Trending 2018: Pipeline Disrupters

Pipeline disruptors are innovative therapies that impact current therapies with significant competition and alter the course of treatment. Industry leaders take a look at three hot areas — regenerative medicine, RNA technologies, and immunotherapies — and their potential impact on the future of medicine.

In recent years, several therapeutic disruptors have hit the market, pushing aside current standard treatment protocols. From hepatitis C cures to immuno-oncology therapies, recent approvals have upended how diseases are treated, providing patients with significant advances.

Pharmaceutical, biotech, and biopharma companies are working on tomorrow’s disrupters. With more than 7,000 medicines in development around the globe, the pipeline is filled with potential first-in-class therapies.

“We currently find ourselves on the cusp of the next therapeutic revolution: the use of cells as medicine,” says Ross Macdonald, Ph.D., managing director and CEO, Cynata Therapeutics, which is one of several companies pursuing stem cell and regenerative medicine. “The approval of Novartis’ Kymriah was a turning point in the validation of cell-based therapies, an area now in the midst of an innovation windfall.”

Stem Cell and Regenerative Medicine

This past summer, the Food and Drug Administration approved the first gene therapy for the treatment of patients with B-cell precursor acute lymphoblastic leukemia (ALL). Novartis’ Kymriah is an immunocellular therapy that is a one-time treatment to enhance cellular expansion.

More recently, a second CAR-T therapy was approved. In October, the FDA approved Kite/Gilead’s Yescarta, a cell-based gene therapy, to treat adult patients with certain types of large B-cell lymphoma who have not responded to or who have relapsed after at least two other kinds of treatment.

Gene and stem cell therapies are the cornerstone of the next wave of regenerative medicine, industry leaders say.

The field of regenerative medicine is an emerging one, aimed at regeneration, repair, or replacement of damaged tissue and organs. Regenerative medicine is defined by the National Institutes of Health as the process of creating living, functional tissues to repair or replace tissue or organ function lost due to age, disease, damage, or congenital defects.

At the close of 2016, there were 804 clinical trials under way involving cell therapy; further, there are a number of approved and/or marketed products worldwide, according to the Alliance for Regenerative Medicine.

Scott Gottlieb, M.D., commissioner of the FDA, said in a statement in August 2017 that regenerative medicine is one of the most promising new fields of science and medicine.

Regenerative medicines are developed by using translational research techniques such as molecular biology, tissue engineering, and gene engineering. Stem cells and tissue scaffolds have effective therapeutic potential, which is increasing the adoption of regenerative medicine.

“These new technologies, most of which are in early stages of development, hold significant promise for transformative and potentially curative treatments for some of humanity’s most troubling and intractable diseases,” Dr. Gottlieb said in the statement.

Dr. Macdonald explains that the advent of regenerative, cell-based medicine has the potential to empower people’s bodies to heal themselves and defend against illness and injury.

“This could translate into a healthier population and allow patients to live fuller lives, while also extending their ability to productively contribute to society,” he says.

Cynata’s Cymerus technology platform addresses a critical hurdle in the application of mesenchymal stem cells (MSCs) as therapeutic agents, by enabling the production of large-scale and consistent MSCs based on a single blood donation from one adult donor.

Atheneus is another company working in the emerging field of regenerative medicine.
FAST FACT

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The company is developing MultiStem, an adult-derived “off-the-shelf” stem cell product platform, for multiple disease indications in the areas of neurological, cardiovascular, inflammatory, and immune disease areas, as well as other indications where there is unmet medical need.

“In the next several years, we’re going to see the approval of therapies that will reshape medicine in some very powerful ways — in fact, it’s already happening with cell therapies like CAR-T,” says Gil Van Bokkelen, Ph.D., CEO of Athesys. “This is exciting; these new therapies have the potential to address some of the areas that are driving healthcare costs, not just now but well into the future.”

Dr. Van Bokkelen says the company’s technology is demonstrating powerful biological activity.

“In situations where there is an injury or some form of tissue damage, the body starts to send out signals and when these cells are administered they respond to those signals,” Dr. Van Bokkelen explains. “The cells home to the site of tissue damage or inflammation, or other relevant organs, and can dynamically regulate what is happening to help promote recovery and repair.”

MultiStem is a biologic product that is manufactured from human stem cells obtained from adult bone marrow. Unlike other cell types, after isolation from a qualified donor, MultiStem consists of a special class of human stem cells that have the ability to express a range of therapeutically relevant proteins and other factors. These cells exhibit a drug-like profile in that they act primarily through the production of multiple factors that regulate the immune system, protect damaged or injured cells, promote tissue repair and healing, and are subsequently cleared from the body over time.

In contrast to other cell therapy technologies or procedures, MultiStem is simple to prepare and administer, using a three-step process that takes only a few minutes. First, a vial of product is removed from the freezer. Second, the vial containing the frozen cells in liquid is thawed.

Cell therapy is maturing as a field, and the indications and markets we are addressing are growing because much of the field is working to address diseases associated with aging.

DR. KARINE KLEINHAUS
Pluristem

Third, using a syringe, the cells are then transferred to an IV bag of saline, and then administered to the patient.

Athesys currently has six clinical-stage programs, including a pending Phase III study in ischemic stroke that has already been given fast track status, an ongoing Phase II clinical study for the treatment of damage from acute myocardial infarction, and an ongoing exploratory clinical study in acute respiratory distress syndrome.

“In addition to their therapeutic properties, there are two other important characteristics of MultiStem,” Dr. Van Bokkelen says. “First, we can administer these cells just like type O blood with no tissue-matching or immune suppression required. Second, we can manufacture the cells that make the MultiStem product in a highly scalable way, meaning we can generate millions of doses using a small amount of material from a single, healthy, consenting donor. That’s a huge advantage, and one of the things that will make these types of therapies a widespread clinical reality.”

Experts say the field holds the promise of regenerating damaged tissues and organs in the body by stimulating previously irreparable organs to heal themselves.

“The cell therapy market is coming into its own,” says Karine Kleinhaus, M.D., divisional VP, North America, Pluristem. “There are a lot of cell therapy trials happening, which