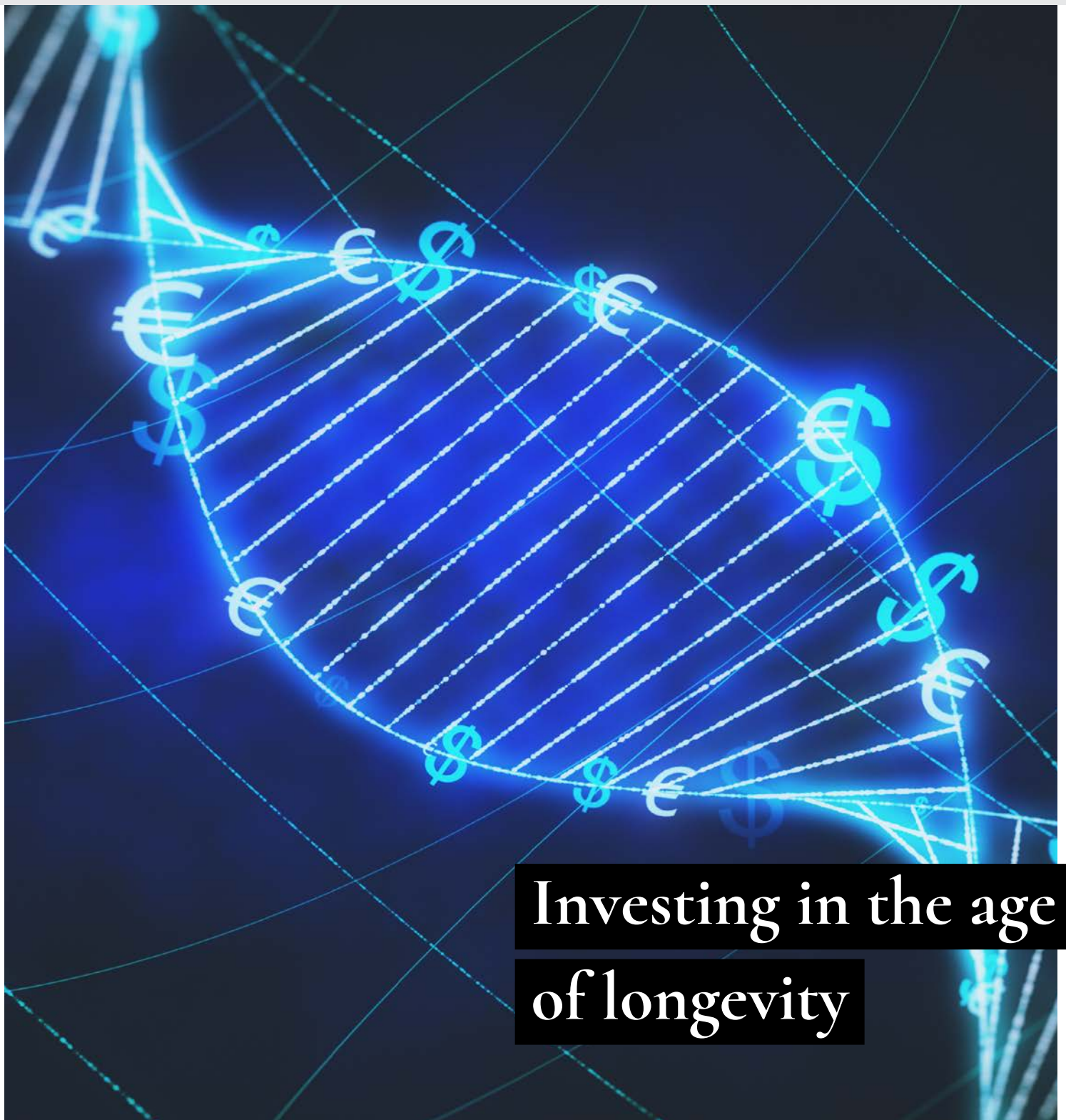


THE EDGE

LONGEVITY | AUTUMN 2019 EDITION



Investing in the age
of longevity

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Master Investor Ltd.
Unit 2, The IO Centre
Salbrook Industrial Estate
Salbrook Road
Salfords, Redhill
RH1 5GJ
United Kingdom

EDITOR
James Faulkner

DESIGNER
Alexandra Mueller

CONTRIBUTORS
Dr Greg Bailey
Michael Corcoran
Dr Raj Dattani
James Lawford Davies
Elizabeth Parrish
Reason
Chris Shilling
Nick Sudbury

Foreword

Dear Reader,

Welcome to the third issue of The Edge. A quarterly supplement to our main publication, Master Investor Magazine, The Edge allows us to take a closer look at specific investment themes. This autumn edition focuses on the potentially transformational developments taking place in the space of longevity and anti-ageing, and ties in with our “Investing in the Age of Longevity” event, which takes place in London on 13th November.



At Master Investor we are very privileged to have Jim Mellon as our chairman. Through his Juvenescence investment company (which you can hear more about on page 12), Jim has been a pioneer when it comes to investing in the anti-ageing space, and he's even written a book on the sector – also titled *Juvenescence*. Jim prides himself on identifying “money fountains” – long-term investment themes that can be relied upon to deliver tremendous returns.

Just skimming through this month's issue, it is clear that the anti-ageing scene fits the bill for a potential money fountain. Elizabeth Parrish, founder and CEO of BioViva, calls longevity science “the best investment on the planet,” adding that “nothing else is likely to yield greater social impact and financial returns in the long run.” Margaretta Colangelo, managing partner at Deep Knowledge Ventures and Longevity Capital claims the longevity industry will reach US\$27 trillion by

2026. Meanwhile, Reason from Repair Biotech reminds us that we are right at the beginning of this growth curve, as “scores of amazing projects” remain “without a champion”.

Indeed, it is hard to imagine a more compelling investment premise than one that offers people a longer, healthier life. But make no mistake – time is of the essence. This technology is being developed right now. As ever, the best returns will be made by those with the foresight to position themselves early, for what promises to be a very exciting ride.

Kind regards,

A handwritten signature in black ink, appearing to read 'J Faulkner', with a stylized, fluid script.

James Faulkner
Editor

Why Invest in Longevity?

By Elizabeth Parrish, Founder and CEO of BioViva



Right now, longevity science is the best investment on the planet. Nothing else is likely to yield greater social impact and financial returns in the long run. Yet, as a topic that has only recently entered public discourse, there are misconceptions about its present state and possible trajectories. A number of companies are investigating in stem cells and pharmaceuticals to address some hallmarks of ageing. Others, like BioViva Sciences, expect gene therapy to systemically tackle multiple hallmarks. Gene therapy works at the cellular level and uses therapeutic genes to stop disease where it starts.

The changing demography of industrialised countries makes it clear that the advancement of regenerative medicine is an economic necessity. Populations in the first world are growing older thanks to increasing life spans and plummeting birth rates. Despite decades of effort, diseases like Alzheimer's remain not just incurable and largely unpreventable, but frustratingly unresponsive to current treatments. For this reason, researchers are now looking at the roots of these diseases. This is why they are setting their sights on the ageing process itself.

One proposal to stem the tide of silver tsunami is to raise the minimum retirement age. Besides being a temporary band aid, altering the age at which we retire will not change the rate at which we age or how we age. We

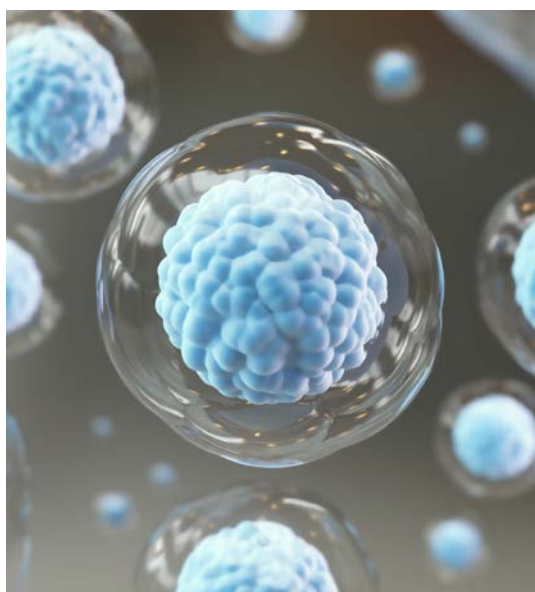
**“The changing demography
of industrialised countries
makes it clear that
the advancement of
regenerative medicine is an
economic necessity.”**

are living longer than ever, but we are not necessarily living better. Hence, it is unrealistic to expect the majority of people to work in certain professions beyond the age of 65. Should someone in the intermediate stages of Alzheimer's be expected to continue working as an air traffic controller? A dramatic example perhaps, but common age-related issues like hearing loss, reduced eyesight, poor quality of sleep, and “normal” cognitive decline can impact job performance.

The job of our air traffic controller has resisted automation because artificial intelligence at this time cannot reliably handle exceptional situations as well as a human being. A lot of faith has been placed in machines for reducing or eliminating the need for human labour. Yes, robots might become decent caregivers in future, but the question is why should there be a need for robotic caregivers, especially if the alternative is giving people back their vitality?

Lifespans can differ between closely related animals. The naked mole-rat can live for over 30 years – nearly ten times longer than similarly sized rodents. The naked mole-rat is also negligibly senescent, meaning it does not show signs of ageing or normally manifest age-related diseases until the very end of its life. Biological ageing is a process that can be understood and managed.

It is also a complex set of interlocking processes. As one would expect, many lines of research are being pursued. Senescent cells no longer replicate and create inflammation. The accumulation of senescent cells is one of the drivers of age-related pathologies. In response to this observation, some companies have looked for senolytics, drugs meant to encourage the clearance of senescent



cells. One problem with this, mentioned by the discoverer of hTert, Bill Andrews, is that elderly bodies are composed largely of senescent cells – getting rid of all of them is hardly feasible, and would subject the patient to too much stress.

Stem cells have been touted as possible cures for a range of illnesses for decades, but so far have largely failed to live up to the hype. Moreover, concerns of oncogenicity (pro-cancer activity) persist. Small molecules, familiar pharmaceuticals like the aspirin in your cabinet, are being investigated to combat aspects of ageing. However, drugs almost always have off-target effects. Metformin, for example, has a long history of human use and appears to protect against certain cancers. For these reasons some longevity enthusiasts are now taking it, including people without reduced insulin sensitivity. Recently, however, it was found that metformin blunts the benefits of exercise. This is clearly not desirable.

George Church, a professor of genetics at Harvard University and BioViva Sciences scientific advisor, states that “finding specific targeting via small molecules is unpredictable and expensive. Developing small molecules that selectively affect a particular protein family member or isoform

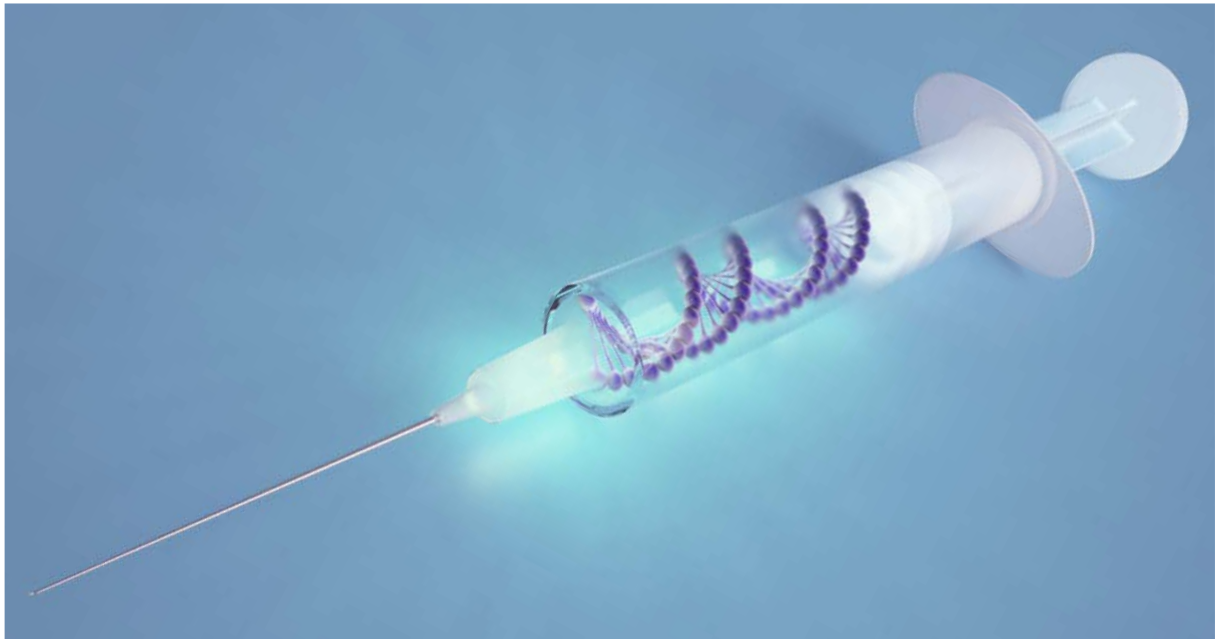
is challenging.” He is interested in engineering longevity from the ground up. Instead of addressing outward manifestation or skimming the surface by tackling a single hallmark of ageing, he wants to get to the bottom of human health and longevity by studying the basic building blocks of our biology. The technology already exists. Gene therapy involves replacing, inactivating, or adding a new gene to treat or prevent a disease. As of March 2019, 372 clinical trials for gene therapy are underway.

Integrated Health Systems, a sister company of BioViva Sciences, is building upon decades of research into telomerase, follistatin, and Klotho gene therapies which, in animal studies, have shown tremendous promise in lengthening lifespan and healthspan. Telomere shortening is one of the major contributors to the ageing process. Another aspect of ageing is muscle wasting, which can be counteracted by follistatin. Klotho, the “king” of anti-ageing proteins, was primarily of interest to kidney specialists. Now it is known to have a crucial role in brain health and mineral metabolism. As powerful and versatile as telomerase, follistatin and Klotho may be, they will not ensure that humans live hundreds or thousands of years. However, the evidence suggests that they can help people stay healthy for longer periods of time.

“Biological ageing is a process that can be understood and managed.”

The long-term profitability of longevity medicine is an understandable concern for investors. What money is there to be made in eradicating the diseases of ageing with a single elixir? As wonderful as this might sound, it is a pipe dream. The complexity of human biology virtually guarantees that longevity medicine will be an area of constant product innovation for decades to come. It is and will remain a vast and fertile territory for scientists, entrepreneurs, and investors. Companies like Celularity and Juvenescence are raising tens of millions of dollars in their series A and B funding rounds. What was once a fringe idea has matured enough to draw the attention of serious investors.

For gene therapy companies like Integrated Health Systems and BioViva Sciences, there is virtually no end to the services they can provide for prospective clients. George Church has provided a wishlist of 45 genes that could help humans live longer and better lives. As



sizeable as this list might seem, it is only the beginning. As the field expands it will become even more bewildering to investors, particularly to those without scientific backgrounds.

Karen Frank, CEO of Barclays Private Bank & Overseas Services, has noted that people “want to understand the technologies that are supporting this kind of advancement, and how we can help them invest and participate.” Non-profits like the SENS Research Foundation and companies like BioViva Sciences have been working tirelessly to explain the latest developments to laypeople. Keeping up with the trends isn’t hard thanks to their diligence. Due to the technical nature of the field, Alice Newcombe-Ellis, a founding partner

at Ahren, advises against investing by yourself. While this is probably a good idea for most of us, there is no lack of quality news outlets in the longevity sphere for solo investors.

Longevity research is of interest not just to those looking to live longer. Heads of state are now acutely aware of its necessity. The fear that these ventures will be underfunded is largely unfounded as this is no longer an issue of individual importance, but a problem with tremendous social, political, and economic ramifications for the world as a whole. As a burgeoning industry, now is the time to begin looking for promising prospects, for the players that are bringing and will continue to bring value and innovation.



Elizabeth Parrish, the Founder and CEO of BioViva, is a humanitarian, entrepreneur,

innovator, author, podcaster, and a leading voice for genetic cures. As a strong proponent of progress and education for the advancement of regenerative medicine modalities, she serves as a motivational speaker to the public at large for the life sciences. She is actively involved in international educational media outreach. Dedicated to the cause of improving and safeguarding more and more lives, Elizabeth asserts, “We are focused on saving as many lives as possible by making tomorrow’s therapies available. This is about Life and Death. Risk aversion and the delaying the approval of therapies that have been successful in research simply kills.”

BioViva

BioViva, a trail-blazing medical data analysis and research and development company, was started to change the face of healthcare treatments by bringing enhanced and definitive solutions for some of the most perilous diseases. The inspiration came from a life-changing incident when the founder’s son was diagnosed with Type 1 Diabetes. On the

path to find the most adequate treatment for him, she was confronted with the reality of children suffering from genetic diseases. She also discovered that, although laboratory animals have been successfully treated for many of these diseases, those therapies haven’t yet been made available to humans, because of the medical profession’s exaggerated risk aversion and the FDA’s precautionary attitude. This meant that despite the discovery of appropriate therapies, the kids die because these therapies have not yet been through a lengthy and extremely expensive chain of paperwork and clinical trials. Determined to change this condition, she established BioViva.

Today, BioViva analyses biomarkers from trials and studies involving patients referred to the clinics by its partner company, Integrated Health Systems. The company is focused on speeding up the number of medical innovations by cooperating with companies that offer consenting patients pioneering therapies that they cannot get in the United States. Using medical researchers to oversee the patients, it beats the gold standard of the US FDA and creates exponential technology for the future. BioViva is the first company in the world to look at the data of regenerative gene therapies in humans.

 <https://bioviva-science.com>

Juvenescence the company

By Dr Greg Bailey, Dr Raj Dattani and Chris Shilling



In this article, the team behind Juvenescence provide some insight into the remarkable opportunities they are seeing as science fiction becomes a reality.

Master Investor asked me to write about Juvenescence, a company that was established by Jim Mellon, Dr Declan Doogan and myself. Two years ago, in October 2017, we began to look for drugs to develop that modify ageing. It has been a remarkable journey for the three of us. The number of compelling therapies we have seen which truly are based on hard science that can modify human ageing, and the amount of capital we have been able to raise to move these projects forward, has been extraordinary. This article is intended to give you some insight into the types of products and the remarkable opportunities we are seeing as science fiction becomes a reality.

Some of you may have heard of us already from the Master Investor show, or through reading about the closing of our latest funding round, a \$100m Series B. Most of you know Jim Mellon and his remarkable business career. Declan and I started as practising physicians who entered the biotechnology sector. Declan was the head of global drug development at Pfizer while I am a serial entrepreneur. We have been fortunate enough to have had a number of shared successes in our companies, notably Biohaven (BHAVN:NYSE). Independently we were involved in two very big success stories

“The number of compelling therapies we have seen which truly are based on hard science that can modify human ageing, and the amount of capital we have been able to raise to move these projects forward, has been extraordinary.”

with Medivation and Amarin before Biohaven. Declan was the CEO at Amarin, where he repositioned their drug for a new indication, taking it through a phase 3 trial and getting it onto the market for dyslipidaemia in under three years. I was involved as a board member and financier of Medivation, which in 12 years went from a \$12 million valuation to being acquired by Pfizer for \$14.3 billion.

When we were founding Juvenescence, we were given the opportunity to design a 21st-century biopharma to take advantage of not only emerging ageing science, but also the

“Selectively killing senescent cells in older animals has been shown to lead to substantial improvement in health.”



emergence of machine learning in drug discovery and development. In fact, our first project was with an artificial intelligence drug company called Insilico Medicine that Jim came across while writing his book *Juvenescence*. Insilico recently published a high-profile paper in *Nature Biotechnology* and closed a \$37 million round of financing.

Artificial intelligence

At Juvenescence we have two joint ventures with machine learning companies – one called GenerAlt focused on drug discovery, which is a joint venture with Insilico Medicine; and StratiPhi, a second joint venture with NetraMark that uses machine learning to optimise drug development and find failed drugs that actually may still be viable but in a specific sub population.

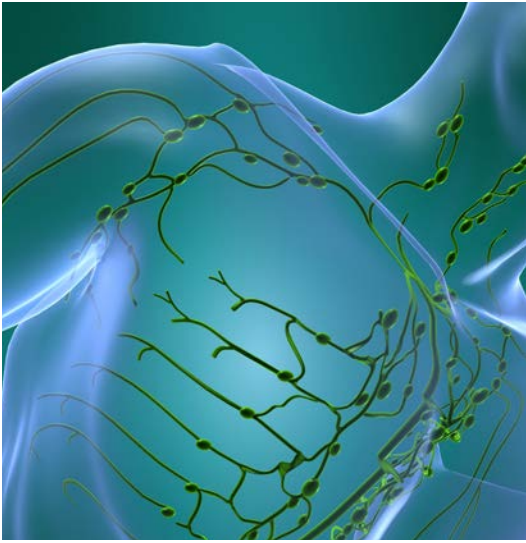
Insilico Medicine, Inc. is a Johns Hopkins-based company that uses artificial intelligence (AI) and deep learning for drug discovery. Insilico Medicine's "end-to-end" AI platform for drug discovery covers target identification and validation, compound generation, and patient selection. Significantly, by using generative adversarial networks, Insilico is able to produce new drug-like chemical compounds and quickly arrive at a clinical candidate without the need for high throughput

screening. Juvenescence and Insilico have created a joint venture, GenerAlt Pharmaceuticals, which every year has the right to choose the top five compounds from Insilico to develop; to date it has identified the first three promising drug candidates.

StratiPhi leverages a novel machine learning technology, NetraAI, based on new mathematical techniques that not only integrates multiple different machine learning algorithms—including gradient boosting, random forests, neural networks, GANs, and quantum computation – but also provides an explainable AI interface. This enables the discovery of patient subpopulations, along with what factors are driving the disease subtypes. The NetraAI system has been utilised to predict placebo response; to discover subpopulations within psychiatric disorders, cancer, and dementia/Alzheimer's; and to make clinical trials significantly more efficient. We plan to use this technology to help companies with failed clinical trials identify overlooked subpopulations of responding patients and to aid in the design of our own trials.

Regeneration

We have two principal projects in the regeneration sphere: Lygenesis and AgeX.



LyGenesis was our second project and is the one nearest to the clinic. The team, based in Pittsburgh, is pioneering the use of a patient's own lymph nodes as bioreactors to regrow functional ectopic organs. Translated to plain English, this means that they are able to use a part of the anatomy (the lymph nodes) which is located close to an organ, as the place to regenerate or "grow" a functional organ to support or replace a diseased one. The first use case is to generate ectopic livers to treat patients with end-stage liver disease. This is a group of patients with no other option but a transplant. The team has tested the approach in multiple small and large animal trials, where this rescue has been repeatedly demonstrated. Appropriate FDA regulatory meetings have been held, and the first human patient is due to be dosed on a trial in the first half of 2020.

AgeX Therapeutics, Inc. (NYSE:AGE) is our largest project by capital investment to date and is traded on the public market. Some of you who attended the Master Investor show in 2019 will have had the benefit of hearing Dr Mike West, its charismatic CEO, speak live. AgeX is based in San Francisco's Bay Area, and is a leading regenerative medicine company focused on cell therapy and human longevity R&D. Its proprietary, novel and potentially industry-changing PureStem® cell manufacturing and UniverCyte™ immunotolerance technologies are designed to work together to generate hypoimmunogenic, off-the-shelf pluripotent stem cell-derived young human cells of any type for application in a range of severe diseases.

These technology platforms are potentially transformative for the cell therapy industry as a whole and enable AgeX to pursue a two-fold business strategy. Firstly, they facilitate a business development and licencing strategy with third parties to bring in early revenue streams as well as allow for the widespread adoption of AgeX's technologies across the cell therapy industry. For example, UniverCyte may solve the biggest challenge facing the allogeneic cell therapy industry, namely immunological rejection of donor cells by the recipient, whilst PureStem could



overcome the high manufacturing costs associated with cell therapies by generating cells with high purity and proliferative capacity.

The second prong of the business strategy is the development of in-house cell therapy products. Current early-stage in-house programmes are for billion-dollar markets, and include AGEX-BAT1 (brown fat cells) for diabetes and metabolic diseases and AGEX-VASC1 (vascular progenitor cells) for tissue ischemia, such as diabetic foot. Excitingly, AgeX is also a leader in the field of partial reprogramming to revert aged cells in vivo back to a youthful state, through its revolutionary induced Tissue Regeneration (iTR) platform, which may have a paradigm-shifting impact on multiple diseases.

“Traditional” biotechnology

All of our projects in this area are not traditional, by virtue of the fact they target ageing pathways rather than disease-specific pathways.

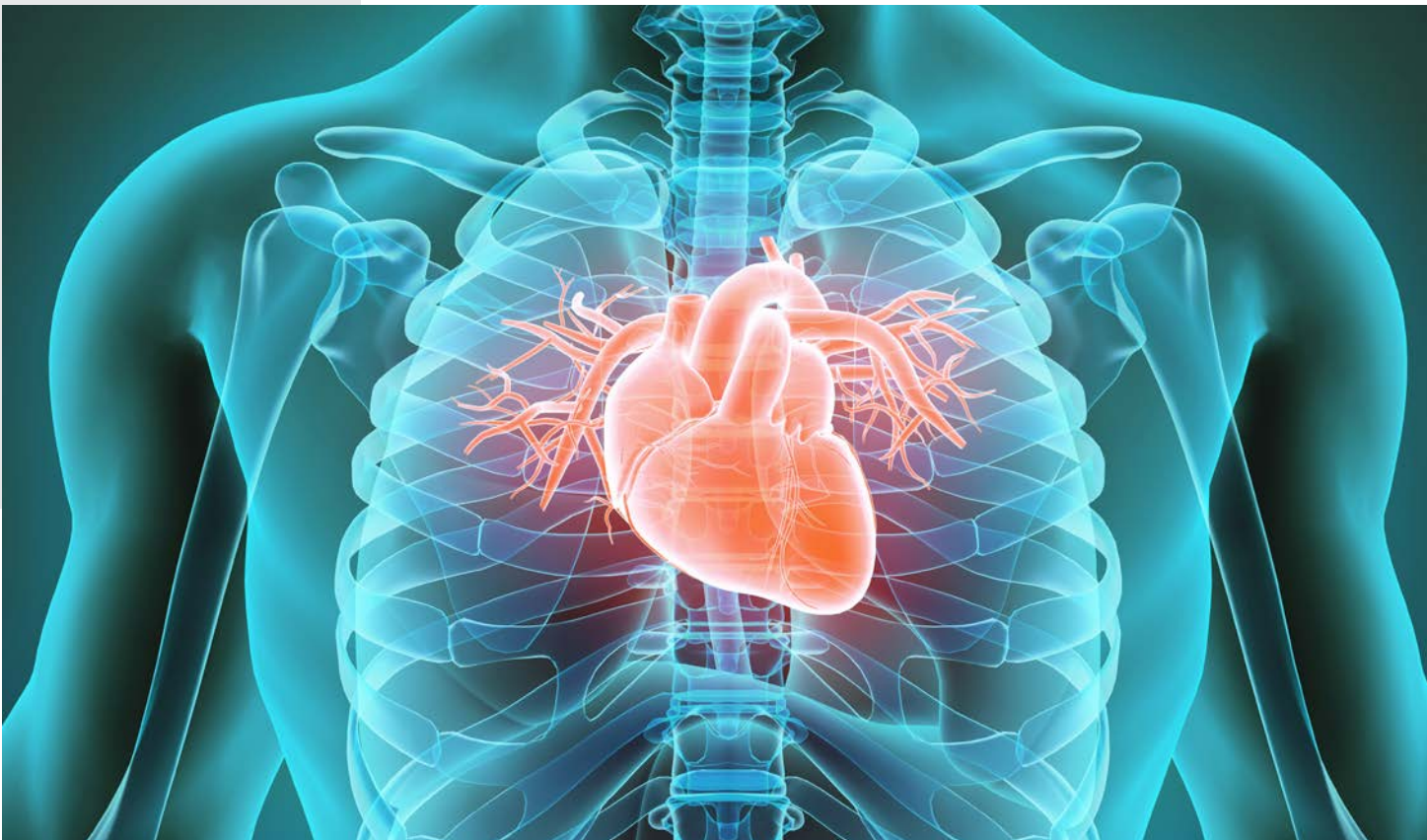
FoxBio is a joint venture between Juvenescence and Antoxerene Inc. (a subsidiary of Ichor Therapeutics). It is focused on developing small molecule “senolytics” that target a major survival pathway relied on by senescent cells. Senescent cells are a key feature of

ageing biology and aged tissues, and many anti-ageing companies have a project focused on them. Senescence occurs due to “stress” signals to the cell such as telomere shortening, oncogene activation, DNA damage, and oxidative stress. Senescent cells remain metabolically active and secrete inflammatory molecules, termed the senescence-associated secretory phenotype (SASP), and it is often this which drives diseases associated with ageing. Selectively killing senescent cells in older animals has been shown to lead to substantial improvement in health.

Napa Therapeutics is a collaboration between Juvenescence, Insilico Medicine, and the Buck Institute for Research on Ageing. Jim Mellon is also a Trustee of the Buck Institute, and the founding scientist of Napa is Eric Verdin, CEO of the Buck Institute. The project focuses on NAD⁺ metabolism. NAD⁺ is a key metabolic molecule which declines with age. The project is a great example of our ecosystem of companies working together, as the chemistry is being supported by Insilico Medicine.

A second project with the Buck Institute is BHB Therapeutics. This is a project focused on a set of novel compounds that have been shown to induce a state of ketosis without carbohydrate restriction. Similar compounds have

“Our first products, which are designed to make the heart more efficient, could be on the market as early as next year.”



recognised applications as a support for athletic performance, and work done at the Buck has identified that long-term exposure to ketone bodies can extend healthy lifespan in model systems, in addition to the potential applications in illnesses like heart failure.

BYOMass is a Massachusetts-based company, the brainchild of Margaret Jackson, our Head of Preclinical Research and Development. It is focused on developing therapeutics to modulate the central control of metabolism associated with ageing and age-related chronic illnesses and for now is operating in stealth mode.

Our most recent addition is Souvien Therapeutics, a project focused on critical epigenetic mechanisms associated with neurodegeneration. Souvien is founded on the pioneering research of Professor Li-Huei Tsai, the director of The Picower Institute for Learning and Memory at MIT, and Associate Professor Stephen Haggarty, the director of the Chemical Neurobiology Laboratory at Harvard Medical School/Massachusetts General Hospital.

These are the initial projects at Juvenescence that demonstrate the breadth and diversity of the various therapeutic candidates that we are developing. Our first products, which

are designed to make the heart more efficient, could be on the market as early as next year. Lygenesis should start its clinical trial next year in humans. The rest of the programmes will enter human trials in two to three years. Then there are a couple of moon-shot possibilities that are spin-offs from these existing projects focused on regeneration. These will take longer but would be transformative to medical care if successful.

As we look to the future for Juvenescence, we are limited by three factors: in-licensing compelling products, hiring seasoned drug professionals and securing adequate capital. The most recent raise of \$100 million enables us to continue our pursuit of finding compelling products and adding to our management team. As Juvenescence has such a lofty goal – to modify ageing – we've been able to recruit extraordinary personnel who are dedicated to, and passionate about, finding scientifically-backed therapies to modify how the human body ages, not just for the wealthy but for everyone. As I said, we are completely surprised by the number and quality of the products that we are seeing that in the next five to 10 years will modify how we live and age. We call it the 'Quiet Revolution' – which will happen so much faster than you expect.



Dr Greg Bailey is the CEO of Juvenescence, a bio-pharma development company leveraging

insights into ageing biology to modify diseases of ageing. Juvenescence has developed an ecosystem of scientists and drug developers enabled by next-generation AI/ML and data science to create therapeutics, from drugs to IP protected consumer products.

Dr Bailey is a proven healthcare company creator and investor. He has been founding and financing companies in this space since 1995. His companies have been traded on NASDAQ, AIM, AMEX and the NYSE, reaching over \$18 billion in market capitalisation.

Dr Bailey received his medical doctorate from University of Western Ontario.

Juvenescence Ltd

Juvenescence is developing multiple therapeutics focused on improving and extending human lifespans. The Juvenescence team comprises proven and seasoned experts in drug development, strategy, structure, commercialization and finance.

From its outset, Juvenescence has staked out a major footprint in AI, and specifically in machine and deep learning through its part ownership of Insilico Medicine and through its ownership in NetraPharma and Juvenescence AI. Access to these two AI engines from our joint ventures will assist our efforts in drug discovery, as well as in optimizing human trials of the therapeutics we develop.

Our company's pipeline consists of pre-clinical candidates that have been joint ventured with leading research institutions and associated scientist inventors. In addition, we are partners with established companies such as Age X, where our role is to provide finance, development expertise and to help guide products with management towards commercialization.

 <https://juvenescence.ltd>

The best biotech trusts and funds

By Nick Sudbury

The ageing population and the healthcare challenges that go along with it have created a huge demand for advancements in medical science. As more and more people make it into their eighties and nineties, their quality of life will depend to a large extent on developments in the biotech sector and those companies that make the biggest breakthroughs will be richly rewarded.

Last year, for the first time in history, people aged 65 or above outnumbered children under five years of age globally. By 2050, one in four people living in Europe and Northern America could be aged 65 or over, while the number of people aged 80 years plus is projected to triple, from 143 million today to 426 million in 2050.

Darius McDermott, MD of Chelsea Financial Services, says that as populations age, biotech and healthcare is likely to become more important, as we are all likely to live longer with health issues.

“Indeed many of us will die with disease rather than from disease, but that’s not the only thing: as more strain is put on governments to provide healthcare solutions, companies that can produce drugs or products that can treat more people for less money should do extremely well.”



Biotech stocks are not particularly sensitive to the economic cycle, with the demand and potential market for their products being mainly driven by the relevant demographics. An ageing population with more complex health needs should provide a favourable long-term environment for the sector to flourish.

Ben Yearsley, a director at Shore Financial Planning, says that he is a big fan of biotech. “Ageing populations and advances in medicine have made this a long-term trend that investors can benefit from. Whether it’s simple medicine or gene cell therapy, as an example, the need for healthcare and biotech products is growing.”

Specialist funds

For many investors the easiest way to profit is to invest in one of the specialist funds that operate in the sector. These are better placed to identify and capture the high potential returns that are available than a more mainstream mandate that will include biotech stocks as part of its wider remit.

“It is a specialist area and the investment teams managing the funds really need proper medical expertise. They don’t

necessarily have to be doctors, but they need to be scientists as well as financiers,” explains McDermott.

Biotech is a volatile sector as it sits at the cutting edge, developing new drugs that may or may not get approval, although it should have faster earnings growth than the wider market going forward.

“For a variety of reasons the biotech sector sits on a low valuation compared to both its own history and the wider market. Part of this is down to politics in the US where both Democrats and Republicans want to lower drug prices,” explains Yearsley.



The constituent companies range from large established organisations such as device or diagnostic businesses, to single product exploration or R&D operations, and therefore the risk and returns can swing to both extremes. This means that it is important to take a diversified approach as the performance can be very mixed.

Capital growth

For investors looking for capital growth, Yearsley recommends the £350m Biotech Growth Trust (LON:BIOG), managed by OrbiMed, one of the largest healthcare focused fund managers in the world with \$12bn of assets under management. They have 84 investment professionals including a large number of MDs, PhDs and former CEOs from the sector.

This high level of expertise enables them to focus on the fundamental research and they have an investment universe of 1,000 companies that range from early stage with pre-clinical assets to the large integrated biopharmaceutical stocks.

“OrbiMed believe that it’s a golden age of innovation, partly due to the favourable regulatory environment with 59 new drugs being approved in the US in 2018.

The trust is a mixture of large established biotech firms and smaller emerging biotech companies,” says Yearsley.

BIOG has a concentrated 43-stock portfolio and has delivered impressive long-term returns with a ten year gain of 378%. Its largest holdings include the likes of Vertex Pharmaceuticals (NAS:VRTX), Sarepta Therapeutics (NAS:SRPT) and Neurocrine Biosciences (NAS:NBIX). The shares are currently available on a five percent discount.

Adrian Lowcock, head of personal investing at Willis Owen, is also a fan and says that the management team combine a deep clinical understanding of scientific developments with a solid investment process.

“It is a thorough, bottom-up process and emphasises investments in companies with technical innovation, underappreciated products in the pipeline, high-quality management teams and adequate financial resources.”

Other growth options

McDermott says that they really like the team at Polar Capital. “They are specialists in this sector and have very



good biotech funds and trusts with the Polar Capital Biotechnology fund worth a look.”

The £369m open-ended fund typically has 40 to 60 different positions. At the end of September its largest holdings included: Alexion Pharmaceuticals (NAS:ALXN), Incyte Corp (NAS:INCY) and Regeneron Pharmaceuticals (NAS:REGN). Since the fund was launched in October 2013 it has returned 182%, which is double the Nasdaq Biotechnology net total return index.

Lowcock prefers the £398m AXA Framlington Biotech fund, managed by Linden Thomson. She sees more long-term growth opportunities in the small and mid-cap biotech stocks rather than the large-caps, some of which are facing challenges to grow revenue beyond their legacy products and do not have the pipelines necessary to drive sustained growth.

“The fund invests in shares of listed companies, principally in the biotechnology, genomic and medical research industry, which the manager believes will provide above-average returns,” he says.

At the end of August it had 47 different holdings with the largest positions including Amgen (NAS:AMGN), Gilead Sciences (NAS:GILD), Alexion Pharmaceuticals (NAS:ALXN) and Biogen (NAS:BIIB). Over the last five years it has returned 42.5%, which is considerably less than the 52.5% produced by its Nasdaq Biotech benchmark.

Income

The biotech sector is normally considered to be a great source of long-term capital growth, but there are also a couple of funds that pay a decent yield if you are more interested in capturing the upside potential in the form of a regular income.

BioPharma Credit (LON:BPCR) is a £1.4bn investment trust that aims to generate sustainable income distributions from exposure to the life sciences industry. It mainly invests in corporate and royalty debt securities



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secured by cash flows derived from sales of approved life sciences products.

BPCR targets an annual dividend of seven cents per share and a net total return on NAV of eight to nine percent per annum in the medium term. The shares are currently yielding seven percent with equal quarterly dividends.

The analysts at Investec Securities say that the investment outlook remains positive, with the life sciences industry expected to have substantial capital needs over the coming years as the number of products undergoing clinical trials continues to increase.

They have recently issued a buy recommendation on the trust, as they

believe that the combination of an attractive yield, low correlation to other investments, low volatility and market-leading management team represents a powerful investment proposition.

Another option is the £230m International Biotechnology Trust (LON:IBT), which is the longest-established of the London-listed funds specialising in the biotech sector. IBT is very unusual as it pays a dividend equivalent to four percent of its preceding year-end NAV in two equal instalments in January and August with the distributions largely paid from capital reserves. It is expected that the total dividends in 2020 will be 24.9 pence per share.

Common holdings and their main focus

Alexion	Rare disease.
Amgen	Broadly-based.
Celgene	Multiple myeloma, psoriasis, oncology and others.
Gilead	Antiviral, including HIV and Hepatitis therapies, haematology/ oncology, cardiovascular, inflammation/respiratory and other.
Regeneron	Ophthalmic, allergic and inflammatory, oncology, cardiovascular and metabolic, neuromuscular, infectious and rare diseases.
Vertex	Cystic fibrosis, inflammation and oncology.

The managers have focused its portfolio in oncology, afflictions of the central nervous system and rare diseases. These are all areas where pricing pressure on drugs and other therapies is less of an issue, which should cushion the fund as we approach election year in the US and the political threats to intervene in drug pricing.

They believe that the secular demand for the biotech sector's products, combined with the growing pipeline of new therapies and IBT's bias towards companies with strong pricing power, should make it resilient in the event of any economic slowdown, or even an outright recession. The largest holdings currently include Celgene (NAS:CELG), Gilead Sciences (NAS:GILD) and Regeneron (NAS:REGN).

Ageing populations and the advances in medical science that they require should enable earnings to grow faster across the biotech sector than the rest of the market, but it will be a patchy affair with a few big winners and plenty of stocks that don't go the distance. The easiest way for those unfamiliar with this area to benefit is to use one of the specialist funds that have the knowhow to navigate the complex science.

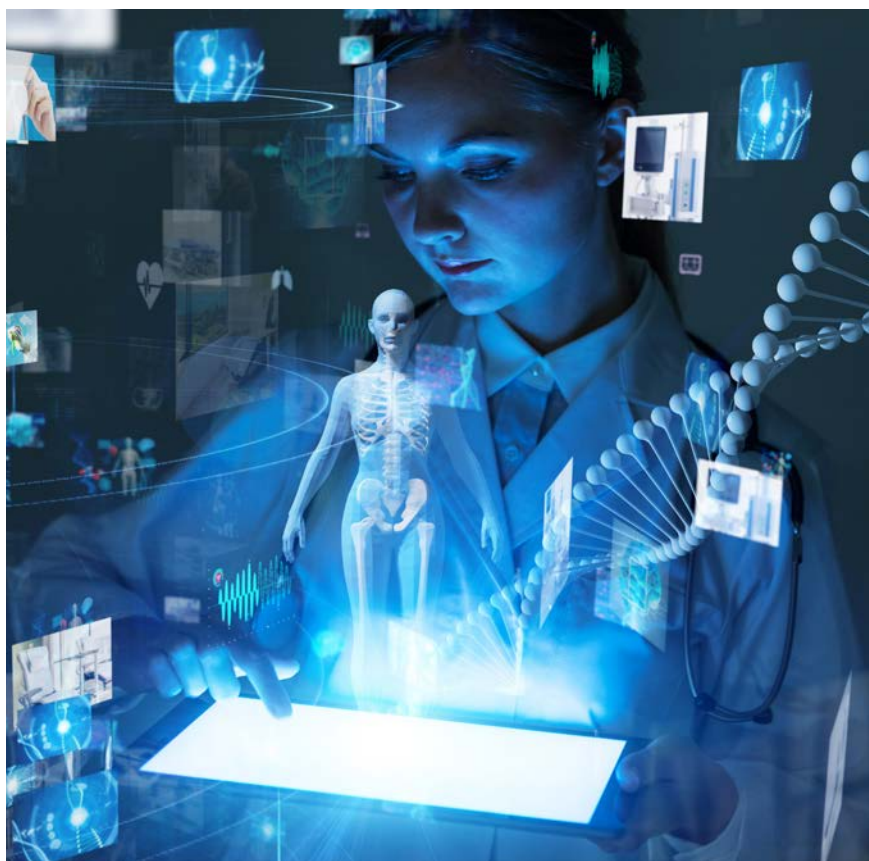
“Ageing populations and the advances in medical science that they require should enable earnings to grow faster across the biotech sector than the rest of the market, but it will be a patchy affair with a few big winners and plenty of stocks that don't go the distance.”



Nick Sudbury is an experienced financial journalist who has written extensively for a range of investment publications aimed at both private and institutional investors. Before moving into journalism he worked both as a fund manager and as a consultant to the industry. He is a fully qualified accountant and has an MBA with finance specialism.

Longevity - Investing in the future

By Michael Corcoran and James Lawford Davies



Investor attention on the industry dubbed “the Biggest and Most Complex Industry in Human History” is growing rapidly. Ahead of London Longevity Week (11-15 November 2019, further details at <https://thelongevityforum.com/the-longevity-week>), James Lawford Davies and Michael Corcoran, Partners in Hill Dickinson’s Life Sciences group, look at recent growth in investment for longevity companies and the continued market focus on the industry’s potential for 2020.

Longevity companies are in the business of finding ways for people to live longer, healthier lives – whether by slowing, stopping or potentially reversing the ageing process. Ageing research and regenerative medicine is expected to grow into a multi-trillion dollar industry over the next few years, and it has now grasped the attention of investors, regulators and governments worldwide. Aside from the obvious benefits of adding additional healthy years onto our lifespans, greater longevity will mean people live and work longer, having significant societal implications that policy makers and social scientists are now having to address.

As in all areas of medical research, clinical trials of new therapies and products require significant funding over a considerable period of time. In this first of a series of articles, we discuss the current trends and our predictions for the future.

Back to the future: longevity science and technology has arrived

The market for investing in longevity has evolved significantly in recent years and it looks likely that 2020 will be the breakout year for capital investment globally in the industry. Venture capitalists are lining up to lead early-stage funding rounds with huge interest, not just on the West Coast of the US (where the longevity industry has its spiritual home), but globally – notably in China and Russia. Investor appetite for longevity-focused companies is borne out by the frequency and size of Series A and Series B funding rounds completed in 2019. The success of early clinical trials completed at the Mayo Clinic utilising senolytic drugs has only added fuel to the fire, such that we may indeed be nearing the point where we can truly interfere in the ageing process in humans. There are, however, a number of other reasons for this trend, including:

**“It looks likely that 2020
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the industry.”**

1. The last 3-5 years have witnessed the launch of a number of longevity-focused funds, taking a portfolio approach to longevity investment. By developing a portfolio of longevity investments, these funds hedge their risk across a number of promising longevity start-ups, thereby increasing their chances of success. In this vein, Juvenescence has created its 'longevity-ecosystem' and now has 15 independent pre-clinical programmes. It successfully raised \$50 million in a Series A financing round in 2018 and recently closed a \$100m Series B round. Other longevity funds (including The Longevity Fund, Longevity Vision Fund, Kizoo Technology Ventures and Felicis Ventures) have raised capital and in so doing allowed investors to access some of the best early stage deals globally. Investment in this space is no longer the preserve of West Coast venture capital.



2. High-profile success stories and public listings have further demonstrated the potential of longevity companies to create enormous shareholder value (particularly for early investors). Unity Biotechnology, a company specialising in senolytics launched an IPO at nearly unicorn valuation and raised \$85 million exemplifying the trend between technological advances and investor interest.
3. Progress in basic science and research into ageing and age-related disease, together with the growing competition within the life science sector, has led to an improved understanding of the ageing process and the causes of disease. A consequence of this is that the rate of progress in the industry has accelerated and there have been notable advances in technology. For example, the advances in ageing



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For more information, please contact:

Michael Corcoran

Partner

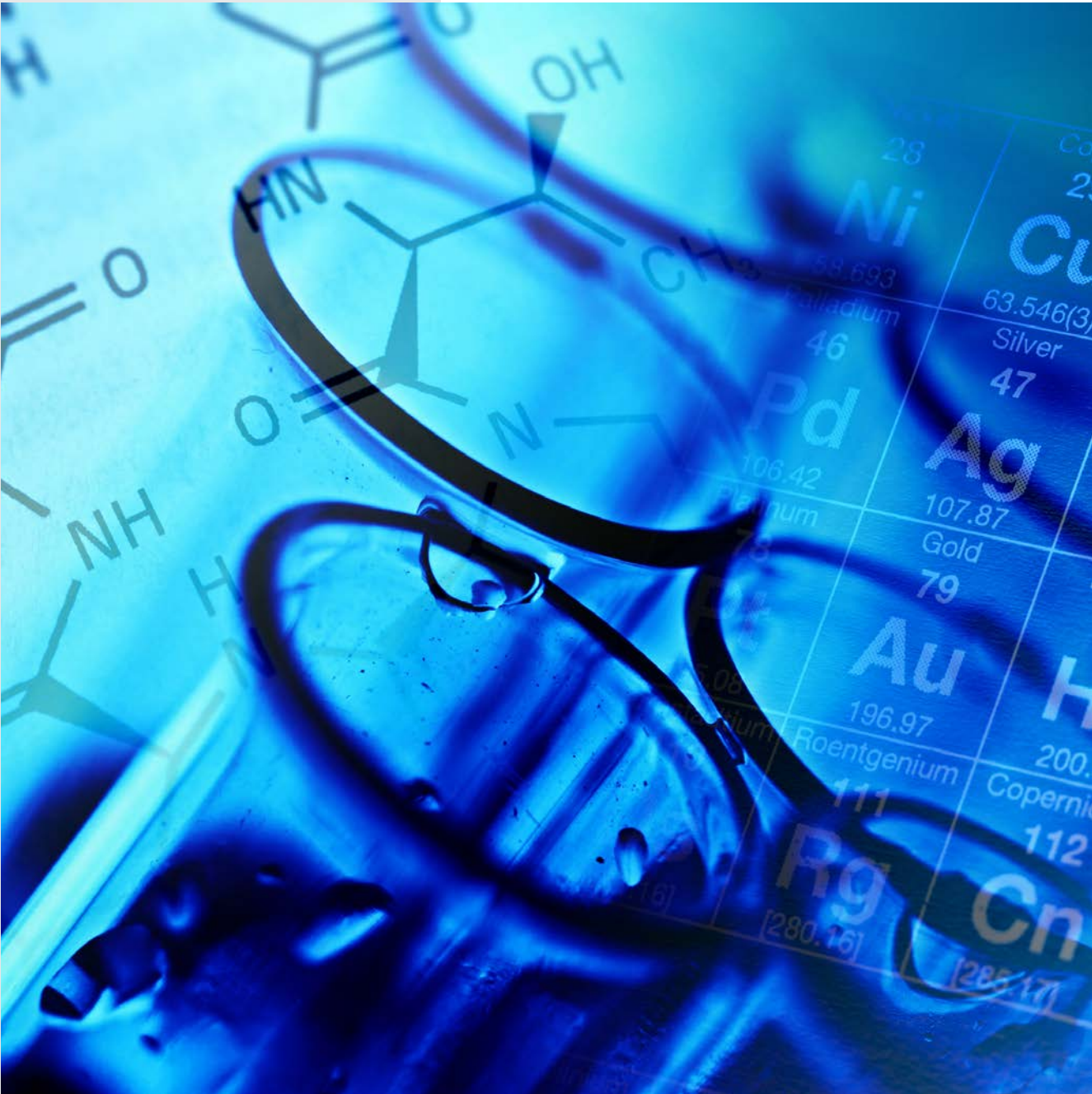
+44 (0)20 7283 9033

michael.corcoran@hilledickinson.com

The Broadgate Tower, 20 Primrose Street, London EC2A 2EW

hilledickinson.com





biomarkers or “ageing clocks” now make it possible to measure the rate of ageing in humans and conduct clinical studies without the need to wait until the end of life. Real results are beginning to convince investors this is a sector worth taking seriously and likely to grow considerably in the coming years.

4. Google’s interest in the area has helped to generate publicity and interest in longevity. Its sister company Calico made the cover of Time magazine when it was set-up in 2013 with the goal of combating ageing and associated diseases. Its 150 employees are currently working on a US\$2.5 billion collaboration with US pharmaceutical company AbbVie, in Calico’s labs in San Francisco, the largest known research project looking at lifespan extension.
5. A series of mega-deals in 2018 sparked the wider attention of investors to the potential of the industry and has helped bolster investor confidence. Samumed raised US\$438 million in a financing round in August 2018 and Celularity raised US\$210 million in a February 2018 Series A round.

**“Margaretta Colangelo,
managing partner
at Deep Knowledge
Ventures and Longevity
Capital claims the
longevity industry will
reach US\$27 trillion
by 2026.”**

Looking to the future

Akin to the PC industry in the early 80s, or the internet in the 90s, Jim Mellon of Juvenescence claims we are at the internet dial-up phase of longevity biotechnology. Investors have an opportunity to cash in at the front end of a huge upward curve. In the short-term, we will see companies progress through their seed and Series A-D rounds, after which some will go public with IPOs. Juvenescence announced recently that they would shortly be initiating their crossover round, with the intention of going public (on NASDAQ) in the second half of 2020. Mellon predicts a proliferation of longevity-focused funds



will form in the next few years, foreseeing that the current 10 or so longevity-focused funds will multiply into the thousands within a decade. Margaretta Colangelo, managing partner at Deep Knowledge Ventures and Longevity Capital claims the longevity industry will reach US\$27 trillion by 2026.

The popularity in the space seems to have recently gained traction with the UK government too: Juvenescence recently visited No.10 to discuss the topic of longevity with a group of industry experts. This meeting is in-line with the development of the Government's national Healthy Longevity development strategy. The All Party Parliamentary Group (APPG) for longevity launched in May 2019 plans to produce the draft National Strategy by early 2020. This Strategy will set out what the United

Kingdom needs to do to meet the goal set by the Government of five more years of healthy life expectancy by 2035. The health secretary Matt Hancock said that the APPG will allow the government to deliver the dream of longer, healthier lives and at the same time close the large social gap in healthy life expectancy.

The newly formed UK Longevity Council, which is co-chaired by Matt Hancock and business leader and industry expert Andy Briggs, will advise how best to use innovations in technology, products and services to improve the lives of our ageing population. The Government has also backed the Ageing Society Grand Challenge, which will run competitions for a £98 million fund to develop products and services that will help people live better and more independent lives as they grow older.



Michael is a partner in the corporate team at Hill Dickinson, having qualified as a solicitor in 2005. He

works primarily with high-growth private companies and small-cap listed companies, particularly in the media, technology, life sciences and resources sectors.

Michael has increasingly focused on matters relating to the life sciences sector over the last five years, working with academics, university spin-outs, venture capital and private equity groups. In particular, Michael has advised Juvenescence Limited, a longevity-focused company, and EMMAC, the leading independent European cannabis company, since incorporation.

Michael has extensive capital markets experience and has led a number of IPOs on the AIM market, the standard list and also the NEX high growth market. In addition, Michael has vast experience advising listed clients on secondary fundraisings, reverse takeovers, schemes of arrangement, takeover offers, tender offers, rights issues, general M&A and private equity.

Michael is noted in The Legal 500 2020 as a 'trusted adviser whose capacity, communication, and commitment to excellence shines through.'

Hill Dickinson: life, longevity and the law

Hill Dickinson acts for a number of longevity focused companies and is a sponsor of London Longevity Week [11-15 November 2019 (further details at <https://thelongevityforum.com/the-longevity-week>)]. Hill Dickinson's Life Sciences team provides practical, commercial legal advice to clients at all stages of development, from start-up to established multi-national. We support clients from an idea in a lab, to helping incorporate the company, raising capital, protecting and licencing intellectual property, signing strategic partnerships and, ultimately, commercialising life-changing treatments and technologies. We also help clients navigate a legal landscape that is continuously evolving in response to innovation as well as societal, regulatory and ethical challenges. Our integrated team provides high-quality, trusted advice to some of the world's leading life sciences companies. Areas of expertise in which we work include healthtech (including AI), pharma, IVF, embryo research, medical cannabis, cell and gene therapies, and genomics.

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The longevity opportunity is waiting to be grasped

By Reason, Co-founder and CEO of Repair Biotechnologies



Repair Biotech co-founder and CEO, Reason, explains how longevity science has moved out of the realms of obscurity to become a very promising and exciting field that's moving towards commercialisation, with two examples of how his own organisation is tackling the scourge of ageing.

In 2018 Bill Cherman and I founded Repair Biotechnologies, one of perhaps 50 to 100 preclinical biotech start-ups making up the newly formed, rapidly growing longevity industry. Our investors include Jim Mellon, Harald McPike, funds such as Emerging Longevity Ventures and Thynk Capital, along with noteworthy organisations in the longevity space such as the SENS Research Foundation and Methuselah Foundation. At Repair Biotechnologies, the capable science team works on gene therapies with the aim of reversing aspects of immune ageing and cardiovascular ageing. We are proud to be doing our part to help bring about a better world, in which ageing does not have to mean disease, suffering, and diminished capacities.

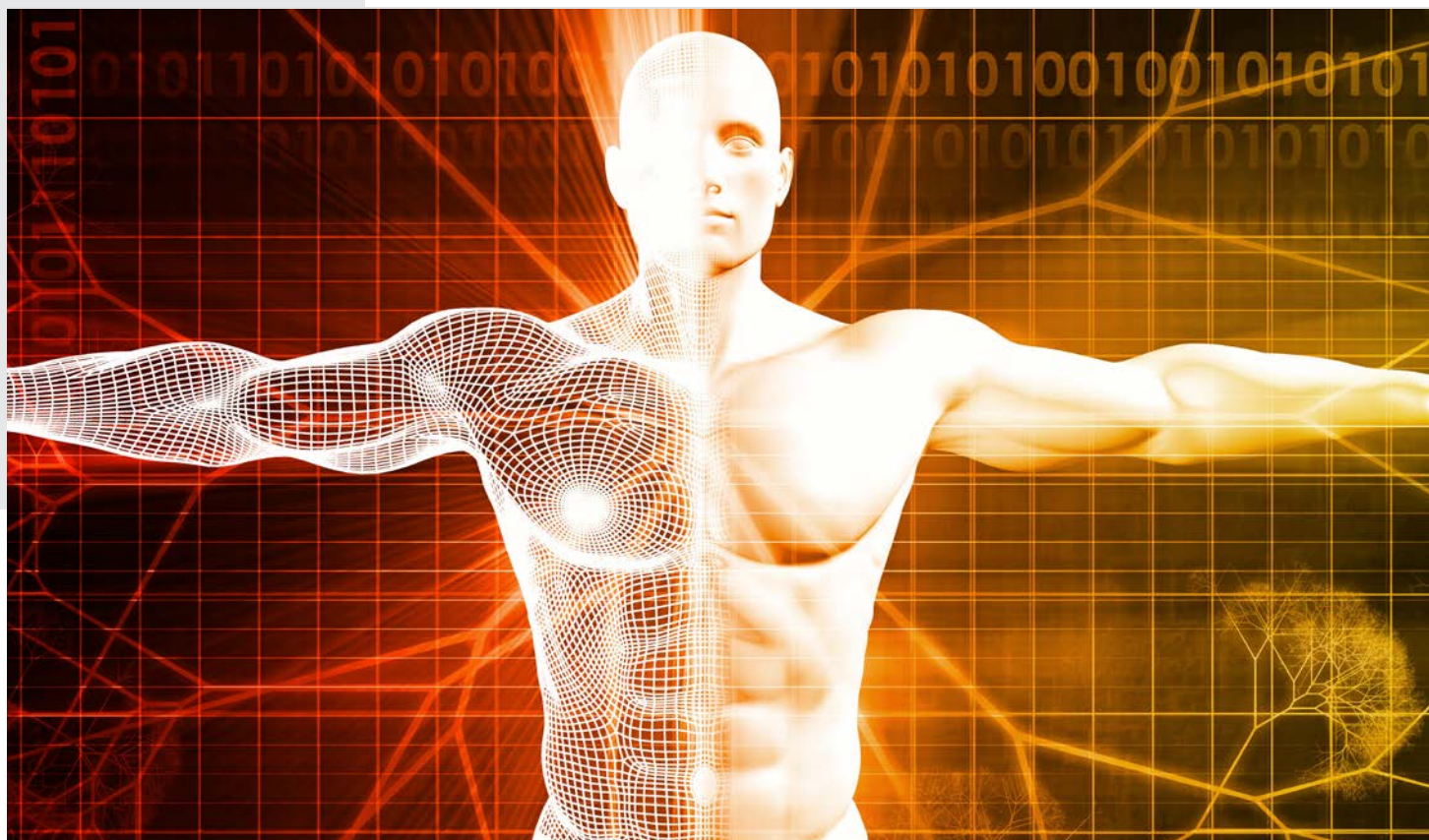
The highly dynamic and exciting longevity industry is perhaps unique amongst human endeavours for the enormous scope of presently unaddressed opportunities to build therapies and companies, coupled with the enormous size of the marketplace for rejuvenation therapies that lies ahead. The present character of the industry and its

participants is an unusual one, the result of a combination of circumstances that is unlikely to ever happen again. It is characterised by the following: (a) novel products for whom the target market is every living human being, and all companion animals as well, while we're at it; (b) decades of active suppression of clinical translation of ageing research, leading to a scientific community cluttered with high quality, high potential, yet effectively abandoned projects; and (c) a sudden blossoming realisation, taking place over just a few years, amongst scientists, futurists, patient advocates, entrepreneurs, and investors, that, hey, this rejuvenation thing is real.

It has been 17 years since Aubrey de Grey and his co-authors declared that existing evidence strongly indicated senescent cells to be a

“We are proud to be doing our part to help bring about a better world, in which ageing does not have to mean disease, suffering, and diminished capacities.”

“There is still a vast accumulation of thirty years of truly compelling projects in the scientific literature, largely untouched and undeveloped.”



cause of ageing, and that the research community should work towards a means of targeted removal of these cells. It was an uphill battle to convince people to in fact work seriously on this project. It has been only eight years since philanthropic funding was used to produce a demonstration of that removal of senescent cells and consequent rejuvenation in mice, a demonstration that was compelling enough to wake up the scientific world and its observers to the very real potential of turning back the course of ageing by tackling its causes. Philanthropic funding was used because no institution or investor was willing to take the risk: for decades prior to that demonstration, nearly everyone and every institution involved in scientific development and clinical translation radically misjudged the potential to achieve rejuvenation, dismissing it almost out of hand.

A sizable part of this dismissal was cultural. Since the 1970s, the existence of the anti-ageing marketplace, equal parts supplements and fraud, caused the leaders of the ageing research community to retreat from any claim or intent to treat ageing as a medical condition. They saw the entire concept of intervention in the ageing process as a poisoned well, and policed their own community quite ruthlessly. They

were wrong to do this, but the damage has been done. Only very recently did this culture of 'look but don't touch' in ageing research begin to thaw into a more reasonable position on intervention. The result is that now, with the sudden acceptance of the ability to treat ageing as a medical condition in order to achieve rejuvenation, there is still a vast accumulation of thirty years of truly compelling projects in the scientific literature, largely untouched and undeveloped. These are legitimate means to treat ageing, or the foundation to produce such a treatment, each of which is in some form of limbo, awaiting a champion to bring it to the clinic.

Hence companies like Ichor Therapeutics, one of the earliest in the longevity industry, arising from the advocates at the SENS Research Foundation, and more recent and well capitalised efforts such as Juvenescence and Life Biosciences. And hence others, including Repair Biotechnologies. All of these ventures exist because we as founders, collectively, looked at the state of the science, at the enormous potential of that science, at the lack of progress towards clinical translation, and we said: "we must do something about this." We picked our favoured projects, and we all got to work. It is less that there are vast returns on investment to be made (though this is certainly true) and far

**“Repair Biotechnologies
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more that ageing might be controlled in our lifetimes, if we all just set to it. Ageing might be made into a condition that no longer kills or incapacitates, because new medical technologies shield us from that fate. At the end of the day, what is the currency of interest, the true measure of wealth – dollars or healthy years? For those of us in this first wave of the longevity industry, it is the healthy years. And if we set our sights on that, the dollars will naturally follow.

There are countless projects that can lead to effective treatments for degenerative ageing, if one only knows where to look, and knows how to evaluate the expectation value of a given approach. By virtue of my long-standing experience and network as

a patient advocate for rejuvenation research, Repair Biotechnologies has the pick of the best projects with the highest expectation values, informed by the SENS viewpoint of the causes of ageing. In the present environment of too few entrepreneurs and companies actively tackling ageing in a serious way, it makes sense to choose ambitious goals – individual projects in medical biotechnology of great enough impact to change the shape of what it means to be old. Ageing is enormously complex, but its roots are far less so. Imagine ageing as analogous to rust in a complex metal sculpture: rust is a simple process, and simple to prevent given the right tools, but let it run and who can predict how exactly the sculpture will collapse? The complexity is in the sculpture itself, not in the process that initiates its destruction. Initiatives that strike at the roots of ageing will be easier to enact, less costly, and achieve greater and more sweeping success than those that attempt to intervene in the downstream complexity of a disrupted ageing metabolism. Senolytics to clear senescent cells are the present best example of this principle, given their demonstrated ability to reverse nearly all of the common age-related conditions in mice, but that is just one of many possible and necessary approaches to the control of ageing.

At Repair Biotechnologies, our first programme of gene therapy development is focused on regeneration of active tissue and restoration of T cell production in the thymus. The thymus is the organ responsible for the maturation of T cells, an essential component of the adaptive immune system. The core problem addressed here is the age-related loss of active thymic tissue, driven by factors such as chronic inflammation and its detrimental effects on tissue maintenance and regeneration, which in turn leads to loss of T cell production and, consequently, immunosenescence. Upregulating the master regulator gene of thymic growth and activity, *FOXN1*, is a straightforward goal and a single well-established therapeutic target, supported by a sizable array of high-quality evidence from the past few decades of research. Yet the immune system is so central to the health of the individual that any form of restoration can beneficially affect a great many other systems. We are not so much repairing damage as we are introducing sophisticated tools into the body, the newly created T cells, that will go on to repair damage.

The immune system is a powerful lever. When restored to a more youthful quality of function, such as by reversing the age-related decline in the supply of new T cells, then it will set forth and

help to fix a number of issues. Cancer risk and senescent cell burden are two of the more important – it isn't just about preventing older people from succumbing to infection, though there is certainly that factor as well.

Our second programme is nothing less than an initiative to cure atherosclerosis, to eliminate the condition completely. Not just slow it down, but get rid of it, prevent it from ever occurring, and hopefully reverse it extensively even in late stages. Does this sound ambitious? To be ambitious is only appropriate: this is an era of radical progress in biotechnology, the potential is there, and we should seize such opportunities where they exist. Atherosclerosis accounts for perhaps a sixth of all deaths, and yet the scope of





the possible is widely seen at present as only a slowing of the condition. It is a field that desperately needs new groups trying new, high expectation value approaches, breaking from the present dominant classes of therapy that can do little to reverse atherosclerosis. This is a common theme in other areas of medical development, such as the Alzheimer's research and development communities, to pick one example. It is time for a change, for radical new approaches informed by what we now know of ageing, for disruption of the failing efforts of the past few decades.

Atherosclerosis is a condition in which fatty deposits called plaques grow to narrow and weaken blood vessels, inevitably leading to rupture

or blockage, heart attack or stroke. It is characterised as a disease of excess cholesterol, but in fact arises from the dysfunction of macrophage cells responsible for clearing cholesterol from blood vessel walls. Macrophages become overwhelmed by cholesterol variants that are increasingly present in old age, and die, adding their corpses to the mass of the plaque that they are attempting to dismantle. We are developing a gene therapy to provide macrophages with the capability to break down cholesterol in situ, thereby becoming near invulnerable to the primary form of dysfunction that both accelerates atherosclerosis and prevents macrophages from doing their clean-up duty. Given invulnerable macrophages, in principle all plaque

will be removed over time, and blood vessels kept clear – just as they are in young people.

These are but two examples of numerous exciting approaches to rejuvenation presently under development in the longevity industry, in the many companies whose founders and staff are working hard to make a big difference to the trajectory of ageing. Yet this industry as it stands today is just the first step. Scores of amazing, promising projects in medical biotechnology for the treatment of ageing remain without a champion. Development programmes focused on all of the major causes of ageing beyond senescent cells, those that are described in the SENS rejuvenation research proposals, lag far behind the present successful clinical translation initiatives for senolytic drugs.

Thus, much remains to be accomplished, and for entrepreneurs and investors not yet involved in this industry, that means that the opportunity for longer healthy lives, greater returns, and a world changed for the better is still largely waiting to be grasped. To all of you as yet uninvolved, I ask: what is it that you are waiting for? An engraved invitation? Consider yourselves invited. There is a lot to do, and the present industry will welcome your assistance.



Reason is co-founder and CEO of Repair Biotechnologies, a biotech start-up working on means of rejuvenation of the thymus and reversal of atherosclerosis. He is the founder and writer of Fight Aging!, which has been a leading voice in the longevity biotechnology and patient advocacy communities for more than fifteen years. Reason is also an active angel investor in the rejuvenation biotechnology space, and has for many years led and aided non-profit fundraising for academic research into rejuvenation via repair of molecular damage.

Repair Biotechnologies

Repair Biotechnologies, Inc. is a biotechnology company with the mission to develop and bring to the clinic therapies that significantly improve human healthspan through targeting the causes of age-related diseases and aging itself. Founded in 2018, Repair Biotechnologies is developing therapies with the goals of regenerating the thymus, treating cancer, and reversing atherosclerosis.

 www.repairbiotechnologies.com

Investor Events Diary

EVERY WEDNESDAY | 12:30**Event:** SR Live webinar**Organiser:** SyndicateRoom**Place:** Webinar**Tickets:** www.syndicatoroom.com/events/sr-live

21 NOVEMBER | 08:00-10:30**Event:** Ready Steady Grow!**Organiser:** EISA**Place:** Engine Shed, Bristol**Tickets:** <https://eisa.org.uk/events>

21 NOVEMBER | 08:30-16:30**Event:** The VCT & EIS Investor Forum**Organiser:** AngelNews**Place:** Leonardo Royal Hotel Tower Bridge, 45 Prescott Street, London E1 8GP**Tickets:** www.thevctandeisinvestorforum.com

22 NOVEMBER | 08:30-19:00**Event:** MoneyWeek Wealth Summit**Organiser:** MoneyWeek**Place:** etc.venues, St Paul's, 200 Aldersgate, London EC1A 4HD**Tickets:** Code: Master20 www.moneyweekwealthsummit.co.uk

26 NOVEMBER | 08:00-10:30**Event:** Ready Steady Grow!**Organiser:** EISA**Place:** Tramshed Tech, Cardiff**Tickets:** <https://eisa.org.uk/events>

27 NOVEMBER | 14:00-21:00**Event:** Future Forward: UKBAA Winter Investment Forum**Organiser:** UKBAA**Place:** CMS, Cannon Place, 78 Cannon Street, London, EC4N 6AF**Tickets:** www.futureforwardukbaa.org

27 & 28 NOVEMBER | 10:00-18:00

Event: Going Global

Organiser: PRYSM Group

Place: ExCeL London, Western Gateway, Royal Docks, London E16 1XL

Tickets: www.goinggloballive.co.uk/tracker.asp?code=MasterInv

5 DECEMBER

Event: Plan to Grow: The essential event to bring you up to date on trends in the EIS & BR markets

Organiser: EISA

Place: The Great Hall, ICAEW, One Moorgate Place, London EC2R 6EA

Tickets: <https://eisa.org.uk/events>

11 DECEMBER | 18:00-20:30

Event: Funders & Founders; Christmas Networking Reception

Organiser: Business Funding Show

Place: WeWork Paddington

Tickets: www.businessfundingshow.com/events

12 DECEMBER | 09:30-17:30

Event: The Sustainable and Social Investing Conference

Organiser: Investor Conferences (UK) Ltd

Place: Novotel London West, 1 Shortlands, London W6 8DR

Tickets: Code MI2019 for £20 off. www.eventbrite.co.uk/e/the-sustainable-social-investing-conference-tickets-65928069631

20 FEBRUARY 2020 | 10:00-17:00

Event: The Business Funding Show

Organiser: Business Funding Show

Place: East Wintergarden, 43 Bank St, London E14 5NX

Tickets: www.businessfundingshow.com/events/the-business-funding-show-2020

28 FEBRUARY 2020 | 09:30-17:00

Event: The London Trader Show

Organiser: Master Investor

Place: Novotel London West, 1 Shortlands, London W6 8DR

Tickets: www.eventbrite.co.uk/e/london-trader-show-2020-tickets-59881575404

28 MARCH 2020 | 09:30-17:00

Event: Master Investor Show

Organiser: Master Investor

Place: Business Design Centre, 52 Upper St, London N1 0QH

Tickets: 50% discount; code: MAG10 <https://masterinvestorshow.eventbrite.co.uk>



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