborations present a win-win opportunity for big pharma and their biotech partners. Pharma companies can use collaborations to supplement their R&D pipelines without the large cash outlays necessitated by acquisitions. By spreading available cash across multiple collaborations, they increase their "shots on goal" of finding the next blockbuster drug/therapy.

Similarly, collaborations are attractive to smaller specialty pharma and biotech companies looking to partner certain noncore assets as a source of nondilutive financing or to accelerate life-saving technologies' path to market. Collaboration arrangements can also serve as a mechanism to validate platform technologies or as a precursor to M&A.

But collaborations are not without risk. A significant number of pharma collaborations fail, often for reasons unrelated to the viability of the subject asset(s). Some common reasons for failure include misalignment of expectations and differing risk tolerances. Therefore, no matter how promising a collaboration may appear, it's essential that the parties anticipate and address potential failure points from the outset.

Defining subjective obligations now helps avoid legal disputes later

In a typical R&D collaboration, two or more companies — often a smaller biotech and a larger pharmaceutical company — enter into a collaboration agreement. This agreement will generally outline the objectives of the collaboration, assign the responsibilities and contributions of each participant, and establish development milestones.

The agreement generally will specify a collaboration partner to oversee and direct the day-to-day activities of the collaboration and require this collaboration partner to use "commercially reasonable efforts" (often referred to as CRE) in progressing the subject asset toward regulatory approval.

Typically, CRE are defined as the same level of effort that the managing partner would use to develop its own products of similar potential. This, unfortunately, is a largely subjective standard. What constitutes a commercially reasonable pace to a global pharmaceutical company can often appear stultifyingly slow to a small, nimble, and singularly focused biotech company. This is particularly true where the smaller company is relying on payment of development milestones under the collaboration agreement or development of certain data/ manufacturing materials by the partner to progress its own internal assets.

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To the extent the parties must use CRE or other subjective terms to measure R&D progress, the parties should include a definition of that term within the agreement that reflects the expectations of the parties. By reaching an agreement at the beginning, it will reduce the potential for conflict later — and hopefully avoid the need for costly litigation after the fact to resolve disagreements on CRE.

Anticipating potential misalignment mitigates risk

Often, parties attempt to mitigate the inherent subjectiveness of the CRE standard by tying it to an agreed upon development plan. But this too has vulnerabilities. R&D does not always unfold consistent with the initial development plan. Unforeseen issues may arise — including worrisome safety and tolerability data and/or increased manufacturing CMC costs that require the parties to re-evaluate the plan.

How the parties evaluate issues relative to the efficacy and commercial potential of the drug/therapy varies widely based on their respective risk tolerances. Often, larger pharmaceutical companies managing the development will be more conservative on these issues than the smaller biotech company partners. Where the former may see an insurmountable issue, the latter may perceive a minor bump in the road. These differing viewpoints can lead to conflict, resulting in termination of collaboration and, in some cases, litigation.

To avoid these unfortunate outcomes, parties should assess potential misalignment at the outset and preemptively address

these issues in their collaboration agreement. Efforts should be made to define objective, measurable criteria on which certain critical decisions will be made. This is especially important with respect to decisions and actions that trigger milestone payments.

Collaboration agreements should have built-in exit strategies that protect both parties' interests and define post-termination obligations.

For example, parties may attempt to define the minimum safety and tolerability data necessary to support an Investigational New Drug (IND) filing, the maximum acceptable dosing to achieve a certain level of efficacy, or the maximum cost per unit necessary to support manufacturing scale-up. In certain cases, these measures may be established in reference to comparator drugs. While the parties have the option to deviate from these measures if they agree, setting objective guardrails can be valuable in situations where the parties cannot reach agreement.

Everyone needs an exit strategy

Sometimes there's no option but to terminate the collaboration arrangement, particularly if the parties are unable to resolve their differences or are adjusting their individual business strategies. Collaboration agreements should have built-in exit strategies that protect both parties' interests and define post-termination obligations.

The collaboration arrangement should at least cover certain critical termination issues, including ownership and control of intellectual property generated during the collaboration (collaboration IP), transfer of any ongoing third-party agreements, and responsibility for any ongoing clinical trials.

Collaboration IP in particular can present difficult issues on termination. It seems intuitive that, on termination, the licensor of the original IP (typically the smaller biotech) should receive, at a minimum, a license to use the collaboration IP so that it can continue development of the original IP on its own or with a new collaboration partner. But this can be challenging when the collaboration IP incorporates the terminating pharma partner's own IP that is used/useful in other non-collaboration products.

It is even more complicated where the terminating pharma partner was performing the collaboration manufacturing work in-house and relying on its own trade secret processes. In these cases, the best hope for the original IP licensor may be a nonexclusive license to use the collaboration IP going forward. Whether this will affect the commercial value of the original IP will vary on a case-by-case basis.

Because each collaboration is unique, and because the reasons for collaboration failure are varied and often unpredictable, it is impossible to address all termination terms up front. For this reason, parties should expect to negotiate a more comprehensive agreement at the time of termination to address unforeseen issues.

Planning ahead can keep a collaboration on track

Overall, it is worthwhile for the parties to spend time as part of the initial contracting process to identify potential areas of misalignment; build in objective, measurable criteria around critical decision points (especially those tied to milestone payments); and, allocate the parties' basic rights and responsibilities in the event of an early termination. This time and effort on the front end of the contracting stage, when the parties are eager to collaborate, can save countless hours and dollars on the back end of the collaboration and, in some cases, may salvage an otherwise doomed partnership.

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This article was first published on Reuters Legal News and Westlaw Today on August 29, 2023.