Q2

ALLIANCE for Regenerative Medicine

2015

Quarterly Data Report

Regenerative Medicine & Advanced Therapies

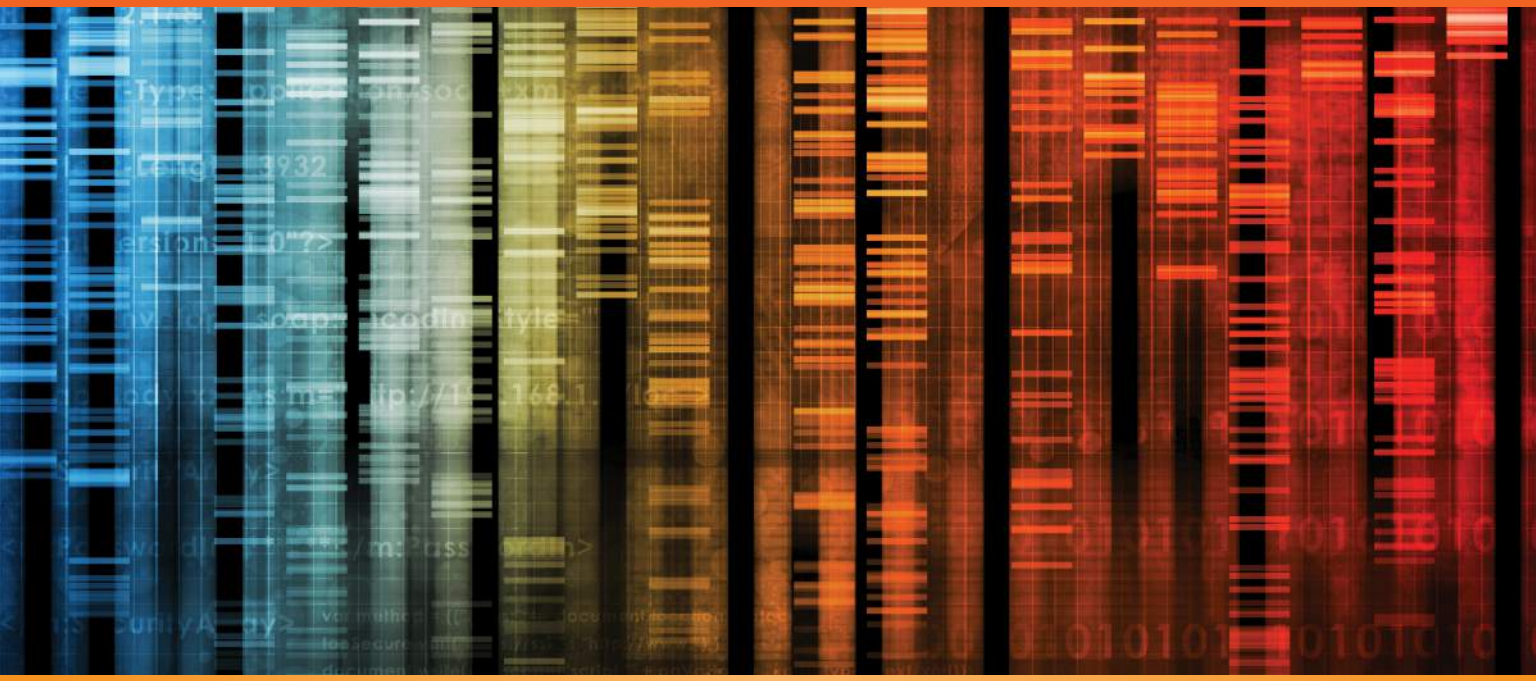
ALLIANCE for
Regenerative Medicine

The Alliance for Regenerative Medicine (ARM) is the preeminent global advocate for regenerative and advanced therapies. ARM fosters research, development, investment and commercialization of transformational treatments and cures for patients worldwide.

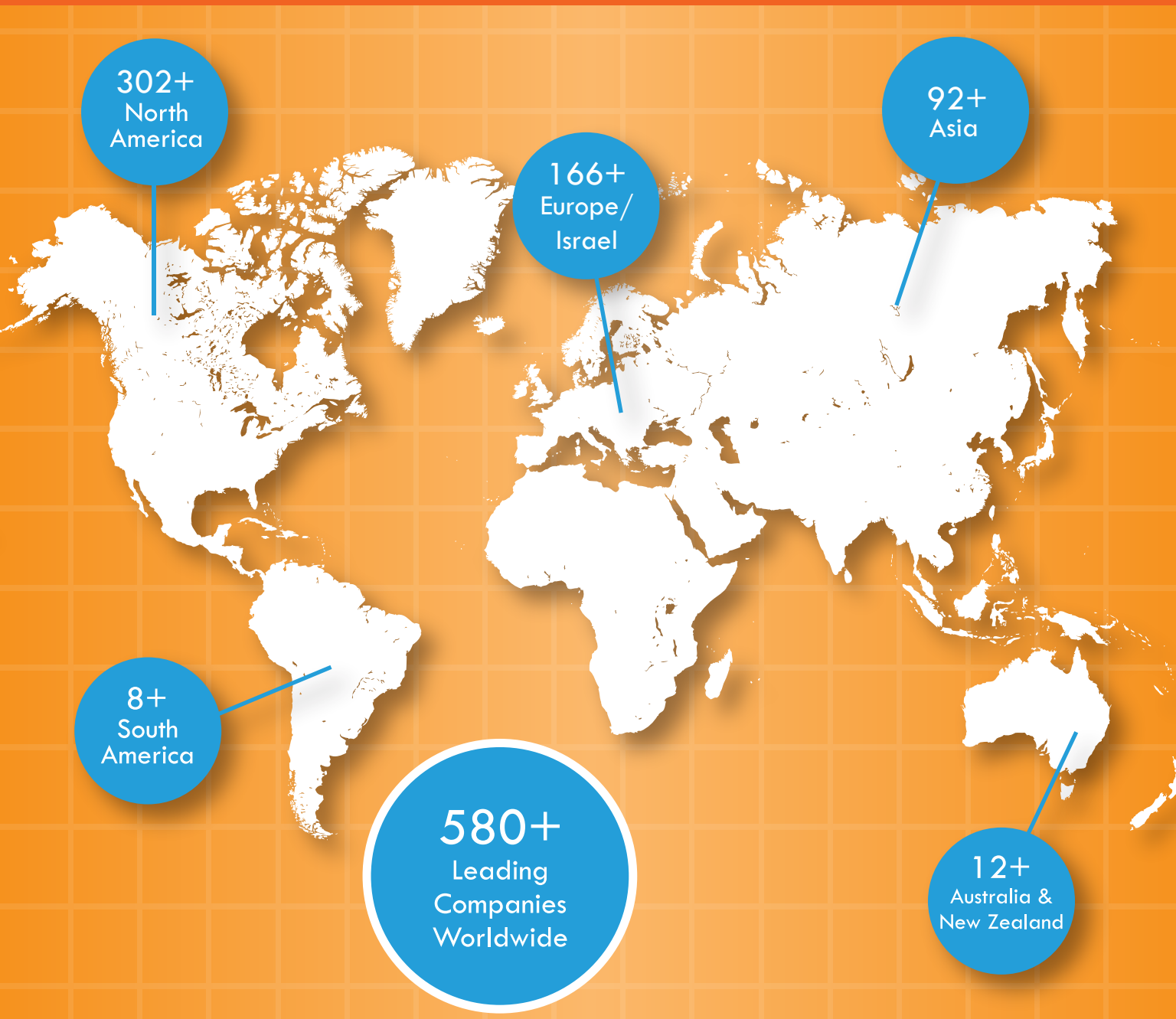
By leveraging the expertise of its membership, ARM empowers multiple stakeholders to promote legislative, regulatory and public understanding of, and support for, this expanding field.

alliancerm.org

Table of Contents



Industry Overview



Industry Overview

Investors in the regenerative medicine and advanced therapies sector remained bullish through the second quarter of 2015. The IPO window continued to be wide open with Benitec Biopharma announcing IPO plans and Kiadis Pharma and CoNKwest (now NantKwest) filing in Q2, while Adaptimmune Therapeutics, Aduro Biotech, Celyad SA and SanBio, Inc. successfully brought theirs to a close. There were also sizable rounds of private capital raised this spring, with REGENXBIO bringing in over $70 million, Dimension Therapeutics and Unum Therapeutics both securing $65 million Series B financings and Third Rock-backed Voyager Therapeutics closing a $60 million Series B round as well. StemCells, Inc. closed a secondary offering yielding almost $27 million while Pluristem Therapeutics, Inc. announced a smaller private placement that should raise $17 million.

This recent quarter also saw several significant sector collaborations, with Bristol-Myers Squibb spending $50 million upfront for exclusive rights to uniQure's gene therapy platform, and Aduro inking an immuno-oncology deal with Novartis worth up to $750 million. bluebird bio, Inc. leveraged its hot lentiviral platform by striking deals with fellow biotechs Five Prime Therapeutics, Inc., converting Five Prime's human antibodies to CAR-T cell products, and Kite Pharma, combining TCR cell therapy candidates with bluebird bio's expertise in gene editing. Astellas Pharma US, Inc. and Anokion SA entered into a partnership to create a new company, Kanyos Bio, looking at antigen-specific immune tolerance in several indications with a total potential deal value of $760 million. AMAG Pharmaceuticals, Inc., looking to expand its maternal health offerings, revealed that it will acquire Cord Blood Registry for $700 million.

There was also a spate of deals from Juno Therapeutics in the second quarter. Juno acquired Stage Cell Therapeutics in May and X-BODY in June. The company announced a joint clinical program with Medimmune, the biologics arm of AstraZeneca, examining the potential of combining CAR-T cell candidates with an early stage PD-L1 inhibitor as a combined therapy in NHL. Juno revealed a partnership with Editas Medicine, paying Editas $25 million upfront and much more for support and commercialization over time for use of their genome editing technologies to uncover therapies for a wider range of cancers. Fate Therapeutics was not left out, receiving a $5 million upfront payment plus stock purchases from Juno for potential small molecule modulators. Most recently, Juno Therapeutics announced a sweeping 10-year global collaboration with Celgene focused on 'transformational' immunotherapies for cancer and autoimmune diseases.

The past three months also reminded us that, especially with new technologies, the path from proof-of-concept to market is not always easy or straightforward, as illustrated by the unsatisfactory clinical trial results reported by Athersys, Inc., Avalanche Biotech and Celladon. But as June drew to a close, bluebird bio posted very promising results on its sickle cell/beta-thalassemia gene therapy in separate studies. In addition, Mesoblast Limited reported positive Phase II trial results from its allogeneic cell therapy product for diabetes and chronic kidney disease and the FDA granted Fast Track designation to ReNeuron for its retinitis pigmentosa cell therapy candidate.

At this mid-year point, optimism in the sector remains high, despite a few wobbles, and the second half of 2015 is poised to reveal significant opportunities in this dynamic field.

-Patricia Reilly
Executive Director, Medtrack

-Nancy Dvorin
Managing Editor – IN VIVO, Start-Up and Medtech Insight

Informa Business Intelligence,
Pharma and Healthcare

Financings

Q2 2015 Total Financings: $4.9B
Up 129% compared to Q2 2014

1H 2015 Total Raised: $7.6B
Up 137% compared to 1H 2014

Gene & Gene-Modified Cell Therapy: $3.3B Raised
Up 200% compared to Q2 2014

1H 2015 Raised: $4.8B
Up 185% compared to 1H 2014

Tissue Engineering: $464.1M Raised
Up 1,057% compared to Q2 2014

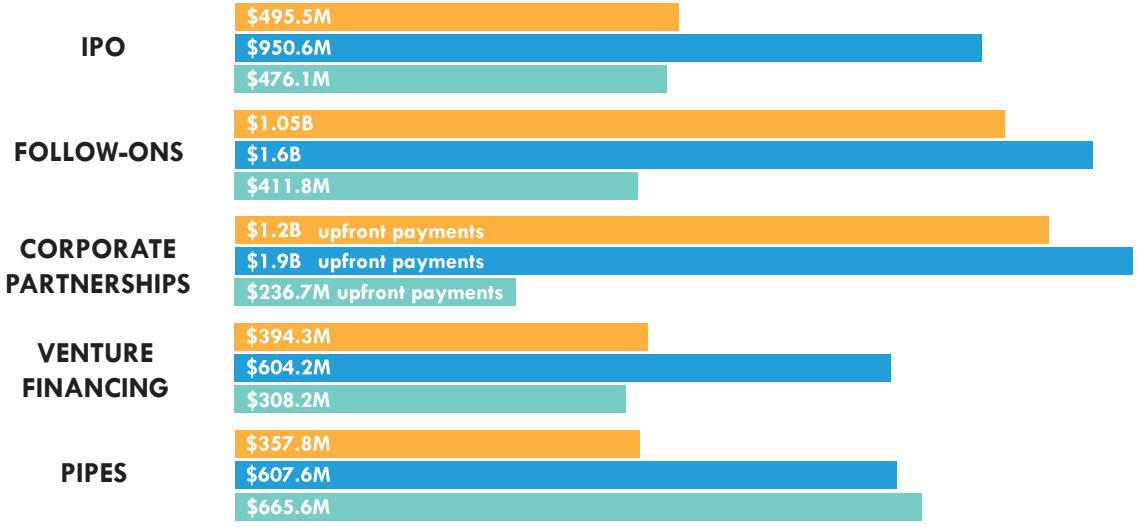
1H 2015 Raised: $617.2M
Up 279% compared to 1H 2014

Cell Therapy: $3.5B Raised
Up 111% compared to Q2 2014

1H 2015 Raised: $5.2B
Up 148% compared to 1H 2014

** Total amount raised represents sector-wide figures; please note that some companies are active in more than one technology group. As a result, the total amount raised does not equal the sum of the raises of the individual technology groups.*

Total financings by type: Q2 2015



Total M&A: Q2 2015

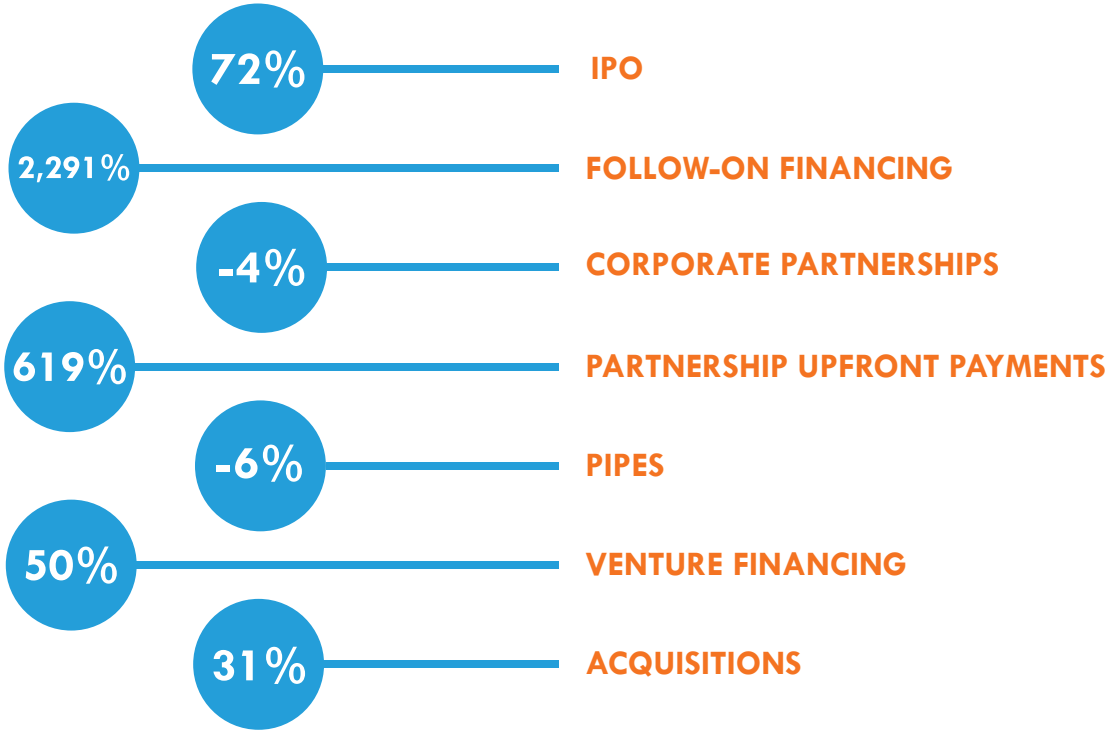
Amounts shown in USD

Q2 2015 total corporate partnerships deal value is $5.3B, compared to Q2 2014 $5.5B total deal value.

Examples of key financings: Q2 2015

IPO:	• Celyad SA raises $100.1 million with NASDAQ IPO – June 19, 2015 • Adaptimmune prices $191.3M IPO – May 6, 2015
FOLLOW-ONS:	• bluebird bio, Inc. prices offering of common stock for $500 million – June 23, 2015 • uniQure N.V. raises $88.5 million in follow-on financing – April 15, 2015
VENTURE FINANCING:	• REGENXBIO Inc. raises $70.5 million in financing round – May 20, 2015 • Dimension Therapeutics secures $65 million in oversubscribed Series B financing – April 21, 2015

Financing comparisons: Q2 2015 to Q2 2014



Sector Commentary

As we continue to investigate the next stages of advanced therapies, we are buoyed and spurred on by anticipated milestones such as the clinical durability of treatments and robust response rates, especially, for example, in relapsed/refractory patients who face situations where they literally have had no medically viable alternatives.

These advances represent potential major paradigm shifts in treatments for patients. Previously, the healthcare industry was largely driven to effectively manage various conditions and/or symptoms of disease, but now, especially in cell and gene therapies, we're focused on harnessing the immune system and, for example, targeting patients' cells with the aspiration to effect cures with our therapies.

Michael Perry, DVM, Ph.D., FRCVS
Chief Scientific Officer
Cell & Gene Therapy Unit
Novartis Pharmaceuticals Corporation

There is a great deal of discussion at present surrounding how to improve manufacturing and how to achieve commercially viable platforms that are automated and scalable – both up and down.

At Memorial Sloan Kettering Cancer Center, we set up and are continuously improving our own manufacturing processes not only for patients' cells, but also to produce our own viral vectors. Since 2013, we have manufactured T cell products for approximately 50 patients per year; with the opening of our new GMP facility, we should be able to double that output within the next few years.

Isabelle Rivière, Ph.D.
Director, Michael G. Harris Cell Therapy and Cell Engineering Facility
Center for Cell Engineering
Memorial Sloan Kettering Cancer Center

Examples of key corporate partnerships & acquisitions: Q2 2015

Celgene and Juno Therapeutics enter into a 10-year collaboration to advance potentially groundbreaking immunotherapies for patients with cancer and autoimmune diseases, including Celgene's initial $1 billion payment	June 29, 2015
AMAG Pharmaceuticals, Inc. announces it will acquire Cord Blood Registry for $700 million	June 29, 2015
Editas Medicine and Juno Therapeutics sign exclusive collaboration valued at $737 million to create next-generation CAR-T and TCR cell therapies	May 27, 2015
uniQure N.V. and Bristol-Myers Squibb enter into exclusive strategic collaboration valued at $2.3 billion to develop gene therapies for cardiovascular disease	May 26, 2015
Juno Therapeutics strengthens multiple capabilities through acquisition of Stage Cell Therapeutics, includes upfront payment valued at $81 million	May 11, 2015

Katrine Bosley, Ph.D.
CEO
Editas Medicine

Over the past couple years there's been a tremendous increase in the number of scientists and companies working in the fields of genome editing and gene therapy as the science has matured. For people who have been working in this area for a long time, it's wonderful to see that work being recognized. Signficant progress has been made and we all hope there's a lot more yet to come.

Clinical Trials & Data Events

528 Clinical trials underway

Ph. I: 169
Ph. II: 304
Ph. III: 55

74 Number of approved and/or marketed products worldwide

Examples of major milestones and key data events: Q2 2015

- Cell Therapy Ltd announces continuing 100% MACE-free survival after two years average follow up in Heartcel clinical trial in advanced heart failure patients at high risk of incomplete revascularization. – June 24, 2015
- bluebird bio, Inc. reports new beta-thalassemia major and severe sickle cell disease follow up data showing two patients with beta-thalassemia major remaining transfusion-independent for 16 and 14 months respectively, with persistent stable expression of HbA^{T87Q}, with neither experiencing a LentiGlobin-related adverse event. The severe sickle cell disease patient, the first to be treated with LentiGlobin BB305 product, was transfusion-free for more than three months without complications and with improvement in hemolysis markers. – June 13, 2015
- Mesoblast Limited announces positive results from Phase II trial in patients with diabetic nephropathy showing that a single infusion of allogeneic MPC product candidate MPC-300-IV is safe, reduces inflammation and preserves or improves renal function over at least 24 weeks. – June 9, 2015
- Asterias Biotherapeutics, Inc. announces positive, new, long-term follow-up data from Phase II trial of AST-VAC1 in patients with intermediate- and high-risk acute myelogenous leukemia, showing that more than 50% of patients had prolonged relapse-free survival. – June 1, 2015
- Juno Therapeutics' investigational CAR-T cell product candidate JCAR015 demonstrates encouraging clinical responses in patients with B-cell cancers. – May 30, 2015
- Juventas Therapeutics presents 12-month data demonstrating single administration of JVS-100 improves cardiac and clinical status in patients with severe ischemic heart failure one year after treatment. – May 26, 2015
- FDA grants Fast Track designation to ReNeuron's retinitis pigmentosa cell therapy candidate. - May 22, 2015

BG Rhee, Ph.D.
President
Green Cross Holdings

We've seen significant developments regarding the potential of cell therapy products in the treatment of various forms of cancer. Our autologous T cell product, ImmuneCell LC, is already approved in Korea. We have completed the first-in-human allogeneic NK cell Phase I trial for hepatocellular carcinoma and are preparing our Phase II trial. Our resources and attention will next turn to the impact of CAR-T and CAR-NK cells to treat patients with solid tumors and we are optimistic about what's achievable in this space.

Current Clinical Trials by Therapeutic Category: Q2 2015

- Nearly 40% of current clinical trials are in oncology
- More than 10% are in cardiovascular

	Cardiovascular 72		Musculoskeletal 37		Dermatology 31		Immunology & Inflammation 24	
Oncology 198		Central Nervous System 37		Infectious Diseases 32		Ophthalmology 29		Endocrine, Metabolic & Genetic Disorders 21
	Hematology 10		Respiratory 5		Ear Diseases 2		Radiation Injury 1	
Gastroenterology 14		Surgery 9		Genitourinary Disorders 4		Lymphatic Diseases 1		Dental 1

I personally view the therapeutic potential for iPSCs very optimistically. There are many diseases that are due primarily to the loss of function of a particular cell type, including dopaminergic neurons in Parkinson's disease, myocardial cells in congestive heart failure, and retinal pigment epithelial (RPE) cells in age-related macular degeneration. Cellular Dynamics International currently manufactures 12 types of iPSC-derived differentiated cells that can be used to treat over 50 diseases. The company's goal is to manufacture these cells under cGMP conditions at a high quality and purity to replace and potentially restore the lost function, revolutionizing the way we treat disease.

Kyle Kolaja, Ph.D.
Vice President, Business Development
Cellular Dynamics International, a FUJIFILM company

We're halfway through 2015, how would you view the performance of the cell and gene therapy sectors so far this year — both Europe as well as the global industry?
Regen med companies continue to attract investment, forge partnerships and license IP to strengthen their competitive position in the market. For example, Adaptimmune's announced IPO in May indicates that the financial sector still sees strength in this industry. And with Juno acquiring Stage Cell Therapies' IP, together with Celgene's investment into Juno, this hints at further consolidation of companies and technology.

What do you see as the primary commercialization challenges facing the sector?
The critical factor now is that none of these technologies have been developed at scale. There's no other field that needs this level of mass customization of production, at scale, and the careful orchestration of both care pathways and production pathways. That's going to take a lot of logistical and infrastructural investment, in particular around IT solutions to manage the industry.

What do you see as the near term and longer term prospects for adoptive T cell therapies and immuno-oncology?
It's a horse race. CAR-T therapies look very promising from an efficacy perspective. That's largely driven the investment in the space over the past 18 months. These therapies look promising for haematological malignancies. What remains to be seen is whether T cell immunotherapy can ultimately be applied to solid tumours, that will revolutionize cancer therapy. Also, we've really not seen too much yet of combination therapies using checkpoint inhibitors along with T cell immunotherapies. That may show promise in new indications as well.

What are the major technology breakthroughs in the last two to three years in the cell-based immunotherapy space that have brought clarity to the commercialization pathway?
First and foremost, the clinical effectiveness has caused people to start whispering about the "c" word: cure. If the efficacy weren't there, we'd be having a very different conversation right now. But, if what we're hearing is true, there is a lot of simplification in process that's taking place, and that will make these therapies easier to manufacture and deliver and ultimately much more cost effective.

What is GE Healthcare Life Sciences looking forward to achieving in the second half of 2015?
We're looking at a number of interesting strategic relationships in the space to consolidate our position as a leading technology provider. We want to continue to build our network of users and to engage in interesting and mutually beneficial consortia of technologists. We plan to continue our strategy of building bespoke unit operations for cell manufacturing, and connecting and digitizing technology beyond that.

Kieran Murphy
President & CEO
GE Healthcare
Life Sciences

European Regional Focus

1H 2015 Total Financing: $1.5B
Up 183% compared to 1H 2014

Gene & Gene-Modified Cell Therapy: $1.4B Raised
Up 195% compared to 1H 2014

Tissue Engineering: $68.9M Raised
No recorded financings in 1H 2014

Cell Therapy: $1.1B Raised
Up 361% comapred to 1H 2014

Whatever one believes, there is no doubt that the landscape of breakthrough medicine available to patients will look much different a decade from now.

Over this time, we will witness the beginning of a seminal transformation from the symptomatic treatment of disease through repeat dosing, to one-time, curative treatments that essentially 'repair' the root cause of the disease itself. We at uniQure are thrilled to play a role in this exciting evolution.

Matt Kapusta
Chief Financial Officer
uniQure

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*** European region also includes companies located in Israel.*

Current Regulatory & Legislative Priorities

- Implementing a federally-directed U.S. national strategy for regenerative medicine and advanced therapies. This includes federal agency coordination, support for research, capitalization for companies and regulatory reform.
- Establishing a Standards Coordinating Body for Regenerative Medicine and Advanced Therapies to create a central clearinghouse for the coordination, development, communication and implementation of technical and process standards and best practices.
- Improving and facilitating the use of FDA incentive programs for Qualified Regenerative Medicine Products (QRMPs). ARM recommends the FDA designate certain regenerative medicine and advanced therapy products as QRMPs, intended for serious or life-threatening diseases with no currently available treatment options. The FDA would meet with the QRMP's sponsors to discuss expedited review opportunities.
- Improved communication and coordination among FDA review centers. ARM recommends the development of a review framework, including timelines, communications and regulatory requirements to facilitate consistency and efficiency among review centers.
- Advocating for reimbursement coverage and coding policies for regenerative medicine and advanced therapies products, promoting a supportive and incentivizing payment structure.
- ARM is reviewing and submitting comments to the European Medicines Agency's recently published draft guidelines on the quality, non-clinical and clinical aspects of gene therapy medicinal products.
- ARM continues to monitor discussions of ATMP regulation and its implementation across EU member states.

Recent regenerative medicine and advanced therapies regulatory initiatives established by Japan and the EU offer examples of very compelling pathways with the potential to significantly improve the commercialization of regenerative medicine, if the regulatory changes are implemented and executed properly. While we must always ensure an appropriate balance between speed-to-market and safety, some of the industry's overall challenges related to the length of time required to develop, manufacture, test and accumulate long-term safety and efficacy data for cell and gene therapy products could be clarified and streamlined in jurisdictions like the United States through regulatory initiatives like Japan's Regenerative Medicine Law or the EU's Adaptive Pathways initiative.

Ann Tsukamoto, Ph.D.
Executive Vice President, Scientific and Strategic Alliances
StemCells, Inc.

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