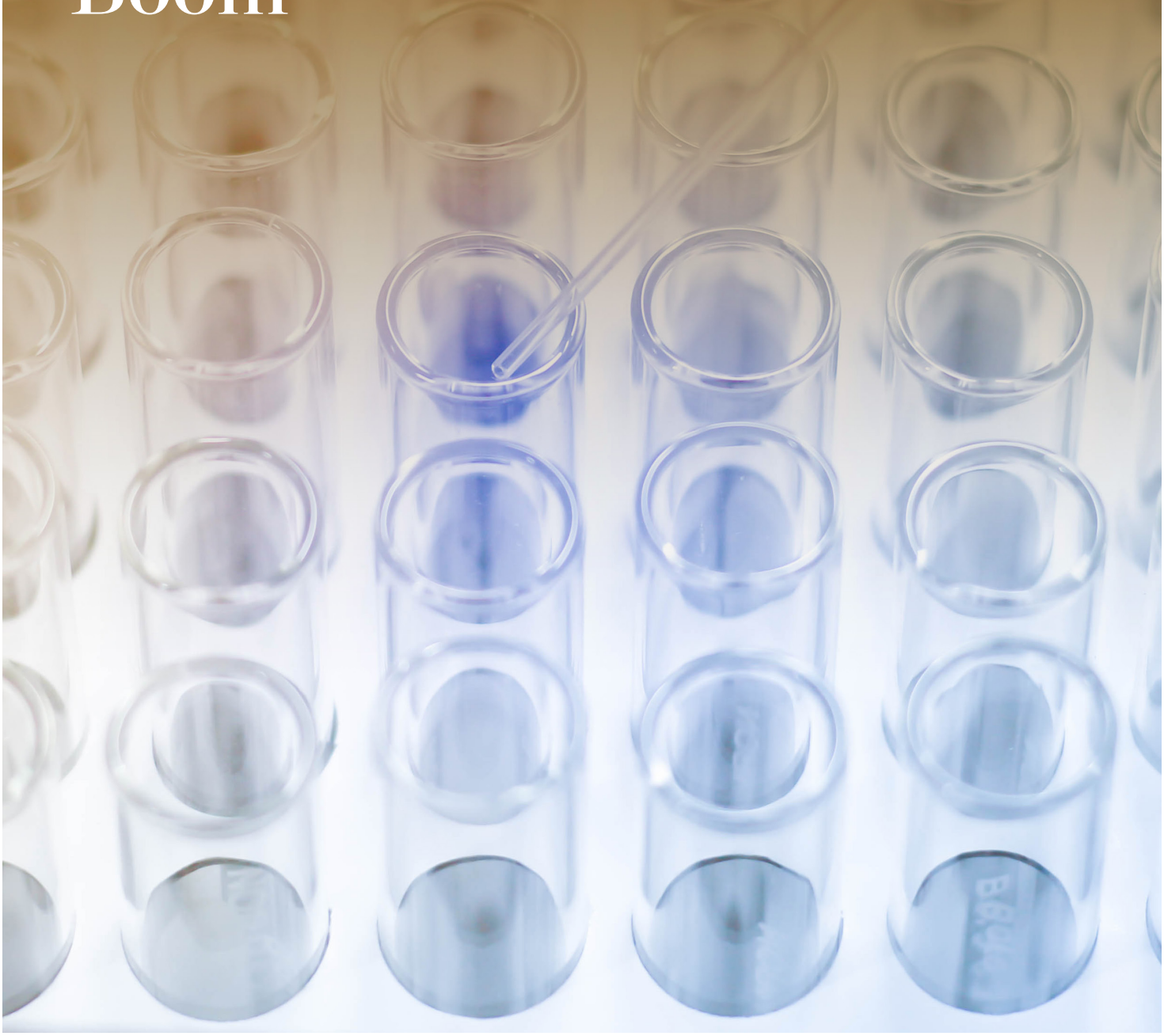
WSJ PRO VENTURE CAPITAL

Tracking The Life Sciences Boom



Tracking The Life Sciences Boom

Venture capital investment in life sciences companies is surging but investors are also changing their models and the sectors in which they're focusing their dollars. In this special report Brian Gormley, a seasoned journalist with WSJ Pro Venture Capital, analyzes the most important trends in the sector. The report draws on the daily reporting on investment, fundraising and trends in WSJ Pro VC. We hope you find this selection of articles a useful guide to an important area of startup investing.

This article appeared originally on April 3, 2018

Startups Return Fire Against Drug-Resistant Bugs

Biotech efforts center on precision therapies that selectively kill harmful bacteria

By BRIAN GORMLEY

Biotech companies are fighting back against drug-resistant bugs.

At least 23,000 Americans a year die from infections caused by antibiotic-resistant bacteria, according to the Centers for Disease Control and Prevention. Drugmakers are countering with a new approach designed to curb the problem.

Conventional antibiotics kill harmful bacteria and beneficial ones needed for digestion and other functions, leading to side effects and drug resistance. Startups like ABAC Therapeutics and Eligo Bioscie ce are using new technology to engineer precision medicines that destroy pathogens and leave helpful microbes unscathed.

"Precision medicine makes sense," said Lilian Abbo, associate professor of infectious diseases at the University of Miami. "You're trying to target the problem and not kill the rest of the good guys."

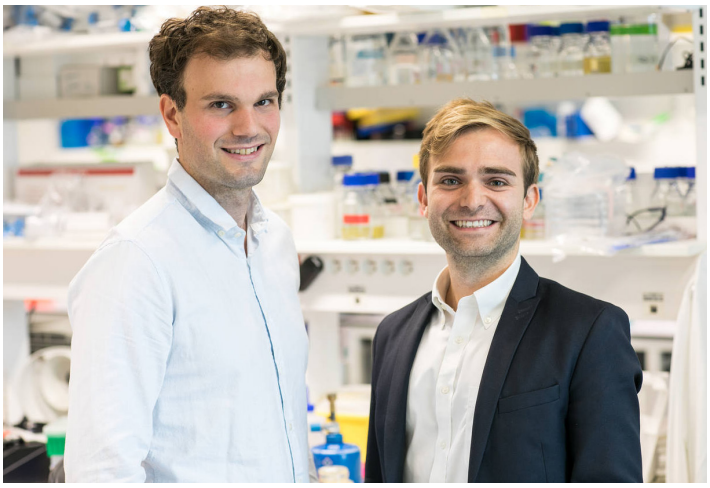
One reason to use antibiotics that kill a range of bacteria is that identifying the infection-causing bug can now be a lengthy process, taking hours to days depending on the organism and the testing technique. Clinicians use broad-spectrum agents to get an infection under control while waiting for tests to pinpoint the specific culprit.

Unlike broad-spectrum antibiotics, precision drugs kill only one type of bug. Consequently, doctors won't use them unless they know which germ caused the illness. To fulfill their promise, precision medicines will have to be paired with tests that rapidly spot specific pathogens, said Jia-Min Zhuo, an analyst with Decision Resources Group.

Precision medicine "can have broad application," Dr. Zhuo said, "if we are able to improve the diagnostics."

Proponents say diagnostics are already improving and will make precision therapy feasible.

ABAC Therapeutics, whose investors include Pontifax, is working with diagnostics companies developing tests that identify Acinetobacter and spot drug-resistant strains of this pathogen within two hours, said co-founder and Chief Scientific Officer Domingo Gargallo-Viola. Today, it takes five to six hours to identify a growing population of Acinetobacter, which causes pneumonia and other infections.



David Bikard, left, and Xavier Duportet, co-founders of Paris-based Eligo Bioscience, which seeks to treat an undisclosed gut infection by selectively eliminating pathogens with a specific gene. PHOTO: ELIGO BIOSCIENCE

Barcelona-based ABAC's first drug attacks proteins in the Acinetobacter cell wall in a novel way and has proven effective against all drug-resistant strains in laboratory tests, said Dr. Gargallo-Viola, who expects clinical studies in patients to begin within three years. The goal is to test high-speed diagnostics along with its drug in clinical trials, he said.

Biotechs are also going beyond the small-molecule compounds typically used against bacteria and devising antibody treatments that home in precisely on their targets. One of them, Visterra Inc., is developing an antibody against Pseudomonas aeruginosa, which causes lung, blood, and other infections.

Since people with these infections often have compromised immune systems, Visterra tagged a microbe-killing peptide onto the treatment to make the therapy even more powerful, Chief Executive Brian Pereira said. Waltham, Mass.-based Visterra, which counts Flagship Pioneering among its backers, expects clinical studies to launch in 2020.

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Another private company, Polyphor, seeks to vanquish Pseudomonas aeruginosa to treat pneumonia in hospitalized patients, including those who need mechanical ventilation to help them breathe. The Swiss company, now enrolling patients in late-stage clinical trials, used its chemistry capabilities to develop its drug, which targets outer-membrane proteins of the pathogen.

Arsanis Inc., which went public in November after raising funds from Polaris Partners, and others, seeks to keep ventilator patients from developing pneumonia from Staphylococcus aureus. Its product, a combination of two antibodies, could make the pathogen harmless by neutralizing its toxins.

"You're telling Staph, 'Produce all the toxins you want,'" said Chief Development Officer David Mantus. "You're essentially rendered benign."

Waltham-based Arsanis is conducting mid-stage clinical trials with a goal of slashing infection rates in ventilated patients at high risk for Staphylococcus aureus pneumonia.

Precision medicine developers are benefiting from research revealing genetic differences among bacteria. Paris-based Eligo Bioscience seeks to treat an undisclosed gut infection by selectively eliminating pathogens with a specific gene.

Eligo, whose investors include Khosla Ventures, targets these genes through drugs that deliver a therapeutic payload to specific bacteria. The startup, which was able to remove strains of antibiotic-resistant bacteria in mouse studies, seeks to launch clinical trials in 2020, CEO Xavier Duportet said. ■

This article appeared originally on March 26,, 2018

Go With the Gut: Intestinal-Focused Startups Win More Funding

'G.I.' research advances propel funding of drugs, tests for gastrointestinal treatments

By Brian Gormley

These venture investors are using their gut instincts.

Funding of intestinal-disease treatments jumped to record levels last year, spurred by advances enabling new ways to tackle common gut conditions.

Startups raised $903.7 million in 2017 across 26 financing rounds, according to market tracker Dow Jones VentureSource. Several large investments helped last year beat the previous record of $704.5 million reached in 2015.

They included a $100 million Series B infusion into Allakos Inc., a San Carlos, Calif., drug developer targeting diseases such as eosinophilic gastritis, an inflammatory condition that causes diarrhea, pain and other symptoms.

Several intestinal diseases represent giant markets, including colorectal cancer and irritable bowel syndrome. Investors are financing new diagnostic and therapeutic technologies for these and other gut conditions.

"The GI space has really taken off," said Leslie Williams, chief executive of biotechnology startup ImmusanT Inc.

ImmusanT targets celiac disease, which affects as many as 1 in 141 Americans, according to the National Institute of Diabetes and Digestive and Kidney Diseases, or Niddk. Celiac patients mount an immune response to gluten found in wheat, rye and barley. This harms the small intestine and can lead to long-term complications such as malnutrition.

Today, patients often turn to gluten-free diets to manage celiac disease. But since gluten is common, avoiding it completely is difficult, even with the rise of gluten-free foods. ImmusanT's Nexvax2 could protect against inadvertent exposure.

Nexvax2, is designed to re-educate the immune system so it doesn't respond to gluten. Cambridge, Mass.-based ImmusanT expects to study the vaccine in Phase 2 clinical trials this year as an adjunct to a gluten-free diet.

Last year, ImmusanT raised $40 million in Series C financing from ARCH Venture Partners and Vatera Healthcare Partners.

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Investors also see unmet need in irritable bowel syndrome, a chronic condition of the large intestine. About 12% of Americans have IBS, according to the Niddk.

San Francisco-based OrphoMed Inc., which raised a $39 million in a Series A last year from New Enterprise Associates, Takeda Ventures, and others, is developing a drug for a form of the condition, IBS-D, marked by abdominal pain and diarrhea.

Today, patients typically initially take Imodium to control the diarrhea. OrphoMed's medication could relieve pain as well as diarrhea. IBS-D patients develop abdominal pain because of hypersensitive intestinal tissue. When this tissue contacts food, it rapidly expels it, causing diarrhea, according to CEO Nikhilesh Singh.

OrphoMed's drug soothes the tissue to control the pain, which in turn leads to control of diarrhea, according to Dr. Singh. The drug, which acts on two receptors in the gut and doesn't affect the central nervous system, is in Phase 1 studies and is expected to enter Phase 2 later this year or early in 2019.

One intestinal disease, colorectal cancer, is highly treatable when detected early. But many people resist the gold-standard screening tool, colonoscopy, and other established screening options, such as stool DNA testing. Colorectal cancer is the fourth most-common cancer, according to the National Cancer Institute.

About 1 in 3 adults aged 50 to 75 haven't been tested for colorectal cancer as recommended, the Centers for Disease Control and Prevention said in 2013.

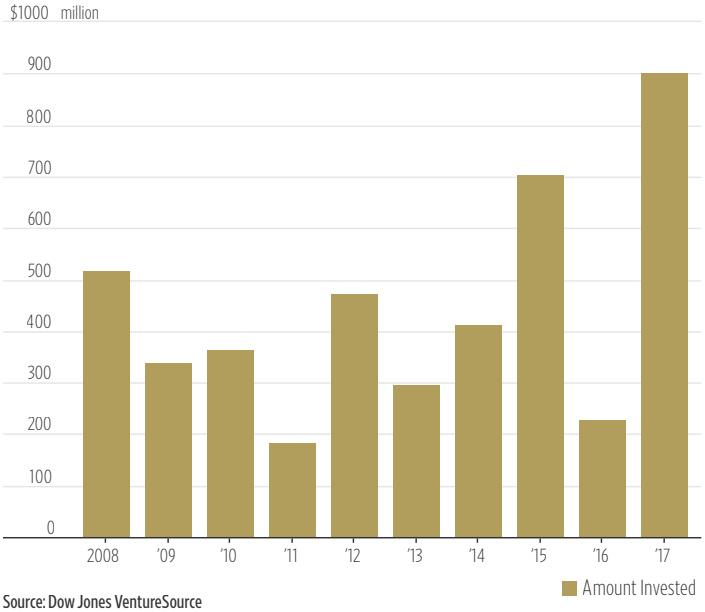
Startup Beacon Biomedical Inc. is launching a blood test to detect the disease. The test, performed in its labs, examines three tumor-associated protein markers. Clinical trials showed the test is 94% accurate in detecting all stages of colorectal cancer, according to Chief Executive Donald Weber.

Patients testing positive would still need a colonoscopy to determine if they have cancer. But the test tells patients "you're at risk, and you should get your colonoscopy," Mr. Weber said.

Phoenix-based Beacon has raised $800,000 in seed financing from Hylascent Ventures and individuals. ■

Gut Checks

Venture investors committed a record amount to gastrointestinal-disease treatments last year.



Source: Dow Jones VentureSource

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This article appeared originally on March 20, 2018

Race for a Cure Spurs Biotechs to Rely More on Nonprofit Backers

Investment arms of foundations help startups with funds, expertise—and access to patients

By BRIAN GORMLEY

As biotech startups race to find a cure for rare and other diseases, they're looking beyond venture capitalists for a leg up.

Increasingly they turn to philanthropists, private foundations and other nonprofits—not only for capital and expertise, but also for a crucial link to patients facing down these diseases.

Although such groups invest alongside venture capitalists, reaping profits is secondary to promoting their cause.

Foundations' growing involvement in the startup ecosystem is becoming more important to biotech companies, especially ones developing drugs for rare conditions that have few or no approved treatments.

"This is going to be a model going forward for a lot of biotechs," said Gini Deshpande, chief executive of NuMedii Inc.

NuMedii's backers include Three Lakes Partners, which formed in 2016 to help companies targeting the rare lung disease idiopathic pulmonary fibrosis. Other new investment groups include JDRF T1D Fund, a venture philanthropy dedicated to diabetes research.

Finding patients for clinical studies of rare-disease medications is often a struggle for startups because conditions affecting few people are often misdiagnosed initially. In devising treatments for smaller populations, companies must understand how a disease affects individuals differently and the specific issues that matter most to patients.

That issue is magnified in an era where drugmakers face growing pressure to justify high prices.

Foundations and other patient groups are plugged into disease communities and can connect companies with clinical experts and people interested in joining drug studies.

Providing grants for basic research isn't new for foundations. But in recent years, several have found it useful to create venture philanthropies to extend their efforts, said Jean-Marc Quach, CEO of the investment arm of the nonprofit Alpha-1 Foundation, which is focused on a genetic disorder that causes lung and liver diseases.

Alpha-1 helps provide startups with disease experts who can brainstorm with management preparing for clinical trials. And since Food and Drug Administration officials want to hear more from patients, an Alpha-1 foundation executive who has the alpha-1 disorder recently joined a company in its meeting with the agency, Mr. Quach said.

Companies the group backs must be financially sound, but the soundness of their therapeutic strategy is most important, he said. It has funded nine biotech companies, including Apic Bio Inc., a gene-therapy startup that raised seed financing in August.

Through their resources disease groups seek to remove obstacles to developing drugs in their disease and draw more into companies into the field. That is the aim of Three Lakes, a Northbrook, Ill.,-based investment and philanthropic firm funded by individuals who have lost a family member to idiopathic pulmonary fibrosis, a rare disease of the lungs.

Foundations and other philanthropic groups aren't as financially driven as venture firms, but that doesn't mean they lack urgency.

"We are not going to sit by the sideline if we believe the operating process is being inefficient," said Ken Bahk, managing director of Three Lakes.

For startups, having philanthropic investors helps to keep up the pressure to discover new treatments. That was top of mind when Myonexus Therapeutics Inc. raised seed financing last year with the Jain Foundation, a nonprofit looking to cure limb-girdle and other muscular dystrophies.

As Myonexus CEO Michael Triplett puts it, "It helps keep everybody focused on the purpose of the company—delivering solutions for patients." ■

This article appeared originally on March 6, 2018

Shakeout Looms for 'Digital Therapeutics' Market

Bets pile up on software aiming to conquer illnesses, from diabetes to drug addiction

By BRIAN GORMLEY

Venture capitalists are betting that software will help conquer chronic diseases.

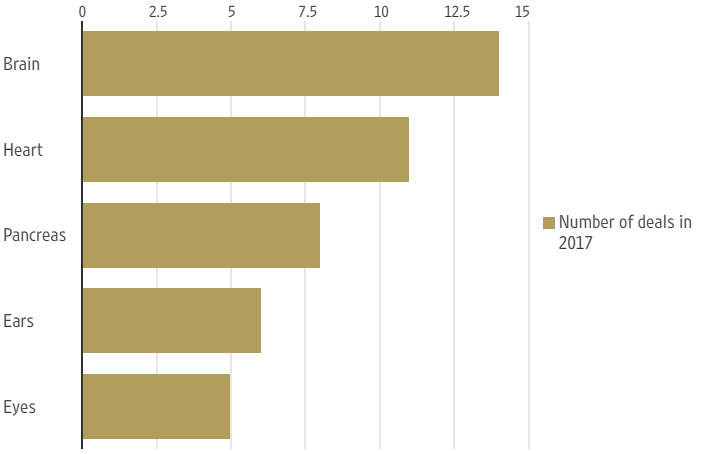
Companies are creating digital tools that treat disease and augment existing therapies. Interest is rising as health care shifts away from fee-for-service and toward a value-based system that rewards improved outcomes, a move that encourages use of technology to help patients better-control diseases outside the hospital.

World-wide, the "digital therapeutics" market will rise to $9.4 billion by 2025 from $1.7 billion in 2016, according to research report last year by Grand View Research.

To capture that opportunity, companies will need generate data showing they have the strongest outcomes.

The Programmable Body

Venture investors supported a record number companies developing software for various health categories last year



Source: Dow Jones VentureSource

But in the coming years there will be a shakeout in which the best startups get acquired or establish themselves as sustainable businesses, said Victor Camlek, an analyst with Frost & Sullivan.

"This is all exciting and all new, but it's going to have to go through the rigor of proving that it does make a difference," Mr. Camlek said.

Brain diseases are seeing the most striking jump. From 1999 through 2012 there was almost no activity. In 2013 brain-software deals increased to five, from two in 2012, and startups completed four deals in 2014, 10 in 2015, nine in 2016, and 14 last year, according to VentureSource.

Federal funding for neuroscience and the emergence of powerful, low-cost digital platforms are leading entrepreneurs to create digital therapeutics for the brain, said Zack Lynch, general partner of Jazz Venture Partners.

Since the brain is an electrochemical system, said Mr. Lynch, digital tools that strengthen neural networks can be effective in treating neurological conditions, especially when married with medication.

Jazz-backed Pear Therapeutics Inc. takes that approach. In September it received Food and Drug Administration clearance for its first product, reSET, a digital treatment for substance use disorder. The product, which includes a smartphone app and a clinician dashboard, teaches user skills to help patients abstain from alcohol, marijuana, cocaine and stimulants.

A study of patients receiving standard face-to-face counseling, or a reduced amount of face-to-face therapy plus reSET, found that Pear's product more than doubled the rate of abstinence, according to the company.

Software may also enable wider use of underused therapies. Education, behavioral-health support and physical therapy can help people with knee and back pain, but these services often don't get delivered, said Daniel Perez, co-founder and CEO of Hinge Health Inc. Doctors have little time to teach patients, and traveling to physical therapy forces people to miss work or family time, he said.

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Hinge delivers digital resources. Patients, who get Hinge through their employer or health plan, receive a tablet computer and wearable sensors. Sensors track body movements and guide users through exercises. Hinge health coaches support patients, and the company's system tracks their usage. This helps people stick with the program.

"Because you know that I know if you've done it or not, that boosts adherence," Mr. Perez said.

Meantime, Tueo Health Inc. wants to help children with asthma maintain good control over their condition. Its system includes sensors installed in the child's mattress that track parameters like heart and respiratory rate. San Francisco.-based Tueo also provides access to asthma coaches.

Tueo, whose investors include Launchpad Digital Health, plans to publish a study regarding the ability to use the sleep monitors' output to assess asthma control and predict adverse factors, co-founder and CEO Bronwyn Harris said.

"In digital health's early days, it wasn't always evidenced-based," Dr. Harris said. Today, he added, "You need results." ■

This article appeared originally on January 19, 2018

Gormley's Take: Quiet Consolidation Coming to Digital Health

As industry matures, venture-backed companies consider opportunities to acquire weaker startups

By BRIAN GORMLEY

Exit activity could pick up in digital health this year—not that the deals will be what investors originally had in mind.

Digital-health venture funding has flourished in recent years, even if exits haven't been as hot lately. In medical software and information services, just a single venture-backed company went public last year, down from three in 2016, according to market tracker Dow Jones VentureSource. And acquisitions dropped to 22 last year from 26 in 2016.

IPOs aren't a good option for most digital-health startups because many are small and have emphasized growth over earnings, said Michael Balmuth, managing partner of SV Health Investors. Long term, the outlook for strategic acquisitions is much better because corporations need growth and will use M&A to bulk up in areas like analytics and medication adherence, he said.

But many startups will falter before capturing acquirers' attention. With digital health maturing, startups with sustainable offerings and strategies to overcome challenges such as long sales cycles are separating themselves.

"There's going to be a lot of road kill in digital health," Mr. Balmuth said. "There will be a flight to quality."

For many digital-health companies the problem isn't underperformance but rather a failure to grow, said Matt Karls, a partner with Echo Health Ventures. Abundant capital has enabled some companies to raise funding at unjustified valuations.

This creates opportunity for venture-backed companies to buy competitors or startups with complementary technology. With little or no fanfare, many startups will fold into other startups, a natural outcome of a maturing market, he said.

"You're going see a lot more of that in the next year, quiet consolidation," Mr. Karls said. "It's often a difficult thing for the companies involved, but it is a healthy thing to happen." ■

This article appeared originally on February 21, 2018

Long Neglected, Rare Muscle Diseases Capture Investors' Attention

Recent scientific progress and large deals raise the prospect of a turnaround in a quiet sector

By BRIAN GORMLEY

Startups tackling rare muscle diseases have never received heavy interest from venture-capital investors. Now, thanks to recent advancements in the sector, more are grabbing investors' attention.

Investment in muscle conditions such as muscular dystrophy peaked at more than $438 million in 2015 before sliding to about $193 million in 2016 and $157 million last year, according to market tracker Dow Jones VentureSource.

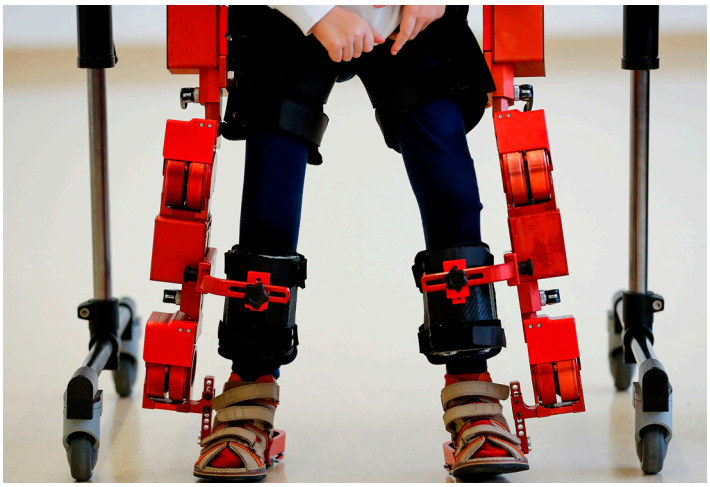
But a better understanding of rare muscle diseases and progress in fields such as gene therapy have opened avenues into treating conditions that once seemed intractable.

Funding in the sector is off to a strong start this year. Scholar Rock Inc. secured a $47 million round, and Expansion Therapeutics Inc. launched with more than $55 million in financing. Late last year Exonics Therapeutics Inc. picked up $40 million and Myonexus Therapeutics Inc. collected $2.5 million in a seed financing that is expected to be a prelude to a larger Series A.

The field "has been somewhat neglected," Scholar Rock Chief Executive Nagesh Mahanthappa said. "But there is growing interest."

Interest is growing along with the success of some drugmakers. Solid Biosciences Inc., a developer of Duchenne muscular dystrophy treatments, went public last month at $16 and now changes hands around $25. Another, Audentes Therapeutics Inc., which targets muscle conditions such as X-linked myotubular myopathy, has seen its shares more than double to $33.51 since going public in July 2016.

That same year publicly held Sarepta Therapeutics Inc. won accelerated Food and Drug Administration approval for Exondys 51, the first drug for Duchenne muscular dystrophy, a genetic disease causing progressive muscle degeneration and weakness. DMD occurs because of a lack of dystrophin, a protein that helps keep muscle cells intact.



A better understanding of rare muscle diseases and progress in fields such as gene therapy have opened avenues into treating conditions that once seemed intractable. Above, a boy diagnosed with spinal muscular atrophy. PHOTO: PAU BARRENA/AGENCE FRANCE-PRESSE/GETTY IMAGES

Sarepta's product, Exondys 51, enables cells to skip over a section or exon in the dystrophin gene. Sarepta gained approval because of an increase in dystrophin protein seen in skeletal muscle of patients treated with the therapy.

In approving the drug, regulators required that Sarepta conduct additional trials to confirm efficacy. Sarepta is in discussions with the FDA about those studies, according to a spokesman. Shares of the company, which launched Exondys 51 in 2017, have more than doubled over the past year.

Steve Brozak, managing partner and president of WBB Securities, said he expects those studies will show efficacy and help demonstrate how to validate the benefits of drugs in this patient population.

Cambridge, Mass.-based Exonics is developing a gene editing-based therapy for DMD that makes a single cut to the DNA and allows the cell to repair the cut. In the process, the cell also repairs the mutated gene and enables production of a functional protein, according to the company.

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Meanwhile, New Albany, Ohio-based Myonexus targets limb-girdle muscular dystrophies, a group of diseases causing weakness and wasting of muscles in the arms and legs. Progression of the disease forces some patients to use a wheelchair.

Continuing research from Nationwide Children's Hospital, Myonexus is developing gene therapies designed to cause therapeutic proteins to be expressed in muscle cells, according to Chief Executive Michael Triplett. These are meant to be one-time treatments, he said.

Another emerging approach is to target RNA. Expansion Therapeutics develops small-molecule drugs targeting RNA to treat diseases such as myotonic dystrophy type 1, or DM1, the leading cause of adult-onset muscular dystrophy.

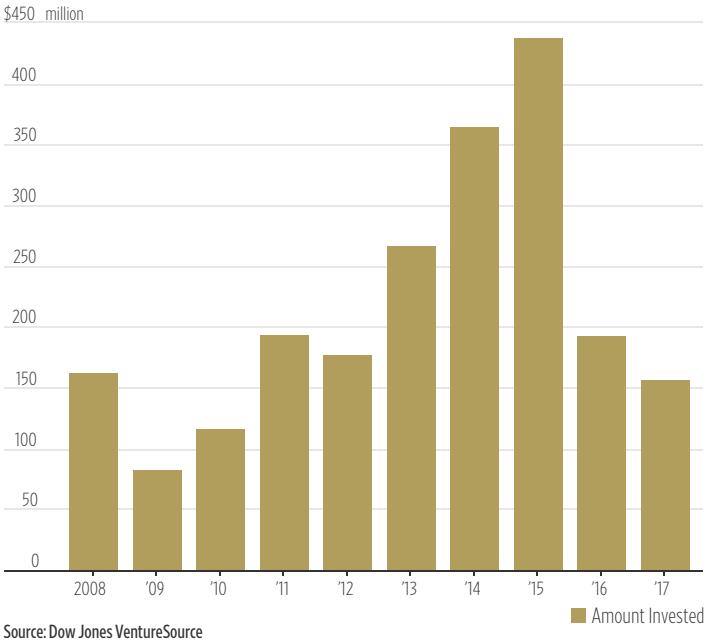
Another recent breakthrough in rare muscle disorders was the 2016 approval of Spinraza, the first drug for spinal muscular atrophy, a genetic disease affecting muscle strength and movement.

Scholar Rock is developing a different type of spinal muscular atrophy treatment. Its drug targets the latent form of myostatin, which is primarily expressed in skeletal muscle cells to inhibit muscle growth.

Cambridge-based Scholar Rock aims to move the drug into clinical trials to test its ability to improve muscle strength and motor function. ■

Muscled Out

Venture investment in muscle-disease treatments fell in each of the past two years.



Source: Dow Jones VentureSource

This article appeared originally on March 2, 2018

Gormley's Take: High Stakes for Next-Generation Cell, Gene Therapy

New products could overcome limitations of existing treatments

By BRIAN GORMLEY

After a landmark year of breakthroughs, venture capitalists are already betting on next-generation cell and gene treatments. This week, Senti Biosciences secured $53 million, while Rubius Therapeutics and Generation Bio each revealed $100 million rounds.

Senti's synthetic biology could make cell and gene therapies more controllable and effective. Generation Bio aims to enable gene therapy to be given repeatedly—today it can only be administered once, thanks to the immune system's defenses. And Rubius is creating a new class of red blood cell products that could treat several diseases.

These startups are new and have yet to enter clinical trials. But investors want them to move fast. Rubius backers urged the company to fill out its pipeline so it could quickly move additional products into clinical trials if the first one shows promise, Executive Chairman David Epstein said.

Investors are chasing the success seen with some companies recently. Gilead Sciences Inc. bought CAR-T company Kite Pharma Inc. for about $11 billion in October, and then purchased startup Cell Design Labs Inc. in December. Celgene Corp. agreed to buy CAR-T company Juno Therapeutics Inc., for about $9 billion, in January, and Spark Therapeutics Inc.'s market value stands at $2.2 billion.

If this next crop of startups succeeds they could deliver similar results. But not all of the recent news has been good. Gene-therapy company Dimension Therapeutics Inc. went public at $13 in 2015 and, after seeing disappointing clinical data, merged with Ultragenyx Pharmaceutical Inc. last year for $6 a share.

Startups are raising large rounds in hopes of building sustainable companies that can survive a hiccup or two. Better to do so now, while investor interest remains hot. ■

Meet the Author

BRIAN GORMLEY is a Special Writer covering life sciences for WSJ Pro Venture Capital, based in Boston. He joined Dow Jones in 2004.

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