

Cell And Gene Therapies Are Driving M&A Deal Activity

By **Adam Golden and Anishiya Abrol** (March 18, 2020)

There have been remarkable advances over the last several years in the development of cell and gene therapies, or CGTs. These therapies represent truly groundbreaking approaches to the treatment and prevention of diseases, many of which have proven resistant to traditional drugs or therapies.

Cell therapy generally refers to the transfer of live cells into a patient to treat a disease. The cells may originate from the patient (autologous therapy), where they are extracted, modified and reinfused into the patient, or from a donor (allogeneic therapy). Gene therapy involves a change in the genetic code of a patient by inserting or removing specific gene sequences.

CGTs as Deal Drivers

The huge potential of CGTs has generated a significant amount of deal activity, including mergers and acquisitions, collaborations between biopharma companies and financings to support the cost of development, as companies look to get into the field or add on to existing CGT platforms.

Examples of significant M&A transactions in recent years involving target companies with significant CGT programs include Bristol-Myers Squibb Co.'s acquisition of Celgene Corp., Novartis Pharmaceuticals Corp.'s acquisition of AveXis Inc., Roche AG's acquisition of Spark Therapeutics Inc. and Biogen Inc.'s acquisition of Nightstar Therapeutics PLC.

Beyond the headline M&A deals, life sciences companies from the biggest pharmaceutical companies to early stage biotechs are collaborating to identify and develop not just CGTs but targets against which they may be effective and numerous technological components that are often needed to make these therapies work.

However, CGTs offer more than potential. So-called CAR-T therapy was one of the first CGTs to be approved and remains an area of continued industry focus.[1] Since then, a number of groundbreaking cell and gene therapies have been approved, indicating that the prospect for these types of therapies is now being proven out.

The U.S. Food and Drug Administration currently cites 17 approved CGT products,[2] including therapies such as CAR-Ts Kymriah (developed by Novartis) and Yescarta (Kite Therapeutics) for certain oncology indications, gene therapy Lexturna (Spark Therapeutics) to treat a rare retinal disease, and gene therapy Zolgensma (Novartis) for spinal muscular atrophy.

What might have seemed like long shots in the past are now becoming successful new treatments.

Another driver for transactions involving CGTs is the fact that these products often involve multiple technologies or components — a viral vector or plasmid to be used as a delivery



Adam Golden



Anishiya Abrol

vehicle, a gene splicing tool, binding agents such as CARs, etc. Many companies don't have all of the technologies needed for a given therapy, so they need to transact — typically through a license or collaboration — to acquire rights to them.

Manufacturing is a critical element for cell and gene therapies and can be highly complex. For example, CAR-T therapy involves extracting T-cells from the patient and sending them to a laboratory or manufacturing facility where they are genetically engineered to express CARs on the surface of the cells, and then returned for reinfusion back into the patient, all under carefully controlled procedures and conditions.

This has driven biopharma companies to make significant investments or in many cases acquire or collaborate to develop the necessary manufacturing capabilities. The potential value of providing such manufacturing capabilities has in turn driven consolidation among contract manufacturing organizations, or CMOs, and contract development manufacturing organizations, or CDMOs, companies who provide such manufacturing as a service to product innovators.

Two notable such deals last year were Catalent Inc.'s acquisition of Paragon Bioservices Inc. and Thermo Fisher Scientific Inc.'s acquisition of Brammer Bio.

Most recently, Catalent agreed to acquire Masthercell Global, a Belgium-based cell and gene therapy CDMO, with Catalent CEO John Chiminski noting that "[b]oth autologous and allogeneic cell therapies provide important new treatment options, with a rising number expected to gain regulatory approval over the coming years."^[3]

Executing CGT Transactions

Executing cell and gene deals can pose a number of challenges, both from a business and legal perspective. Some of the key considerations that go into any transaction include the following:

Valuation

Competition for CGT assets has caused significant increases in valuations for many of the companies developing them.

Beyond competition driving up prices, developing a financial model to value these assets and businesses can be quite challenging for a number of reasons, including the risks and high cost of development, uncertain pricing environment for pharmaceuticals generally and in particular the administration of CGTs, and the commercial challenges of launching and manufacturing these therapies. As a result, valuations based on future revenue streams can be difficult.

Payments to Third Parties

As noted above, CGTs can incorporate multiple components which often need to be acquired or licensed by the innovator from other companies. Each of these can carry its own set of monetary obligations such as payments due upon achievement of development, regulatory or commercial milestones, and royalties on sales of the ultimate product incorporating the component.

CGT developers need to carefully assess the various rights that may be needed to commercialize the therapy and the aggregate associated cost likely to be due to third

parties.

In particular, when separate royalty streams on the sale of a product are owed to multiple parties (so-called royalty stacking), the overall royalty burden can significantly eat into the financial return that innovators need to achieve in order to fund the development of the CGT and other therapies.

In licensing deals, the impact of these potential payments is typically mitigated to a certain extent through risk sharing mechanisms such as anti-stacking provisions which allow the licensee to offset a portion of royalties or other payments that may become due to other parties against the payments to the licensor.

The extent of such offsets are often highly negotiated, including around issues such as the portion of the third-party payments that can be offset and whether there is a floor below which royalties or other payments to the licensor may not be decreased.

Another area of focus for licensing deals are the payment mechanics. Royalty provisions typically provide for pro rating the amount of net sales on which royalties are payable for purposes of traditional combination products, i.e., products that include multiple active ingredients.

Components combined to form many cell and gene therapies don't necessarily neatly fall into this construct as they wouldn't necessarily be considered active ingredients in the traditional sense. Therefore, combination products and how they are addressed in royalty payment provisions need to be carefully considered given the potentially significant impact on future costs associated with the product.

Similarly, understanding these payment obligations is a significant due diligence point for acquirers in M&A deals as it is one of the factors affecting the valuation of the potential acquisition. One of the first things our buy-side clients look at is to understand all the licenses and collaborations that a target company has and to calculate the projected royalties and other payments that will become due to third parties on the target's key products.

This can be a complex exercise, requiring input from patent lawyers, licensing lawyers and the finance teams charged with calculating these payments. However, a meaningful valuation of the target business and its key products cannot be determined unless these payment obligations are understood.

Where there are numerous third-party payment obligations, sellers can get out ahead of this issue by providing summary calculations as part of the due diligence process. Buyers will always do the confirmatory diligence, but sellers can gain a lot of credibility and facilitate a speedy auction by offering this sort of assistance.

Exclusivity

Licenses and collaboration agreements often include noncompete or exclusivity provisions designed to protect licensees from dilution of the value of their license by restricting licensors from licensing its technology to other parties for competing uses.

While less common, such licensors may seek to commit the licensee to their specific technology through an agreement not to use competing technologies. These provisions are typically highly negotiated and rightly so given that they can impose significant and

potentially long-term restrictions on the parties' businesses.

Further licensors' and licensees' interests are not necessarily aligned depending on the parties' respective business models. Companies with platform technology which can be used in a variety of products or fields need to maintain the ability to license their technology to multiple parties in order to capitalize on the value of the platform while licensees of these novel technologies need to maintain the flexibility to utilize alternative products and technologies that may ultimately prove to be better than the license technology.

This is particularly true in the cell and gene space given the rapidly changing landscape of therapies and technologies. Lastly, deal-makers should also be careful to review the scope and duration of exclusivity provisions in order to ensure they don't run afoul of the antitrust laws, which can vary significantly based on jurisdiction.

Intellectual Property

Ultimately, intellectual property is the key value driver for most life sciences companies and therefore intellectual property due diligence by specialists is a key element of these transactions. Similarly, in the context of negotiating licenses and collaborations and diligencing these agreements for acquisitions, contractual provisions around ownership of new IP, control over prosecution and maintenance and the right to enforce patents are critical issues which are key to maintaining the value of the relevant products or technologies.

These provisions can have significant long-term business effects and therefore are not solely the purview of the IP lawyers. Again, given the many emerging technologies types of therapies that CGTs present, they are of particular importance for deals for these therapies.

Conclusion

CGTs offer exciting opportunities for cutting-edge therapies. There are many challenges ahead in the continuing journey to discover and most importantly make these therapies available to patients. Deal-making will remain an important piece of this puzzle, and will implicate many of the issues discussed herein as well as others.

With proper attention to these issues and disciplined deal-making, industry players are successfully navigating the world of cell and gene therapies transactions and we have no doubt they will continue to do so.

Adam Golden is a partner and Anishiya Abrol is counsel at Hogan Lovells.

The opinions expressed are those of the author(s) and do not necessarily reflect the views of the firm, its clients or Portfolio Media Inc., or any of its or their respective affiliates. This article is for general information purposes and is not intended to be and should not be taken as legal advice.

[1] CAR-T stands for chimeric antigen receptor (CAR) T cell therapy which is a process of modifying a patient's T-cells to express a receptor that recognizes and binds to an antigen on the surface of malignant cells. American Society of Gene & Cell Therapy (<https://www.asgct.org/education/more-resources/gene-and-cell-therapy-faqs>).

[2] U.S. Food & Drug Administration (<https://www.fda.gov/vaccines-blood-biologics/cellular-gene-therapy-products/approved-cellular-and-gene-therapy-products>).

[3] <https://www.businesswire.com/news/home/20200203005176/en/%C2%A0Catalent-Acquire-Leading-Cell-Therapy-Company-MaSTherCell>.