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Intense Transactional Activity Continues To Propel Biopharma Growth

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Outcome Capital analyzed transactional activity by the largest biopharmaceutical companies in the three-and-a-half-year period between January 2017 and June 2020 to reveal development and therapeutic areas trends.

Transactional activity – mergers, acquisitions and alliances – is an important tool that allows big pharma companies to maintain a competitive edge, ensure a healthy pipeline and reduce developmental risk by allocating resources towards promising candidates. Importantly, these transactions allow large companies to access innovation, typically provided by smaller entrepreneurial players.

For investors in the target companies, the prospect of an acquisition or partnership represents an attractive exit window with substantial returns and far increased likelihood that candidate therapeutics reach patients. There are innumerable benefits of early partnerships for earlier stage target companies. Beyond providing a flow of cash, partnership transactions enable rapid discovery, development and scale-up, access to knowledge and expertise, essential resources, third-party validation and credibility and overall risk mitigation.

Understanding the rationale behind these transactions and the intended strategic direction of acquirers is key for CEOs when considering how to position their companies in a market-aligned manner. To that effect, Outcome Capital analyzed transactional activity by the largest biopharmaceutical companies in the three-and-a-half-year period between January 2017 and June 2020. Our analysis describes the type and frequency of acquisitions and collaborations in the biopharmaceutical industry and reveals sectors and stages of development in which transactional activity in concentrated.

Transaction Trends

The drug development priorities and resource allocations of major pharmaceutical companies are ever changing with risk/reward calculations constantly determining the direction of the research and development. Efforts may be shifted away from disease indications that have proven particularly challenging and towards indications and therapeutic types that are beginning to show promise. To understand transaction trends in the biopharmaceutical industry, Outcome Capital examined M&A and partnership transactions made by the largest 24 biopharmaceutical companies by market cap from 1 January, 2017 to 30 June, 2020 (*see Table 1)*.

Acquisitions that pertained to therapeutics intended to treat human disease that were in discovery/preclinical development, clinical trials, or already approved were considered in this analysis. Transactions that pertained to other areas including animal health, facilities, software/database development, and assay development were excluded. Of the 156 transactions identified, 73 met these inclusion criteria. We analyzed these transactions by various market parameters including transaction value, disease indication, and phase of development of the lead asset. Notably, three companies, AstraZeneca, Zoetis, and Regeneron did not make any acquisitions relevant to this research and thus were not considered in subsequent analyses.

Transactions with disclosed financial details (n=62) were analyzed by deal value. The average transaction value was approximately $5.5bn and median value was $914m. The separation between the average and median transactions values was due, in part, to the inclusion of *Takeda Pharmaceutical Co. Ltd.*'s acquisition of Shire and *Bristol Myers Squibb*'s acquisition of Celgene, both transactions valued well in excess of $50bn (these transactions were considered outliers and were not included in subsequent analyses).

The analysis found that 69.4% of the transactions had a total deal value between $250m and $5bn indicating that, with some exceptions, the big pharmaceutical companies generally do not engage in acquisitions smaller than $250m. Thus, companies valued below this apparent threshold are unlikely to be targeted by the largest players. These data also reveal that transactions valued at greater than $5bn are relatively rare events that require a unique set of circumstances to be advantageous for both parties, including priority focus on a disease indication, clinical progress showing promise, and/or significant and sustained revenue generation for the acquirer.

The number of deals per year was largely steady for the three years analyzed here (*see Exhibit 1A*). However, in 2017 the $57bn cumulative value of all deals was greater than cumulative deal values in either 2018 or 2019 (excluding outliers; *see Exhibit 1B*). The larger amount in 2017 was primarily driven by *Johnson & Johnson*'s $30bn acquisition of Actelion Ltd., the pulmonary arterial hypertension-focused Swiss biopharmaceutical company. Despite uncertainty surrounding the impact of the Covid-19 pandemic on the broader economic landscape, M&A expenditure in 2020 is on pace to surpass 2018 and 2019, driven by *Novartis AG*'s nearly $10bn acquisition of The Medicines Company. In total, the top pharmaceutical companies spent

approximately $162.5bn on acquisitions of companies with relevant therapeutic assets during this three-and-a-half-year period.

Exhibit 1.

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Source for all exhibits: Outcome Capital

Important insights can be gleaned from analyzing the number of deals and total deal values by acquiring company. The most acquisitive companies over this period were *Astellas Pharma, Inc.*, Novartis, and *Merck & Co., Inc.* (*see Exhibit 2*). The amount of deals made by Astellas is particularly notable as they are the smallest company by market cap of those considered here. Astellas' acquisitions were primarily focused in oncology and ophthalmology, which are two stated core interests for the company. This level of activity by a comparatively small player signals ambition to quickly establish a dominant position in these sectors. In contrast, *Pfizer Inc.* was the least acquisitive of the top five companies (J&J, Roche, Merck, and Novartis being the other four), making only two acquisitions from 2017-2020. This may not be surprising in light of their focus and ultimate failing in 2016 to acquire the medical aesthetics giant, Allergan. In fact, the company made no deals in either 2017 or 2018 and replaced their CEO in early 2019.

Exhibit 2.

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It is especially informative to consider the number of deals by company in the context of total money spent on acquisitions. Of the three most acquisitive companies, Novartis spent a total of approximately $26.7bn and Merck spent approximately $7.3bn. Despite being the smallest company, Astellas spent a total of $5.5bn, though more than half of this came from their $3bn acquisition of the neuromuscular disease focused, Audentes Therapeutics in 2020. Aside from this large acquisition, Astellas spent a total of $2.5bn on seven other acquisitions. Consistent with this relatively low total, four of the seven acquisitions made by Astellas were of companies with lead assets in Phase I clinicals trials and the remaining deals were all in preclinical development. These low-value early-stage acquisitions highlight Astellas' ambitious posture. In accordance with their market capitalization, the company is taking a series of relatively low-cost calculated risks in the hopes of achieving significant growth and increased market share.

Outcome Capital also analyzed deals made by stage of development and disease indication of the target company's lead asset. There were only two deals done involving discovery phase companies, indicating that the large pharmaceutical companies generally do not seek the earliest

stage acquisition targets. Eighteen companies were acquired in preclinical development which exceeded the number of acquisitions at any other developmental stage (*see Exhibit 3A*). Acquisitions involving clinical stage companies and companies with marketed therapeutics were similar. Interestingly, the average deal value for a preclinical stage acquisition ($765m) exceeded the average acquisition value of companies in Phase I clinical trials ($543m). As progress towards FDA approval increased, so did the average valuation. Companies engaged in Phase II clinical trials were acquired for average of $1.4bn, while companies in Phase III were acquired for an average of $2.7bn. Companies with therapeutics already on the market were acquired for an average of $8.5bn (excluding outliers; *see Exhibit 3B*). These data indicate that while there is significant interest in acquisitions of preclinical and early clinical companies, the heightened risk of failure keeps valuations at these stages relatively low. Reaching a Phase III clinical trial represents a dramatic increase in value for companies involved in drug development.

Exhibit 3.

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To understand how these transactions were distributed, deals were analyzed by disease indication. While immuno-oncology (IO) has made headlines lately, activity in non-IO oncology remained high. Together, nearly half of all acquisitions made in this period came from these two sectors (*see Exhibit 4A*). Despite similar numbers of transactions, approximately 60% more money was spent to acquire companies focused on non-IO oncology *(see Exhibit 4B*).

This discrepancy can best be understood by examining in which phase of development these acquisitions occurred. Nearly half of all oncology acquisitions involved companies with approved therapeutics, while nearly half of all IO acquisitions were of companies in preclinical development (*see Exhibit 5*). This suggests that there is increased demand for IO acquisitions among the large pharmaceutical companies, perhaps due to perceived break through potential, which has resulted in the acquisition of several early stage companies. There was also significant activity in immunology and rare disease, and deal values in rare disease in particular were similar to IO.

Exhibit 4.

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Although there were only two acquisitions of companies developing therapies for cardiovascular indications, each acquisition was of a revenue generating company with marketed drugs. These two large acquisitions exceeded the expenditure in any sector aside from oncology. Consistent with the much-publicized withdrawal from R&D efforts in psychiatry, there was only one deal

made in this sector valued at $45m. Together, these analyses demonstrate that acquisitions made by the largest pharmaceutical companies are highly concentrated in a few key sectors, with a particular focus in oncology (including IO).

Exhibit 5.

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Large Acquisitions

During the time period analyzed, three M&As in excess of $50bn garnered much attention: BMS' acquisition of Celgene, *AbbVie Inc.*'s acquisition of Allergan (although not closed during the time period analyzed) and Takeda's acquisition of Shire. Outcome Capital examined these deals and comments made by the CEOs to understand the circumstances that incentivized these exceptionally large transactions.

In early 2019, BMS announced a deal to acquire oncology-focused, Celgene, for $99bn. At the time, BMS' largest therapeutic franchise was Opdivo (nivolumab), a PD-1 inhibitor IO drug, which was losing market share to Merck's PD-1 inhibitor, Keytruda (pembrolizumab). Celgene's largest revenue generator was Revlimid (lenalidomide), a treatment for multiple myeloma, which was facing a 2022 patent cliff. However, unlike BMS, Celgene had a strong oncology pipeline. Thus, the acquisition allowed BMS to bolster its development pipeline, stabilize revenue, and establish itself as a dominant player in oncology.

In June of 2019 AbbVie announced its acquisition of Allergan for $86bn. AbbVie's most profitable drug was the TNF alpha inhibitor, Humira (adalimumab), which was approved for the treatment of a variety of inflammatory conditions and accounted for 70% of the company's revenue. Humira was facing a 2023 patent cliff in the US and was already losing ground to biosimilars in Europe. The acquisition allowed AbbVie to reduce their reliance Humira by adding Allergan's $4.5bn medical aesthetics business primarily driven by the success of Botox. Allergan also brought immediate R&D capabilities, particularly in immunology and neuroscience, and a global sales presence. The acquisition allowed AbbVie to diversify, stabilize revenue and grow their R&D capacity in key disease sectors.

Takeda announced their planned acquisition of Shire for $80bn in April of 2018. This acquisition differs from the previous two discussed, as Takeda was not a dominant pharmaceutical company seeking to maintain and solidify their position. Rather, the company sought the Shire acquisition for the purposes of expansion. Takeda was primarily focused on development in immunology (GI in particular), neuroscience and oncology. The acquisition of Shire expanded their portfolio, giving them a major presence in rare disease and plasma-derived therapies. Perhaps most importantly, the deal resulted in their listing on the New York Stock Exchange and positioned

Takeda as a global player.

Taken together, stabilization of revenue and expansion into new markets or sectors are clear drivers for these large-scale mergers. They allow for a company to quickly and dramatically bolster their pipeline while also diversifying revenues that may be highly concentrated in a single program. Because these transactions require a specific set of circumstances, they are rare occurrences. One such factor is the attitude of the CEO. Many CEOs are wary of the perils of sudden expansion. Emma Walmsley, the CEO of *GlaxoSmithKline plc*encapsulated this notion upon taking her position in 2017 by stating, "Companies can die of indigestion just as easily as they can die from starvation." Though clearly not without risk, these transactions alter the global biopharmaceutical landscape.

Partnerships

Though acquisitions in the biopharmaceutical industry often garner much attention, partnerships and collaborations are actually much more common. Outcome Capital compared the number of partnership agreements with the number of acquisitions in 2019 (with no exclusions) and found that partnerships occur about six times as frequently as acquisitions. Collaborations can vary significantly in their size, area of focus, and scope.

As observed in M&A activity, the developmental stage of the therapeutics involved correlates with the size of the transaction. Early stage transactions are the smallest and deals involving late clinical and marketed therapeutics are larger. For large companies, partnerships can be a value tool in accessing specialized technology to identify novel drug targets, bolster development pipelines by codeveloping already promising therapeutics, and gaining access to new sectors and global markets. For smaller companies, these deals are important liquidity events that do not necessarily require giving up equity. Given the massive expenditure required to bring a candidate therapeutic through multiple clinical trials, these deals are a means of ensuring that a promising drug has the maximum chance of success without delay.

One type of partnership agreement common amongst biopharmaceutical companies is a collaboration for the purposes of drug discovery. These types of collaborations allow a large company to gain access to new and specialized technologies as well as the expertise of the developers. These deals are typically three to five years in length and focus on a specific set of disease indications. The specific financial structures vary, but they commonly include an upfront payment as well as milestone payments at various stages of clinical development and future sales royalties for the smaller company. In exchange, the larger company gains exclusive rights to any drug candidate programs arising from the partnership.

For example, in January of 2020, *Bayer AG* announced a three-year collaboration with Exscientia to develop novel small molecule therapeutics for cardiovascular and oncological diseases using Exscientia's proprietary, AI-driven, drug development technology. In exchange for access,

expertise, and exclusive developmental and commercial rights to resultant therapeutics, Bayer made an undisclosed up-front payment. In addition, Exscentia was eligible for various development milestone payments potentially worth $267m as well as future sales royalties. These development deals benefit both parties, as the larger company gains specialized R&D capacity while the smaller company gains liquidity without giving up equity.

While drug discovery partnerships may be relatively small transactions, collaborations involving clinical stage therapeutics are generally larger. One common type of collaboration involves a larger company agreeing to manage and finance clinical development of a drug that has shown preclinical promise in exchange for exclusive commercialization rights. Though larger, the structure of these deals is generally similar to drug discovery collaborations, as they involve an upfront payment, as well as developmental and commercialization milestone payments and potential sales royalties. An example of a clinical development partnership is Sanofi's 2018 collaboration with Denali Therapeutics. Denali had preclinical success with two candidate therapeutics, one for neurodegenerative disease and one for systemic inflammatory diseases. Sanofi agreed to fund initial clinical trials for both compounds, as well as the majority of Phase III trials in neurodegenerative diseases. In exchange, Sanofi gained commercialization rights for neurodegenerative disease (ex US and China) and exclusive developmental and commercialization rights for the inflammatory diseases therapeutic. Denali received a $125m up-front payment and eligibility for developmental and commercialization milestone payments potentially worth $1bn as well as a sales royalty.

This type of backloaded deal structure is a common way to minimize the risk of clinical trial failure. The more successful the program, the more money both parties make. Again, these deals benefit both parties. Sanofi gains access to two promising candidate therapeutics while avoiding the risk of initial drug discovery and preclinical development. Denali gains the resources and expertise of Sanofi to fund and run clinical trials, and, importantly, receives immediate capital with the potential for much more without surrendering equity.

Finally, though clinical developmental partnerships are commonly sought by companies that have a small pipeline, they can also useful for much larger companies. In July of 2019, *Gilead Sciences, Inc.* announced that it would enter into a 10-year global research and development agreement with Galapagos NV, a Belgian immunology-focused pharmaceutical company. At the time, Galapagos had six candidate therapeutics already in clinical trials, complemented by a large preclinical pipeline and a proprietary drug discovery platform. As part of the collaboration, Galapagos would develop all programs through Phase II clinical trials. Gilead received the right to option any program following the completion of a Phase II study for further development and eventual commercialization outside of Europe, where Galapagos would obtain commercial rights. In exchange, Gilead made a $3.95bn up-front payment and made a $1.1bn equity investment in Galapagos.

This agreement benefited Galapagos by providing them with substantial and immediate capital, allowing them to avoid having to fund and manage all Phase III clinical trials, and allowing them to retain and build their European sales presence. Gilead benefited by gaining immediate access to a large immunology-focused pipeline and obtaining commercialization rights for several potential programs outside of Europe. Though a partnership of this scope is relatively rare, this deal aligns with the values of Gilead CEO, Daniel O'Day, who has emphasized his preference for partnerships over acquisitions as partnerships tend to keep key native scientific and development teams in place resulting in expertise conservation.

Key Takeaways

Due to the risks, costs, and required specialization associated with research and development, acquisitions and partnerships have become powerful and frequently used tools for large pharmaceutical companies to ensure continued growth. Outcome Capital's analysis of M&A by the largest pharmaceutical companies over the past three-and-a-half-years reveals some important trends. Most acquisitions are valued between $250m and $5bn, and the majority involve companies with clinical stage assets. Nearly half of all acquisitions made were focused in oncology. IO has garnered a lot of interest lately, and increased competition in this sector has driven earlier stage acquisitions. However, there remains significant activity in non-IO oncology, and these acquisitions tended to involve later stage companies with substantially higher valuations.

Over the period analyzed there were three mergers that exceeded $50bn. These transactions were driven primarily by a need to ensure future revenue and reduce reliance on a major therapeutic franchise facing the threat of competition, compounded by an insufficient internal development pipeline, or as a means of rapid expansion into new markets and disease sectors. Understanding the precursors to such transactions can shed light on the state and strategic direction of these large companies.

Outcome Capital also analyzed partnership agreements and found they are significantly more common than outright acquisitions. Whether focused on early or clinical stage development of a single asset or a vast pipeline, partnerships allow for the augmentation of development pipelines with reduced risk and enhanced flexibility.

For a CEO considering how to position his/her company to best gain market access, understanding the factors that drive M&A and partnership transactions is invaluable. The large biopharmaceutical companies have continued to concentrate their efforts in a select few sectors, most significantly in oncology. The presence of specialized technology, phase of development, strength of developmental pipeline, and disease indication are all critical factors that determine likelihood of acquisition or collaboration engagement.

Table 1.

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Methods

The M&A activity of the top 24 biopharmaceutical companies by market cap as of 1/30/2020 was identified using Capital IQ. Only transactions closed between 1/1/2017 and 6/30/2020 were included in this analysis. Each transaction was cataloged based on a number of factors including disease indication, phase of development of the lead asset involved, and deal financials. Transactions in which the acquired company did not have a lead asset involved or previously involved in the clinical development pipeline were excluded. This resulted in the exclusion of transactions related to medtech/medical devices, business development, real estate, veterinary medicine, etc. Deal financials were obtained from Capital IQ.

Outcome Capital identified 156 total transactions, 73 of which met our criteria for further analysis. 62 of the 73 transactions had disclosed financial details. Of the companies considered, AstraZeneca, Regeneron, and Zoetis did not have M&A activity relevant to this analysis. Thus, transactions from 21 companies were considered. Information on partnerships was obtained from various databases and Outcome Capital internal resources.