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07 Aug 2017 | **Analysis**

Strong Market For Regenerative Medicine Deals Drives Value

by Amanda Micklus

Untapped market opportunities for treating and possibly curing underserved diseases have spurred an active deal-making environment in regenerative medicine, according to a new report from Datamonitor Healthcare.

Regenerative medicine, while not a new area of medical research, has advanced within the last several years to emerge as one of the best hopes for addressing, and even curing, diseases that until now had few or no treatment options. These regenerative methods have far-reaching potential and mark an important next wave of research into targeting genetically defined diseases, as well as chronic or life-threatening disorders that are underserved or not yet addressed.

These untapped market opportunities provide for an active deal-making environment around these assets, and there is great investor interest in financing companies working in this area. In addition to the active internal research and development being performed in regenerative medicine, there are many efforts underway in external innovation, through mergers and acquisitions (M&As) and partnerships.

Datamonitor Healthcare's new report, "Regenerative Medicine Landscape," states that between 2012 and 2016, there were just over 100 regenerative medicine M&As announced, and the five-year M&A value reached an aggregate $68 billion (note that not all M&As had disclosed values). (*See Exhibit 1*.) The steady climb in deals annually reflects the strong demand for regenerative medicine assets, including cell therapies, gene therapies

Methodology: Regenerative Medicine Deals

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The methodology behind Datamonitor Healthcare's new *Regenerative Medicine*

Landscape report.

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and tissue regeneration products. Further, for those transactions with disclosed values, most of that money goes into investors' pockets right away, signifying a vote of confidence for these products. Of the $68 billion of total potential deal value, $61 billion has been paid to the acquirers up front, as opposed to being tied up in earn-outs, which aggregated a smaller portion of $7 billion. This was also the case on an annual basis, except in 2014, when significantly more of the total value was attributed to earn-outs. No single agreement was responsible for this, but rather it occurred because most of the M&As that year ended up having lower up-front payments than earn-outs.

The volume of deals showed annual increases year-on-year. The same was true of transaction value, but 2015 was an outlier year in that metric with $51 billion worth in M&As, or 75% of the total five-year deal value. Two mega regenerative medicine takeovers occurred: *Shire PLC*'s $32 billion acquisition of Baxalta*[See Deal]*, and Zimmer's $14 billion merger with Biomet to form *Zimmer Biomet Holdings Inc.[See Deal]*

Exhibit 1

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SOURCES: Medtrack; Strategic Transactions | Pharma Intelligence, 2017

By and large, biotech firms have been the most acquisitive in regenerative medicine, acting as the acquirers on more than 60 deals (or about 63%). (*See Exhibit 2.*) As more companies combine in this way, it furthers the development of the various underlying regenerative medicine technologies. A factor in many of these combinations is likely to be forward planning to a further exit via acquisition by a larger company. *Intrexon Corp.*, for instance, has been actively buying fellow regenerative medicine players. In 2013, it paid $19.5 million for *MediStem Inc.*, with plans to use the latter's engineered multipotent endometrial regenerative cells in tandem with synthetic biology technologies to modify genetic material within the cells to improve therapeutic effect, and to deliver secreted proteins, among other uses. Two years later, Intrexon acquired *ActoGeniX NV*for $60 million, gaining the company's genetically engineered food-grade microbes, which convert into what are called *ActoBiologics*. These are used for expression and secretion of orally delivered therapeutic proteins and peptides. *[See Deal][See Deal]*

Exhibit 2

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SOURCES: Medtrack; Strategic Transactions | Pharma Intelligence, 2017

Of the top 10 M&As, five acquisitions in the regenerative medicine market surpassed values of $1 billion during 2012–16. (*See Exhibit 3.*) Leading this group was Baxalta's $32 billion takeover by Shire in 2015 (finalized in 2016). Newly spun off from *Baxter International Inc.* at the time*[See Deal]*, Baxalta enriched Shire's rare diseases pipeline in hemophilia and brought a promising gene candidate for hemophilia B: BAX335. Shortly after the acquisition of Baxalta, Shire terminated development of the drug because of inconsistent clinical results. Shire does continue to work on other hemophilia gene therapies. During the 2012–16 period, Shire also performed a smaller regenerative medicine takeover, paying $200 million in up-front and earn-out payments for *Pervasis Therapeutics Inc.*in 2012.*[See Deal]* Pervasis focused on endothelial cell technology used in tissue repair and vascular healing, using intellectual property discovered at the *Massachusetts Institute of Technology*. *[See Deal]*

Exhibit 3

Year	Acquirer	Target	Target's Regenerative Medicine Focus	Deal Value ($m)
2015	Shire	Baxalta	Hemophilia gene therapy	32,000
2015	Zimmer	Biomet	Hard- and soft-tissue regeneration	14,000
2016	AbbVie	Stemcentryx	Rovalpituzumab tesirine (Rova-T), a cancer stem cell-derived therapy for small cell lung cancer	9,800
2016	Allergan	LifeCell	Dermal matrices, human- and animal-based allograft tissue, and grafting devices	2,900
2015	Mallinckrodt	Theranos	Fully integrated system called Therakos that administers autologous immune cell therapy through extracorporeal photopheresis	1,325
2015	AMAG	Cord Blood Registry	Stem cell banking	700
2016	Pfizer	Bamboo Therapeutics	Gene therapies in neuromuscular and central nervous system diseases	645
2014	Novartis	Gamida Cell*	Stem cell transplantation and technologies	635
2014	Baxter	Chatham Therapeutics	Hemophilia gene therapy	630
2015	Valeant	Dendreon**	Autologous dendritic cell therapy Provenge (sipuleucel-T)	495

*The Novartis/Gamida Cell deal was later terminated.

**Valeant divested Dendreon to the Sanpower Group in 2017.

SOURCES: Medtrack; Strategic Transactions | Pharma Intelligence, 2017

Partnerships in regenerative medicine tend to center around cell therapies, with a higher volume of alliances conducted for these treatments in comparison to gene therapies and tissue regeneration products. With deal values it was a slightly different story. Starting in 2014, the monetary value attributed to gene therapy deals began taking off, surpassing that of agreements for cell therapies, and reaching $11 billion to $12 billion during 2015–16. (*See Exhibit 4.*) In those two years, there were several billion-dollar gene therapy agreements, led by *CRISPR Therapeutics AG*and Vertex Pharmaceutical Inc.'s $2.6 billion partnership.*[See Deal]* They are using the clustered regularly interspaced short palindromic repeats (CRISPR)/CRISPR associated protein (Cas9) method to target genetic defects that cause or contribute to diseases, such as cystic fibrosis (an area of expertise for Vertex through its marketed product portfolio) and sickle cell disease. Vertex holds exclusive worldwide options to six candidates.

Exhibit 4

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SOURCES: Medtrack; Strategic Transactions | Pharma Intelligence, 2017

Across all modalities, there have been 12 partnerships with a value of $1 billion or higher, and most of the agreements included big pharma or mid pharma in-licensers. (*See Exhibit 5.*) Topping the list was *Celgene Corp.*'s $3.3 billion alliance in 2013 with *OncoMed Pharmaceuticals Inc.* to develop up to six cancer stem cell therapies*[See Deal]*, including inhibitors of delta-like ligand 4 and T-cell immunoreceptor with Ig and ITIM domains (TIGIT). The anti-TIGIT compound OMP-313M32 is the most advanced, in Phase I for solid tumors. Celgene is quite active in regenerative medicine deal-making overall, and has a high-valued CAR-T deal with *Juno Therapeutics Inc.[See Deal]*

Exhibit 5

Year	Licenser	Licensee	Subject of Deal	Deal Value ($m)
2013	OncoMed Pharmaceuticals	Celgene	Cancer stem cell therapies	3,332
2014	Cellectis	Pfizer	CAR-T immunotherapies for up to 27 total targets	2,855

2015	CRISPR Therapeutics	Vertex Pharmaceuticals	CRISPR/Cas9 gene editing to correct genetic defects causing cystic fibrosis and sickle cell disease	2,625
2016	Selecta Biosciences	Spark Therapeutics	Synthetic Vaccine Particles technology for co-administration with up to five gene therapies, including one for hemophilia A, with an option for an additional four	2,183
2016	University of Pennsylvania	Biogen	Gene therapies and gene editing technologies focused on ophthalmic, musculoskeletal and neurological diseases	2,000
2016	Precision BioSciences	Baxalta	CAR-T therapies for up to six cancer targets	1,705
2015	BioNTech	Sanofi	Up to five cancer immunotherapies based on BioNTech's messenger RNA platform	1,560
2015	Kite Pharma	Amgen	CAR-T therapies developed using Kite Pharma's engineered autologous cell therapy platform	1,110
2015	Juno Therapeutics	Celgene	TCR and CAR-T therapies in cancer and autoimmune disease	1,100
2015	Bavarian Nordic	Bristol-Myers Squibb	PROSTVAC (rilimogene galvacirepvec) for asymptomatic or minimally symptomatic metastatic castration-resistant prostate cancer	1,025
2013	Immatics Biotechnologies	Roche	Using XPRESIDENT technology, discovery and development of tumor-associated peptide vaccines and immunotherapies	1,017

Notes: Cas9 = CRISPR associated protein 9; CAR-T = chimeric antigen receptor T cell; CRISPR = clustered regularly interspaced short palindromic repeats; TCR = T-cell receptor

SOURCES: Medtrack; Strategic Transactions | Pharma Intelligence, 2017

Editor's note: This article is adapted from Datamonitor Healthcare's July 2017 report, "Regenerative Medicine Landscape." For more information about Datamonitor Healthcare, or this particular report,

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