

## Client Focus

# Regenerative Medicine: Today's Health Revolution

Rapid advances in gene research is  
creating medical miracles

### CLIENT PROFILE

New stem cell therapy at  
Rush marks breakthrough  
for paralysis

### EQUITY RESEARCH

Regenerative medicine zeroes  
in on underlying cause of  
an ailment

### CLIENT FOCUS ONLINE

[williamblair.com/CFsummer2018](http://williamblair.com/CFsummer2018)





## Navigating the Markets

As the markets have absorbed a steady pace of captivating headlines over the past few months, we've seen volatility continue. Remember we are here to help you navigate the market swings and to help you plan for the future.

It is also healthy to take a step back and look at some of the bigger trends driving investments both in the United States and around the world. At William Blair we focus on the long term, searching for companies and sectors that have the potential for growth.

We recently hosted our 38th Annual Growth Stock Conference, a three-day event held in Chicago during June. A record 246 public companies attended as top executives presented their outlooks for the year. Companies represented six market sectors—consumer; industrials; financials & tech; global services; healthcare; and tech, media, communications.

Overall, the companies were optimistic about the current economic environment. While many said growth accelerated in 2017, growth this year was increasing at a faster rate and more than they expected.

One of the growth areas in the healthcare sector we find interesting

is regenerative medicine—the reengineering of cells and tissues to zero in on the underlying cause of diseases and fixing them for good.

While the science is in its early stages, scientists, healthcare professionals and government officials say it holds transformative promise for patients. Given the possibilities, we wanted to spotlight some of the latest advances in this issue of *Client Focus*.

Hundreds of companies around the globe are working on these technologies. While new regenerative therapies are beginning to reach the market, researchers say, the next generation of therapies are benefiting from earlier discoveries. It is that potential along with recent therapy approvals by the U.S. Food and Drug Administration that is capturing the attention of big pharmaceutical companies.

One example of the possibilities is the pioneering work of Dr. Richard Fessler, a neurosurgeon at Rush University Medical Center, a long-time institutional client of William Blair.

He led a 12-month study of a new regenerative stem cell therapy for patients paralyzed by cervical spinal cord injuries. For the first time, the

therapy helped reverse some of the paralysis. It is a fascinating story and offers hope for others.

I'm also pleased to share some recent industry honors. In March William Blair was named 2018 Investment Bank of the Year by *Mergers & Acquisitions* magazine. In May we received the 2018 Corporate Partner Award from Chicago-based Bunker Labs in recognition of our leadership in helping military veterans start their own businesses.

On behalf of everyone with William Blair, thank you for the trust you have placed in us. Wishing you and your family a safe and enjoyable summer.

Sincerely,

John Ettelson  
President and CEO

# Regenerative Medicine: Finding Ways for the Body to Heal Itself

One of the most exciting areas in healthcare today is regenerative medicine. This simple term encompasses a rapidly expanding revolution in medical research, which in its application by physicians is allowing the body to heal itself in ways never before seen.

Hundreds of companies and universities around the world are working on regenerative technologies to cure leukemia, hemophilia and other devastating diseases or repair injured organs and tissues such as spinal cords, retinas and hearts.

Of the 946 regenerative clinical trials going on at the end of 2017, more than half were in cancer. Nearly 10% were related to heart disease and 6.5% were addressing diseases of the brain and spinal cord.<sup>1</sup>

By exploring the mysteries of DNA, scientists are successfully engineering stem cells and tissues that are then injected into patients and actually fight diseases at their roots or “regenerate” tissue to heal patients—fundamentally advancing medicine beyond its traditions of just treating symptoms.

## FDA promises support

The Food and Drug Administration is promising to support accelerated paths for product approvals in many fields.

“We’re at a key point when it comes to cell and gene therapy. These therapies have the potential to address hundreds, if not thousands, of different rare and common diseases,” FDA Administrator Dr. Scott Gottlieb told the Alliance for Regenerative

Medicine’s (ARM) annual board meeting in Washington on May 22.

“For a long time, they were largely theoretical constructs. Now they’re a therapeutic reality. And it’s my expectation that they will soon become the mainstay of how we treat a wide range of illnesses.”

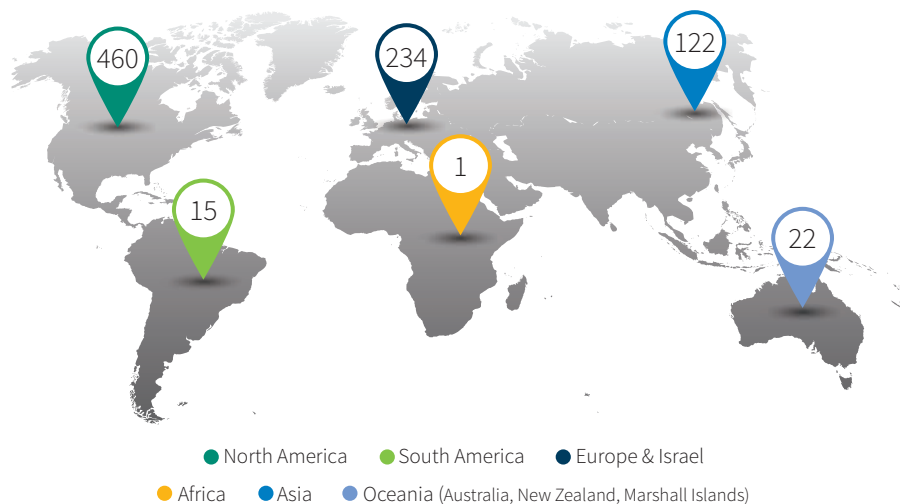
In the fall of 2017, the FDA for the first time approved not one but two of the new gene therapies for general use.

Novartis’s Kymriah, used to attack leukemia, became the first gene therapy available in the United States. That was followed by Kite/Gilead’s Yescarta to fight non-Hodgkin’s lymphoma. Both involve genetically altering a patient’s own immune cells to fight a disease, known as CAR T-cell therapies.

## No longer science fiction

ARM CEO Janet Lambert says 2017 was groundbreaking for the sector and

## Regenerative Medicine Companies Worldwide



Source: Alliance for Regenerative Medicine, 2017 Annual Report

trends continue to be strong. Global financings for IPOs in the sector at the end of first quarter 2018 were already 90% of the investment seen for all of 2017. First-quarter mergers and acquisitions were also strong, nearly 70% of full-year 2017.

“It’s scientifically disruptive that we can now tackle the cause of the disease,” Lambert says. “Once these products get to market you’re in a whole new world, greatly expanding their access beyond the limited number of patients participating in trials.”

“Some of the most exciting are the CAR-T focused therapies and cell-based immune oncology,” she says, adding there has been much success in fighting “liquid” tumors such as blood-based cancers. Hopes are high that regenerative medicine will soon be successful battling “solid” tumors like those of the lung, prostate, breast and colon.

“These concepts are no longer the stuff of science fiction, but rather real-life science,” Gottlieb said at the time of the first 2017 approvals.

### Big pharma and biotech deals

The applications of this scientific revolution have grabbed the attention of big pharma in particular. Just from August of last year to this April, there have been three multibillion-dollar acquisitions centered on regenerative medicine made by Gilead, Celgene and Novartis.

*“These therapies have the potential to address hundreds, if not thousands, of different rare and common diseases.”*

Swiss drugmaker Novartis’s purchase of AveXis, an Illinois biotech company, closed in May for \$8.7 billion—a 72% premium to AveXis’s 30-day volume-weighted average stock price.

“There’s significant excitement about the potential of cell and gene therapies to transform the treatment paradigm for several diseases, and that’s reflected in these valuations,” says William

Blair analyst Raju Prasad, who covers biotech companies including AveXis.

Novartis was particularly interested in AveXis’s new gene therapy to treat spinal muscular atrophy (SMA), a disease that prevents the body from producing muscle and is the leading genetic cause of infant deaths.

AveXis engineered a gene that is missing in children suffering from SMA, then delivered it to them using a virus. Of the 15 patients in the Phase I clinical trial, all were alive after 24 months and the young children achieved many important motor nerve milestones after getting treatment.

AveXis is currently enrolling a Phase III trial, with early results from that study presented at the American Academy of Neurology annual meeting in April 2018, corroborating the impressive results seen from the Phase I trial.<sup>2</sup>

### Revolution in its early stages with hurdles ahead

Such promise of medical miracles drives both the basic science and the

## Clinical Trials Worldwide 2017



Source: Alliance for Regenerative Medicine, 2017 Annual Report

# Regenerative Medicine: Early Innings, Exciting Gains

applied medicine of regenerative therapies. Scientists say the revolution is still in its early stages with next-generation therapies primed for FDA-approved clinical trials.

*“These concepts are no longer the stuff of science fiction, but rather real-life science.”*

Practical hurdles remain. Hopes are soaring—but so are costs. How many people can pay for a million-dollar injection? What will be government’s role? For now, Gottlieb promises a sharp eye to protect consumers and researchers.

The FDA is cracking down on touted but unregulated and unapproved procedures or claims it says put patients at risk, as it did at stem cell clinics in Florida and California in the past year.<sup>3</sup>

## Challenges ahead

“This field is moving really fast but there’s still going to be a lot of challenges and missteps along the way,” said Matt Phipps, a William Blair analyst who covers the biotech sector.

“People get very exuberant on the prospects. But at the end of the day, biology is really complex. On top of that, the thing people worry about is our healthcare system really isn’t set up to pay for one-time cures,” he adds.

*“The most profound story is curing one individual at a time.”*

Still, challenges on how treatments will be paid for have not yet slowed interest in the burgeoning regenerative medical revolution.

“We’re just beginning to scratch the surface that this sector is going to be able to deliver for patients and families,” Lambert says. “The most profound story is curing one individual at a time.”

Regenerative medicine is still in its early stages. But the science, many analysts agree, has the potential to change the course of healthcare. Instead of constantly treating a disease, regenerative medicine zeroes in on the underlying cause of an ailment and fixes it for good.

“That’s why people are excited about it and why investors are flocking to it,” said Matt Phipps, a William Blair analyst, who covers the biotech sector. “If you have the ability to cure a patient, that’s going to make other drugs obsolete. And that changes a lot of those markets.”

Take hemophilia. A hemophilia patient may need two to three infusions a week of a protein they lack to prevent them from bleeding. Those drugs can cost \$300,000 to \$400,000 a year, or millions over a lifetime; a one-time regenerative cure could cost a million dollars, Phipps says.

Researchers are currently testing therapies for hemophiliacs to fix a faulty gene with such one-time cure-all remedy. Biotech companies Spark Therapeutics and BioMarin are each conducting clinical trials in hemophilia with impressive results seen to date, including little to no infusions needed for the patients treated over the course of one to two years.

## New therapy for vision loss

Spark also received FDA approval in late 2017 for a new gene therapy, Luxturna, to treat children and adults with an inherited form of vision loss that may cause blindness. Luxturna is the first gene therapy approved in the United States that targets a disease caused by mutations in a specific gene.

“What’s impressive is the therapeutics getting approved now are seen as late-stage, first-generation products and part of a larger kind of growth and expansion in this field,” says Raju Prasad, an analyst and member of William Blair’s biotech research team.

“What’s next? What’s coming? That’s what gets me excited,” Prasad says. “There are tons of private companies, some public companies that are already working on bigger, better versions of these products.”

A year ago William Blair expanded its biotech research coverage to provide clients with a deeper level of investment insights on companies leading such regenerative innovation.

“We are committed to providing our clients best-in-class service and insights into this vital sector,” said John Moore, head of institutional equities and research.

*To receive William Blair research reports, contact your advisor. Visit [williamblair.com/ResearchCoverage](http://williamblair.com/ResearchCoverage) for disclosure information.*

<sup>1</sup> Alliance for Regenerative Medicine

<sup>2</sup> AveXis study

<sup>3</sup> FDA



# Dr. Richard Fessler Leads Breakthrough Research for Paralysis

*New Stem Cell Treatment at Rush University Medical Center Restores Movement.*



Dr. Richard Fessler

Dr. Richard Fessler has spent much of his 30-year career as a neurosurgeon treating patients with spinal cord injuries. He has always aspired to be a healer, even a miracle worker. But it was just a year and a half ago he experienced his biggest breakthrough moment.

He led a 12-month study at Rush University Medical Center that involved injecting a new regenerative stem cell therapy for people paralyzed by cervical spinal cord injuries. Of the six patients who participated, all regained some upper-body movement. Four got two levels of movement back and one patient got three levels back. So a patient who could only shrug his shoulders before the procedure is using his hands to eat, write, and do other tasks.

“These are tremendously exciting results,” Fessler says. “It was the first time in recorded history we made progress in reversing spinal cord injury. This is really the first step. But I learned it is possible that some day we will have a cure for paralysis.”

Rush was one of nine medical centers across the country studying this new therapy. Patients received an injection of 10 million cells in a fluid drop near the spinal cord injury. The cells, engineered by San Francisco Bay-area biotech Asterias Biotherapeutics, were derived from stem cells—the basic building blocks of all human cells.

Created in the lab, the cells can enable the body to reproduce new spinal cord cells, liver cells, heart cells, and so on, offering scientists a key to regenerate diseased and injured parts of the human body.

Fessler says the Asterias AST OPC1 cells make a protein coating, myelin, missing in damaged spinal cord cells. Once injected into the patient, the cells only have to grow 1 to 2 cm before the nerve regains enough functionality to improve the quality of life of the individual.

One Rush patient in the trial was Illinois native Chris Block, an athletic young mechanical engineer. He was working in Indiana after graduating from Virginia Tech in mechanical engineering when a bicycling accident changed his life on July 23, 2016. Block sustained a spinal cord injury to his C5 vertebra that left him paralyzed. Two weeks later, while lying in a hospital bed in Indianapolis, his doctor mentioned a new stem cell therapy.

“I was immediately very interested in learning more and to be a guinea pig for the program,” Block says.

He said the results have boosted not just his movement but his hopes. Before surgery all Block could do was shrug his shoulders and raise his right arm a little bit. After the stem cell injection he was first able to recover feeling in his left arm, then raise his left hand to his face and eventually raise both arms above his head.

“Five to six months after the stem cell injection, I was able to dress the upper half of my body, shower my upper body,” Block said.

Fessler, who became involved in spinal cord research 20 years ago at the University of Florida, acknowledges that the new stem cell therapies have a long way to go. But the spectacular results with Block and other patients have raised his hope for a cure.

“It was the first time in recorded history we made progress in reversing spinal cord injury.”

“For the first time ever we are seeing real positive results,” Fessler says. “We are very early in the research. But we are seeing these changes. Normally after a spinal cord injury, you’ll see improvement for a month or two and that’s it. We’re 12 months out, and these patients are still getting better. That’s remarkable.”

Buoyed by the results, Fessler opened a new stem cell lab at Rush this spring. He plans to continue working with Asterias and the company’s lead scientist on the AST OPEC1 stem cell line, who was a former colleague from the University of Florida and Rush.

“Physicians like to help patients. That’s why we do this. To be able to

help someone who never has been able to be helped before...,” Fessler says, pausing for the right word to sum up his feelings. Then, he finds it. “Wow!”

*Rush is a William Blair client and Dave Coolidge, vice chairman of William Blair, has been a Rush board member since 1986.*

## Profile in Courage: the Spirit of Christopher Block



Chris Block, one of the spinal cord patients helping to pioneer new stem cell therapies aimed at a cure, has always been competitive and goal oriented. He played college lacrosse at Virginia Tech as an engineering student and was ramping up as a road biker while working in Indiana after graduation when he incurred his paralyzing injury in July, 2016.

His spirit and courage are carrying him through. Today, two years into his recovery at Rush and the Northwestern-affiliated Rehabilitation Institute of Chicago (RIC), Block continues to excel in his extensive physical therapies including standing frame exercises, hand/upper-extremity cycling, functional electronic stimulation (FES) rowing, and even horseback riding and scuba diving. But his thanks are for others.

“Something like one in 10,000 people has a spinal cord injury. So it’s rare but those of us who do have an injury, our lives are so much more enhanced by the people dedicated to helping those with spinal cord injuries like Dr. Fessler,” Block says.

Block first heard of the new stem cell therapy in his Indianapolis hospital bed. His first goal was to be transferred to Chicago so he could begin his rehab at RIC and be closer to his family in Lake Forest. His second goal was to learn more about the stem cell treatment led by Dr. Fessler at Rush.

But two significant meetings helped Block make his decision to go ahead with the stem cell surgery, which he qualified for. He reached out to Mark Stephan, another native of Chicago’s North Shore who had broken his neck 10 years earlier. Stephan gladly became a mentor for both Block and his parents.

“You’re confused with things going on with your own body and there’s a million things you’re thinking about,” Block recalls. “You’re wondering if you’re going to walk again, you want to get your life back. Without talking to Mark Stephan and Dr. Fessler and getting a warm fuzzy feeling, I would not have done the surgery.”

Block said he was also lucky to meet Adam Chaffee, a spinal cord patient who received an earlier experimental stem cell injection. “One of the 2 million cell guys,” Block calls Chaffee, who happened to be at Rush for his one-year checkup the day before Block was scheduled to get his 10 million cells.

“He’s like a big brother to me,” Block says. “Without him being one of the guys to take 2 million cells, it would not have been possible for me to get any cells at all.

“I am super fortunate,” he says. “I am lucky to get out of my wheelchair almost every day.”

# Internet Fosters Connectivity, Community for Families of Barth Syndrome Patients

*Families of children suffering from a rare genetic disease known as Barth syndrome are finding each other online, sharing experiences and support.*

“When you have a rare disease it is a lonely experience. It’s likely you don’t know anyone else who understands what you’re going through,” says Emily Milligan of the Barth Syndrome Foundation (BSF). “The internet has revolutionized the ability to connect, especially for caregivers.”

Barth syndrome is a genetic disease found in males that can severely affect the heart, muscles and a type of white blood cell that fights bacterial infections. There are only a couple hundred people worldwide known to suffer from Barth syndrome. There are no approved therapies to treat or cure Barth syndrome.

Three mothers led the creation of the Barth Syndrome Foundation in 2000, which had its roots in these families who found each other online in the late ‘90s. Today, families representing more than 230 confirmed cases from around the globe are sharing experiences and knowledge online to support loved ones, Milligan says.

Marc Sernel, a William Blair client who served as BSF board chairman the past five years, became involved with

the foundation in 2006 shortly after his son Ryan was diagnosed with Barth syndrome in his first year of life. Tragically, the end of Sernel’s three terms on the board coincided with the sudden passing of his son in March.

“To be plugged into all that knowledge, experience and wisdom from families and doctors in every corner of the world is a godsend for all of us,” Sernel says. “That connection and information helped my son live a good life for 12-1/2 years. I hope it leads to longer and better lives for those affected by Barth who follow in my son’s footsteps.”

Social media also helps the foundation’s fundraising to support research and its biennial conference which connects patients, families and scientists. Sernel says the first clinical trial focused on treating Barth syndrome is now underway.

“The medicine is moving forward and I have great hope in the coming years there will be some treatment for Barth syndrome,” he says.

## CLIENT SERVICE

### New Publication on Managing Market Risk Available

Investors have seen a jump in stock market volatility in 2018 triggered by a variety of factors: political uncertainty, the specter of trade wars, rising inflation, the jump in oil prices, speculation on interest rates, and more.

Volatility tends to raise risk, a basic market fact. The first step is evaluating your risk exposure.

Our latest publication—*Risk: Understanding and Managing an Inevitable Part of Investing*—is available online at [williamblair.com/risk](http://williamblair.com/risk) and zeroes in on the current risk factors and their likely impacts.

Helping you understand and manage risk is central to William Blair’s approach to wealth management. To discuss strategies to help manage market risk, please contact your William Blair advisor.

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