

In this issue:

- Beyond the obvious
- A pipeline of breakthrough drugs
- Insanity prevails

Secrets of the “Second Brain” revealed

Eoin Treacy, Investment Director



“The brain, the masterpiece of creation, is almost unknown to us.”

So said the Danish anatomist Nicolaus Steno in 1669. Steno deserves his place in history as someone who helped advance humanities understanding of perhaps the most important and complex living thing in the known universe: the human brain.

That may sound like hyperbole, but it's emphatically not. We shouldn't forget that we're all born with what amounts to a supercomputer in our skulls, capable of building everything

in the modern world, from the modern medicine industry to cars that drive themselves to great works of art, music and comedy.

We may never comprehend the full complexity of the brain. But our understanding has come a long way in a relatively short period of time. It wasn't long ago that the world's best minds knew nothing about the brain. Aristotle described the brain as a kind of radiator, with all “thinking” being done in the heart. It's only in the last two centuries that neuroscience has developed.

The point being, it's possible for science to dismiss... or completely misunderstand... parts of the

human body that are vital to our health. The topic of this month's issue is one such example. It's been called the “Second Brain”. It's a part of the body that is as complex, and – as we're discovering – just as important to our wellbeing. But historically it's been neglected by research.

That's all changing now. As R&D efforts ramp up, treatment of the Second Brain could yield some incredible new treatments, to ailments as diverse as X and Y... and even to old age itself.

With that in mind, I want to introduce you to one of the only “pure plays” on this burgeoning industry I know of. It's a firm with a great pedigree, a highly



respected senior leadership team and some high potential drugs in its pipeline.

We'll come to that shortly. First, let us discuss the mysteries of the Second Brain. My own understanding of this area has been something of a personal journey. I thought I'd share that story with you, because ultimately medical breakthroughs like this *are* highly personal as well as financially lucrative. Let me explain.

after our second daughter, so we lost it all, but then we moved to the US and I topped out at 215lbs or 97.5kg about two years ago.

I finally had to sit down and figure out why my weight was seesawing so wildly with each successive peak getting heavier and heavier. I knew that if I did not learn how to control my diet I would end up with health problems I certainly do not want. My cholesterol was already dangerously high and I was a

that is thirsting for a sugar rush. I had transformed my personal microbiome into a junkie, which was willing to pull any deception in order to get its fix. I knew then that if I wanted to lose the weight, and more importantly keep it off, I would have to conquer my gut and rehabilitate my microbiome.

It wasn't my liver or pancreas, heart or brain that was craving chocolate it was my "Second Brain", the billions of microbiota that make up a significant part of my digestive tract. Some of these bacteria, viruses and fungi thrive on sugar which contributes to it being such an addictive substance. But importantly when these bad microbiota thrive they crowd out the probiotics, which contribute to so many health-inducing results.

I had transformed my personal microbiome into a junkie, which was willing to pull any deception in order to get its fix.

When small is BIG

I've always struggled with my weight. I was a sturdy child but when my parents relented and bought my brothers and I an Amstrad 464, we stopped going outside to play and instead camped out to play *Harrier Attack* and *Bridge It*. We were in our element. It was about a year later I picked up the moniker "Battle of the Bulge".

When I took up rowing I lost it all again, but when I gave up rowing I put it all and more back on. When I was backpacking in Australia I lost it all, but when I started travelling for Bloomberg on expenses I ballooned. I started going to the gym so I lost it all again. Then I got married and it looked like both of us were pregnant. We both converted to the Weight Watchers religion

prime candidate for diabetes and heart issues.

The answer was simple enough, cut out sugar. I'm a demon for chocolate so I have tended to go cold turkey when I want to lose weight because I can't have just one.

However, what I noticed over time was that whenever I gave up chocolate my alcohol consumption went up. I did some research and realised this is not a coincidence. My body was dependent on heightened sugar consumption and by cutting out chocolate it simply shifted my craving on to another ready source of sugar – beer.

Once I realised it was my body making these requests for sugar it dawned on me that it is not my body but what is inside it

The "Second Brain" in your stomach could be the key to long-lasting good health - and huge profits

The microbiome is a story that's all about inner space. But unfolds into an epiphany for how we perceive the world and what's going on in it.

In short, there is another world we hardly spare a moment to think about until something goes wrong with it.

The human body is home to trillions of bacteria, fungi and viruses and without them we would be unable to function. In fact, each of us carries around 2.5lbs of them. That's a lot of bacteria when you consider they are microorganisms.



The human race is expected to hit peak population of around 12 billion people sometime this century but our bodies are home to trillions of microorganisms. A handy way to think about the role they play in our lives is they have much the same effect on their environment that we do on ours.

Perhaps describing the microbiome as “important” is an understatement. Try “crucial to every aspect of our health and wellbeing” and you’re closer to the mark.

The 1,000 different species of microbe in the gut, lung and

function of the immune system and immune-mediated inflammation, especially locally. When the human microbiota is dysbiotic, the body can be left more susceptible to infections, metabolic disorders, allergies, autoimmune disease, inflammation and other conditions.

Modern research into the microbiome is probably a good century or two behind neuroscience.

The human microbiota consists of 10-100 trillion symbiotic microorganisms (including bacteria, fungi and viruses) that reside in every person and mostly hang out in our guts. Here’s where it really gets to be fun. We share about 8% of our microorganisms with other people. The other 92% are individual to us in one regard or another, which means our individual microbiomes are as unique as we are.

If you want to think about overpopulation, the number of bacterial cells alone are thought to outnumber the body’s own cells by a ratio of ~3 to 1. The number of neurons in the gut is greater than in the spinal column at about 100,000,000 so it is often referred to as the “Second Brain”. Just like with the brain in previous centuries, our understanding of the microbiome is fairly rudimentary. We’re only just understanding just how important it is.

other areas, (including skin and hair), with close to 7,000 different strains, or subtypes, found in the gut mean that the Second Brain is dealing with a political balancing act. The colonies of inhabitants that call our gut home have an inordinate effect our everyday health.

Many of those colonies are responsible for key biological processes, most notably digestion and immune function. The gut microbiome is especially important in efficiently digesting complex carbohydrates in the diet. Many polysaccharides and oligosaccharides are broken down by enzymes produced by the microbiome rather than those produced in gut tissues.

As a Cowen and Co report I came across recently put it:

The interaction between the immune system and the microbiome is thought to be key in the development, regulation and overall

Don’t worry I had to look up what dysbiotic meant too. The definition of dysbiosis is basically the condition that evolves when the bad bacteria gain the upper hand and most particularly contributes to the development of irritable bowel syndrome (IBS) and autoimmune reactions like arthritis.

The Human Microbiome Project

To go back to my Second Brain analogy, modern research into the microbiome is probably a good century or two behind neuroscience.

Like I said, we’re starting to realise that the microbiome may well be as important as the brain... but that understanding is still more vague than specific.

From an investment perspective that’s exciting. This is an area of medicine that’s still on the frontier of our comprehension. As we discover more about how the microbiome affects our health, the opportunities for new medical breakthroughs are enormous.

Still, research has identified many ways in which the microbiome



impacts our health. These go far beyond “obvious” ailments like IBS, stretching all the way from our entire immune system to mental health and beyond.

The microbiome was first identified in the 1880s and over the course of the next century progressively more of the microbes that call humans home were identified. But it was only

In all they collected 14.23 terabytes of information.

The project has now moved into its second phase, which is focused on identifying exactly how the microbiome affects our health. The data is being collated into longitudinal studies, which will in all likelihood form the basis for major healthcare breakthroughs over the coming decade.

seed our immune systems.

Getting children off to a good start with their microbiomes represents a beachhead in the battle against allergies which are growing in prevalence all over the world.

IBS

Inflammatory bowel disease affects about 1 million people in the US. When Mrs Treacy had a part-time job as a translator at a Chinese health clinic in Bethnal Green, while she was pursuing her MBA, the number one complaint was IBD. As the American Centers for Disease Control and Prevention has to say on the subject, “The cause of IBD is unknown, and until we understand more, prevention or a cure will not be possible.”

That’s not an encouraging statement but it highlights just how important this kind of work is.

IBS is part of a number of number of gastrointestinal problems that many people will be familiar with such as ulcerative colitis and Crohn’s disease and for all the wrong reasons.

There is a realistic possibility that imbalances within the gastrointestinal tract between the good and bad microbes is the root cause behind these kinds of problems.

Diabetes

Type-2 diabetes has reached pandemic proportions over

The data will in all likelihood form the basis for major healthcare breakthroughs over the coming decade.

with the invention of genetic sequencing and big data that the full scope of the microbiome was appreciated.

In fact, it was not until 2007 that the scientific community turned its attention to the sector as a serious area of study. The Human Microbiome Project began in 2008 and ended in 2013 and was the first concerted effort to characterise the full extent of what has come to be known as the human microbiome.

In seven years, researchers harvested microbial communities from 300 healthy individuals, focusing on the nasal passages, oral cavity, skin, gastrointestinal tract and urogenital tract. The aim of the project was to ascertain whether there is a core healthy microbiome that could be used to guide further study into what is required to create a healthy gut environment.

Additionally, they are focusing on three main fields of study that represent high probability targets for drug and treatment discovery. These are: pregnancy and preterm birth; onset of inflammatory bowel disease; and onset of type 2 diabetes.

The reasons for these three choices are simple enough. They’re the most obvious – but not only – manifestations of how the microbiome affects our health.

In the womb

When we are within the womb we begin to develop our microbiome courtesy of our mothers. During birth and immediately afterwards we are exposed to the microorganisms present both inside and outside our mother’s body while breast milk represents a treasure trove of biological data that helps to



the last decade, which has represented a boom for companies like Novo Nordisk which dominate the market for therapies.

Novo has a handy business model which revolves around increasing dosages as the patient ages and the severity of the condition deteriorates. That leads to outsized profits but it represents an unsustainable model for treating large numbers of people much less affording the escalating cost of treatment. As a Deutsche Bank report on the topic put it:

It should also be noted that diabetes is a progressive disease, where insulin resistance and ongoing beta cell death result in the patient progressing from a single oral therapy, to multiple oral therapies, to finally requiring insulin. At the time of diagnosis, only about 50% of pancreatic beta-cell function would remain, and this is estimated to continue to decline at an average of 4% a year. About 50% of patients will require more than one anti-diabetic medication by three years after their initial diagnosis, and this increases to 75% at nine years.

Exploration of the microbiome represents an uncharted path for the development of diabetes medication and represents a compelling hope for overcoming the spiralling cost of treating this disease, which is growing everywhere but most especially in emerging markets as living standards rise to levels where

physical activity declines.

Beyond the obvious

But as I said earlier, the story doesn't end there. Beyond the more obvious impacts the microbiome has on our health, lie a plethora of wider avenues

including self-injury.

** On a separate two-day period, another spike in H. parainfluenzae correlated with another increase in self-injurious behavior – but this time without any change in stool consistency or obvious*

It was estimated in 2000 that autism effected 1 in 150 children in the US – recent estimates now say it is as high as 1 in 45.

for discovery... each of which could lead microbiome research companies to new lucrative breakthroughs.

Take autism. Here again there are interesting initial signs that the microbiome plays an integral part in how this syndrome both develops and persists. Here is a section from a report by Autism Speaks:

All of the daily stool samples from the child with autism contained four organisms that earlier research had associated with autism. These included Sarcina ventriculi, Barnesiella intestihominis, Clostridium bartlettii, and Clostridium bolteae. By contrast, none of these bacteria appeared in the stool of the unaffected sibling.

** The bacterium Haemophilus parainfluenzae appeared in the stool of the child with autism during a three-day period when the child experienced GI pain, diarrhea and a spike in challenging behaviors*

signs of GI pain.

The heartbreak of discovering one's child lies somewhere on the autism spectrum is unimaginable for those of us who have not had to deal with it, but it is a subject that is gaining progressively more attention – not least because the incidence of autism in children is trending higher. It was estimated in 2000 that autism effected 1 in 150 children in the US – recent estimates now say it is as high as 1 in 45.

On this topic, I came across an interesting report from the Harvard College Global Health Review that's worth sharing with you:

Many scientists theorize that other factors may also be responsible for the increasing rates in post-industrial countries. Some claim that about one third of ASD is due to immune dysregulation during pregnancy. That is, anything that causes an inflammatory response in the pregnant



mother, such as infection or an immune disorder, may expose the fetal brain to inflammatory signals and disrupt development. For example, mothers with celiac disease have an increased chance of autism by 350 percent, while those with rheumatoid arthritis have an elevated risk of 80 percent.

Pharmaceuticals have been developed to treat some of the symptoms of autism, but none the cause – should a company develop a microbiome treatment for it they shall have no competition.

Drawing this together, it has been proven that the bacteria in our guts are capable of producing neurochemicals which affect mood. These micro-organisms produce chemicals like dopamine, serotonin and gamma-aminobutyric (GABA), all of which have proven effects on mood. Here is an important quote from a New York Times article:

“It has enormous implications for the sense of self,” Tom Insel, the director of the National Institute of Mental Health, told me. “We are, at least from the standpoint of DNA, more microbial than human. That’s a phenomenal insight and one that we have to take seriously when we think about human development.”

In very simple terms we exist in a carefully balanced symbiotic relationship with billions of microbes. When everything is going well, we live a long and healthy life. However, when

that balance is upset we become susceptible to all manner of life-altering afflictions which modern medicine has difficulty treating.

It’s even more important than

number of potential treatments.

That is equally true today.

The kind of business model it follows is referred to

The CEO Daphne Zohar is one of the most influential women in biotech.

that though because of the compounding effect an out-of-kilter microbiome can have on mood. It is very hard to adopt a better lifestyle if our brains aren’t getting the positive feedback loop from happy microbes in our guts. Comfort eating, lethargy, depression and obesity are all interrelated functions of a wider ecosystem where the microbiome plays an important role.

It really does all come back to Hippocrates’ maxim “Let food be thy medicine and medicine be thy food.”

The frontier of medicine and finance: how to claim your stake in this new industry

Which brings me to my recommendation on how to invest in the microbiome.

It’s a quality company with world-class research talent, major partnerships with well-funded pharma firms and an innovative business model. The business was founded in Boston in 2001 as a highly diversified biotechnology company investing in a large

as “intellectual property commercialisation”. That means it goes to the people who are the best in their field in the world and helps them to commercialise their ideas. That is why taking a look at the star-studded board is so important.

The CEO Daphne Zohar is one of the most influential women in biotech according to publications like The Boston Globe and Boston Business Journal. She was named one of the MIT Technology Review’s 35 under 30 to watch in 2010 because of the company she built, which is developing medicines at the interface of the brain, gut and immune system.

Her co-founder is Robert S Langer is an institute professor at MIT, its highest accolade. He is quite simply the most cited engineer in history with more than 1,260 issued and pending patents worldwide. As his bio at MIT puts it,

He is one of 4 living individuals to have received both the United States National Medal of Science (2006) and



the United States National Medal of Technology and Innovation (2011). He also received the 2002 Charles Stark Draper Prize, considered the equivalent of the Nobel Prize for engineers, the 2008 Millennium Prize, the world's largest technology prize, the 2012 Priestley Medal, the highest award of the American Chemical Society, the 2013 Wolf Prize in Chemistry, the 2014 Breakthrough Prize in Life Sciences and the 2014 Kyoto Prize. He is also the only engineer to receive the Gairdner Foundation International Award; 83 recipients of this award have subsequently received a Nobel Prize. In 2015, Dr. Langer received the Queen Elizabeth Prize for Engineering.

That's real pedigree. Talent at the top is always important, since these are the people we're essentially backing with our money when we claim a stake. A world-class leadership team, respected across the industry, is a great sign for us as investors.

For example, Robert Horvitz is the David H. Koch Professor of Biology at MIT, but is also the company's scientific advisory board chair and received the Noble Prize for Physiology.

Raju Kucherlapati is another notable board member because he has founded two companies which have been taken over. The first was Abgenix which was acquired by Amgen, the second was Millennium Pharmaceuticals which was acquired by Takeda.

Then you have the contracts the business already has with major pharma companies. The company is already collaborating with the companies like Amgen, Shire, Merck, Pfizer, Johnson & Johnson and Novartis.

In the last week of 2017 it announced a \$5 million investment from Eli Lilly. These companies represent the aristocracy of the pharmaceuticals world and the fact they are investing is a testament to how close the potential for game-changing treatments for chronic conditions

spend all their own money on developing a potentially useless product. In effect that means they have outsourced R&D to the biotechnology sector.

The fact so many companies are collaborating with our investment candidate helps to highlight they have multiple avenues for investigation but also how narrow the field of potential investments is. Everyone wants in on the microbiome because of the potential it has to treat chronic conditions which are traditional money spinners for the pharmaceutical sector. The challenge they have is this is still a very new sector. That represents a considerable opportunity for this company.

The company I'm talking about is PureTech Health (PRTC). It's a UK-listed small cap I believe has a big future. Let's have a look at what its star-studded research team is working on... and what's got so many outside backers excited.

A pipeline of breakthrough drugs

PureTech is focusing on the brain-immune-gut (BIG) axis. It's one of the very few pure plays on the microbiome and it is listed in the UK because we tend to be more welcoming to intellectual property commercialisation businesses than the US.

Everyone wants in on the microbiome because of the potential it has to treat chronic conditions.

It doesn't end there, either. Zohar's time at MIT afforded her the opportunity to also bring other highly influential people into the fold of this evolving company.

are.

The nature of the medical sector's R&D is such that big companies are willing to collaborate with small companies so that they diversify their risk and don't

The microbiome represents one of its biggest bets and not least because it was able to get in on the ground floor of the evolving sector. The move to an initial public offering (IPO) in 2015 was in large part due to the increased



need for funding that comes from developing a next generation centre of excellence for what is a very new field in the medical arena.

Right now, it has a number of active trials underway. Two of these are in Stage 3 trials and are therefore closest to commercial utility. I'll let you know more about these in due course, but I want to focus more on the microbiome products it has in development that hold the greatest promise for the growth of the company.

PureTech is one of the leaders in the field of defined microbial consortia for auto-immune disorders, infection and immuno-oncology. It has some of the earliest intellectual property in the microbiome field and is collaborating widely to develop treatments that have commercial utility.

A simple way of describing what the firm is doing in the microbiome space is to think of a "living drug" – a dose of bacteria in pill form designed to rebalance the gut and treat specific ailments.

As the company itself puts it, it's developing a consortium of "immune-modulating bacteria that could potentially restore colonization resistance against gut pathogen and stimulate protective immune responses." These bacteria are being designed to treat *Clostridium difficile* infection (CDI) by helping the microbiome respond to the spread of the alien bacteria. The drug it is producing for this is

called Vedanta and is now in Stage 1 trials.

CDI kills as many as 30,000 people in the US annually. It's essentially caused when traditional drugs destroy the nature balance of bacteria in the microbiome. Together with MRSA it is one of the most commonly contracted secondary infections in hospitals. Solving the threat represented by this aggressive bacteria is one of the most urgent challenges of the medical professions and represents a significant prize for the company that can come out with a viable product first.

Importantly, while today fecal transplants are a growing sector, this company is pioneering a pill-based approach which has obvious benefits and much less of an icky factor compared to transplanting someone else's poop into our intestines.

One of the additional potential uses for Vedanta will be in helping to arrest the spirally incidence of allergies in developed world populations. Today, approximately 8% of children experience some form of allergy and it represents a \$25 billion opportunity cost for the US economy alone. Right now avoidance is the most common approach, gradual desensitisation is fraught with risk and potentially results in multiple hospital visits. If proven effective, the introduction of Vedanta has the potential solve for allergy in a much less problematic fashion by populating the gut with tolerant bacteria that re-educate the immune system to reclassify the allergen as friend rather than foe.

But Vedanta is just one drug PureTech has under development. It has a much wider pipeline of drugs that make it a compelling investment proposition.

Take cancer. Cancers are often experts at avoiding the immune system. The evolving immuno-oncology sector aims to re-educate the immune system so it can identify and therefore kill cancer.

Checkpoint inhibitors are one of the primary tools created by the immuno-oncology sector because they stop both cancer cells and t-cells from producing proteins that reduce their ability to identify each other. The introduction of the right kind of bacteria may help to improve the success rate of checkpoint inhibitors beyond the current 20%-30%.

In the developed world incidence and prevalence of asthma, diabetes, obesity and allergies in children is trending higher all the time. The earlier the microbiome of an at-risk child is assessed the better the chances they will have of living a happy and healthy life. With that in mind, this company is actively developing rationally defined consortia of bacteria as therapeutics to tackle what are now unmet needs for children. Its product Commense (COM101) is currently in preclinical trials.

These are developing technologies and as I said earlier, they are the company's future. They're also likely to take a while to reach the market (though successful trials could send the



firm's share price rocketing). That's why I wanted to show you the other drugs PureTech is developing, which are likely to come to market much quicker...

Obesity, autism, diabetes - PureTech is on the frontier of drug development in multiple sectors

Gelesis 100 is a pill which contains hydrogel particles derived from food which expand in the stomach by absorbing water to make patients feel fuller.

The increased elasticity of the stomach contents delays gastric emptying as the stomach contents flow into the small intestine. The particles then slow down glucose absorption and restore the mucosa and epithelial barrier. As it moves into the large intestine, water is released, reabsorbed by the body and the particles are excreted.

Gelesis is aiming squarely at the obesity and diabetes markets by controlling appetites but also by moderating the absorption of glucose, which helps to keep one's glycemic intake under control. It also smoothens out the gut, which helps with inflammation and associated maladies.

With 11% of all US healthcare spending dedicated to the treatment of diabetes, and the global anti-obesity drug market forecast to hit more than £17.5 billion by 2027, PureTech stands to gain significantly should Gelesis be successful.

The company's second Stage 3

candidate is a computer game which is designed to assess and diagnose attention deficit hyperactivity disorder (ADHD) in children, autism spectrum disorder (in collaboration with Autism Speaks), depression, Alzheimer's diseases and traumatic brain injury. Using games to act both a diagnostic tool and also as a treatment mechanism is a wholly new field and holds great promise to assist people with these ailments.

The reason these two candidates are so close to commercial reality is because they are not new chemicals and are therefore not held to the same burden of proof as conventional pharmaceuticals.

The company is also developing a TORC1 Inhibitor, which is aimed at increasing lifespan and ameliorate multiple ageing-related diseases. Generally speaking our immune systems have a decreased ability to fight infection as we age, which contributes to a higher risk of

going on and I wanted to bring this particular aspect to your attention because I intend to write more about ageing in 2018 and am actively searching for suitable investments.

PureTech could double in 2018

PureTech Health is listed in the UK with the ticker PRTC. It has a market cap of £356.1 million.

It is a development stage company so it does not have positive earnings, but that has the potential to change over the next coming 18 months as its Stage 3 trials move out of the lab and into the real world.

Importantly, the company's cash and cash equivalents figure has risen from \$8.9 million in 2013 to \$248.4 million as of 30 June 2017. This suggests the company has ample capital to conduct its research over the coming couple of years.

The global anti-obesity drug market is forecast to hit more than £17.5 billion by 2027.

cancer and declining organ function. The company has now initiated a Phase 2b trial, which will build on the Phase 2a trial that produced promising results from 500 elderly individuals.

While this is not a microbiome product, it is another example of the breadth of research

Nevertheless, the closer the company comes to commercial reality the greater the likely need for fresh capital so dilution does represent a risk.

The share hit an important low in March 2017 near 110p and is now trading in the region of 150p. The average recommendation



from the five analysts covering the share is a price of 258p over the next 12 months. I believe the potential for revenues to increase in 2018, the scope for positive news to come out with regard to its efforts to commercialise the microbiome and the increasing popularity of the subject justify a higher estimate with a doubling likely in 2018, a three-year target of 450p and five-year target of 800p. I recommend buying PureTech Health Plc below 170p with an upside target of 250p in the next 12 months.

To put that into context, if I'm right that'd be a 500%+ return in the next five years. There's huge potential here.

As with so many promising biotechnology companies the potential for a takeover cannot be ruled out which could accelerate the realisation of these estimates.

An important point to consider is the PureTech has a lot of irons in the fire with a very deep pipeline and multiple areas of investigation. Success in any of these areas, but most especially in the emerging microbiome sector, has the potential to cause a step change in the price action. That is the primary reason I am writing to you now. Gelesis is expected to reach FDA approval sometime in late 2018 and the price has potential to rise significantly ahead of a positive outcome to that decision.

The first risk, as with any small emerging company, regardless of promise, is that some other company beats them to the punch and gets a product out first. The

second risk, as discussed above, is the need for an additional capital raise which would act as a brake on price appreciation. However, the greatest risk is if clinical trials do not pan out as expected.

Nevertheless, considering the potential this sector represents, where we are talking about life-changing treatments for chronic conditions, I believe the future for PureTech Health is very encouraging.

Name:	Puretech Health PLC
Ticker:	PRTC UK
Closing price as of 06.11.2017:	150p
Buy up to:	180p
52-week high/low:	152p/110p

Figures accurate as of last market close: 08.01.2018

Performance since inception:

2015: -4.11% | 2016: -27.68% | 2017: +27.25%

How understanding the microbiome could disrupt modern medicine for the better (and help solve the NHS crisis)

James Allen,
Associate Publisher

It didn't take long, did it?

Before most heads had fully cleared from our New Year celebrations, then we were already waking up to new stories that the NHS was in crisis.

Or not.

On Wednesday, just the second day back to work for many in the country, Prime Minister Theresa May was forced to deny that the NHS was itself in a state of emergency.

Though I'm not sure too many people were buying the denials. The front pages that day splashed on the news that tens of thousands of non-urgent NHS operations and procedures in England may be deferred until 31 January, due to winter pressures.

Officials told hospitals to delay routine outpatient appointments to concentrate on emergency care.

That could affect around 55,000 operations.

Other unprecedented measures NHS England imposed included cancelling outpatient appointments and day case surgery, and deploying consultants in A&E units to assess if patients really are a medical emergency.

Some hospitals have put themselves on their most severe pressure level – an official admission that they cannot



cope – with doctors’ leaders and hospital chiefs saying this is the most intense strain the NHS has faced in decades. A doctor in Stoke even apologised on Twitter for “third world conditions” in the hospital where he works. Official figures from NHS England later confirmed the evidence from earlier in the week: that the NHS is more stretched than ever before.

This is not to beat up on the NHS. The doctors and nurses who work for them do a mighty fine job under severely strained, underfunded conditions. They are a credit to their profession.

Indeed, the service is always under great pressure at this time of year as patients put off going to their doctors and hospitals over the festive season before going to A&E.

But a wider issue is at stake, one that goes to the heart of why “NHS-in-crisis” stories are such a staple of our Google News alerts.

And it’s all to do with how we diagnose, treat and cure patients, particularly those with chronic disease.

To put it simply, the NHS and other health organisations like it spend extortionate amounts of time and money trying to treat chronic disease.

As my colleague Eoin Treacy writes, chronic disease is crippling the ability of the NHS – as well as other health services around the world – to provide effective care.

Eoin has researched the industry extensively for the latest issue of *Frontier Tech Investor*. In the issue, he notes how the cost of care balloons to treat patients with diabetes, renal failure, IBD or a host of other chronic conditions because they don’t get cured. Instead the patients get levelled off and sent home until the next time they are readmitted.

The current treatment of type 2 diabetes, for instance, which has reached pandemic proportions over the last decade, revolves around increasing dosages as the patients age and the severity of the condition deteriorates. That represents an unsustainable model for treating large numbers of people with an escalating cost of treatment.

Something has to give.

But perhaps help is on the way.

Eoin says the key to give the NHS and its ilk an effective way to treat chronic disease could lie in developing a greater understanding of the 10-100 trillion or so of symbiotic microorganisms (including bacteria, fungi and viruses) that live in and on the human body – known collectively as the microbiome.

In recent years, scientists have learned that the microbiome is intimately involved with many aspects of our health, including the robustness of our immune system, our risk of developing asthma and allergies and even neurological and psychological disorders.

The microbiome offers enormous potential to define and influence the DNA record of the bacteria, information that will allow researchers and later doctors to diagnosis, prevent or treat a huge assortment of health conditions, from infectious disease and obesity, to cancer and digestive disease.

You see, modern medicine is finding it increasingly difficult to treat life-altering afflictions when the balance in the microbiome is out of sync – costing health services time and money, and causing misery to those afflicted.

But as scientists and researchers investigate how the microbiome impacts us all, many experts foresee disruptive changes in the way doctors diagnose and treat disease.

“Someday soon, you and I will go into the doctor’s office, and the doctor will prescribe medicine that won’t be a chemical from a lab, but may be live bacteria,” says Sarkis Mazmanian, a microbiologist at Caltech in Pasadena, California.

“In addition to blood work, yearly physicals may include fecal samples to profile the microbiome,” tracking changes in bacteria to predict your risk for illness, sometimes long before symptoms appear.

Indeed, bacteria could eventually be used in lieu of chemical treatments, according to John Cryan, a neuroscientist at University College Cork in Ireland, who’s even coined a



term to describe the possibility: psychobiotics. “Within five years, we’ll have specific microbial-based treatments,” he says.

In fact, we’re already seeing changes in the way doctors treat certain conditions, such as for infections with the deadly bacterium *Clostridium difficile* infection (CDI).

Doctors are already using fecal transplants fecal material taken from someone with a healthy microbiome and delivered to the patient’s colon to treat and cure the notoriously difficult

motor deficits in a mouse model of Parkinson’s disease, the second most common neurodegenerative disease; while a group from the Weizmann Institute of Science discovered that gut microbes are the reason you regain weight after dieting, a potentially huge step forward in treating the obesity epidemic.

Last year, a group of researchers, including from Peking University First Hospital in Beijing, said gut microbiome therapies show promise for treating autism; another group discovered gut microbiota

pouring into the space, including from venture capital, as the science and understanding of the microbiome develops. Between 2011 and 2016, funding in microbiome startups grew from around \$20.5m to over \$600m, a figure likely to have been broken last year.

There are now hordes of microbiome-specific venture capital firms closing funds at increasing sizes, with dozens of companies, as well as the major pharmas, dedicated or involved in harnessing the microbiome to treat disease.

Eoin says the microbiome is rapidly becoming a game-changer in the healthcare industry. Understanding it could revolutionise treatment and medicine and one day stop the drain on hospitals and doctors in health services such as the NHS.

Between 2011 and 2016, funding in microbiome startups grew from around \$20.5m to over \$600m.

condition. By introducing helpful bacteria, the treatment can combat CDI better than antibiotics can.

But more treatments are on the way, with the last few years seeing huge and potentially game-changing microbiome discoveries.

In 2016, among a host of other breakthroughs, scientists at the University of California San Francisco identified a specific pattern in the gut microbiome of babies that can predict if they will be more likely to develop asthma or allergies later in life; a team from Caltech demonstrated that gut microbiota promote neuroinflammation and

amino acids are linked to disease severity in Crohn’s; while a new review article published just last month in Mayo Clinic Proceedings said advances in microbiome science will play a key role in a new era of patient care, enabling precision diagnostics and personalised treatment strategies.

Imagine how much time and money could be saved if we could all access personalised disease diagnosis and drug therapies.

What will be discovered in 2018 is unknown.

But one thing we know for sure is that more and more money is

He thinks the microbiome will be used to discover the next frontier in improving healthcare and will reshape the way we treat some of today’s most critical diseases.

And he’s found a way that you can already profit from it, in PureTech Health.



Insanity prevails

Sam Volkering

Panic, fear, mayhem best sums up the last 24 hours in crypto markets. Less than 24 hours ago the crypto market was a “bloodbath”.

A quick glance at Coinmarketcap.com would reveal almost universal losses across all major crypto. Ripple, Cardano, NEM, Stellar and IOTA all down double digits. That wiped *billions* from their “market cap”.

Bitcoin and Ethereum were down too. While not as dramatically, still enough to wipe *billions* from their market cap. In fact at one point the total “market cap” of all cryptocurrencies was up around \$830 billion. And then in a matter of minutes it was closer to \$700 billion.

What was the reaction of most crypto traders? Panic. Sell, sell, sell. It was like the opening of the doors on Boxing Day. Remember those pictures of men and women climbing over each other just to get their hands on a “cheap” LED TV?

Picture that again, except to sell off their crypto holdings.

Insanity prevails.

Except it was on false pretences.

You see most new people (noobs) to the crypto world have a very shallow understanding of how things really work. Their

experience so far is randomly choosing crypto, “investing” their money and seeing the things rocket in price.

What really happened is that Coinmarketcap decided to stop using inflated prices from Korean exchanges in calculating the average crypto prices. That meant an *instant* reduction in “price” for crypto across the board.

What happens next?

It is a bit like shooting fish in a barrel at the moment. Anyone can do pretty well out of it. The problem is that makes everyone thinks they’re a crypto genius. However, it doesn’t last like this forever.

I know because I’ve seen mania like this before. Albeit on a

Everyone thinks they’re a crypto genius. However, it doesn’t last like this forever.

Due to bizarre overinflated trading in Korea, everyone had an artificial view of crypto markets. That’s because the only thing people could see was price and only on Coinmarketcap.

The reality is there was absolutely no change whatsoever to the value of any crypto. It was just that one price-tracking site chose to do its calculations differently.

But when people saw the new calculations they freaked out. And panic sold. But as you’d expect, the market readjusted and all those that dumped their “bags” were left looking the sucker.

It’s why you cannot step into this world and pretend to be a guru with no more than a few months’ experience. It’s simply not that easy to navigate with certainty or any confidence.

smaller scale in 2013 and 2014. This is exactly what happened to crypto back then. 10x, 100x gains in a matter of days and weeks. What happened out the back end was many of the “s**tcoins” eventually tanked and become worthless.

Until 2017 that is. And the truth is the exact same thing is going to happen this time around as well. Maybe the peak runs higher and harder for longer. But at some point the fakery and fraud will be found out.

The projects with little to no development will not survive. When the announcements start to come they’ve run out of funds, then what next? What happens when these crypto projects that have run up millions in contributions... need more money to survive? Then what?

Just issue more tokens even though they said they wouldn’t?



No. They disappear. Bye bye. This <i>will</i> happen again. But just like 2013 and 2014, it <i>won't</i> happen to all crypto. Some of them, the best of the best, the cream of the crop, will go on to become even bigger and better than now. Some of them will continue to deliver 10x, 100x, 1,000x gains to smart investors.	But what it requires is the expertise to find those that have the right project, the right team, the right community, and technical proficiency – all the pieces of the puzzle. This market is still the single biggest opportunity to build life-changing wealth I've ever seen. In fact, I think it's the biggest wealth-creation event the world will see	this century. That is, so long as you know how to avoid the traps and pitfalls – like freaking out when a website recalculates its prices. But if you can avoid the dangers and find the right crypto, then you may very well be on track to mint yourself a crypto fortune.
---	--	---

Risk warning

Your capital is at risk when you invest in shares – you can lose some or all of your money, so never risk more than you can afford to lose. Bid/ offer spreads, commissions, fees and other charges can reduce returns from investments. The Frontier Tech Investor portfolio is not intended to represent the exact price at which you could buy or sell a share. Our reference price is the closing price the day before issue is published. Sometimes readers will achieve better entry/exit prices; sometimes worse. All gains are gross, and returns will be affected by dealing costs and taxes. Profits from share dealing are a form of capital gain and subject to taxation. Tax treatment depends on individual circumstances and may be subject to change in the future. The information and opinions expressed do not necessarily reflect the views of other editors/contributors of Southbank Investment Research Ltd. Small cap shares - Shares recommended may be small company shares. These can be relatively illiquid meaning they are hard to trade and can have a large bid/offer spread. If you need to sell soon after you bought, you might get back less than you paid. This makes them riskier than other investments. Small companies may not pay a dividend. Full details of our complaints procedure and terms & conditions can be found on our website southbankresearch.com Investment Director: Eoin Treacy. Frontier Tech Investor is issued by Southbank Investment Research Ltd. Registered in England and Wales No 9539630. VAT No GB629 7287 94. Registered Office: 2nd Floor, Crowne House, 56-58 Southwark Street, London, SE1 1UN. Southbank Investment Research Ltd is authorised and regulated by the Financial Conduct Authority. FCA No 706697. <https://register.fca.org.uk/>. ISSN 2398-2470. © 2017 Southbank Investment Research Ltd.

Energy



Company	Ticker	Rec Date	Price Then	Price Now	Gain/loss %
Orocobre Ltd	ORE.AX	07/04/16	A\$ 2.92	A\$ 7.14	144.52
Ormat Technologies	ORA on NYSE	06/06/17	\$58.79	\$65.25	10.99
Smart Metering Systems	SMS LN	03/10/17	735.5p	834p	13.39

Technology



Company	Ticker	Rec Date	Price Then	Price Now	Gain/loss %
Cyberdyne	7779	30/05/16	JPY 2,353	JPY 1,973	-16.15
IBM	IBM LN	07/06/16	\$153.33	\$163.47	6.61
SAIC	SAIC US	05/07/16	\$58.20	\$78.68	35.19
Garmin	GRMN US	02/08/16	\$55.75	\$60.34	8.23
2U INC	TWOU: US	06/02/17	\$33.25	\$63.36	90.56
Cisco Systems Inc.	CSCO: US	03/04/17	\$33.80	\$39.94	18.17
Advanced Micro Devices	AMD US	26/07/17	\$14.76	\$12.28	-16.80
Microsoft	MSFT	31/07/17	\$73.04	\$88.28	20.87
Northrup Grumman	NOC US	06/07/17	\$301.66	\$308.26	2.12

Medical



Company	Ticker	Rec Date	Price Then	Price Now	Gain/loss %
Terra Tech Corp	TRTC	11/10/16	\$0.41	\$0.37	-10.68
Autodesk	ADSK	19/07/17	\$108.83	\$111.42	2.38
Abcam	ABC	07/03/17	907.5p	1150p	26.72
Zynerba Pharmaceuticals Inc	ZYNE: US	03/04/17	\$20.10	\$12.55	-37.56
Illumina	ILMN	04/09/17	\$207.15	\$227.06	9.57

Moonshot



Company	Ticker	Rec Date	Price Then	Price Now	Gain/loss %
SolarWindow	WNDW	07/04/16	\$3.96	\$8.88	124.12
Alkane Resources Ltd	ALK: AU	05/09/16	AU\$ 0.31	AU\$ 0.36	18.03
Editas	EDIT: US	07/03/17	\$21.02	\$30.02	41.07
Haydale Graphene Industries	HAYD	02/5/17	178.5p	116.50p	-34.73