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Progress in the Tissue Engineering and Stem Cell Industry

"Are we there yet?"

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This report presents a detailed update to our 2008 publication on the tissue engineering (TE) and stem cell industry. Data are reported through mid 2011 showing an almost three-fold growth in commercial sales over the past 4 years. In addition, the number of companies selling products or offering services has increased over two-fold to 106, and they are generating a remarkable $3.5 billion in sales. Overall, the TE and stem cell sector is spending $3.6 billion and employing almost 14,000 employees. These data suggest the TE and stem cell industry has stabilized and is on a path pointing toward continued success.

Introduction

The tissue engineering (TE) industry has hardly traveled a smooth path toward success, experiencing a roller coaster ride over the last quarter century. The late Michael Lysaght devoted five articles analyzing this path over time, the first reported in 1995 and the last in 2008.[1–5] Lysaght's analyses outlined the emergence and hype, growth, downward trend, and rebound of the field and are eloquently summarized in Nerem's article.[6] Briefly, the TE industry began to develop in earnest in the 1990s and grew to 3300 full time employees (FTEs) working in over 70 companies at the end of 2000.[1] By 2001, a number of TE products had reached the market, including Organogenesis' Apligraf® and Genzyme's Carticel®. Expectations and hype were high both in the science and TE business communities and in the news. In 1999, a *Good Morning America* report described TE as one of the greatest scientific accomplishments of the 20th century.[7] Soon after the turn of the century, however, the industry entered a dark period. Private sector activity decreased 20% and the capital value of publicly traded TE companies fell a staggering 90 percent.[4] This was in part due to a poor economy and the consequent decrease in investor interest, and also due to failed product launches and disappointing results from Food and Drug Administration (FDA) clinical trials. Incredibly, the industry had rebounded by our 2008 report and was back on track to meet the expectations set in the '90s.[3] The capital values for public TE companies increased over 10-fold compared to 2003 and products were entering FDA clinical trials, achieving FDA-approval, and in some cases becoming profitable. Today, as the data reported here indicate, the industry is on a path pointing toward continued success.

Lysaght *et al.* describe, in detail, the history of the name "TE" and the emergence of both the research field and the industry in the 20th century.[3] However, it is interesting to note that the ancient Egyptians may have been the first to apply TE principles to wound care around 1500 B.C.[8] In the Papyrus of Ebers, there is a description of how skin wounds were treated with lint, grease, and honey. It is believed that the lint served as a fibrous scaffold to guide wound regeneration, the grease provided a barrier to environmental pathogens, and the honey acted as an antibiotic.[8] It is not clear how this product was sold in ancient Egypt and whether they had any competitors, but it is clear that the field might be much older than we think.

Centuries later, in 1993, Langer and Vacanti defined TE as an "interdisciplinary field that applies the principles of engineering and the life sciences toward the development of biological substitutes that restore, maintain, or improve tissue or whole organ function".[9] Generally, the term TE is now accepted to include regenerative medicine and stem cell therapeutics. In this report, TE and regenerative medicine are used interchangeably. Further, stem cell therapeutics are included, consisting of both cell-based therapies and stem cell banking. These terms have become rather commonplace in today's mass media culture. Google searches for the term "TE" produces 3.3 million hits and "regenerative medicine"

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2.8 million hits, roughly double the hit rate compared to 4 years ago.[3] Likewise, a Google search of "stem cell" produces over 23 million hits.

Several other authors have evaluated the progress of the TE field. Most recently, Mason examined the cell therapy industry and characterized it as a distinct health care sector rapidly growing and transitioning into a successful multi-billion dollar industry.[10,11] It is important to note that Mason makes a clear distinction between regenerative medicine and cell therapy, which we do not. Therefore, it is difficult to compare the two analyses, other than to say that Mason's findings represent a portion of our findings. Similarly, Martin *et al.* have done a comprehensive survey focused on the cell therapy sector.[12] To the best of our knowledge, others have not done a broad TE and stem cell industry analysis as we have defined it.

Here we present an update to our 2008 publication (containing data analysis for 2007), which was coauthored by the late Michael J. Lysaght, in our continued efforts to follow the progress of this industry. Data are reported through mid 2011 and confirm that the industry is moving onward and upward. Compared to 2008, the current data show significant increases in commercial stage spending, number of FTEs and sales.

Methods

Compiling of company list

A list of companies in the TE space was prepared from the following:

1. The 2008 version of this report,[3] where the existence of each company was verified by checking the website and doing an internet search. Companies that no longer exist or were bought by another company were removed.
2. Daily Google Alerts derived from the terms "regenerative medicine," "stem cell," or "TE" between April and June 2011. Company names were found in news articles that were reported in these alerts.
3. Internet searches.

Company inclusion/exclusion criteria

Contract research organizations (CROs) that provide services for other TE firms were included. Organizations selling goods (e.g., laboratory equipment) or unrelated services (e.g., financial service firms) to operating firms were not included. Bioaesthetic products were excluded (e.g., creams prepared from conditioned media), except those products involving cell transplantation. In addition, the following were fully excluded: not-for-profit cord blood banks, veterinary firms, clinical services, organ or tissue allografts, conventional bone marrow transplantation for blood-borne cancers, transfusion medicine, and educational, media-based, or financial services.

The line between TE technology and other types of medical technology is often not clear and highly dependent upon the definitions imposed at the time. Although Dendreon's recent success with Provenge®, a cell-based immunotherapy for cancer treatment, is often touted as a breakthrough TE technology, we have elected not to include this type of product in our analysis. We excluded this because the cell-based therapy does not provide any regenerative or reconstructive function to a damaged organ or tissue. Dendreon is at the commercial stage and generates about $72M in sales. Had they been included, the industry market cap would have been drastically increased by $1.86B. Further, we have excluded those research efforts focused on "cancer stem cell" therapy and all medical technology in the cancer space.

It is important to note that we included stem cell banking companies in our industry analysis as commercial entities in the stem cell sector. The therapeutic potential of these stored cells to provide future regenerative function clearly enables this technology to fall within our definition.

Gathering company data

The following data were collected for each company from their respective websites. Founding year, location, and website address were obtained. Companies' underlying technology, or sector, was categorized as biomaterials, cells and biomaterials, stem cells (adult and embryonic), or other. These characterizations were based on the company's regenerative medicine portfolio and not by an individual product. For example, Genzyme (Sanofi) has three products, Carticel (cells), Epicel® (cells), and Maci® (cells and biomaterials), and therefore was classified as a "cells and biomaterials" company. Further, companies with products containing synthetic or biologically-derived materials, including proteins such as growth factors, were labeled as "biomaterials." Cell type used (autologous, allogeneic, and/or xenogeneic), development status (preclinical, clinical trials, or commercial), clinical trial status (phase I, phase II, phase III) if applicable, and focus (e.g., wound healing, orthopedic, platform, etc.) data were also collected.

The size of a TE company was quantified by the number of FTEs and by overall operating expenditure. FTE counts were found in SEC reports, on company websites, and through email communication with companies. When not available by these methods, FTE counts were found on professional networking sites like LinkedIn. In the case where FTE counts were reported as a range (e.g., 1–10) the high and low ends of the range were averaged.

In those instances where overall operating expenditure was not available, estimates were calculated based on comparables with FTE counts. We determined a ratio of $265,900 spending per employee based upon a linear regression of annual spending against the number of employees for 39 TE companies for which both sets of data were available ($R^2 = 0.96$). Excluded from this regression were diverse companies with a primary function other than TE, such as medical device companies and pharma.

For those companies with diverse product lines spanning TE and non-TE areas, we scoured SEC filings and press releases for revenue, spending, and FTE figures for the TE portion of the company. Only TE portions of diverse company statistics were included in any analysis. We estimated the percentage of the diverse company focused on TE mainly based upon revenues and used these percentages to calculate any applicable market caps. Spending and FTE were calculated using the aforementioned regression curve when both figures were not independently available from reported data.

Table 1. Key Industry Parameters: Tissue Engineering and Stem Cell Therapeutics

Worldwide estimates (in millions)	*2007*	*2011*	*Factor*
Total sector activity	$2400	$3600	1.5x
Total commercial stage spending	$1600	$2820	1.8x
Total development stage spending	$860	$780	0.9x
Number of FTE's	6100	13,810	2.3x
Capital value of listed firms (36)	$4700	$6580	1.4x
Number of companies	171	202	1.2x
Number of companies in commercial stage	47	62	1.3x
Number of companies providing services		44	
Number of companies with products in clinical trials	57	60	1.1x

FTE, full time employees.

We recognize that the data set presented is not perfect; companies may have been overlooked, estimates of FTE and/or sales values based on our regression may not be truly representative of actual data, data for some companies are missing, data may be outdated as the field is moving rapidly, and estimates of the percentage of company involvement in TE for companies researching in diverse areas of science may have a degree of error, among other things. However, we are confident that the data are representative of current trends and, if anything, are an underestimate. The field is growing and certainly these numbers will change in future analyses.

Results

Appendix A contains 202 companies that met the inclusion criteria. The company's name, location, sector (biomaterial, cells & biomaterial, stem cells, other), stage (preclinical, clinical trials, commercial, and service), and website are listed. For subsidiaries, the parent company name was included in parenthesis.

Table 1 summarizes key industry parameters for the TE and stem cell companies. Total sector activity is defined as total spending by companies on TE or stem cell products or services. Our analysis estimates this at $3.6 billion, which constitutes a 1.5-fold increase since our last analysis of data from 2007.[3] Total spending for commercial TE products or services is almost twice (1.8-fold) that of 2007, at $2.8 billion. The number of employees in the TE industry has increased by just over two-fold (2.3 ×) from 6100 to 13,810. Most of the remaining parameters had only slight increases since 2007. There are now 202 companies in this sector and 62% of them are U.S. based. A total of 122 companies are either in commercial or clinical trials stage, while 44 companies are providing services such as stem cell banking and CROs. The only parameter that showed a decrease in value, since the previous study, was development stage spending. Table 2 lists sales of TE or stem cell products by focus. Orthopedics leads the field at $1.7 billion in sales, followed by wound healing at $0.74 billion. Companies focused on multiple areas (e.g., wound healing and orthopedic) have $554 million in sales, while stem cell banking sales are at around $312 million. Specialties such as cardiovascular and fertility are grouped together as "other" and have $144 million in sales.

Table 2. Sales for Commercial Products or Services

Commercial products (# of companies)	*2011 Sales (in millions)*	*%*
Orthopedic (19)	$1713	50
Wound healing (15)	$738	21
Multiple (16)	$554	16
Stem cell banking (18)	$312	9
Other (5)	$144	4
Total:	$3461	

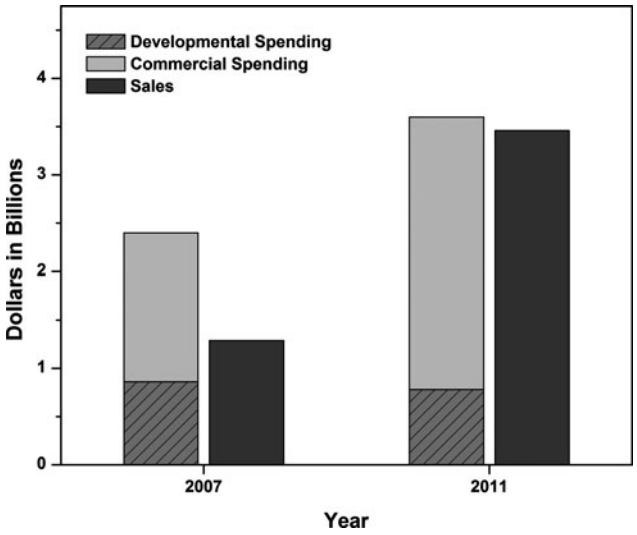

FIG. 1. Spending and sales (black) in billions for tissue engineering and stem cell therapeutics for 2007 and 2011. Preclinical and clinical trials stage spending is shown in ash gray while commercial stage spending is light gray.

Figure 1 summarizes spending data listed in Table 1 and compares it to commercial sales for 2007 and 2011. In 2007, sales were half that of spending for the industry, while in 2011 sales nearly equaled spending (0.96 ×). In addition, sales increased almost three-fold (2.7 ×) in the 4 year period depicted. Figure 2 shows a detailed breakdown of spending by industry segment and stage. Preclinical (62%) and clinical trial (73%) stages of company development are dominated by stem cells, while the commercial (76%) and service (92%) stages are overwhelmingly populated by biomaterials and stem cell banking, respectively. Figure 3 illustrates total spending and number of companies with respect to stage. Spending is dominated by commercial stage companies (64%), while the number of companies operating in the four stages is about even. Figure 4 details the worldwide distribution of companies by spending, highlighting that the United States is leading the field with 81% of the worldwide investment.

Discussion

Perhaps the most important result of the presented data analysis is that sales for the TE and stem cell industry are $3.46B, which is approaching total spending ($3.6B) (Fig. 1). For the first time since Michael Lysaght started these analyses, the TE and stem cell industry is essentially breaking even.[1–5] These data are in stark contrast to 2007 data, where product sales were about half of the spending volume.[3] Not only is TE a billion dollar industry, it is now close to operating in the black. This is quite an accomplishment

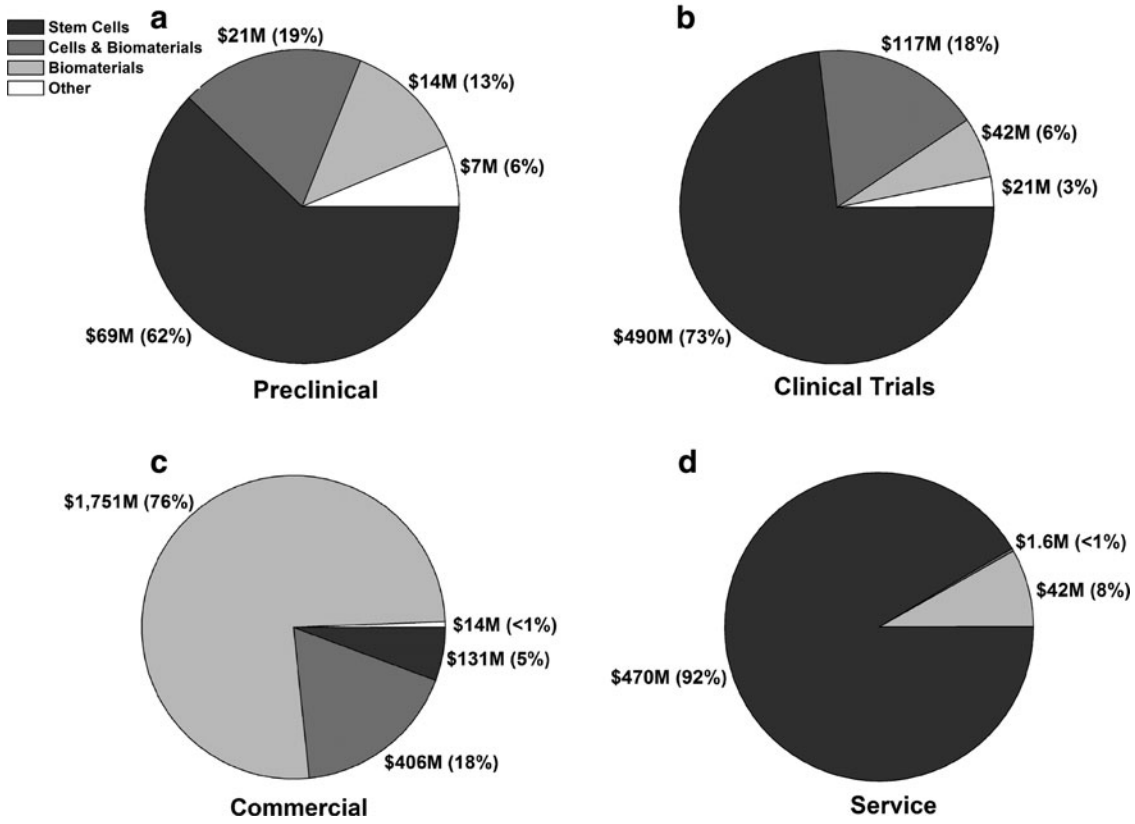

FIG. 2. Breakout of spending (in millions) by product platform for the four development stages: preclinical **(a)**, clinical trials **(b)**, commercial **(c)**, and service **(d)**.

considering the recent U.S. and global financial meltdown over the last 4 years.

As indicated in Table 1, almost all key industry parameters for this sector have increased compared to our 2007 data.[3] Overall spending for the field has increased from $2.4B to $3.6B, including a 1.8-fold increase in commercial stage spending from $1.6B from $2.8B (Fig. 1). Total spending increased 1.5-fold in the last 4 years, however, sales have increased 2.7-fold, indicating that sales increased at almost twice the rate of spending. Interestingly, development stage spending is the only industry parameter that has decreased over this time period. This could be due to several factors, including firms gaining market clearance and transitioning from development to commercial status, firms being bought out by larger commercial partners, and firms shutting down altogether. Only time will tell whether this decrease in the development sector will have an impact on pipelines and the number of products entering the market in the future. After all, it takes spending money in the short term to make money in the long term.

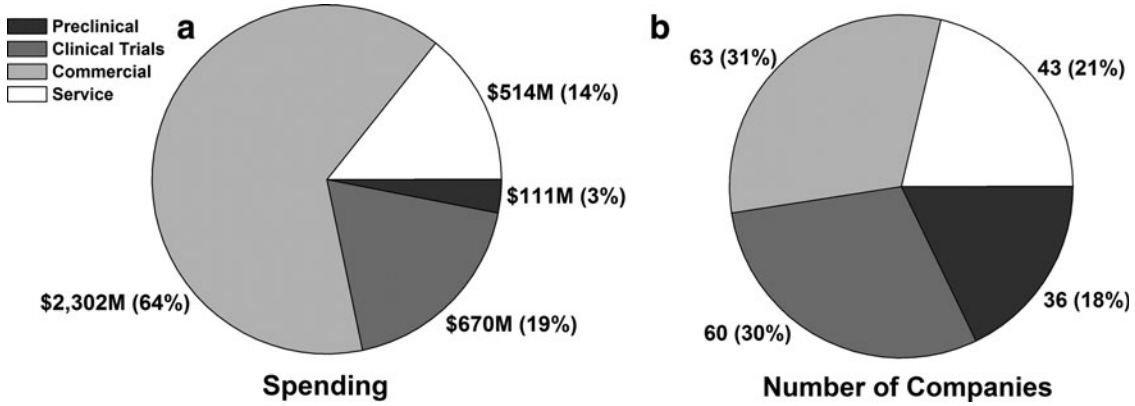

FIG. 3. Tissue engineering and stem cell therapeutics developmental stages by total spending (in millions) **(a)** and by number of companies **(b)**.

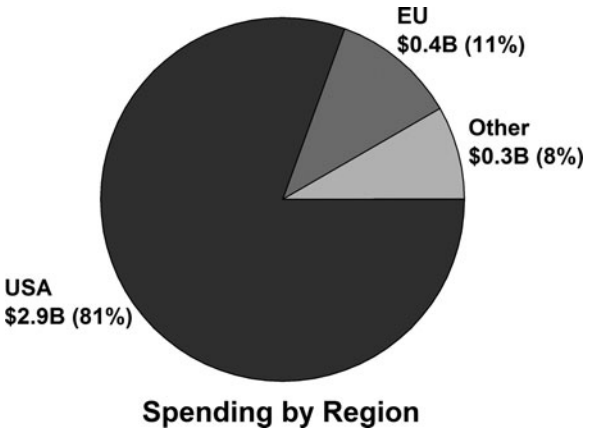

FIG. 4. Worldwide geographical distribution of spending.

Even though development stage spending has decreased, there is still significant growth as the industry has generated over 7710 jobs in the last 4 years, a 2.3-fold increase compared to the 2007 analysis. Moreover, the total number of companies in TE has increased from 171 to 202 and in each stage of development indicating that the field is not only progressing but also sustaining itself. That is, as companies are moving products to market, others are entering the space with new technologies. Currently, 31% of the companies are in commercial product stage and another 21% of the companies are service based (e.g., stem cell banking), resulting in over 52% of the companies generating revenue for the industry. Another 30% of the companies are now in the clinical trial period, indicating a robust TE pipeline and a field that is expected to grow. However, the number of companies with products in clinical trials did not grow at the same rate as those with commercial products (1.1× vs. 1.3×, respectively). One reason for the larger growth of the commercial sector could be due to the poor economy. Perhaps financially transitioning from a successful clinical trial to a commercial product is easier compared to transitioning into clinical trials, where the risk is much greater. In addition, commercial-stage firms might be acquiring preclinical and clinical trial companies, which would deplete the number of companies in these two categories from our analyses.

It should be noted that we deviated from previous analysis methods and made a distinction between commercial-stage companies and service-based companies, that is, stem cell banks and CROs. We felt that this designation was more appropriate as these service companies do not follow a traditional product pipeline. In our previous analysis we included these companies at the commercial stage and had we done the same here, the increase in commercial stage companies would have been 2.2-fold higher, emphasizing again the successful integration of TE products into the health care market. It is no surprise, then, that the capital value of publicly traded companies in this space increased from $4.7B to $6.6B. This 1.4-fold increase in economic activity from 2007 to 2011 is not as dramatic as the five-fold increase from 2002 to 2007. However, previous accelerated growth has been attributed to the industry reorganizing itself and getting back on track from a low point. Today, the industry has begun to understand how to manufacture and market TE and stem cell products, sustaining itself and still growing.

Focusing just on commercial stage companies, the breakdown of sales by application specialty is summarized in Table 2. Orthopedics dominates the field at 49% or $1.7B in revenue with 19 companies. Not surprisingly, a large portion of this revenue is from Medtronic, which brings in an estimated $750M in sales with their bone graft product Infuse®. It is difficult to predict the future of Medtronic's dominance in this space as there has been a controversy regarding this blockbuster product. The scientific community recently raised concerns that clinical studies conducted with Infuse overstated benefits and understated risk.[13] One thing is for sure: a flurry of legal action will persist for years to come. There are certainly others that will be greatly affected—one way or the other—by the outcome of these developments. Baxter's bone graft product Actifuse® and their regenerative medicine business group show $527M in sales. Depuy, Orthovita, and Olympus Biotech report the next highest revenues in this specialty area, generating around $95M each. Depuy, a Johnson & Johnson company, has seven bone graft products on the market. Orthovita sells Vitoss™, a bone graft substitute, and Olympus, after acquiring Stryker Biotech in 2010, has two commercial products, OP-1™ Putty and OP-1 Implant.

Wound healing is the second largest specialty area by sales at 21% with 15 companies and $738M in revenue. There are three major players in this area: Kinetic Concepts, Advanced BioHealing, and Organogenesis. Kinetic Concepts generates $340M in revenue with Graftjacket®. Advanced BioHealing, a Shire company, lists about $150M in sales with their Dermagraft® skin product. Organogenesis, one of the original TE companies founded in 1985 and whose progress has been well documented in earlier analyses,[3] is making around $100M in revenue with Apligraf.

The category "multiple" includes 16 companies that have products in more than one application specialty and their estimated sales are $554M. For example, Integra Life Sciences has both orthopedic products (Accell Evo3®, Mozaik™ and Allograft Cancellous Sponge) and a wound healing product (Dermal Regeneration Template) and brings in around $170M annually. Similarly, Covidien has DuraSeal™ for wound healing and Collagen Repair Patch for orthopedic applications, generating revenue around $95M.

Stem cell banking is the third most profitable specialty area with sales at $312M. These companies have a very efficient service business model based upon liquid nitrogen storage capabilities and limited personnel oversight. Typically, they collect one-time initiation fees and subsequent annual storage fees for up to 20 years. The utility of this service is not clear as little evidence exists about the viability of cord blood cells (or fat stem cells, dental stem cells, and other types of stem cells that can be banked) over a 20 year span. Further, it is not yet known how banking can significantly help the elderly population, who arguably have the most need for TE engineering therapies. Nevertheless, these businesses thrive and make 9% of the industry revenues in our analysis.

Finally, five companies were listed under "other" as they are focused on cardiovascular, fertility, or platform technologies. This group brings in around $144M in sales and is dominated by Cryolife ($116M in sales) which has SynerGraft® platform for cell transplantation.

Overall, these data are encouraging and indicate that the TE and stem cell industry is alive and well. About 42% of the companies at the commercial stage are generating a profit,

which leaves 58% that are not. This breakdown will most likely shift in the future as the health care field becomes more familiar with TE and stem cell technologies and these products become common therapeutic options. Further commercial success will also depend on companies having a better understanding of the FDA approval processes.[14] Even with the introduction of the FDA Office of Combination Products in 2002, a recent survey found that one of established companies' (defined as companies with ongoing, predictable product sales and growth) most difficult hurdles is working with the FDA.[15]

A detailed breakdown of spending by industry segment (i.e., product platform) and stage is illustrated in Figure 2. The preclinical stage is dominated by stem cells at 62% ($69M), followed by cells and biomaterials at 19% ($21M). Biomaterials and other constitute 13% ($14M) and 6% ($7M), respectively. A very similar trend follows for the clinical trials stage, indicating that stem cell-based therapies are dominating the product pipeline (Fig. 2a, b). These data suggest that stem cell-based products and combination products (cells and biomaterials) will be entering the market in the next 5–10 years. Their entrance into the commercial space will be interesting to watch as recent actions within the FDA and with the 510(k) process will greatly affect the commercialization of these products.

Of particular note is the entrance of embryonic stem cell (ESC)-based therapies into clinical trials for the first time. Geron's Phase I clinical trial for GRNOPC1 in spinal cord injury was given a green light in the summer of 2010 and the first patient was enrolled later that year.[16] Advanced Cell Technology (ACT) quickly followed behind with two Phase I/II trials with their human ESC (hESC) derived retinal pigment epithelial (RPE) cell therapy for dry age-related macular degeneration and Stargardt's macular dystrophy. The first patients for these studies were dosed in July of this year.[17] Interestingly, on November 14, 2011 Geron announced on their website that they are discontinuing their stem cell program to focus on their cancer therapies. Geron was considered a leader in the stem cell industry; their clinical trial experiences are of great interest not only to industrial competitors but also to academics. Regardless of their outcomes, these stem cell trials are the first of their kind and they are likely to have a large impact on the future of ESC-based therapies.

A breakdown by cell source shows that companies with stem cell-based products favor autologous cells (59%), followed by allogeneic (39%) and only 2% utilize xenogeneic cells. In addition, the majority (58%) of stem cell companies are utilizing adult stem cell technologies, while only 10% are specializing in ESCs. The remaining 32% are focused on stem cell banking services. Again, the outcome of the Geron and ACT hESC clinical trials could initiate a shift in trend for autologous versus allogeneic stem cells and for adult stem cell versus ESCs.

Biomaterial-based products are overwhelmingly present in the commercial stage with 76% ($1.8B) in spending. Combination products and stem cells follow at significantly lower volumes of $406M and $131M, respectively. Such products are generally classified as devices and have an easy path to market through the FDA, so it is not surprising that they are the frontrunner in this industry sector. Hopefully, as the cell-based sector gains more experience with the FDA, and vice versa, the path to market will be clearer for these products.

The FDA has started responding to the emergence of the TE field and is adapting quality systems and regulatory pathways to the specialized nature of TE products. Importantly, it was not until 2005 that current good tissue practices were mandated ensuring quality manufacturing procedures for human cell, tissue, and cellular and tissue-based products. Since the regulatory aspects of this industry are only beginning to develop and distinguish from other health care products, we believe that there will still be some uncertainty as more complex TE products move through the pipeline and the policies are refined and adapted accordingly. With this in mind, we think that the CROs for the TE industry will thrive when R&D firms find it difficult to keep up with these regulatory changes and the very specialized nature of the manufacturing and quality systems necessary for TE market approval.

Though we have paid particular attention to the role of the FDA approval process in achieving sales, it is important to consider that simply gaining FDA approval does not guarantee success. Another critical element of commercial success is achieving reimbursement.[18] As the TE industry is gaining experience with the FDA process, reimbursement is becoming the new grand hurdle. The "black box" of coverage, payment, and coding associated with reimbursement can lead to the failure of an FDA-approved TE therapy. Once reimbursement has been decoded (if reimbursement can be decoded), perhaps the sky is the limit!

Finally, service is dominated by stem cell banking firms and CROs performing the manufacturing for TE companies (Fig. 2d). As mentioned above, the stem cell banking business model is rather simple and one might expect that it will grow and continue to lead in this area.

Spending in the TE and stem cell sector by developmental stage is shown in Figure 3a. Here, commercial stage spending is at $2.3B (64%) and is separated from service ($514M, 14%), in contrast to the analysis in Table 1 and Figure 1. As one would expect, most of the spending is done by companies that have products on the market, followed by companies in clinical trials and service. Finally, the least amount of spending is done by companies at the preclinical stage. This is expected as one proceeds down the regulatory pathway for product approval, the costs for product development increase. The number of companies at each stage of development are not as skewed (Fig. 3b). Both clinical trials and commercial stage companies are approximately equal at 30%, and service and preclinical are even at about 20%. This further emphasizes the increase in spending at the clinical trial and commercial stages of product development. Comparing these data with our 2007 analysis, we note some interesting changes. For example, the number of commercial companies (including service) increased two-fold from 47 to 106 and the number of preclinical stage companies decreased almost two-fold from 67 to 36. As discussed above, this increase and decrease could be attributed to more products flowing down the pipeline to the market. Other possibilities include acquisitions by larger firms or going out of business. The spending distribution by geographic region (Fig. 4) still shows that the United States is leading by over 81%, a 7 percentage point increase from 2007. This indicates that the distribution of spending for the TE and stem cell industry has not drastically changed and that the United States is still the dominant player in this area.

The analyses presented show that the TE and stem cell industry is just attaining profitability and that it appears to be on a positive trajectory. Although it seems that the industry is on a smoother path now than it probably ever has been, we do anticipate that there may be growth pains as the industry matures.

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Disclosure Statement

No competing financial interests exist.

References

1. Lysaght, M.J., and Reyes, J. The growth of tissue engineering. Tissue Eng **7,** 485, 2001.
2. Lysaght, M.J., and O'Loughlin, J.A. Demographic scope and economic magnitude of contemporary organ replacement therapies. Asaio J **46,** 515, 2000.
3. Lysaght, M.J., Jaklenec, A., and Deweerd, E. Great expectations: private sector activity in tissue engineering, regenerative medicine, and stem cell therapeutics. Tissue Eng Part A **14,** 305, 2008.
4. Lysaght, M.J., and Hazlehurst, A.L. Tissue engineering: the end of the beginning. Tissue Eng **10,** 309, 2004.
5. Lysaght, M.J. Product development in tissue engineering. Tissue Eng **1,** 221, 1995.
6. Nerem, R.M. Regenerative medicine: the emergence of an industry. J R Soc Interface **7 Suppl 6,** S771, 2010.
7. Gillian, M. Body Doubles. Good Morning America. April 29, 1999.
8. Nahmias, Y., and Yarmush, M. Tissue engineering application in general surgery. In: Meyer, U., Meyer, T., Handschel, J., and Wiesmann, H.P., eds. Fundamentals of Tissue Engineering and Regenerative Medicine (1st edition). Berlin: Springer, 2009.
9. Langer, R., and Vacanti, J.P. Tissue engineering. Science **260,** 920, 1993.
10. Mason, C., Brindley, D.A., Culme-Seymour, E.J., and Davie, N.L. Cell therapy industry: billion dollar global business with unlimited potential. Regen Med **6,** 265, 2011.
11. Mason, C., and Manzotti, E. Regenerative medicine cell therapies: numbers of units manufactured and patients treated between 1988 and 2010. Regen Med **5,** 307, 2010.
12. Martin, P.H., Hawksley, R., and Turner, A. The Commercial Development of Cell Therapy–Lessons for the Future? Nottingham, UK: Institute for Science and Society, University of Nottingham, 2009.
13. Carragee, E.J., Ghanayem, A.J., Weiner, B.K., Rothman, D.J., and Bono, C.M. A challenge to integrity in spine publications: years of living dangerously with the promotion of bone growth factors. Spine J **11,** 463, 2011.
14. Lee, M.H., Arcidiacono, J.A., Bilek, A.M., Wille, J.J., Hamill, C.A., Wonnacott, K.M., *et al.* Considerations for tissue-engineered and regenerative medicine product development prior to clinical trials in the United States. Tissue Eng Part B Rev **16,** 41, 2009.
15. Johnson, P.C., Bertram, T.A., Tawil, B., and Hellman, K.B. Hurdles in tissue engineering/regenerative medicine product commercialization: a survey of North American academia and industry. Tissue Eng Part A **17,** 5, 2011.
16. Barker, C., Culme-Seymour, E., Dalton, S., Hayek, A., and Genbacev, O. The year in regenerative medicine. Regen Med **6,** 21, 2011.
17. ACT Announces First Patients Undergo Embryonic Stem Cell Transplantation Treatment for Stargardt's Disease and Macular Degeneration at UCLA's Jules Stein Eye Institute. Advanced Cell Technology, 2011. http://www.advancedcell.com/news-and-media/press-releases/act-announces-first-patients-undergo-embryonic-stem-cell-transplantation-treatment-for-stargardts-disease-and-macular-degeneration-at-uclas-jules-stein-eye-institute/index.asp
18. Ginty, P.J., Singh, P.B., Smith, D., Hourd, P., and Williams, D.J. Achieving reimbursement for regenerative medicine products in the USA. Regen Med **5,** 463, 2010.

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(*Appendix follows* →)

Company	*Location*	*Sector*	*Stage*	*Website*
3DM	Boston, MA	Biomaterials	Preclinical	www.puramatrix.com
Aastrom Biosciences	Ann Arbor, MI	Stem Cells	Clinical trials	www.aastrom.com
ACell	Columbia, MD	Biomaterials	Commercial	www.acell.com/
Advanced Biohealing (Shire)	New York, NY	Cells and Biomaterials	Commercial	http://advancedbiohealing.com
Advanced Cell Technology	Worcester, MA	Stem Cells	Clinical trials	www.advancedcell.com
Advanced Technologies and Regenerative Medicine	Raynham, MA	Cells and Biomaterials	Clinical trials	www.atrm.com/
Aldagen	Durham, NC	Stem Cells	Clinical trials	www.aldagen.com
Allocure	Burlington, MA	Stem Cells	Clinical trials	www.allocure.com/
Altrika (Ilika)	United Kingdom	Cells and Biomaterials	Commercial	www.altrika.co.uk/
American CryoStem	Red Bank, NJ	Stem Cells	Service	www.americancryostem.com/
Amni Bioscience	Lebanon	Stem Cells	Preclinical	www.amnibioscience.com/
Amorcyte	Allendale, NJ	Stem Cells	Clinical trials	www.amorcyte.com/
Angioscaff	Switzerland	Biomaterials	Preclinical	www.angioscaff.eu
Aquamed Technologies (Alliqua)	Langhorne, PA	Biomaterials	CRO	www.aquamedinc.net/
Arbios	Los Angeles, CA	Cells and Biomaterials	Clinical trials	www.arbios.com
ArBlast USA	Japan	Cells and Biomaterials	Clinical trials	www.arblast-usa.com/index.html
Arteriocyte	Clevand, OH	Stem Cells	Clinical trials	www.arteriocyte.com/
Arthro Kinetics	Germany	Cells and Biomaterials	Commercial	www.arthro-kinetics.com
Athersys	Clevland, OH	Stem Cells	Clinical trials	www.athersys.com/
AuxoCell Laboratories	Cambridge, MA	Stem Cells	Service	auxocell.com/
Avita Medical	Australia	Other	Commercial	www.avitamedical.com/
Axcelon Biopolymers	Canada	Biomaterials	Commercial	www.axcelonbp.com/
Azellon	United Kingdom	Stem Cells	Preclinical	www.azellon-ltd.com/
Bacterin International	Belgrade, MT	Biomaterials	Commercial	www.bacterin.com/index.htm
Baxter	Deerfield, IL	Biomaterials	Commercial	http://baxter.com
Bayer Innovations	Germany	Stem Cells	Preclinical	www.bayer-innovation.com
Beike Biotechnology	China	Stem Cells	Clinical trials	www.beikebiotech.com/
BetaCell	Belgium	Cells and Biomaterials	Preclinical	www.beta-cell.com
Biocell Center	Boston, MA	Stem Cells	Service	www.biocellcenter.com/
Biocomposites	England	Biomaterials	Commercial	www.biocomposites.com/
Bioheart	Sunrise, FL	Stem Cells	Clinical trials	www.bioheartinc.com
Biomerix	Fremont, CA	Biomaterials	Commercial	www.biomerix.com/
Biomet	Warsaw, IN	Biomaterials	Commercial	www.biomet.com/corporate/index.cfm
Biomimetic Therapeutics	Franklin, TN	Biomaterials	Commercial	www.biomimetics.com
Bionova	Australia	Cells and Biomaterials	Commercial	www.bionova.com.au/
BioParadox, Inc	Menlo Park, CA	Other	Preclinical	http://plateletcelltherapy.com/
Biosurface Engineering Technologies	Rockville, MD	Biomaterials	Clinical trials	www.biosetinc.com/
BioTime, Inc	Alameda, CA	Stem Cells	Preclinical	www.biotimeinc.com/
BioTissue AG	Miami, FL	Cells and Biomaterials	Commercial	www.biotissue.com/
Biotissue Technologies	Germany	Cells and Biomaterials	Commercial	www.biotissue.de
BrainStorm Cell Therapuetics	Israel	Stem Cells	Clinical trials	www.brainstorm-cell.com
California Stem Cell	Irvine, CA	Stem Cells	Preclinical	http://californiastemcell.com/

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Appendix A. (Continued)

Company	*Location*	*Sector*	*Stage*	*Website*
Cardio	Japan	Cells and Biomaterials	Preclinical	www.cardio.co.jp
Cardio3 BioSciences	Belgium	Stem Cells	Clinical trials	www.c3bs.com/
Cardiocreate	San Diego, CA	Stem Cells	Preclinical	www.cardiocreate.com
Cardium Therapeutics	San Diego, CA	Biomaterials	Clinical trials	www.cardiumthx.com/
CBR Systems	San Bruno, CA	Stem Cells	Service	www.cordblood.com/
Celgene	Summit, NJ	Stem Cells	Service	www.celgene.com/
Cell Care Australia	Australia	Stem Cells	Service	www.cellcareaustralia.com/
Cell Matrix AB	Sweden	Cells and Biomaterials	Commercial	www.cellmatrix.se
Cellerant Therapeutics	San Carlos, CA	Stem Cells	Clinical trials	www.cellerant.com
Cellerix	Spain	Stem Cells	Clinical trials	www.cellerix.com/
CellGenix Technologie Transfer GmbH	Germany	Stem Cells	Commercial, CRO	www.cellgenix.com
Celling Technologies	Austin, TX	Stem Cells	Clinical trials	www.cellingtechnologies.com/
Cells for Life	Canada	Stem Cells	Service	www.cellsforlife.com
Cephalon	Frazer, PA	Stem Cells	Clinical trials	www.cephalon.com/
Cerco Medical llc	San Francisco, CA	Cells and Biomaterials	Preclinical	www.cercomedical.com
Co.don	Germany	Cells and Biomaterials	Commercial	www.codon.de
Cognate BioServices Inc	Baltimore, MD	Stem Cells	CRO	www.cognatebioservices.com
Cook Biotech Ltd	West Layfayette, IN	Biomaterials	Commercial	www.cookbiotech.com
Cord Blood America	Los Angeles, CA	Stem Cells	Service	www.cordblood-america.com/
Cord Blood Bank of Canada	Canada	Stem Cells	Service	www.cordbloodbankofcanada.com
Cordbank	New Zealand	Stem Cells	Service	www.cordbank.co.nz
CordLife Limited	Singapore	Stem Cells	Service	www.cordlife.com/
Covidien	Ireland	Biomaterials	Commercial	www.covidien.com/
Cryo-Save	Netherlands	Stem Cells	Service	www.cryo-save.com
CryoCell	Oldsmar, FL	Stem Cells	Service	www.cryo-cell.com/
Cryocord	Malaysia	Stem Cells	Service	www.cryocord.com.my/
Cryolife	Atlanta, GA	Biomaterials	Commercial	www.cryolife.com/
Cryosite	Australia	Stem Cells	Service	www.cryosite.com/
Cytograft	Novato, CA	Cells and Biomaterials	Clinical trials	www.cytograft.com
Cytomedix	Gaithersburg, MD	Cells and Biomaterials	Commercial	www.cytomedix.com/
Cytonet Hannover Gmbh	Germany	Stem Cells	Clinical trials	www.cytonet.de
Cytori Therapeutics	San Diego, CA	Stem Cells	Commercial	www.cytoritx.com
Depuy (Johnson & Johnson)	New Brunswick, NJ	Biomaterials	Commercial	www.depuy.com/
Educell	Slovenia	Cells and Biomaterials	Commercial	www.educell.si
EndGenitor Technologies	Indianapolis, IN	Stem Cells	Preclinical	www.endgenitor.com
Escape Therapeutics Inc	San Jose, CA	Stem Cells	Preclinical	http://escapetherapeutics.com/
Eticur	Germany	Stem Cells	Service	www.eticur.de
Eufets AG	Germany	Stem Cells	CRO	www.eufets.com
Euroderm Biotech	Switzerland	Cells and Biomaterials	Commercial	www.euroderm-biotech.de
Exactech Inc	Gainesville, FL	Biomaterials	Commercial	www.exac.com/
Excorp	Minneapolis, MN	Cells and Biomaterials	Clinical trials	www.excorp.com/
Eyegenix (Cellular Bioengineering)	Honolulu, HI	Biomaterials	Clinical trials	www.eyegenix.com/
Family Cord	Los Angeles, CA	Stem Cells	Service	www.familycord.com/

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Appendix A. (Continued)

Company	*Location*	*Sector*	*Stage*	*Website*
Fate Therapeutics	San Diego, CA	Stem Cells	Clinical trials	www.fatetherapeutics.com/
FCB-Pharmicell	Korea	Stem Cells	Service	www.fcbpharmicell.com/english/
Forticell	Englewood Cliffs, NJ	Cells and Biomaterials	Commercial	www.forticellbioscience.com/
Future Health	United Kingdom	Stem Cells	Service	www.futurehealth.co.uk
Gamida Cell Ltd	Israel	Stem Cells	Clinical trials	www.gamida-cell.com
Genegrafts Ltd	Israel	Other	Preclinical	www.genegrafts.com
Genevrier (Endocell)	France	Cells and Biomaterials	Commercial	www.laboratoires-genevrier.com
Genzyme (Sanofi)	Bridgewater, NJ	Cells and Biomaterials	Commercial	www.genzyme.com/
Geron	Menlo Park, CA	Stem Cells	Clinical trials	www.geron.com
Healthpoint Biotherapeutics	Fort Worth, TX	Stem Cells	Commercial	www.healthpointbio.com/
Histogen Inc	San Diego, CA	Biomaterials	Clinical trials	www.histogen.com/
Histogenics	Waltham, MA	Cells and Biomaterials	Clinical trials	www.histogenics.com
Histostem	South Korea	Stem Cells	Commercial	www.histostem.co.kr/english/english_1.htm
Humacyte	Research Triangle, NC	Biomaterials	Preclinical	www.humacyte.com
Hybrid Organ GMBH	Germany	Cells and Biomaterials	Clinical trials	www.hybrid-organ.com
Inion Ltd	Finland	Biomaterials	Commercial	www.inion.com/
Innovacell	Austria	Other	Clinical trials	www.innovacell.at
Integra Life Sciences	Plainsboro, NJ	Biomaterials	Commercial	www.IntegraLife.com/
IntelliCell BioSciences	New York, NY	Stem Cells	Preclinical	www.intellicellbiosciences.com/
Intercytex (Regenerative Solutions)	United Kingdom	Cells and Biomaterials	Clinical trials	www.intercytex.com
International Stem Cell Corporation	Carlsbad, CA	Stem Cells	Preclinical	www.internationalstemcell.com
International Stem Cell Institute	San Diego, CA	Stem Cells	Commercial	www.istemcelli.com/
InVivo Therapeutics	Cambridge, MA	Stem Cells	Preclinical	www.invivotherapeutics.com/
iPierian Inc.	San Francisco, CA	Stem Cells	Preclinical	www.ipierian.com/
ISTO Technologies Inc.	St Louis, MO	Cells and Biomaterials	Commercial	www.istotech.com
Ivy Sports Medicine	Franklin Lake, NJ	Biomaterials	Commercial	www.regenbio.com/
Japan Tissue Engineering Co	Japan	Cells and Biomaterials	Commercial	www.jpte.co.jp/english/
Kensey Nash	Exton, PA	Biomaterials	Commercial	www.kenseynash.com/
Keranetics	Winston-Salem, NC	Biomaterials	Preclinical	www.keranetics.com
Kinetic Concepts Inc	San Antonio, TX	Biomaterials	Commercial	www.kci1.com/KCI1/home
Kuros Biosurgery	Switzerland	Biomaterials	Clinical trials	www.kuros.ch
Lazaron Biotechnologies	South Africa	Stem Cells	Service	www.lazaron.co.za
Lifeforce Cryobanks	Altamonte Springs, FL	Stem Cells	Service	www.lifeforcecryobanks.com/
Lifeline	Cyprus	Stem Cells	Service	www.lifelinecordblood.com/
Living Cell Tehnologies	Australia	Cells and Biomaterials	Clinical trials	www.lctglobal.com
Medistem Laboratories	Tempe, AZ	Stem Cells	Preclinical	www.medisteminc.com
Medtronic	Minneapolis,MN	Biomaterials	Commercial	www.medtronic.com/
Mesynthes	New Zealand	Biomaterials	Commercial	www.mesynthes.com/
MiMedx Group, Inc	Marietta, GA	Biomaterials	Commercial	www.mimedx.com/
Miromatrix	Eden Prairie, MN	Biomaterials	Preclinical	www.miromatrix.com/
Morphogenesis	Oldsmar, FL	Stem Cells	Preclinical	www.morphogenesis-inc.com
Nanotope	Skokie, IL	Biomaterials	Preclinical	www.nanotope.com/
NeoMend	Irvine, CA	Biomaterials	Commercial	www.neomend.com/

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Appendix A. (Continued)

Company	*Location*	*Sector*	*Stage*	*Website*
NeoStem	Agoura Hills, CA	Stem Cells	CRO, Service	www.neostem.com
Neotherix	United Kingdom	Biomaterials	Preclinical	www.neotherix.com/index.php
Neuralstem	Rockville, MD	Stem Cells	Clinical trials	www.neuralstem.com
NeuroGeneration	Beverly Hills, CA	Stem Cells	Clinical trials	www.neurogeneration.com
Neurotech	Lincoln, RI	Cells and Biomaterials	Clinical trials	www.neurotechusa.com
New England Cord Blood Bank	Newton, MA	Stem Cells	Service	www.cordbloodbank.com
NsGene	Denmark	Cells and Biomaterials	Clinical trials	www.nsgene.dk
Olympus Biotech	Hopkinton, MA	Biomaterials	Commercial	www.op1.com/
Opexa Therapeutics	The Woodlands, TX	Stem Cells	Clinical trials	www.opexatherapeutics.com
Organogenesis	Canton, MA	Cells and Biomaterials	Commercial	www.organogenesis.com
Organovo	San Diego, CA	Cells and Biomaterials	CRO, Preclinical	www.organovo.com/
Oristem (Pharmacells Ltd.)	Scotland	Stem Cells	Service	oristem.com/
Orthovita	Malvern, PA	Biomaterials	Commercial	www.orthovita.com
Osiris	Baltimore, MD	Stem Cells	Clinical trials	www.osiris.com/
Pathfinder Cell Therapy	Iselin, NJ	Biomaterials	Commercial	www.pathfindercelltherapy.com/
Pervasis	Cambridge, MA	Cells and Biomaterials	Clinical trials	www.pervasistx.com
Pioneer Surgical	Marquette, MI	Biomaterials	Commercial	www.pioneersurgical.com
Plasticell	United Kingdom	Stem Cells	CRO	www.plasticell.co.uk/
Plureon Corporation	Winston-Salem, NC	Stem Cells	Preclinical	www.plureon.com
Pluristem Therapeutics	Israel	Stem Cells	Clinical trials	www.pluristem.com
PrimeGen Biotech Corporation	Irvine, CA	Stem Cells	Preclinical	www.primegenbiotech.com
Provia Labs	Lexington, MA	Stem Cells	Service	www.provialabs.com/
Q Therapeutics	Salt Lake City, UT	Stem Cells	Preclinical	www.qthera.com/
Q-Med	Sweden	Biomaterials	Commercial	www.q-med.com/
Regenerative Medical Systems	United Kingdom	Cells and Biomaterials	Commercial	www.rmsbio.net/
Regenicin, Inc.	Little Falls, NJ	Cells and Biomaterials	Clinical trials	www.regenicin.com/
Regenics A/S	Norway	Stem Cells	Preclinical	www.regenics.no
Regenocyte	Bonita Springs, FL	Stem Cells	Commercial	www.regenocyte.com/
Regentec	United Kingdom	Cells and Biomaterials	CRO, Preclinical	www.regentec.net/
Regentis Biomaterials	Israel	Biomaterials	Clinical trials	www.regentis.co.il
Reneuron	United Kingdom	Stem Cells	Clinical trials	www.reneuron.com
RhinoCyte	Louisville, KY	Stem Cells	Preclinical	www.RhinoCyte.com
RNL Bio (EHE Biocell)	Korea	Stem Cells	Clinical trials	www.rnl.co.kr/eng
SanBio	Mountain View, CA	Stem Cells	Clinical trials	www.san-bio.com/
Scil Technology	Germany	Biomaterials	Clinical trials	www.sciltechnology.com/
Secant Medical	Perkasie, PA	Biomaterials	CRO	www.secantmedical.com/
Securacell	Canton, OH	Stem Cells	Service	www.securacell.com
Soluble Systems	Newport News, VA	Cells and Biomaterials	Commercial	www.solublesystems.com/
SpineSmith	Austin, TX	Cells and Biomaterials	Preclinical	www.spinesmithusa.com/
Stem Cell Assurance	Jupiter, FL	Stem Cells	Service	www.stemcellassurance.com/
Stem Cells for Hope, Inc	Calverton, NY	Stem Cells	Commercial	www.stemcellsforhope.com/
Stemagen	San Diego, CA	Stem Cells	Preclinical	www.stemagen.com
StemCells	Palo Alto, CA	Stem Cells	Clinical trials	www.stemcellsinc.com

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Appendix A. (Continued)

Company	*Location*	*Sector*	*Stage*	*Website*
Stemcyte	Arcadia, CA	Stem Cells	Service	www.stemcyteinc.com
Stemedica Cell Technologies, Inc.	San Diego, CA	Stem Cells	Clinical trials	www.stemedica.com/
Stemlife	Malaysia	Stem Cells	Service	www.stemlife.com/
Stemnion Inc	Pittsburgh, PA	Stem Cells	Clinical trials	www.stemnion.com
Stempeutics	India	Stem Cells	Clinical trials	www.stempeutics.com/
StemSave	New York, NY	Stem Cells	Service	www.stemsave.com/
TEI Biosciences	Boston, MA	Biomaterials	Commercial	www.teibio.com/
Tengion	East Norriton, PA	Cells and Biomaterials	Clinical trials	www.tengion.com/
Tepha	Cambridge, MA	Biomaterials	Commercial	www.tepha.com
Tetec	Germany	Cells and Biomaterials	Commercial	www.tetec-ag.com/
Theradigm	Baltimore, MD	Stem Cells	Preclinical	www.theradigm.com
Theregen	San Francisco, CA	Cells and Biomaterials	Clinical trials	www.theregeninc.com
TiGenix	Belgium	Stem Cells	Commercial	www.tigenix.com
Tissue Genesis	Honolulu, HI	Stem Cells	Clinical trials	www.tissuegenesis.com/
Tissue Regeneration Therapeutics	Canada	Stem Cells	Commercial	www.verypowerfulbiology.com/
Tissue Regenix	United Kingdom	Biomaterials	Commercial	www.tissueregenix.com/
TissueGene	Gaithersburg, MD	Other	Clinical trials	www.tissuegene.com
Tornier	Edina, MN	Biomaterials	Commercial	www.tornier.com/
TotipotentRX Cellular Medicine	Los Angeles, CA + India	Stem Cells	CRO, Service	www.totipotentrx.com/
Tristem Corporation	United Kingdom	Stem Cells	Clinical trials	www.tristemcorp.com
VasoTissue Technologies	Germany	Cells and Biomaterials	Clinical trials	www.vasotissue.com
Veltion Cell Therapeutics Limited	United Kingdom	Stem Cells	Preclinical	www.veltioncell.com/
Vescell	Thailand	Stem Cells	Commercial	www.vescell.com
ViaCord (PerkinElmer)	Cambridge, MA	Stem Cells	Service	www.viacord.com/
ViaCyte Inc.	San Diego, CA	Stem Cells	Preclinical	www.viacyte.com/
Virgin Health Bank	United Kingdom	Stem Cells	Service	www.virginhealthbank.com
VistaGen Therapeutics Inc.	Durham, NC	Stem Cells	Clinical trials	www.vestatherapeutics.com
Vita 34 AG	Germany	Stem Cells	Service	www.vita34.de
Vital Therapies	San Diego, CA	Cells and Biomaterials	Clinical trials	www.vitaltherapies.com
ViviCells International	Evanston, IL	Stem Cells	Service	www.vivicells.com
Zimmer	Warsaw, IN	Cells and Biomaterials	Commercial	www.zimmer.com/