



CRA Insights: Life Sciences

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Trends in cell and gene therapy financial deals

Introduction

Cell and gene therapies (CGTs) are coming of age, with most healthcare leaders expecting them to be ready for widespread delivery within the next 3 to 10 years.¹ They can be considered the new “magic bullet,” which is reminiscent of monoclonal antibodies (mAbs) some 20 to 25 years ago. At the time, mAbs represented a breakthrough: large proteins with capacity to target specific antigens in a world of small molecules. The mAbs brought with them much hope and significant activity amongst biotech and pharma companies worldwide, in terms of mergers and acquisitions (M&As), collaborative deals, and licensing opportunities. They have since delivered (and are still delivering) great progress in the treatment armamentarium of autoimmune diseases, cancers, and more.

But what does the deal landscape look like today for CGTs as these technologies begin to reach their potential? Will the same trends in licensing or acquisitions manifest in the CGT space as they did for mAbs? Or, given the lack of commercial benchmarks and uncertainties in long-term valuation for these therapies, can we expect new trends to emerge? To help answer these questions, we have looked at recent M&A and collaborative activity in the space, with an eye toward size, pace and focus of companies involved, deal structure and value, and the number and clinical stage of assets, to draw similarities and parallels between mAbs and CGTs.

Finding 1: The pace of CGTs deals and partnerships is greatly accelerated compared to those historically seen for mAbs, with Big Pharma eager to establish an early presence in this space

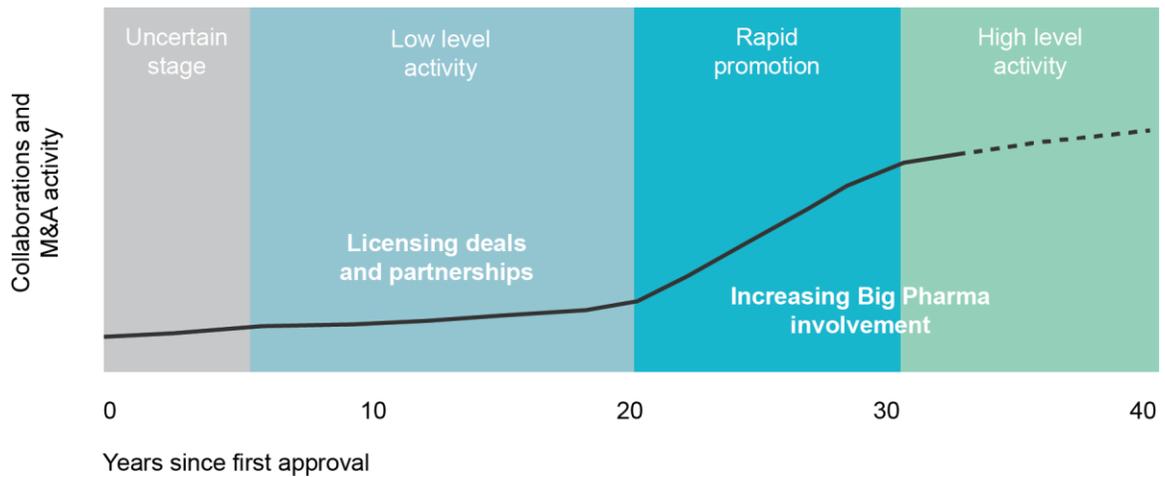
Previous analysis of mAb collaborations showed four distinct phases of activity: an uncertain stage, a stable stage with low level activity, a rapid promotion stage, and a stable stage at high level of activity.² The approval of the first mAb in the mid-1980s marked the beginning of the unstable stage, where interactions were mostly limited to collaborations and licensing deals, and were predominantly between small biotechnology firms. Activity did not reach ‘rapid promotion’ until two decades later, when Big Pharma began to show real interest in acquiring assets and developing collaborations, and the number and size of deals began to ramp up (Figure 1a). Conversely, deals within the CGT space have shown a much faster uptake, quickly growing in momentum since the approval of the first CGTs in the early 2010s (Figure 1b). Over 50 CGT-related partnerships and investments were made between 2010-2016, with Big Pharma involvement from the beginning.³

2010 started with a partnership worth a potential \$213.6 million (excluding royalties) between Novartis and GenVec for the development of adenovirus-based gene therapies, and later in the year saw a strategic alliance between GSK and the Telethon Institute of Gene therapy (TIGET), also for gene therapy research and development.^{4,5} Since 2016, activity in the CGT space has continued apace, with more companies betting on the value of CGTs and trying to establish a presence in this promising space (Figure 2).

Figure 1: The pace of CGT deals and partnerships has been much faster than previously observed within the mAb space.

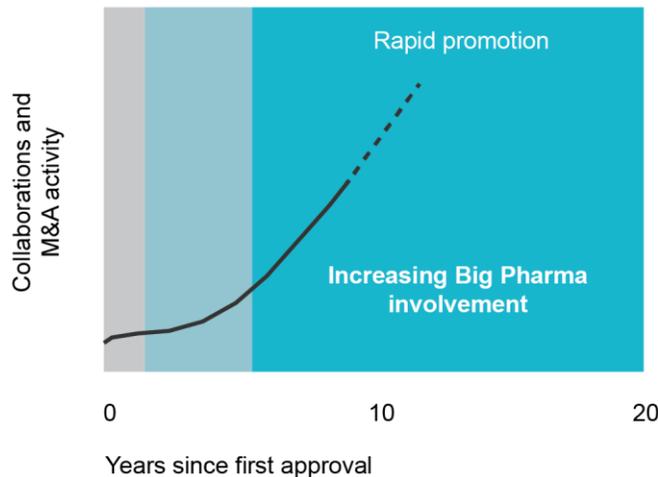
a. Monoclonal antibodies

Interest in setting up partnerships for mAb technologies and assets was originally slow and Big Pharma involvement was not observed until the mid-2000s



b. Cell and gene therapy

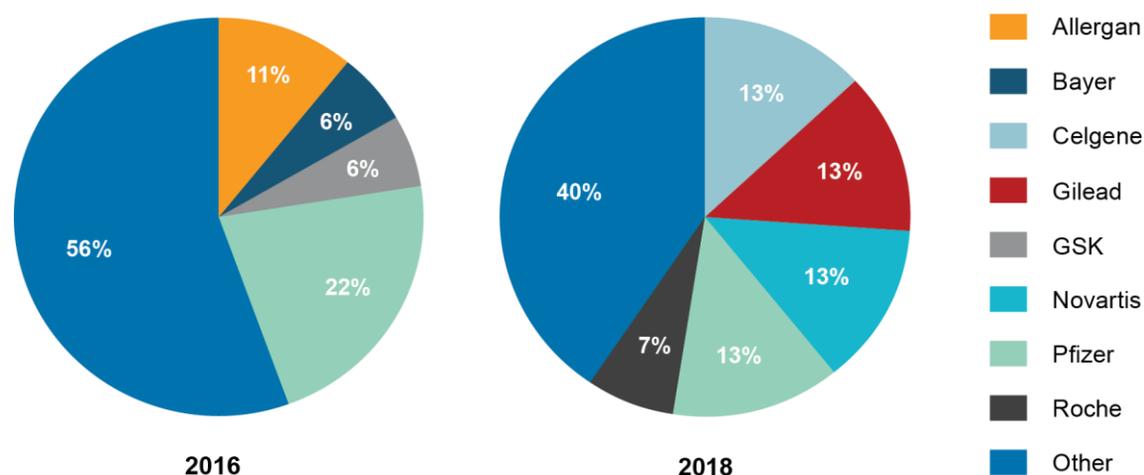
The pace for CGT deals and partnerships is greatly accelerated compared to that of mAbs, with large biopharmaceutical companies being faster to embrace the potential of these innovative therapies.



Source: EMA; CRA analysis

Figure 2: Big Pharma is increasingly involved in M&A and collaborative activity within the CGT space.

Unlike in the early years of mAb activity, large pharmaceutical companies are not waiting for the CGT space to become well established before forming partnerships and making acquisitions. Figures show percentage involvement in deal volume of Big Pharma companies (defined as those within the top 20 highest revenue companies in 2018) in all M&A and collaborative activity within the specified year.



Source: EMA; CRA analysis

This acceleration of Big Pharma’s foray into CGT is also exemplified in the difference between CGT and mAb products commanding premiums. The largest mAb deals were characterized by the acquisitions of late stage and marketed products – evidence of Big Pharma waiting for low-risk products in a developed space. Most major CGT acquisitions are for product pipelines – large numbers of early stage products and the accompanying platform technologies and manufacturing capabilities that require building from the ground up.

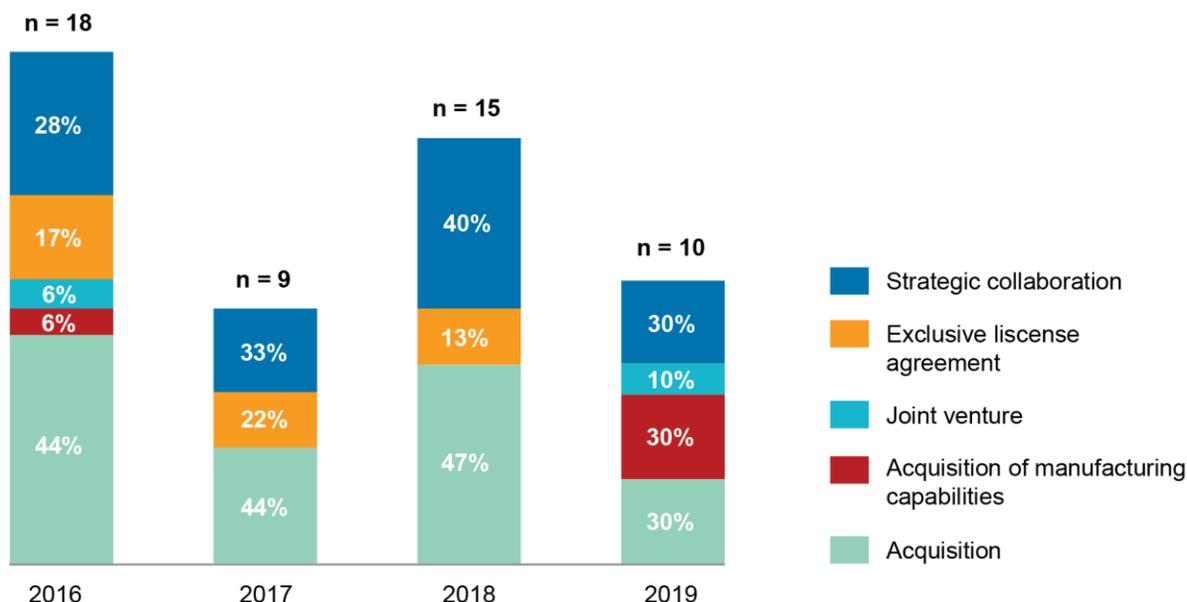
Finding 2: Although overall deal activity in the CGT space is high, the proportion of licensing deals and partnerships relative to M&A operations remains relatively constant as uncertainties remain about the long-term commercial potential of novel CGTs

While Big Pharma appears to show less hesitation in embracing CGTs, the types of deals have evolved. Analysis of highly publicized deals that took place during the ‘rapid promotion’ phase of mAb transactions shows a high proportion of M&A relative to licensing and collaborative deals. This trend differs from that observed for CGT, where licensing and collaborative deals continue to play a dominant role. Given the relative infancy of CGT technology, this is unsurprising, as uncertainties over valuations and technical barriers remain. Partnerships provide a lower risk option to the licensor or investor to expand CGT offerings, without assuming full financial responsibility and without suffering the disruption to productivity often associated with M&A (Figure 3).

Interestingly, within the first half of 2019, three contract development and manufacturing organizations (CDMOs) with CGT capabilities were acquired by major industry players. These substantial investments in manufacturing capability address an important historical concern about manufacturing scarcity associated with new technologies and may indicate a growing confidence in the long-term potential of CGTs.

Figure 3: The proportion of strategic collaborations and licensing agreements compared to M&A activity in the CGT space remains high.

Over the past three and a half years, the proportion of collaborative agreements and partnerships relative to M&A deals, has remained more or less constant. We believe this indicates companies are still somewhat reluctant to invest heavily in CGT, whilst there are still hurdles that these technologies must overcome to reach their full potential. n = total number of deals per year.



Source: CRA analysis

It is not just financial investment that is driving CGT deal-making; there is also an emphasis on accessing complementary capabilities through collaboration. This can be in terms of expertise from the licensor point of view, or technical abilities and assets that ‘fit’ the current portfolio from the licensee perspective. The partnership between Neurocrine Bioscience and Voyager Therapeutics exemplifies such a synergistic collaboration, with Neurocrine providing central nervous system (CNS) drug development expertise, as well as much needed financial support for the clinical development of gene therapies for Parkinson’s disease and Friedreich’s ataxia. In return, Neurocrine gained the opportunity to co-commercialize and potentially obtain global rights to these portfolio-compatible therapies.

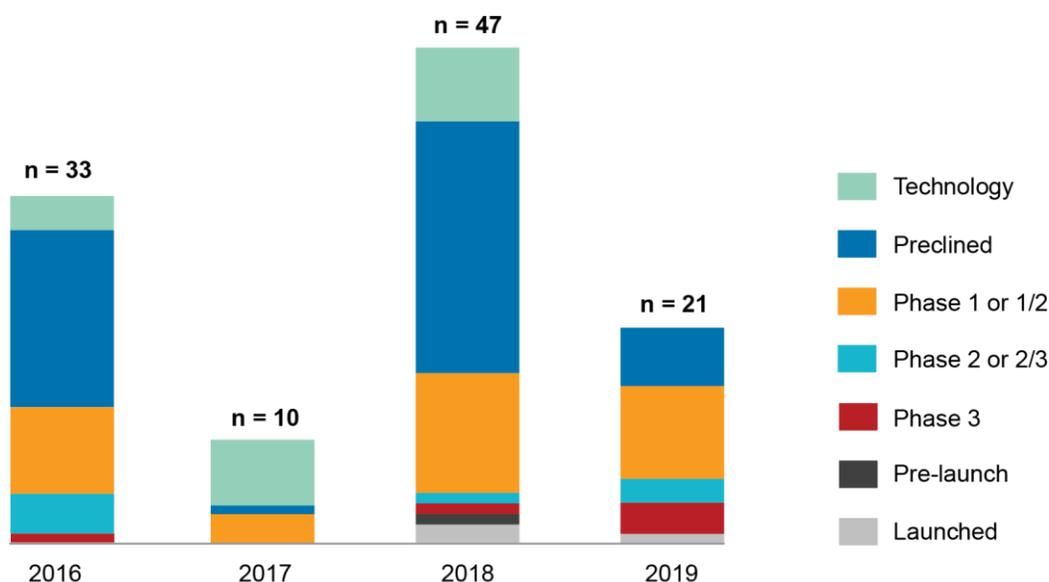
As assets approach regulatory approval, we expect that the structure and value of deals in the CGT space will mature. Companies will exercise the option to follow up on previous collaborative deals, punctuating the space with massive exclusive licensing deals and acquisitions. Early indications of this change have already been observed in recent years. The \$11.9 billion acquisition of Kite (including near-launch asset Yescarta) by Gilead in 2017, and Roche’s \$4.8 billion bid for Spark Therapeutics (including marketed Luxturna), may be early indicators of the rise of the billion dollar deals that previously characterized the mAb ‘rapid promotion’ phase.

Finding 3: Despite the infancy of the CGT space and hurdles that may limit its potential, Big Pharma is aggressively pursuing CGT opportunities, even targeting early development assets with limited supportive clinical data

A striking difference between recent CGT deals and earlier mAb ones is the number involving assets without robust supportive clinical data (Figure 4). Historically, there was a high interest in acquiring late stage or already marketed mAb products, to minimize potential risks associated with drug development. Interest in CGTs, however, has shifted to earlier stage opportunities, with a high proportion of partnerships involving Phase I, II, or even preclinical assets. Pfizer’s first move into CGTs, for example, was through a collaboration for the development and commercialization of Spark Therapeutics Phi/II hemophilia gene therapy SPK-FIX. Subsequent efforts to expand Pfizer’s CGT offerings include the acquisition of Bamboo Therapeutics in 2016, which provided one Phase I and several pre-clinical assets, as well as an early 2019 deal collaborating on the development of Vivet Therapeutics’ Phase I/II asset VTX-801.

Figure 4: Partnerships, licensing deals, and M&A activity primarily involve very early stage clinical assets.

Many products involved in CGT deals are not supported by robust trial data given their early stage of clinical development. n = total number of technologies or assets involved in all deals per year.



Source: CRA analysis

To further examine this finding, various factors associated with mAb and CGT deals between 1999 and 2019 were assessed quantitatively (see footnote). Big Pharma’s preference for late stage and marketed mAb products was clearly observed with a close correlation between a product’s phase and deal value, with later stage products associated with the highest deal value. Conversely, recent CGT deal valuations show a slight negative correlation with product phase, indicating that it is early stage products that are key contributors to the value of these deals. Contrasting relationships are noted also for mAb and CGT deals in the number of products included in the deals. For mAbs, an inverse correlation to the number of products in the deal is evident, as the largest deals involve the acquisitions of few, very late stage, or marketed, products, typically without a play in platform technologies. The number of products in CGT deals, however, has a strong impact on deal valuation, as the inclusion of many incremental early stage products has an outsized impact on CGT deal value.

Conclusion

CGTs are shaking up the pharmaceutical and healthcare landscape. In providing innovative platforms to treat disease, there is hope that these technologies can provide significant improvements to treatment and may even represent one-time cures for diseases where limited management options have previously only been available. For insurance and coverage, new payment and contracting schemes are being developed to handle the often substantial upfront costs yet long-term value offered by CGTs. For pharmaceutical companies, these products represent areas of unprecedented activity and opportunity.

While the entrance of every new technology sparks interest and deal making activity, the CGT space is proving to be unique. It took twenty years for collaborative activity around mAbs to reach a “rapid promotion” phase of significant Big Pharma interest and billion-dollar deal-making. CGT deals have reached this phase in under ten years. The differences in M&A and collaborative activity extend beyond the pacing of activity, with contrasting trends in terms of deal structure, average phase of development, and number of products all resulting in a clear distinction between the therapy types (Figure 5).

Figure 5: Key similarities and differences in CGT and mAb deal trends.

| | mAb deals | CGT deals |
|---------------------------|--|--|
| Pace of activity | <ul style="list-style-type: none"> • Slow pace, reaching high rapid promotion phase at 20 years • Early activity primarily between smaller biotech, Big Pharma cautious to engage in deal making until therapy class was established | <ul style="list-style-type: none"> • Fast pace, reaching high rapid promotion phase at 5-6 years • Big Pharma quick to establish presence in the space |
| Deal type | <ul style="list-style-type: none"> • Rapid promotion phase characterized mainly by high value M&A deals | <ul style="list-style-type: none"> • Rapid promotion phase characterized by mixture of M&A deals and licensing partnerships and collaborations |
| Deal value | <ul style="list-style-type: none"> • High value acquisitions throughout • Consistent growth in deal value | <ul style="list-style-type: none"> • Infrequent blockbuster acquisitions • Smaller value for licensing deals |
| Product phase | <ul style="list-style-type: none"> • High interest in acquiring late stage or already marketed mAb products | <ul style="list-style-type: none"> • High proportion of assets not yet supported by robust trial data • Many products still in preclinical or Phase I/II at the time of the deal |
| Number of products | <ul style="list-style-type: none"> • Most deals involve only one asset (or in some cases a few late stage assets) | <ul style="list-style-type: none"> • A mixture of deals involving only one asset with those containing multiple assets at various points along the clinical development pathway |

Sources: CRA analysis, GBA, AEMPS

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Footnote on quantitative methodology

To identify and describe trends in CGT deals and valuations from a quantitative perspective, we analyzed 32 CGT deals between 2016 and June 2019, and compared them with 29 mAb deals between 1999 and 2013 based on data from company press releases and other publicly available media. In particular, we looked at correlations among the following factors: deal value and structure (total value, upfront payment, milestones and royalties); products involved (number, development phase, indication).

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