

Irish Medtech
Association
Ibec

The Medtech Entrepreneur

Founders share their stories of starting and growing a business in Ireland

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Finding your purpose, a passion for medtech innovation

“I’ve worked in the medtech sector for over a decade, but I’m still amazed by the passion and sense of purpose that people bring with them to change lives daily by developing innovative technologies,” Irish Medtech Association Director Sinead Keogh reveals.

The new millennium marked the beginning of a new age for medtech innovation and growth in Ireland.

Since the Irish Medtech Association was established as part of Ibec in 2000, under Sharon Higgins’ leadership, we’ve witnessed a wave of entrepreneurs emerge and a multitude of new medtech startups born in Ireland. Since I joined Ibec in 2006 I’ve enjoyed being part of this important work to help Ireland’s medtech industry move up the value chain. While we continue to be recognised internationally for manufacturing excellence, companies here have taken ownership of complete supply chains, increased the level of R&D, as well as embraced smart manufacturing,” she adds.

Ireland’s medtech sector now boasts more than 450 medtech businesses, including 9 of the world’s top 10 medtech companies.

continued overleaf



*John O'Brien,
Sinead Keogh
and Conor Hanley*

“ We must continue to speak out as the voice of Irish medtech to help develop policies and conditions to ensure entrepreneurship can thrive.”



Global trends and growth

Globally the top three areas dominating market share will continue to be invitro diagnostics at 13.4% with sales of €71 billion, cardiology at 12.2% with €65 billion, and diagnostic imaging at 8.6% with €45 billion, by 2024. But, Neurology is set to be the fastest growing device area with 9.1% growth (CAGR) reaching €14 billion by 2024.

Orthopaedics, connected health, as well as ear, nose and throat (ENT) will continue to be strong growth areas with growth of 3.7%, 5.9%, and 5.7% respectively. Orthopaedics will reach €42 billion in sales by 2024, while connected health reaches €15.7 and ENT reaches €12 billion.

Of the 450 medtech businesses here, 60% are homegrown and as many as four out of five are startups or SMEs.

“The success of Ireland’s global medtech hub has seen €316 million in investments and 2,300 jobs, as well as €178 million financing raised by startups, publicly announced in the past couple of years. The continued growth of Ireland’s medtech sector is a bet worth taking, with a growing number of successful acquisitions making headlines.” Keogh remarks.

The Irish medtech community connects people, she explains “Ireland now boasts some worldclass medtech serial entrepreneurs and founders like Ian Quinn, John O’Shaughnessy, John Power and John O’Dea who shared their stories with us here.”

“You can never underestimate the power of people coming together to deliver a shared vision and that’s what we do in the Irish Medtech Association. We’ve been blessed with experienced CEOs and senior business leaders sitting around a table together to guide the industry to success by setting out an ambitious strategy for future growth.”

“And we couldn’t achieve this without our numerous working groups who offer specialist expertise to champion key priority areas such as advanced factory, digital health, leadership development and regulatory affairs.”

Keogh has been bowled over this year after setting-up the Founders Circle, “I have a deep admiration for entrepreneurs. I’ve had the opportunity to hear about the highs and lows of starting a business. The successes which we applaud and

promote, but also those who have tried, failed, and then tried again. It takes great courage to believe in yourself and take risks by founding a startup.

“We’re lucky in Ireland to not only have some exceptionally talented people but also a supportive ecosystems with a range of supports like Enterprise Ireland, BioInnovate Ireland, and the Health Innovation Hub Ireland to name but a few of the key players profiled here.”

But more can be done to realise the sector’s potential, “My big ambition for Ireland is to be a location of choice not only for startups, but also for investors. We need to attract more global investment into Ireland to help transformative technologies get to patients.”

“The Irish Medtech Association will continue to nurture entrepreneurship as the voice of Irish medtech and part of Ireland’s leading business group Ibec. We’re calling on the Government to help the industry succeed by developing the right policies and conditions to encourage risk taking.”

She adds, “If we get this right we can make Ireland one of the top 10 global startup communities, with more startups founded here and international business leaders choosing to grow their business here.”

“We hope that aspiring entrepreneurs will be inspired by the success stories presented in The Medtech Entrepreneur. I’d like to thank all our members who shared the lessons they learned on their journeys starting and growing businesses in Ireland, and I’d also like to recognise Irish Medtech Association Executive Ciara Finlay’s role bringing their stories together here.” Keogh concludes.

Positioning startups for success

“The Irish Medtech Association is pushing Ireland forward to cement its position as an international leader in connected health,” says Irish Medtech Association Chair and FIRE1 CEO Conor Hanley.

The company was set-up in Dublin five years ago where it's developing a novel remote monitoring solution to improve outcomes for heart failure patients.

Heart failure affects around 90,000 people in Ireland with up to one in five people will developing it at some point during their lives. It affects mainly middle-aged to older people, while over 50yrs are the group most at risk younger people can develop it.

Globally it's estimated that at least 26 million people suffer from heart failure, with an ageing population the impact of heart failure is expected to increase substantially.

“Heart failure is a life-threatening disease and a significant burden on patients and the health system. Managing patients at home

with novel digital health-enabled solutions will promote better patient pathways with a reduced need for hospitalisation,” Hanley advises.

“Given the strength of Ireland's business and medtech ecosystems, we're in a strong position for FIRE1 to accelerate the development and commercialisation of our first product which has received strong support from global investors, having announced a €40 million financing investment last year.”

Serial entrepreneurs are common in the medtech industry and Ireland has some of the best in the world. Hanley adds, “I know from my own experience that startups play a unique role in the medtech ecosystem.



Conor Hanley

They help drive innovation and develop novel life changing technologies. I have seen personally with FIRE1, and before that BiancaMed, that Irish startups stand out with worldclass teams, technologies and the drive to develop amazing solutions to improve lives and help people get healthy.”

He cautions that, “While collaboration between large multinationals and startups is proven formula for getting transformative technologies to the market, more needs to be done to help small businesses make it big. The top ten medtech companies in the world occupied 39% of the market, in 2017.”

As Chair of the Irish Medtech Association, Hanley says Ireland needs “The right business environment to scale and drive sustainable growth. Or risk losing promising startups to relocations to Silicon Valley or Israel and other locations known for thriving entrepreneurial bases.

To help us better compete we’ve identified the, one, two, three of supporting startups:

- Attracting and retaining talent with share options
- An appropriate venture capital ecosystem
- Encouraging risk taking and reinvestment with incentives like a competitive CGT rate

Ireland is the greatest employer of medtech professionals, per capita, in Europe with 38,000 people working in the sector and 4,000 jobs to be added by the end of 2020.

“To compete with global multinationals, medtech startups need to be in a position to attract and retain talent. To do this we’re calling on the Government to introduce a new, best in class, flexible share option scheme that’s easy to use.”

Hanley highlights the fact that venture capital is the lifeblood of any thriving

startup ecosystem, but it’s a lifeline for medtech startups, “To get medical technologies into the health system and to patients, startups must overcome numerous hurdles, from proving technological feasibility and clinical trials, to getting regulatory approval to get market access, this takes funding. The number of VC firms and dedicated health technology funds here is not sufficient to meet the ambition of this growing sector.”

“But, there’s an opportunity to expand our VC landscape and build more partnerships between firms here and key locations such as California. To secure this vital element of the startup ecosystem, the Government must adopt a proactive approach or risk losing Irish businesses to more competitive startup hubs.”

Lastly, we need to address our uncompetitive Capital Gains Tax. “Ireland has the third highest rate of CGT in the OECD at 33%. Improvements made

under the 2016 Financial Act did not go far enough to bring us in line with our nearest competitor, the UK. We need the right business environment to support reinvestment and serial entrepreneurship,” he warns.

Hanley concludes, “Success doesn’t happen overnight. We will continue to engage with our members, as well as government and policymakers, as we work to bring in a more supportive tax environment, better access to funding and talent for startups in Ireland. It took many years for Ireland to become a global medtech hub. Now, as we look to the future, we must ensure that entrepreneurship and innovation remain at the heart of what we do. And that we take advantage of avenues for future growth.”

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A go-to destination for growth markets

“Medtech is an critical industry that’s not only driving growth it’s also improving lives,” Vice Chair of the Irish Medtech Association and S3 Connected Health CEO John O’Brien highlights.

John O'Brien



“ This trend is driving healthcare, lifescience and medtech organizations to develop services and solutions that demonstrably improve outcomes for patients through solutions that support, enhance, augment and sometimes replace their products.”

Medtech sales worldwide are forecast to reach €530 billion by 2024.

This represents growth of €168.6 billion between 2017 and 2024.

“In Ireland there is an established ecosystem of medtech, pharma and tech companies and so you have mix of people from these background with worldclass skills. These are some of the key ingredients you need to build a connected health company,” O’Brien notes.

As part of the Irish Medtech Association O’Brien wants to “Put Ireland on the map as a go-to destination for connected health innovation, development and commercialisation.”

With sales of €15.7 billion forecast by 2024 it’s an attractive area for both FDI multinationals and startups to explore.

Ireland is a strategic location of choice not only for global medtech, but also as a base to tap into the second biggest global medtech market, Europe accounting for 27% of the world market at €115 billion.

O’Brien adds, “The medtech industry is a very

prominent and successfully sector in Ireland and is constantly innovating. The move to value-based care and payment for outcomes is already influencing medtech and I want to help where I can in driving awareness and knowledge of how connected health solutions in medtech are a key part of addressing this challenge.”

Healthcare spending in the OECD grew an estimated 2.5% in 2017, with increased demand for services, ageing populations and the rise of chronic diseases putting pressure on health systems.

Hospitals account for 40% of health spending, but connected health presents an opportunity to develop technologies that empower patients, and help them get on the right care pathways.

“In S3 Connected Health we believe that the move to value-based care and payment for outcomes is happening and will accelerate. This trend is driving healthcare, lifescience and medtech organizations to develop services and solutions that demonstrably improve outcomes for patients through solutions that support, enhance, augment and sometimes replace their

products,” he explains.

Talking about his own company, O’Brien says, “S3 Connected Health works with global medtech and lifesciences companies to design, develop and deploy digital therapy and patient support programs that increase awareness, assist self-management, gather real-world-evidence, and improve access, adherence and outcomes for patients and healthcare professionals.”

O’Brien offers advice for aspiring entrepreneurs, “When building a company in the connected health space a critical learning is to understand that an effective technology solution alone is not enough. You need to understand how your solution will fit in into care pathways and that these care pathways can be quite resistant to change. Your solution needs to be very low friction and must bring benefits to all stakeholders in the system and have a path to scale.”

The Medtech Entrepreneur showcases inspiring examples of the dynamic medtech startups leading across exciting growth areas with advice from leading CEOs and Founders.

Irish medtech's first champions

Ireland's ability to attract foreign direct investment helped set the scene for a worldclass manufacturing hub. Medtech's founding fathers used their experience as global suppliers for ICT businesses and R&D leaders in medtech FDI multinationals to follow their passion and make a difference. Taking a risk on medtech has paid off for these entrepreneurs and they're paying it forward by investing both their time and money in the next generation of medtech leaders. By learning from their fears, hopes and dreams we can ensure that medtech startups achieve new heights in the future.





From entrepreneur to investor

Over the course of 40 years, Ian Quinn has gone from someone who had little knowledge of medtech to becoming a major player in the industry with his company Creganna Medical and now an advocate and financial supporter of medtech startups in Ireland.

For Ian Quinn, the “oh my goodness” moment in his medtech journey came in 1995 when the company he co-founded in 1980, Creganna, was approached by medtech giant Boston Scientific.

“Our original market base was mini computer manufacturing, which had disappeared by 1995. In survival mode, we became a company that solved unusual manufacturing problems. Boston Scientific came to us with just that. It was to do with a component for an angioplasty catheter used to unblock the coronary arteries,” recalls Quinn.

“We solved the problem for Boston Scientific; then essentially got all of its business for that component worldwide. At that time, we had no experience of medical devices as such. The rest of the medtech companies in

the minimally invasive vascular surgery space came to us. The result was that over a few years, Creganna gained 80% of the world supply of that component and to this day it has retained that market share.”

It was a scramble to meet demand initially, but once that was achieved a decision had to be made about what to do next. In 2003, Creganna divested its operations in all other industries to focus solely on the medtech sector.

“We had heavy dependence on this one component and didn’t want to risk it being discontinued or taken from us. Customers had started asking us to do prototypes to help them with next generation products involving that component, so we decided to become medical device designers and developers,” explains Quinn.

“That brought us into the entry stage for fresh

product development and new components. Being first to come in through the design route worked like a dream. We graduated to also becoming manufacturers of the components.”

This was the catalyst for a whole series of development within the company. Processes and capabilities were added and a strategic decision was made for Creganna never to compete with its customers. “We also put Chinese walls in place as we were designing and developing for competing customers, so they had to trust us. Our customer base came to include all the major medtech companies in the vascular area and a large number of minor ones,” says Quinn.

In 2005, Quinn sold a minority stake in Creganna to a New York private equity firm, stepping back as CEO but continuing to contribute at

board level as chairman. Five years later, he sold his majority stake to global investment firm Permira, which subsequently sold Creganna to sensor and connector manufacturer TE Connectivity for €820 million.

Giving something back

Over the years, Quinn had diagnosed the medtech industry as being over-dependent on foreign multinationals and felt there weren’t enough smaller Irish companies. Following his substantial dividend from selling his stakes in Creganna, he decided to put money aside to be made available for investment in medtech startups.

“There is a myriad of medtech startups at various stages all over the country and – unlike computer manufacturing or textiles – this

What would you do differently knowing what you know now?

“I would hire great engineers and managers earlier. For too many years I tried to do everything myself. The company was getting very big and needed management skills that perhaps I didn't have. I was great at the startup stage, in building the company and at customer service, but I could see I needed to step back as CEO in 2005 and become chairman. In the early stages, I was very afraid of debt, but I should have been less afraid which would have enabled the company to move faster and purchase better equipment.”

is an industry that's here to stay. My objective is to make sure it does stay by having a mix of foreign multinationals as well as Irish startups and mid-sized companies that hopefully might soon become multinationals themselves,” he says.

Having been inundated with proposals from startups looking for investment, Quinn introduced the criterion that candidates must have gone through the BioInnovate Ireland programme and achieved commercialisation funding from Enterprise Ireland before he will consider them. So far he has invested in a number of such startups, including Embo Medical.

“The companies that emerge from the BioInnovate programme are better thought out than startups in general. They have gone through the wringer and competed for Enterprise Ireland commercialisation funding

with a high success rate,” says Quinn.

While pursuing his interest in startups, Quinn was given a tour of the design courses available at Stanford University in the US. “One of them, BioDesign, struck me as being particularly suitable for Ireland. I happened to meet President of NUI Galway Jim Browne and told him about it,” he says. Soon after, in 2011, BioInnovate Ireland came about and Quinn was asked to chair its advisory board, which he did for a number of years.

“The programme has done just what I said it would. In practice, over half of the teams go on to implement business plans and bring their startups to a stage where they are investable by angel investors,” he notes.

“I have been asked back to Stanford to give talks to Fellows of the BioDesign course. When they heard about the commercialisation funding available through Enterprise Ireland they went green with envy. There is no such thing in the US.”



Ian Quinn

“ There is a myriad of medtech startups at various stages all over the country and – unlike computer manufacturing or textiles – this is an industry that's here to stay.”

John O'Shaughnessy has played an important role in the evolution of the medtech cluster in Ireland from managing a global business to founding two very successful companies. He wants to see that cluster growing in strength so it can have an even greater impact on medical science, employment and the economy of the country.

*John
O'Shaughnessy*

Going out on your own

From a very early age John O'Shaughnessy had strong thoughts and feelings about wanting to set up his own business some day. As he puts it, he effectively began his "apprenticeship" in medical devices in 1982, by jumping at the opportunity to join CR Bard when it set up in Galway. One year later and at the age of 34 he became the company's General Manager. Bard (now Medtronic in Galway) was the world's pioneer in the development of minimally invasive medical devices for the treatment of cardiovascular diseases. O'Shaughnessy spent 16 years with the company in ever-increasing senior management positions. During that time, he set up the very first medical device research and development function in the country and prior to leaving had full business responsibility for Bard's Cardiovascular Products Division outside the US.

What would you do differently knowing what you know now?

“The experience I gained with Bard was priceless but I could have left at least five years earlier than I did and started more companies. The landscape for financing startups has much improved over the past years. If I were starting out today I would be setting my sights on scaling the startup in order to develop the company with a global reach and resist the path of early exit or sale of the business.”

“I saw opportunities to realise my ambition of starting my own business in 1996 and took the risk of leaving a very high profile senior management position with a global company to set up MedNova along with three others,” says O’Shaughnessy.

Headquartered in Galway, MedNova pioneered the development of medical devices for the treatment of atherosclerosis in arteries leading to the brain in order to prevent stroke. As its CEO, O’Shaughnessy led two fundraising rounds in excess of €20 million. In conjunction with the investment arm of Deutsche Bank, he managed a structured sale of MedNova to Abbott Laboratories.

“Abbott Laboratories’ initial investment came in 2001 culminating in a final exit in 2005. The investors realised an exit valuation of US\$120 million. MedNova proudly became the first successful exit of an Irish-founded and venture-capital backed medical device startup in the country,” notes O’Shaughnessy.

Co-founding Neuravi

With a successful exit under their belts, Eamon Brady, the former Chief Technical Officer and co-founder of MedNova and O’Shaughnessy researched over 20 medical treatment opportunities. “These had either been brought to our attention or were ideas which we pursued independently. We finally focussed on ‘acute ischemic stroke’ and formed Neuravi where Eamon assumed the role of CEO and I became part-time Executive Chairperson,” O’Shaughnessy explains.

Acute ischemic stroke is caused when a blood clot

travels to the brain, lodges in an artery, and restricts blood flow. Over 80% of all strokes are caused by acute ischemic events. Until recently the “treatment time window” was treated with a clot-dissolving drug that had to be administered in a specialised stroke unit within four hours of the onset of symptoms.

“We identified the need for an alternative treatment, and developed EmboTrap, a device which would mechanically remove the clot. We raised over €25 million in venture capital funding, including from Fountain Health Care Partners and Delta Partners, both Irish VCs,” says O’Shaughnessy.

Halfway through Neuravi’s US clinical trial the co-founders received several offers of interest from various suitors. This resulted in the recruitment of JP Morgan Bank to run a sale and auction process. Johnson & Johnson became the successful bidder during the early part of 2017 with an all-cash, 100% upfront offer which the shareholders accepted. The VC investors made in excess of nine times return on their investment. Neuravi’s EmboTrap product is now sold by Johnson & Johnson in markets all over the world.

Other medtech business interests

At present, O’Shaughnessy is Chairman of Irish medtech companies Vistamed, Cambus Medical and Loci Orthopaedics and was previously Chairman of Crospon.

With 500 employees in Carrick-on-Shannon, Co Leitrim and Roosky, Co Roscommon, Vistamed is a world leader in the provision of thermoplastic extrusions to

the minimally invasive medical device industry.

Cambus Medical is also world leader in metallic and plastic micro-components for medical devices and employs around 140 staff at its headquarters outside Galway in Spiddal.

A medtech spin-out from the BioInnovate programme, Loci Orthopaedics is finalising the development of the InDx thumb implant to reduce pain and improve mobility in thumbs affected by arthritis.

“I very much enjoy being involved in medical device innovation. There was a two-year gap from the time of selling MedNova to starting Neuravi and I had many offers of directorships,” says O’Shaughnessy. “I chose Crospon, Vistamed and Cambus because they were all very innovative and trading internationally and I felt I could contribute to their future growth plans.”

In the case of Loci Orthopaedics, O’Shaughnessy put an investor syndicate together. That investment, which was conditional on him being the Chairperson, made up a substantial part of the overall €2.8 million seed round.

“Apart from funding, I bring contacts with key medical opinion leaders, financial institutions, State agencies and with the global medical technology business,” says O’Shaughnessy. “My involvement adds to the company’s business credibility and it strengthens its image as a well managed company with good corporate governance. Good corporate direction and the development of management skills in leaders is a key component of the growing medtech ecosystem in Ireland.”

The first generation of medtech startups

Having started, built and successfully sold two Irish medtech companies, John O'Dea has seen significant evolution in the industry and is passionate about encouraging new startups led by unmet clinical needs.

When John O'Dea founded respiratory company Caradyne in 1997, he was part of the first generation of indigenous finished device medtech startups in Ireland. A true engineer, he was working in an R&D management position at Nellcor Puritan Bennett when he decided to go it alone with his own company.

"The only indigenous companies around at that time were sub-suppliers to the medtech industry. When Caradyne, MedNova and Aerogen were formed in 1997/1998, this represented the beginning of medtech startups creating devices for end users in Ireland. All of the founders came from R&D groups in multinationals. We were all learning as these were our first companies in this space," says O'Dea.



John O'Dea

John O’Dea’s top tip for startups: How to traverse the journey to market

“Rather than trying to raise a lot of money to build a big team, keep things tight in the early years. You will only have a couple of bites at the funding well, so delay this by being really lean early on and do as much as you can on a shoestring.”

“There was a different support infrastructure back then as Enterprise Ireland was only in its infancy. Our first steps were also Ireland Inc’s first steps into finished devices and we paved the way for other companies.”

Caradyne designed and manufactured non-invasive ventilation and humidification technology at its base in Galway. “Building a device and building the clinical evidence base is a long journey. With Caradyne, we started off with a basic R&D platform and went into manufacturing. There comes a point where you have got to invest in sales or marketing or look for a partner. For me as an R&D guy, learning about sales and marketing was great training. We found a large US distributor to work with and grew from there,” says O’Dea.

In 2004, US company Respironics acquired Caradyne, which broadened Respironics’ existing ventilation offering from hospital and home care settings into paramedic and emergency room settings.

Two years after this, O’Dea felt he had the confidence to go again with another medtech startup in Ireland and chose to do this rather than moving to work in the US. “I was interested in certain medical areas and 2006 was a better time for funding a company than in 1997. The fact that I had a track record made it easier to bring in funding as well. All of

the ingredients were right – I had a ready-made team of eight people from Day One who had worked with me at Caradyne,” he recalls.

“Things didn’t go as smoothly as with Caradyne. We went through two product development phases, as we quickly realised the first idea wasn’t working. Having started out with a device for glucose monitoring for diabetes, we made a quick twist to endoscopic diagnostics,” says O’Dea. “If a concept isn’t working, you have to know when to kill it and execute Plan B.” The concept behind Crospon’s product Endoflip originally came from technology licensed from Professor Barry McMahon who was in Tallaght Hospital at the time.

Crospon’s Endoflip and Esoflip technologies are changing the face of esophageal function testing. The minimally invasive medical devices transform the patient experience when it comes to swallow testing and deliver a whole new diagnostic tool into the hands of gastroenterology professionals.

In 2017, Crospon was acquired by Medtronic and integrated into its Respiratory, Gastrointestinal & Informatics business. The acquisition strengthens Medtronic’s position as an end-to-end leader in the esophageal disease space with innovative solutions from diagnosis to therapy.

“The increasing number

of acquisitions such as this in recent years is a success story for the Irish medtech industry. It shows that Ireland is not just a country of ideas with a strong manufacturing base, but is also an execution country where companies can get products out to the market. Lots of points are aligning to confirm that Ireland is a major centre for medtech startups. The ecosystem is as good as it gets in the world,” says O’Dea.

“One of the challenges coming from this success is that early-stage seed funding is more constrained than it used to be as there are more startups going after the same pot.”

Aside from setting up and running his own businesses, O’Dea has generously given of his time to the medtech industry over the years as Chair of the Irish Medtech Association and Chairman of the External Advisory Board for BioInnovate Ireland.

“The Irish Medtech Association is a fantastic networking resource, allowing large and small companies to meet each other in an informal way. It is also important in terms of lobbying. During my time as Chair, in 2013, we did some early work on lobbying for the establishment of a single, cohesive national research ethics committee structure in Ireland,” says O’Dea. Last February, the Government approved proposals by Minister for Health Simon Harris TD to prepare a General Scheme of a Bill to provide for national research ethics committees.

In O’Dea’s opinion, the BioInnovate programme has fundamentally changed the medtech startup landscape in Ireland. “It is the most fertile source of new startups we have seen. With the support of Enterprise Ireland, the power of this programme is incomparable.”

What would you do differently knowing what you know now?

“Endoflip was a great story that worked out. There was nothing like it before and we built a brand new market. However, Crospon was very technology-led rather than led by having identified a clinical need. Crospon is not a template I would use now if I was doing a medtech startup, especially after seeing the success of the BioInnovate Ireland programme, which is focussed on identifying and assessing unmet clinical needs. Being technology driven is a very difficult road to travel. A lot of things have to fall into place, which thankfully they did for us after ten years with Crospon. It is very challenging raising funding for a device business that does not meet a clearly defined clinical need, and a key thing I would do differently again would be to focus on establishing that first.”

Making a difference, not just making a living

It is no wonder that budding medtech entrepreneurs find founder and CEO of Aerogen, John Power, inspiring. Even in the face of adversity, he never lost faith in his ground-breaking product for aerosol drug delivery over the past 22 years.

Founder and CEO of Aerogen John Power believed he could develop the best solution possible to address a clear unmet clinical need for an aerosol drug delivery system for ventilated patients. His unwavering belief in the product ever since has brought the company to a point where this year it will have been used to treat more than 7 million patients around the world.

Aerogen's aerosol drug delivery system can reduce the length of time a patient needs to be on a ventilator or treated in an Emergency Department. Improved aerosol drug delivery means they recover faster and have a shorter stay in hospital. Its proprietary vibrating mesh technology turns liquid medication into a fine particle mist, gently and effectively delivering drugs to the lungs of critically ill patients.

"As a Design Engineer I could have had a career in any area of engineering, but I wanted to work in a sector in which I believed I could make a meaningful difference and that's why I love working in the medtech sector. When I go into hospitals and see patients on life support equipment supported by Aerogen's drug delivery system I know how critical it is to them," he says. "It is not like we are an alternative version to

what is already there. This is a complete step change in terms of drug delivery and efficiency for patients most in need of it. That sort of satisfaction is hard to achieve in other sectors."

A chartered engineer, Power had over 20 years' product design and commercialisation experience in the aerospace, automation and Med-tech sectors in various roles before he decided to establish his own

“ Having associations under one umbrella (Ibec) representing medtech, ICT and pharmaceuticals is very helpful as technologies are converging now. You can't look at medtech in isolation anymore.”



medtech company in 1997. “I had been involved in both MNCs and in startups so had a good grounding in the entrepreneurial process along with the discipline and more formal experience within international businesses. Back then, there wasn't the sort of funding available that there is now. I had to raise the money myself and remortgaged the house twice over the years to pay the company's bills.”

John Power

Surviving a hostile takeover

In 2000 Power merged his medical device company (then called Cerus Medical) with a US bio-pharma company Aerogen Inc which he helped to bring public on Nasdaq later that year. The company was subsequently acquired by San Carlos based Nektar Therapeutics and in 2008 Power led a leveraged management buyout of his strategic business unit from Nektar.

“We went public very successfully at a US \$300 million market valuation. I did the roadshow alongside the CEO Dr Jane Shaw and we got ‘out the door’ just before the markets crashed when the dotcom bubble burst. Shareholders switched from long play investments to those with a fast return on investment. Aerogen back then was a typical bio-pharma business with long development times and so funding dried up and eventually the company was put on the market. This meant any company could buy it, including a competitor and that's exactly what happened when Nektar acquired us in 2005 says Power. Working in a MNC again did not suit me and by 2008 I negotiated to buy out my part of the business, raising money from high net worth individuals. It was tough starting again from scratch effectively having to buy my own business back after ten years. I wouldn't

What would you do differently knowing what you know now?

"I could have done without the sleepless nights and fear of losing my house when I was trying to support a young family. But every part of the entrepreneurial journey makes you more resilient. There is great strength in knowing you can hit the bottom of the barrel and still climb out."

I was lucky to crack a good idea early on and make it successful, but I strongly believe in continuous learning both formally and through business experience. You can always pick up ideas and strategy from other sectors. For example Aerogen's strategy of integrating technology inside ventilation platforms could be compared to what "Intel Inside" did with chips in computers.

There are an infinite number of needs that often don't get recognised. As people go through a process of work, they don't realise it could be done differently. We should think about medtech now in the same way as consumer products – everyone uses an iPad now, but did we think we needed a computer without a keyboard when it didn't exist?"

have done it if I didn't totally believe in the product and the potential impact it could have."

From the outset as a medtech entrepreneur in Ireland Power recognised the need to be global and the importance of protecting intellectual property to achieve that. "We have been granted over 100 international patents since 2000. As some expired over the years, we needed others in support of them. The category we are in represents the most patents issued in Europe. We filed heavily all around our area as competitors from the Far East would try to copy us and try to sell into Europe."

Investing time

A prominent figure on the medtech scene in Ireland now for many years, Power was a member of the board of the Irish Medtech Association (previously the Irish Medical Devices Association) for about nine years up until 2018.

"We were focussed on pushing entrepreneurship and R&D, looking to encourage new startups and more R&D within existing multinationals. The Government eventually responded with new research grants and tax incentives," says Power. "Having associations under one umbrella (Ibec) representing medtech, ICT and pharmaceuticals is very helpful as technologies are converging now. You can't

look at medtech in isolation anymore."

Power is an adjunct lecturer at NUI Galway and a founding member of the BioInnovate Ireland programme which is located there. In 2016 he received an honorary doctorate from NUI Galway for his outstanding contribution to the medtech industry along with four others in the region. Aerogen employs 250 people, most of whom are based in Galway.

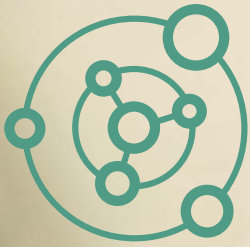
"Half of our workforce came out of NUI Galway and Galway Mayo Institute of Technology. We have a great allegiance with NUI Galway so I try to give as much of my time as I can as an adjunct lecturer. One of the interesting things has been that I have ended up giving lectures to students of engineering, science and business courses and was also involved in BioInnovate – there are not too many people who have been involved in all four faculties in the university," says Power.

"One of the great things about BioInnovate is that it gives startups the opportunity to get commercialisation grants", in Power's view. "With this programme, success is not measured by how much money you make. If a team doesn't manage to get a company off the ground, they have still gained tremendous experience. It is all part of the learning curve as an entrepreneur."

What's next?

As for what's next, well Power firmly believes if you don't move forward you are moving back. For the past four years Aerogen has been investing its own money in the development of Aerogen Pharma and specifically in two drugs combined with its next generation aerosol technology. "I believe Aerogen has the opportunity to build a major Irish Speciality Pharmaceuticals business to go alongside its medtech success," Power notes, "We now have two drugs in the clinic and successfully through phase 2a and will be starting 2b trials in Q3." One of the drugs in particular held a special interest for Power for many years and that is inhaled surfactant for premature babies.

He explains pre-term babies are often lacking this essential lubricant for the lung and as such currently go through a very invasive procedure to apply it, delivery of Aerogen's surfactant in aerosol form through a nasal cannula will be minimally invasive and Power believes could result in the biggest positive impact to pre term infant mortality rates seen in the last 30 years. Now that is worth going to work for.



Ireland is one of top 5 global medtech hubs and the seventh most competitive economy in the world

As many as 9 of world's top 10 medtech businesses have a base here



The greatest employer of medtech professionals in Europe, per capita, with 38,000 professionals

Ireland is one of the top exporters in Europe at €12.6 billion



Top 10 steps for starting and growing a startup



Ciara Finlay

Startups fuel the innovation pipeline for the medtech sector. These businesses are founded by highly motivated doctors, engineers and business professionals to develop new technologies that transform healthcare and improve patient's lives.

There are a number of key milestones on the road to success for medtech startups, Irish Medtech Association Executive Ciara Finlay tells us, from identifying an unmet clinical need and commercial opportunity, to attracting funding, then getting to market and driving sales. This journey takes time and money; some startups run out of both along the way. Those who succeed can either grow their business by adding new markets and products or exit and start all over again with a new startup. Here we explore the top ten most common steps for starting and growing a medtech business to help you on your journey.

1. Identifying an unmet clinical need and commercial opportunity

The first question you must ask yourself when starting a medtech business is, is there a sizeable market opportunity? This involves identifying an unmet clinical need, having an idea about a health technology or product that can address patient needs and add economic value. If you have a good idea, you need to make sure that it stands out. Does your proposed

technology address these needs in an innovative way and what are the potential risks? Understanding the clinical need is not enough, you need to consider the clinical commercial context to understand the financial drivers behind your technology. Once you find the problem which your technology is trying to solve you need to ask, are there any competitors? If there are, how is your product differentiated?

2. Getting your leadership team right

Once you have a good idea, you can start to build your business around. There are two key streams for this, technology development and attracting funding to help your business reach key milestones. But first you need to bring together a team that has a strong track record to help you realise your ambition. When putting together a team you need subject matter experts that can help give you an advantage. You also need to add experience with your board who will help steer you on the right path and avoid common pitfalls. This will help build trust with potential investors and re-assure them that your new startup is less of a risk.

continued on page 24

Medtech Brew

For nearly four years we have run Medtech Brew with BioInnovate to help startups get insights from industry experts, share best practice and network. It has grown in popularity with 80+ people attending the first event and up to 180+ people attending. Areas covered to date include:

2016

- Starting, sustaining, and growing a medtech company
- The commercial model – the journey to your first sale
- Access to funding for startups

2017

- Innovation for medtech: clinical collaboration with business
- Design with the patient in mind
- Building your leadership team and board for success

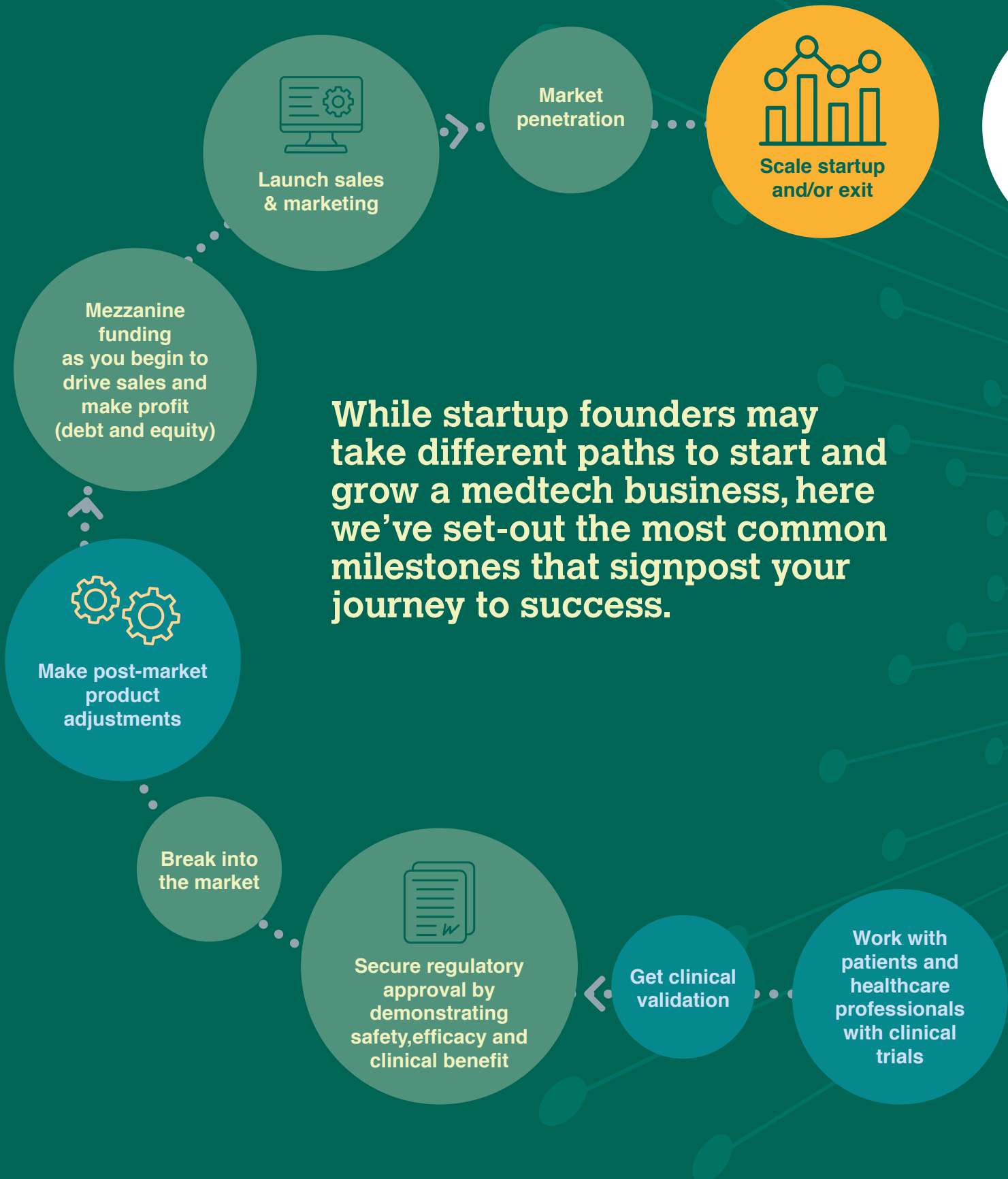
2018

- Standing out from a crowd: PR for small businesses
- Connected health: The new frontier for startups
- Top trends in quality and regulatory affairs and what it means for your business

2019

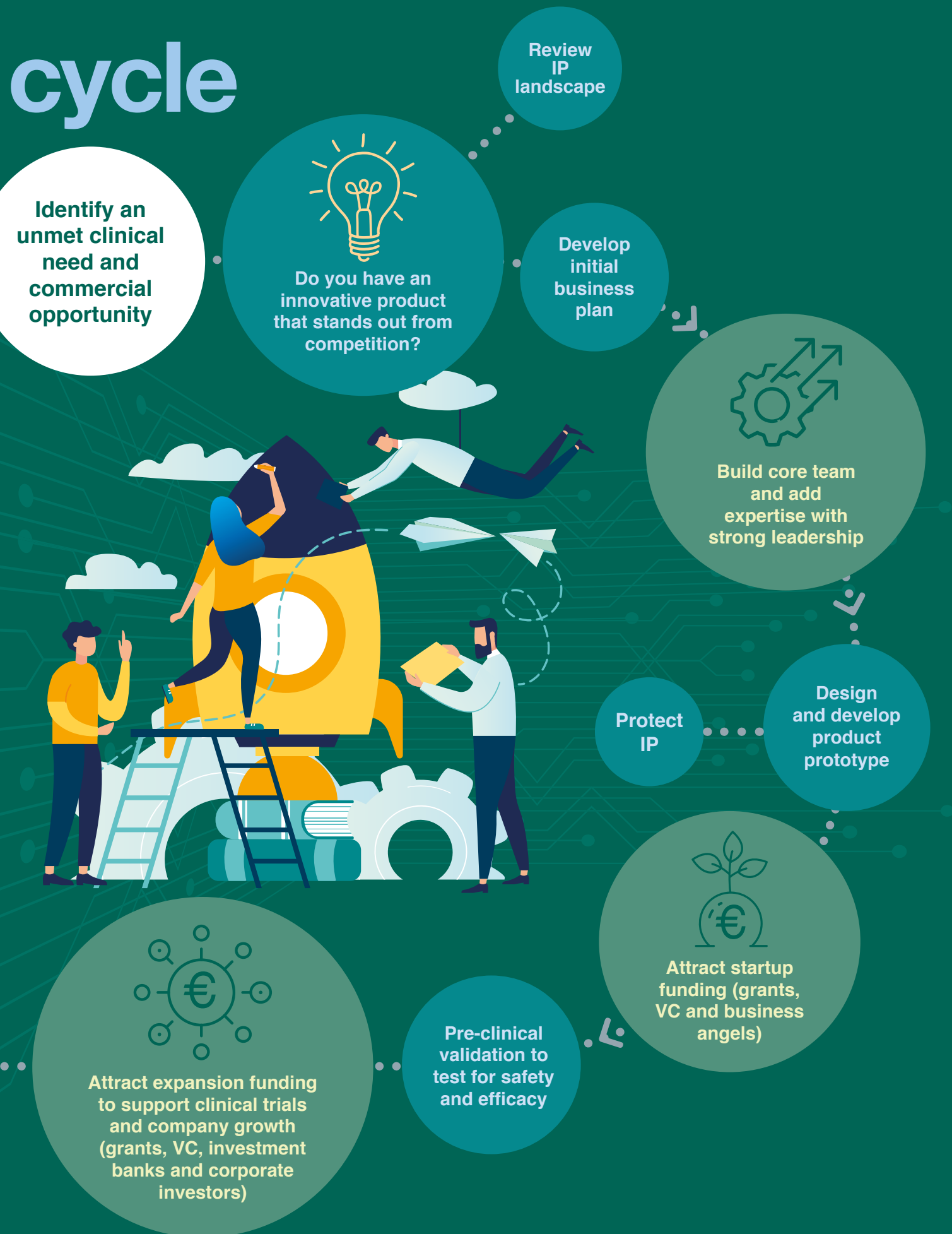
- Supporting innovation and growth with IP
- The clinician/innovator: Identifying and addressing unmet needs

The medtech startup



While startup founders may take different paths to start and grow a medtech business, here we've set-out the most common milestones that signpost your journey to success.

cycle



3. Addressing clinical need and device development

Now you can begin to develop your technology. First you need to develop a prototype as proof of concept. Then as you continue to design and develop your technology you need to identify any potential risks and ensure technological feasibility.

4. Your business plan

Along with developing your technology, you need to build a business plan to help you on your journey to market and raise funding along the way. A good idea is not enough to get ahead. You need a practical business model. You must ask, how much do you need to raise to support R&D, clinical trials, regulatory approval, market access, distribution costs and still make a return on investment in an acceptable time frame. To sell your technology you need to ask, what's your reimbursement strategy. When you've identified which country you're going to market in first you need to understand the implications of this such as regulatory pathways and the implication of different health systems. Then you need to consider whether you'll sell on a fee-for-service basis or value-based payments, remember that you're generally not selling directly to clinicians, you're dealing with hospitals, third party organisations and government health systems.

5. Intellectual property

Medtech is arguably the most innovative sector in Europe with nearly 14,000 patents filled with the European Patents Office. As you begin to grow your startup you need to do a review of the IP landscape to ensure your position is not already taken. Then you need to protect your IP to avoid copycats and dissuade early competition. There are three different ways to do this including, patents, trademarks and registered designs. But to protect your idea, you need to identify how 'inventive' your device is early on to demonstrate that it's a novel or unique device. Early strategic work with IP experts can save you down the road and increase your technologies attractiveness with investors.

6. Financing

As you begin on your startup journey your company's worth is low, you're high risk and raising money can be expensive. Pre-money valuation will give an early indication of your worth by checking your leadership team, similar companies, reviewing the market size along with key players, and identify how much money you need to reach key milestones. As you move from one milestone to the next, raising money gets less expensive if technical and commercial milestones are well managed as the risks are reduced for investors. But you should always include safety amounts to help you manage potential delays or overruns.

There are a number of key funding milestones you need to reach to move from one stage to the next or risk failure. Then, you can progressively raise more to support expansion with hiring, production, marketing, and value building activities. The key funding milestones take you from:

- Concept, usually with seed funding
- Establishing your startup, with funding from state grants, venture capitals and business angels
- Testing the safety and efficacy of your technology with clinical trials, with expansion funding from venture capitals, family, investment banks, and corporate investors
- When you've gone to market, had your first sale and are trying to drive profits, you may reach the mezzanine funding stage underpinned by debt and equity
- Once you've achieved liquidity, you may look to scale your businesses or exit by being acquired.

The market opportunity to justify returns for VCs can be as large as €320-500 million per year. The capital required will be different for each opportunity, a large funding injection will be predicated on a greater market opportunity to satisfy the need for significant returns from investors.

7. Clinical investigations

Early engagement with clinical and ethics experts can help you successfully manage clinical studies. Once you have developed your technology, you must begin to test it for safety and initial efficacy with pre-clinical validation. Early engagement with clinical and ethics experts can help you successfully manage clinical studies. When you've had success in this stage, you may move on to first in human clinical investigations to gather more data and build clinical experience of the product in use. After the technology has been successfully used in the pilot trial and clinical endpoints have been reached, then you get clinical validation.

8. Identifying the right regulatory pathway

For your product to get to market, you need regulatory approval. To get regulatory approval you need to demonstrate product safety, efficacy and clinical benefit. The Food and Drug Administration is the regulator in America, the channels for regulatory approval are either the 510(k) demonstrating equivalence to another legally marketed technology or premarket approval (PMA) to go to market by demonstrating sufficient scientific evidence to provide assurance. In Europe the regulations are set by the European Union and companies are held to a high standard to achieve a Conformité Européenne (CE)

mark. While the EU set the regulations CE marks can be granted under these rules by any one of 58 notified bodies.

Achieving regulatory approval is not only an important step for selling your product, it's required for most companies that may wish to exit. The majority of startups are acquired post-commercialisation, and you must plan ahead to make it to this milestone. Once your technology has gone to market and is in use you will begin post-market surveillance. At this stage there may be further product updates to improve clinical as well as cost-effectiveness of the technology.

9. Breaking into the market

Your first sale is an important step on the road to success. The most common market medtech startups pursued first are either the USA which is the largest medtech market (43% of the global market) or the European Union (28% of the global market). As both the largest global market and a single market, the USA is an attractive first destination. To get there you need to identify the right distribution channels. Then as startups look to grow they develop sales & marketing strategies to drive sales and break into new markets.

10. Exiting or scaling

When you've achieved significant market penetration, you can either develop a strategy to scale your business or look to exit by being acquired or go public with an IPO. Many startups pick the acquisition route with entrepreneurs using the experience to then start new companies, but competition is getting tougher with changes in M&A. Global medtech firms are becoming more strategic making fewer, larger deals, the value of mergers and acquisitions grew 178% globally and were worth €49 billion in the first half of the 2017 alone. This activity is complemented by divestments as companies refine their business plans.

Only 1 in 4 medtech acquisitions occur within

six years of a company's existence. For any VCs these first six years are focused on building and growing portfolios. Finding the right VC at the right time to invest in your business is a major driver of success. The following four years then focus on portfolio maintenance and realisation of investments. Sometimes, funds have a one or two year extension.

An acquirer's willingness to pay depends on profits and how the startup can strategically enhance its portfolio by expanding either its product range or creating a gateway into new markets. The average time-to-exit for medtech startups is 7-9 years. By this time companies have spent an estimated €40 million growing their business. Nearly one in five medtech M&A deals are around the €45-€90 million valuation range.

“Achieving regulatory approval is not only an important step for selling your product, it's required for most companies that may wish to exit. The majority of startups are acquired post-commercialisation, and you must plan ahead to make it to this milestone.”

Why Ireland?

There's no place like home for these experienced business leaders who've become ambassadors for Ireland's medtech hub, attracting international attention. Ireland is a location of choice for medtech business, thanks to our strong business environment, the availability of talent, our track record for manufacturing excellence, and our medtech community that connects you to the global market.

A culture of innovation and top talent

Veryan Medical was formed in 2003 as the result of a technology spin-out from Imperial College London in the UK. When Paul Gilson joined its board as Chief Scientific Officer in 2007, along with Chas Taylor as Chief Executive Officer, they convinced the other directors that Galway should be chosen as the location for the company's research and development facility.

Taylor and Gilson had been asked by the technology transfer office of Imperial College London to take the university spin-off company to the next level. Based on pioneering research by Colin Caro, Professor of Bioengineering at Imperial College London, the patented technology needed commercial and regulatory expertise to manage its transition from laboratory to marketplace.

"I had been around the block before, having co-founded MedNova in 1995 and

Novate Medical in 2006 and understood the environment here [in Galway]," says Gilson. "There was no other place I was ever going to select for a medtech operation."

For Gilson, the main reason to locate in Galway is people and talent. "A very strong medtech cluster has developed in Galway, particularly in the western region, and there are skilled and experienced people in a whole range of fields," he says.

"The culture of innovation that exists is well supported by the State and the third-

level institutions have a good feel for what is required by the medtech sector. There is also a well developed supply industry."

Veryan has designed, patented and developed a highly innovative stent technology, the BioMimics 3D Vascular Stent System, which is based on the link between vessel geometry, blood flow mechanics and vascular disease.

Used to reopen narrowed regions of a femoropopliteal artery, in the upper leg, caused by atherosclerosis, the

BioMimics 3D Vascular Stent System acts as a support to hold open the narrowed artery and improve blood flow to the leg. Atherosclerosis is the collection of fatty substances that form “plaque” along the lining of the arteries. This narrowing of the femoropopliteal artery may limit blood flow to the leg and lead to pain when walking.

Further to the BioMimics 3D Vascular System achieving US Food and Drug Administration approval last October, Veryan was acquired in December by Japanese company Otsuka Medical Devices. Veryan and Otsuka plan to collaborate on developing Swirling Flow stents for use in the treatment of vascular disease.

Currently employing a team of 35 people, Veryan’s operations in Galway will be retained to play a key role in the continued development of this technology. At the announcement, Taylor said: “Becoming part of Otsuka Medical Devices will allow Veryan to build on the strong clinical data with the BioMimics stent and realise the potential to significantly advance the treatment of peripheral vascular disease.”

Ireland stands-out for global leaders

The founders of 4Tech Cardio are based in Israel, Italy, Belgium and Switzerland but when they reached a stage

when they felt their idea could be turned into a company, they picked Ireland as the ideal location.

Incorporated in Delaware in the US, but based in Ballybrit, Co Galway since 2011, 4Tech Cardio is developing a minimally invasive alternative solution for the treatment of functional tricuspid regurgitation.

The TriCinch Coil System is a simple device designed to help blood flow problems in the heart by reducing tricuspid regurgitation by means of tricuspid valve remodelling. This is done via a unique nitinol coil anchor that is tensioned by a nitinol stent in the inferior vena cava.

“Initially Carine Schorochoff [co-founder and former 4Tech Cardio CEO] was working with a couple of physicians and engineers on the idea. They had done some garage-type work in Israel and moved it to a point where they were ready to build a company around it,” says current 4Tech Cardio CEO Tom Fleming.

“They picked Ireland to do this because of the availability of talent, the strong medtech community and the opportunity to get Government supports such as R&D tax credits. The decision to locate in Galway was because it really is the centre for catheter-based technologies in Ireland.”

After 20 years working at Boston Scientific in the US, Fleming took over as CEO of

4Tech Cardio in March 2018, managing around 40 people in the Galway facility, which is the company’s main area of operations. “I didn’t take the decision to move to Ireland lightly,” he says. “I like the structural heart space and had seen what technologies can do for patients. I had developed good relationships with some of the best cardiovascular physicians in the world while at Boston Scientific and knew that the area 4Tech Cardio is involved in is one they are excited about.”

Being based in Galway has allowed things to progress for 4Tech Cardio, notes Fleming. “The initial design had worked well in terms of safety in a clinical setting, but didn’t really do all the founders had envisioned. The process was redesigned with one of the components,” he explains.

“The community supports in Galway should not be understated. A company such as ours needs to have a number of components supplied to us. We need external suppliers to be successful. There are so many supply companies in Galway that understand the needs of the medtech industry, from manufacturing to milling, extrusion, metals, sterilisation and regulatory requirements on the supply chain.

“It has been so beneficial to expand our network here. We are always running into people from Galway Mayo

Institute of Technology and NUI Galway who are involved in this space. I have found people engaged with medtech generally in Galway to be very welcoming, open and generous with their time.”

Last year, 4Tech Cardio conducted a US feasibility trial and implantations and has achieved some very promising results with patients. It is starting its first implantations in Europe soon and hopes to achieve the CE mark towards the end of this year.

“This is a very unique technology because patients that have functional tricuspid regurgitation don’t really have good surgical options. The mortality rate is very high, so surgeons typically won’t operate for that reason,” explains Fleming.

“Our solution allows the tricuspid valve to start functioning more normally by changing some of the geometry of the right ventricle. This condition is usually associated with patients that have heart failure, who tend to be mostly elderly. The question about whether intervening earlier would be helpful to those patients will be answered through our ongoing clinical studies and trials.”



Taking a chance on success

One of the qualities which sets entrepreneurs apart is their ability to spot an opportunity. A disused facility or your job going down in flames would not inspire most people, but these medtech entrepreneurs combine their scientific backgrounds with a flair for business to help them make a difference.

Hatching a plan for bone grafts

Ten years ago, Declan Clarke and Ronnie Robins decided to turn a disused salmon hatchery in the Inagh Valley near Recess in Connemara into an innovation hub. Together with the Inagh Valley Trust, chaired by Mr Howard Kilroy, they sought to bring highly innovative people and ideas together with the most

advanced research thinking. The hub, or Hatchery of Ideas, has resulted in a number of startups being formed, including Zoan BioMed, which Clarke and Robins founded in 2016 specialising in medical-grade coral for bone healing and repair.

Zoan's coral scaffolds are ideal as bone graft substitutes.

They have the internal porosity and structure of human bones and over time are resorbed to be replaced with patients' own bone.

"We began in 2009 when we started out by looking into the cytotoxic potential of the compounds within marine coral tissues. These compounds form part of the corals defence system, with some unique toxicity profiles, but we quickly realised this was blue sky in

its ambition. However, in the process, we developed the ability to consistently produce biomaterial formed of high-grade scaffolds, which the coral create and build as a skeleton on the outside," explains Clarke, who is a marine zoology graduate and completed a master's in zoology at NUI Galway in 1995.

They then explored how to take this into the field of bone healing. "One of our big moments was when we realised coral had been used clinically in orthopaedics since the 1970s, but supply from the wild is terminal," says Clarke.

"We sought to contribute to the global need for bone graft material and contribute to the exciting field of Orthobiologics, where more and more biological solutions are meeting needs.

By the time we launched we had grown hugely as a team and we were working with expertise from very exciting and different sectors. James Martin, with a marine background was refining



Declan Clarke

the scaffold production to a commercial art and PBC BioMed were working hard to help us develop the idea into a business, covering regulatory and product development aspects. Dr Cynthia Coleman's research was our first cellular test and we were all inspired with the outcome.

"By pure coincidence, coral when building scaffolds have the same blueprint as human bone. This makes our biomaterial ideally suited to bone grafts because of its flow structure, natural porosity and strength."

The gold standard in orthopaedic trauma operations is autograft, where tissue is transplanted from one part of the body to another on the same individual, which is declining in use. This procedure requires a second operation to harvest bone from the patient, increasing the risk of infections, adding costs and slowing healing times. Additionally increasing incidence of diseases such as osteoporosis limits the number of patients who may avail of the autograft.

Recognising the demand for new bone graft materials, the team were convinced they were dealing with something quite unique and wanted focus and bring the first product, a highly porous bone graft substitute, in easy to use granular form, to market. "We were really committed to getting it off the ground and put everything we had into it," says Clarke.

Since Zoan BioMed was officially incorporated as a startup in 2016, Dr Cynthia Coleman of the Regenerative Medicine Institute at NUI Galway has completed further biocompatibility trials with its biomaterial and concluded it to be an excellent environment for stem cells to grow. Zoan BioMed's strategic partnership with, medical device innovation partners PBC Biomed, is helping the team to refine regulatory submissions. Zoan also worked with Dr Eamonn Sheehy of the Royal College of Surgeons

in confirming the hospitable nature of the scaffolds to human stem cells.

"We have taken a few great leaps in the past eight to ten months. We've brought commercial expertise and investment on board and taken steps to manufacture to controlled production scale, says Clarke. "We are running animal trials and our plan is to be on sale in the US in the fourth quarter of 2020."

To achieve this, Zoan BioMed is going to go through the Food and Drug Administration's 510(k) process as there are a number of successfully marketed coral-based devices it can compare its biomaterial with as being substantially equivalent in terms of safety and efficacy.

"Our portfolio development has grown quite a lot. The same platform can deliver product presentations across a number of different clinical applications, all of which are under R&D at the moment," says Clarke.

"We have started the process of talking to potential distributors and co-developers in the US, Asia Pacific and Canada and we plan to achieve the CE Mark in Europe."

Rising from the ashes

One Monday morning in 1993 Evelyn O'Toole turned up for work at Gaelic Seafoods in Connemara, Co Galway and was told the building had burnt down over the weekend and all the jobs were gone. Aged 25 at the time, she had been laboratory manager there for two and a half years.

"It was pretty dramatic. But within two weeks, I decided to try and set up an independent testing lab based in Connemara, which became Complete Laboratory Solutions [CLS]. The opportunity just presented itself," she recalls.

O'Toole had studied applied biology for two years in Athlone Institute of Technology and environmental science in Institute of Technology Sligo. While at college, she undertook a marketing elective, which was an unusual choice for a science student. "Unknown to myself, this would feed into my psyche and future. I liked the whole idea of having a technically challenging job and living in the West of Ireland, but in the back of my mind I loved business," she says.

In terms of starting a medtech business, O'Toole believes CLS is "a lovely example of success through support", both from the business community around her as well as State agencies. "Udarás na Gaeltachta has been fantastic. Once I supplied a business plan and made a commitment to employ five people, they gave me two employment grants and premises in Rosmuc free of charge for a year. I have used every other available fund since."

O'Toole kicked off by approaching the fishing industry for her first contacts and won business testing fish and factory hygiene. She drove around in a van collecting samples from clients. This evolved to microbiology testing for water and she added an environmental lab to the facility. Then, in 2006, two large pharmaceutical

companies asked the company to supply trained testing analysts on contract, which represented O'Toole's first steps into life sciences arena.

"We started to reach out to medtech companies in Galway one by one to do non-core testing such as clean room monitoring," says O'Toole. "We have organically grown since in that space, developing a sister plant in Galway City geared towards pharmaceuticals and medical devices."

CLS's GMP-approved, state-of-the-art facility in Galway City works in partnership with the medtech sector to support current and next generation products through routine analysis, method development, stability testing and various process validations.

"We have an array of clients I could have only dreamed of including Boston Scientific, Medtronic and Cook Medical, and will be developing another space in Galway City this year, which will increase our footprint by 50%," says O'Toole.

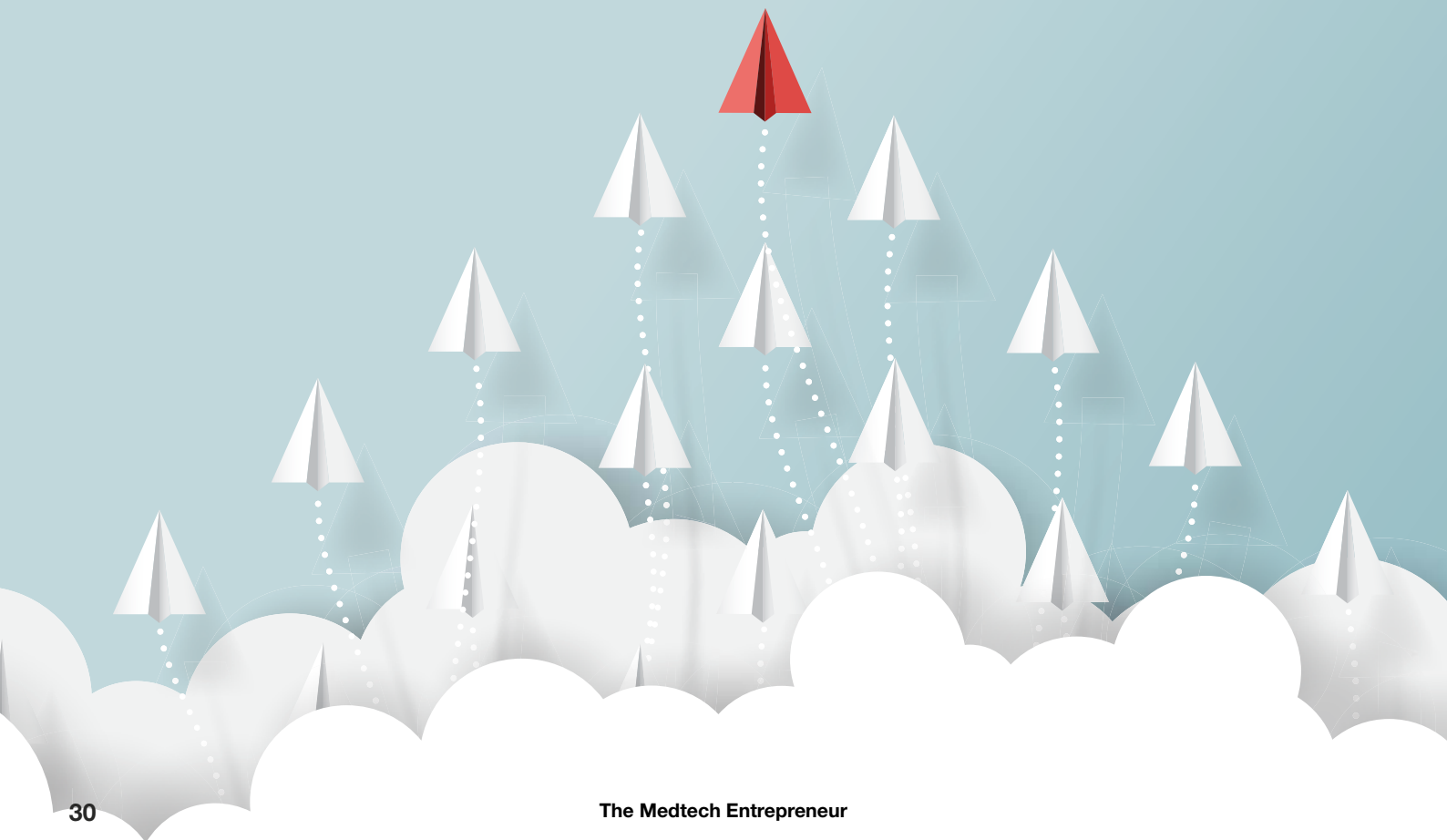
Having achieved Health Products Regulatory Authority approvals in 2008 and 2009, CLS currently has trained lab analysts contracted out to work at 20 different life sciences sites in Ireland. It employs a total of 175 people. "My first hire is still with us and is now leading a team of analysts at Diageo," notes O'Toole.



Evelyn O'Toole

Getting your leadership right

To grow a startup, everyone on your team needs to be a leader and offer something unique to give you an edge. Bringing engineering and commercial skills is an important balancing act for many medtech startups. But what often makes the greatest difference, is adding experience with a board who can help you avoid pitfalls by guiding your strategy development and reducing risks.



Finding a co-founder for your startup journey

Wayne Allen and Liam Mullins know each other well, having co-founded Embo Medical in 2012 and brought it to the point where it was acquired by CR Bard subsidiary Clearstream for almost €43.5 million in early 2016.

A spin-out from the NUI Galway BioInnovate programme, Embo Medical developed innovative medical device technology to treat diseased peripheral vascular vessels and organs. Its unique platform technology is designed for use in the field of vascular embolization.

“Liam and I have complementary startup skills. He is a mechanical engineer and I have a commercial background,” says Allen. “After the successful exit of Embo Medical, we took time out and decided to go into partnership again. From my previous experience of working with Liam, I knew he was the right partner for me to move into the next venture with – it wasn’t any more complicated than that.

“The cycle of company foundation, growth and exit is quite a windy road. The fact that we came out the other side and still wanted to go into partnership together was a great sign. We knew

each other’s strengths and weaknesses and what was ahead in terms of securing funding and the journey ahead.”

Allen and Mullins looked at 20 unmet medical needs that they had observed and collated. The project they decided to move forward with was a solution to treat acute ischemic stroke. They founded Perfuze in 2018 and closed a €3 million seed investment fund in January 2019, led by Earlybird Ventures, with backing including Enterprise Ireland and a syndicate of Irish medtech sector veterans and stroke physicians.

Perfuzé’s technology is intended to provide superior clinical outcomes in shorter procedural times; resulting in safe, cost-effective therapy.

“About 80% of strokes are ischemic and involve a clot lodging in the brain. At a macro level one third of patients die, one third are permanently incapacitated and one third make some kind of recovery. Of the patients that make it to surgery, only about 20% are functionally independent post procedure. Our clinical objective is to improve that 20% level so that more people can have a quality of life after an ischemic stroke,” explains Allen.

With Allen as Chief Executive Officer and Mullins as Chief Technical Officer,



Eoin Bambury

Perfuzé currently has a team of six engineers and a number of product builders. It recently took on Anne Marie Gannon, previously Regulatory and Design Assurance Manager at Novate Medical as Consultant Quality and Regulatory Director.

“With any senior role, it’s important that the person coming into the company hits the ground running and is bringing something to the table that we don’t have,” says Allen. “The clock is always ticking and there is constant pressure in terms of time, money and execution. We felt Anne Marie had the skills to direct us so we can push ahead with our strategy and not take months to get up to speed.”

Mentors and networking for success

Eoin Bambury and Moshe Zilversmit had both worked in medtech startups and

multinationals for many years by the time they met on the NUI Galway BioInnovate programme in 2013/14.

The company they spun out from the programme, Signum Surgical, is focussed on developing innovative solutions to treat patients with colorectal diseases, starting with anal fistula. Its groundbreaking bioabsorbable implant is designed to prevent reinfection and promote healing.

“For both of us as co-founders, this represented the first time we were running a company ourselves,” says Bambury. “We wanted to have an experienced board to help guide the company – to find people who had seen the pitfalls and issues an early stage medtech company can have.”

Bambury and Zilversmit talked to a lot of people from the mentor network they had built up during their careers, as well as those they met through BioInnovate, and drew up a shortlist of candidates



Wayne Allen

they thought would be the most suitable. The end result is that they now have Jeff Grainger as Chairman and Non-executive Director and Alan Levy and Declan Quinn as Non-executive Directors on the board.

"We approached Alan as we're working with bioabsorbable materials. He was the inventor of an absorbable surgical suture in the seventies and has also run and sold numerous medtech companies," says Bambury. "Alan is the kind of mentor who understands where we are and likes what we're doing. He can guide us on the technical side and the positioning strategy and has a huge network in the medtech community worldwide."

Zilversmit knew Grainger from his time working in the San Francisco Bay Area. A mechanical engineer and patent attorney, Grainger has over 20 years' experience in the medical device industry. Most recently, he was Managing Partner at The Foundry, a leading incubator that has started more than a dozen pioneering companies that have transformed the treatment of a variety of widespread diseases.

"Jeff is a hugely valuable member of our board because of his experience of founding companies and intellectual property (IP). He is helping us to build out our IP strategy to ensure optimal protection in appropriate territories," explains Bambury.

Quinn represents the medtech syndicate which led Signum Surgical's Series A investment round. A mechanical engineer with a background in medtech

manufacturing, he has specialised in product and technology transfer management for minimally invasive procedures.

"As well as representing the investors' perspective, Declan can give us technical guidance. We are happy to have an investor/director like that in the background," says Bambury. "Our entire structure is set up to give guidance and advice at the early stage, not just to report from a corporate governance point of view."

Getting the balance right while expanding

Chief Executive Officer and co-founder of Vivasure Medical Gerard Brett also co-founded Zerusa, where he led the development and commercialisation of its hemostasis technology in the EU and the US prior to Zerusa's acquisition by Vascular Solutions in 2011.

Currently employing 25 people in Galway, Vivasure is pioneering novel fully absorbable technology for percutaneous vessel closure. Six members of the team had previously worked at Zerusa and some are in leadership roles at Vivasure, including co-founder and Chief Technical Officer Dr Chris Martin.

"As we transitioned from Zerusa to Vivasure, some design engineers, quality, regulatory and clinical specialists came with us," explains Brett. "In looking to expand, we had to balance between building in-house expertise and bringing it in on an as required basis. This is a really important balance

for a med-tech startup which has to use cash as efficiently as possible."

Vivasure's current management team of eight people have very wide experience across multinationals and SMEs in the medtech, pharma and finance sectors. All of them have international experience and strong track records in the previous companies they worked for.

"We hired our Chief Commercial Officer from Belgium as this is one of the areas that is a bit challenging. Ireland is good in terms of manufacturing, R&D, regulatory and quality talent but we don't have a big population of medtech commercialisation expertise," says Brett.

For Brett, any member of Vivasure's leadership team has to have entrepreneurial thinking in their DNA. "It is just necessary to deal with the highs and lows of the type of work we do. People who join us get the opportunity to see

the full story of a company and wear a lot of different hats in the process."

Vivasure's strong leadership team is backed up by an experienced board, including Chairman Dr Bernard Collins, who also serves on the board of directors of several US and Irish life sciences companies.

Gerard Brett



David Townley (L)
and Brian Shields

Adding experience to guide strategy

When co-founders of Neurent Medical Brian Shields and David Townley went about building out their board of directors, they wanted to satisfy three criteria: to find someone with deep commercial experience of their domain, someone with relevant startup experience and to have an individual on the board to represent investors.

A spin-out from the NUI Galway BioInnovate programme, Neurent Medical is developing a minimally invasive, hand-held radio-frequency device which ear, nose and throat (ENT) surgeons will be able to use to treat patients with rhinitis in an office setting. It will remove the complications and costs associated with most surgical procedures.

“We felt we needed to go outside Ireland to find someone with deep

commercial experience in ENT as Ireland does not have the same wealth of experience in ENT as it does in other domains such as cardiovascular and orthopaedics,” says Shields. “We approached Mark Fletcher, who had just retired as President of Medtronic’s ENT business. We got to know him over three or four months and subsequently appointed him to the board in 2017.”

Justin Lynch, Partner and Chief Financial Officer, Fountain Healthcare Partners joined the board of directors of Neurent Medical in May 2018 as part of its Series A financing round, which raised €9.3 million. Fountain Healthcare Partners

led the funding round with participation from Atlantic Bridge Capital, the Western Development Commission, Enterprise Ireland and a syndicate of Irish and US medical device veterans.

A couple of months after that Shields and Townley managed to secure Eamon Brady, former CEO of Neuravi, to complete Neurent Medical’s solid board of five directors.

“Eamon had done the startup journey a couple of times so knew what it took. He has been a phenomenal addition for us,” says Shields. “We spent a lot of time trying to get the right board around us and this has proven to be a very worthwhile effort. It is all about getting the strategy right – doing the right things in the right sequence to maximise the outputs.”

The company strategy is to focus on the US as its initial market. “Having the correct board in place is important in the validation of this strategy and while working through the clinical and regulatory milestones required for a successful US commercial launch. We have deep experience to draw from in terms of the pros and cons of taking particular actions,” explains Shields.

“In Shields’ view, you don’t need a big leadership team in the traditional sense as a medtech startup. However, you do need everybody involved to be a leader, to take ownership of what they’re doing and be experts in their own domain.

In Shields' view, you don't need a big leadership team in the traditional sense as a medtech startup. However, you do need everybody involved to be a leader, to take ownership of what they're doing and be experts in their own domain. With this in mind Neurent Medical is currently running a leadership development programme for its entire team.

Collaborating with key opinion leaders

Chief Executive Officer of Neuromod Devices, Dr Ross O'Neill convinced Dr Hubert Lim to join the company as Chief Scientific Officer in January 2018. The world-renowned scientist in auditory neuroscience and neurostimulation was considering a number of senior government research agency roles in the US at the time.

Based in the Digital Hub in Dublin, Neuromod has developed and patented a new home-use technology that it is evaluating for neurological disorders including chronic tinnitus. The technology works by stimulating key nerves in the body to tone down misbehaving nerve cells in the part of the brain that is responsible for the unwanted sound. Neuromod's approach doesn't require surgery and takes the form of a handheld device no bigger than a mobile phone. It is used with Bluetooth over-ear headphones. O'Neill founded the company as a spin-out from Maynooth University in 2010.

At the University of Minnesota in the US, Lim had been independently working on similar scientific approaches in animal models of tinnitus. He, and separately another independent research group led by Professor Susan

Shore of the University of Michigan, had published papers and gained recognition for the work they were doing in this area. Meanwhile, Neuromod's research had advanced beyond the animal research stage, and they were already manufacturing a home-use device and running late-stage clinical trials, which gave the company first mover advantage.

"Hubert had made significant contributions to the understanding of how to activate nerves to treat tinnitus. We were introduced to Hubert by members of our Scientific Advisory Board and we got on very well. He wanted to see this scientific approach working in humans as soon as possible and has been a fantastic addition to the company."

Following his appointment, Lim undertook an ambitious schedule of presentations at many of the leading ENT and audiology meetings in the world to promote Neuromod's technology and highlight the results that were emerging from its clinical trials. "We completed some of the largest ever device trials for tinnitus involving more than 500 participants. The results coming from these trials suggest that the technology can achieve meaningful and sustained relief from the condition" says O'Neill. "Hubert is well connected in the ENT and audiology areas. Having him present the results with me really helped to socialise the data and build awareness of the technology. A lot of very serious people in the field are now talking about Neuromod's approach as the big breakthrough treatment for tinnitus."

Another major coup for O'Neill was securing Chris Smith, former CEO of Cochlear, the global leader in cochlear implantation

technology. Chris joined as a member of the board of directors in January 2019 after serving as strategic advisor to the Chairman and CEO for nearly six months.

"I wanted to flesh out the board with some big names in the hearing space and was constantly looking out for news of CEOs stepping down. After Chris Smith announced in December 2017 that he planned to retire from Cochlear, I flew out to Denver for the company's quarterly

results announcement and secured a meeting with him," recalls O'Neill.

"Chris has helped us to connect with people at the highest level within the corporate hearing aid and implant areas. It has meant we have pressed ahead with commercialisation and have already had various partnering discussions. All of the hearing companies we have spoken to recognise the huge global unmet need of tinnitus."

Dr Ross O'Neill



Transforming lives by developing new technologies

Most innovation in global medtech companies is iterative. The innovation pipeline for this dynamic industry is fuelled by startups that take on risk to drive radical innovation in the face of unmet clinical needs that represent significant commercial opportunities. Medtech startups are transforming lives, and those who succeed get acquired to manufacture their technologies to meet global demands.





David Vale

Deep understanding drives success

Founded in 2009 by David Vale, Eamon Brady, John O’Shaughnessy and Dr Mahmood Razavi, Neuravi invested extensively in scientific research for many years on the varieties of clots that cause acute ischemic stroke while creating its successful EmboTrap revascularisation device.

Ischemic strokes occur as a result of an obstruction, typically a blood clot, blocking blood flow to the brain, accounting for almost 90% of all strokes. Rapid restoration of blood flow is of utmost importance when treating patients suffering this condition.

EmboTrap targets these occlusive blood clots, capturing them within the device and allowing for immediate restoration of blood flow while also cleaning up any particles disturbed during the clot removal.

In 2017 Neuravi was taken over by Johnson & Johnson company Codman Neuro in a deal estimated to be worth several hundred million euro. Vale and Brady had previously worked together at MedNova, a medtech startup that was acquired by multinational healthcare firm Abbott Laboratories in 2005.

“A lot of the R&D done in big medtech multinationals tends to be iterative, such as additions to a size range and/or fairly minor design enhancements. Significant innovation generally entails significant risk, and larger companies often prefer to let smaller startups carry this risk and then acquire them after they have overcome or mitigated the majority of these risks. To be the startup that gets acquired (and not the one of the many that fail!) you need to create a truly differentiated product, that can generate market share through superior performance, cost, usability or other attribute.

Vale’s experience has shown him that a medtech startup has to have a really deep understanding of a problem if it is to be successful. “It can take years to develop this level of understanding. With Neuravi we started with a huge and largely unaddressed market and a clear unmet need, as the existing mechanical thrombectomy technologies at the time were failing to restore adequate flow in about a third of cases, and were not resulting in good patient outcomes. We felt confident that we could create a far superior solution to this, however, having raised seed money based on our initial design concept, we stood back and took the time to ensure we really understood the problem we were trying to solve. After two years conducting further research and recreating stroke on the bench, we ended up with a device that was wildly different, and far superior, to the first one we envisaged.

Vale has stayed on to work 3 days a week at Cerenovus (the new entity created by J&J through the merger of Codman Neuro, Neuravi and another acquisition – Pulsar medical), focusing on R&D and next generation products. “There has been very strong investment in R&D since the acquisition - the company has doubled in size and continues to grow,” he says.

Making connections to deliver treatments

While working as part of a machine learning and computational neurobiology group at Maynooth University, founder of Neuromod Devices Ross O’Neill connected with two key people who would help him to confirm what he saw as a huge unmet need– leading ear, nose and throat (ENT) surgeon Brendan Conlon and audiologist Caroline Hamilton, who was increasingly moving into the area of tinnitus treatment.

At the same time, he reconnected with Stephen Hughes, now Chief Technical Officer at Neuromod Devices. They had previously worked together as post-grad researchers at MIT Media Lab Europe.



Now based in the Digital Hub in Dublin, Neuromod has developed and patented a new home-use technology that it is evaluating for neurological disorders including chronic tinnitus. The technology works by stimulating key nerves in the body to tone down the misbehaving nerve cells in the part of the brain that is responsible for the unwanted sound. Neuromod's approach doesn't require surgery and takes the form of a handheld device no bigger than a mobile phone.

"The four of us were involved in designing the technical prototype for clinical use. Brendan and Caroline were on the coalface of being aware of a huge unmet need, with thousands of patients every year coming to them with tinnitus," says O'Neill.

It is estimated that 10-15% of the population has tinnitus. 1-2% of the population are so badly affected by tinnitus that it greatly reduces their quality of life.

"Many people visit their doctors about their tinnitus.

Mostly the doctor tells them that there is nothing that can be done about tinnitus and that the patient must learn to live with it. This opinion is gradually changing, as GPs are starting to refer patients to ENT surgeons. The challenge for ENT surgeons is that unless the cause of the tinnitus is a tumour or vascular compression, which are rare, there is relatively little that they can do within their practice."

While a causal link is yet to be proven, it is widely believed that tinnitus is related to hearing loss. There is a large overlap between the two conditions: most people with tinnitus have some hearing loss, and many people with hearing loss have some tinnitus. Therefore, people with tinnitus are generally referred to audiologists to manage their care. Audiologists typically address the hearing loss with hearing aids and may offer versions with built-in features such as noise masking. Ultimately though, they have little to offer if the patient is not interested in a hearing aid. I believe that our device offers

patients a treatment that they can use in the comfort and privacy of their own home that is backed by evidence from more than 500 clinical trial participants," says O'Neill.

Neuromod Devices achieved the CE mark in 2014, allowing for its device to be sold in Europe.

"There was a lot of scepticism and hesitation among ENT surgeons and audiologists about tinnitus. Instead of investing in expanding an initial sales pilot in Ireland in 2015, we decided to invest in large-scale clinical trials working with many of the top scientists in the space, funded by our Series A investment round led by Fountain Healthcare," says O'Neill.

"We now have a wealth of information from our clinical trials that includes 3 months of treatment and 12-months of follow up data— some of the biggest and longest-term clinical trials ever in tinnitus – and are ready to restart commercial activity."

A one-stop-shop to bring ideas to life

Derek Young began his career as an inventor and a design engineer in the automotive industry and over the years he became involved in a number of medtech startups and has been named on at least 36 patents. "I have taken a good few medtech startups from start to finish, adding teams and a business case, conducting clinical trials and taking them to a stage where they can be acquired," he says.

While working as Head of the Centre of Innovation in Surgical Technology at the Royal College of Surgeons in Ireland (RCSI), Young had a vision: to set up a one-stop-shop to allow clinicians to come with their unmet clinical needs and ideas for innovation.

"After a couple of years, we realised our academic focus meant we weren't reaching all clinicians and were isolating ourselves from the true market where unmet clinical needs and ideas come from – within hospitals," says Young. With

"We now have a wealth of information from our clinical trials that includes three months of treatment and 12-months of follow up data— some of the biggest and longest-term clinical trials ever in tinnitus – and are ready to restart commercial activity."





Derek Young

the support of RCSI and Cleveland Clinic Innovations in the US, i360medical was spun out as a company in 2012. It now employs 8 full-time and 8 part-time people, including engineers, clinicians, market expertise, commercialisation and quality assurance expertise.

Central to i360medical's success and sustainability as a company is the turnkey model it has developed, involving a formal seven-stage process to take an idea from inception to becoming a real-life product in the marketplace.

"Academic research is important, but you have to look at how to make an idea become a reality within a timeframe," says Young. "We have proven this model from stages one to seven with 5 different partners around the globe. We also work with a large cohort of key opinion leaders, both clinical and commercial, in Ireland and internationally."

i360medical's international partners are a mixture of hospital systems, multinationals and mid-tier medtech companies. "Multinational companies are not set up to look for ideas in hospital systems as this could cause conflict of interest. We bring projects to a point of value where they are ready to spin out as companies on their own per se. We already have four projects at the point of being special purpose vehicles (SPVs), with another three coming down the line," says Young.

"Our commercial partners have the option to structure deals to acquire these SPVs. Approaching things in this way de-risks projects for them while also lowering our own risk profile, as we can operate separately from the startups."

Clinical strategy, the cornerstone of medtech

Identifying the right clinical strategy pays off for medtech startups. While some ideas originate with clinicians and key opinion leaders, other businesses benefit from early and regular engagement with the clinical community to take their technologies from validation to commercialisation.

Early detection for safer pregnancies

With a vision of making pregnancy safer, Metabolomic Diagnostics has developed technology that analyses the levels of particular combinations of biomarkers present in a person's blood. These biomarkers are selected so that their combined levels can provide information of this person's risk of developing a certain condition.

"Most bad outcomes of preeclampsia occur when the disease occurs before week 37 in a pregnancy. Our goal was to have the ability to predict in early pregnancy, a woman's risk of developing

pre-term preeclampsia, up to five months before any symptoms would typically occur," says CEO Charles Garvey.

"When we went to do this, we found the tools weren't really there and we spent years building them. We have researched and patented novel analytical and statistical methods which now allow us to match biomarkers to specific disease phenotypes. Part of the magic in our work is that we can now analyse large numbers of metabolites across a huge variety of classes. In a study last year we looked at 90 different biomarkers to identify those which relate to a risk of preeclampsia."



Charles Garvey

Metabolomic Diagnostics has carried out retrospective trials, testing its techniques on specimens donated during pregnancy. “We looked at samples of blood from thousands of women to allow us to go back and say, ‘If we had been able to measure the biomarkers at this point in time, what would we have said?’. Then by looking at the database and the outcomes we could see that we would have got the predictions right,” Garvey explains.

Being able to predict who is at risk of preterm preeclampsia could really make a difference. In another EU funded project, 35,000 pregnancies were analysed to evaluate the ability of aspirin to reduce the risk of preeclampsia among high risk women. The results were published in October 2017. They showed that giving aspirin to high-risk women significantly reduced their risk of preeclampsia before 37 weeks of pregnancy. Preterm preeclampsia developed in 1.6% of the high risk women given 150mg of aspirin daily, compared with 4.3% who took a placebo.

“It is essential therefore, to be able to identify early enough who is at risk

of developing preterm preeclampsia and would therefore benefit most from aspirin. That is where we came in,” says Garvey. “This is a very exciting study, which will make it possible to eliminate two thirds of the worst cases of preterm preeclampsia.”

How local knowledge drives clinical and commercial success

Neurent Medical will embark on its first formal clinical trial of its rhinitis treatment device in the second quarter of 2019 partnering with a top tier academic centre in the US, which the company is targeting as its initial market. The device it has developed is a minimally invasive hand-held, radio-frequency device which ear, nose and throat surgeons will use to treat patients in an office setting.

“The first clinical trial involves the recruitment of 15 patients to demonstrate, primarily, that our device has an appropriate safety profile for the indicated patients in the specific treatment setting” says CEO Brian Shields. “We will also study the efficacy of the device

and how well it is working for those 15 patients over 6 months. This is an important milestone for the company as it will determine the design of further clinical trials as we prepare for and enter the commercialisation phase”

Shields and his co-founder David Townley plan to conduct further clinical trials in the US, the first being next year, to demonstrate superiority of the device. “Successful commercial launch has a high bar when it comes to clinical evidence, we were very conscious of that in the design of our clinical strategy.”

The positioning of Neurent Medical's device has been carefully considered in terms of achieving buy-in from clinicians. “It is important to look at the dynamics of the domain you're in. As a startup we're not trying to change too many things, in particular how surgeons work. In the US, ENT surgeons already frequently carry out procedures in the office setting. We aim to leverage that and bring an exciting new therapy to them and their patients.

“Most rhinitis patients are treated by medical therapy, which does not work for certain patients. Our solution requires the surgeon being more hands on in their intervention for the patient and means that the patients can be relieved of the requirement of long term medication with a single visit to their ENT.”

How research is helping heal high risk patients

Cork-based startup OrthoXel has introduced the world's first implantable nails with controlled axial micromotion fixation. The Apex Tibial and Femoral Nails are the next evolution in fracture fixation for lower extremity long bone fractures – the first and only systems to promote secondary bone healing with controlled axial

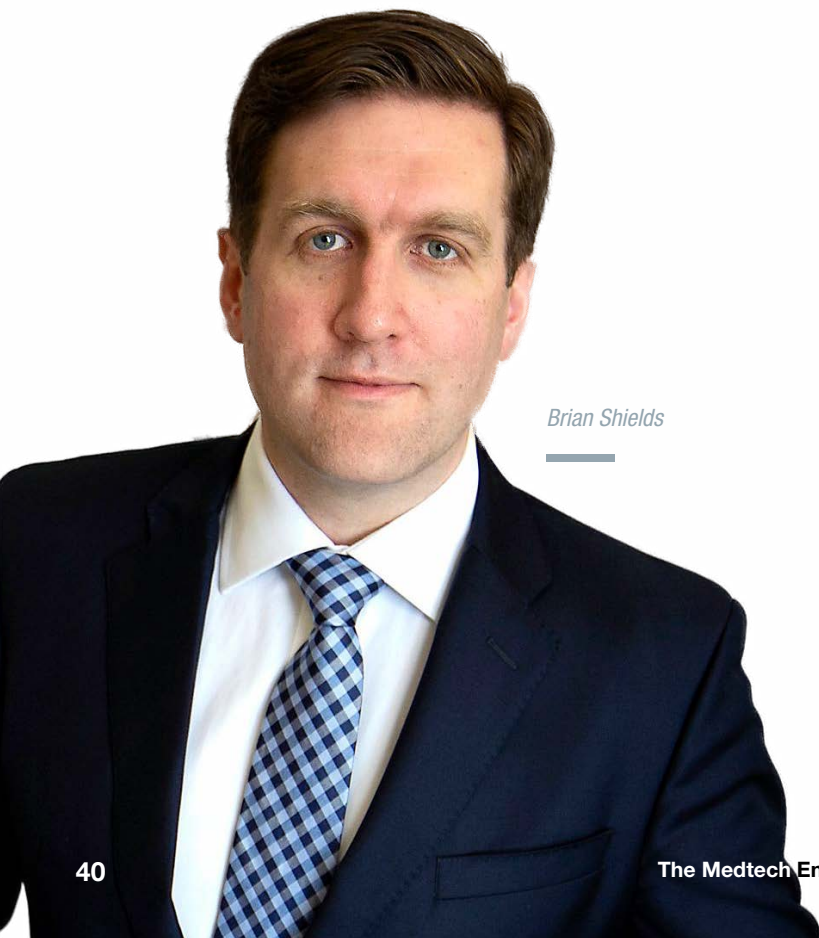
micromotion and outstanding torsional stability. OrthoXel's products can be used to treat the estimated 400,000 annual tibia and femoral fracture patients Europe and US.

The company's flagship tibial and femoral nail products grew out of five years of research and development work in the Medical Engineering Design and Innovation Centre (MEDIC) at Cork Institute of Technology, where co-founder and CEO Pat O'Connor was centre manager.

“Prior to incorporating the company, we had collaborated on the original fracture device with orthopaedic surgeon James Harty who had approached CIT's MEDIC centre with an idea around tibia nail dynamization. Working with James, we turned this original idea on its head several times before arriving at an axial micromotion technology which we brought to the point of proof of concept,” says O'Connor. The proof of concept work established that the optimal healing conditions for lower extremity long bone fractures requires rotational stability of bone fragments combined with approximately 1mm of axial micromotion”.

“The principles of axial micromotion combined with rotational stability had already demonstrated accelerated healing on external fixation devices. OrthoXel is the first company to apply these principles to intramedullary nails for use in tibia and femoral fractures.

OrthoXel recently published a white paper highlighting four surgical case reports of patients who were considered high-risk (comorbidities, high grade fractures etc) in terms of delayed fracture healing. All four patients healed very well in a short time following the use of the Apex Tibial Nailing System. These four patients are a subset of a clinical study that is assessing the performance of OrthoXel's Apex Tibia Nail across a broad spectrum of patient profiles.



Brian Shields



Pat O'Connor

"The ongoing clinical study shows how effective the system is, even in high-risk patients," says O'Connor. "The US is a key market for us and we wanted to get a clinical white paper into the public domain before we travelled to the American Academy of Orthopaedic Surgeons convention in Las Vegas in March where we had planned meetings with a number of US surgeons."

OrthoXel has secured European CE Mark and US FDA Regulatory approval for both of its products, which means that we are legally permitted to implant our innovative tibia and femoral nail products in patients in Europe and the US respectively. "We are in the midst of our European clinical case studies with 30 patients implanted to date in Cork University Hospital. Patient recruitment and data generation is ongoing. We plan to implant our first US patient in Q2 of this year with a view to completing a US clinical study throughout 2019 and into 2020. The US is a key target market for us so it is important that we get US surgeon endorsement and market validation in that market."

Clinical innovation informed by personal experience

Elbe Valley Medical in Mullingar, Co Westmeath is developing a therapy which it hopes will add to the treatment options for patients with solid tumour cancers. Aimed at end-of-life patients when chemotherapy and radiation have failed, the technology will target any unwanted tissue that shows up on an MRI scan through the injection of nanobots into the blood.

In 2014, a random health check organised by his employer in Germany, led Rob Reynolds to found and become CEO of Elbe Valley Medical, fearing he may have a brain tumour (which turned out not to be the case).

"I came up with this therapy as a result of what happened to me. I felt there should be a fast, non-invasive way to treat tumours," he says. "I'm a big fan of negative innovation – as time passes I aim to make the technology less and less complex by taking features away rather than adding them so you end up with the bare minimum of what is needed. It's the opposite of what everybody else does."

So far, Elbe Valley Medical has conducted pre-clinical work with the University of Sheffield and is moving on to more pre-clinical work in Ireland early next year.

"Our next trial will be a dress rehearsal for our first-in-man study, which will take place in late 2020, early 2021 overseas. Ireland has some great first-in-man and clinical facilities for conducting trials. But there's an opportunity now to grow this important element of the innovation ecosystem to meet the demand of the dynamic medtech industry by expanding our capabilities to support the development of transformative technologies," says Reynolds.

Professor Frank Sullivan at NUI Galway recognises there is a need to develop such capability and is working on it. "I believe it is really key to driving Ireland up the leader

board in healthcare globally."

"'First-in-man' studies are complex, and patient safety is paramount. There is also a need to balance optimism for novel therapies, with the reality of dealing with refractory cancers in late stage patients. That said, Ireland has the facilities and expertise to expand this effort. Other startups and multinationals would benefit from expanding 'first-in-man' facilities in Ireland. It would mean life-saving therapies could be brought to market in shorter time. Furthermore there is evidence that patient care benefits, when well-designed clinical trials are incorporated into existing care facilities"

Elbe Valley Medical currently employs five full-time people and a couple of part-time staff. In hiring mode currently, Reynolds is looking to open a US office later this year.



Rob Reynolds

From iterative to dis

For medtech startups your first idea might not be your best idea, entrepreneurs in this industry are devoted to continuous research and testing to ensure safety and efficacy. Device development is guided by thorough research and regular testing to ensure only the best version of medtech products make it to market.

Neuravi: device design and development

Developing Neuravi's EmboTrap device didn't happen overnight. Designing a transformative medical technology takes time and thought, according to Neuravi co-founder and Chief Technology Officer David Vale.

Stroke is the second leading cause of death and the third leading cause of disability worldwide, according to the World Health Organisation. "We started with a pretty clear unmet need: restore blood flow to the brain, quickly, and without causing secondary harm," says Vale. That's how the idea for the EmboTrap began. The device developed by Neuravi, and acquired by Johnson & Johnson in 2017, captures and removes clots from blood vessels to restore blood flow quickly and safely.

"A good decision we made on day one was not to assume that our initial concept was the optimal solution for this need. We had raised seed funding on this idea, but we

didn't take it for granted that this was the best we could do. We set about comprehensively brainstorming all the different ways in which this need could be addressed. Then we filtered this through increasingly detailed rounds of prototyping and testing to funnel down to our final design solution," he says.

"The real secret to getting this right was the level of realism we managed to get in our testing, and the research we carried out into understanding the properties and behaviour of blood clot itself was key to this. Neither a bench nor an animal test can fully represent clinical reality, but the closer you can come to a realistic test the more meaningful and valuable will be the results you get," he adds.

"Our bench simulations of stroke cases had limitations, but they offered a fresh perspective to physicians on the mechanism of interaction between the clot, the blood vessel and the treatment device. Seeing this happen in front of your eyes is very

different than seeing it in a black and white x-ray image. Bringing this level of research to the table enabled us to have lengthy and engaging conversations with physicians, with information and learning flowing both ways."

Vale concludes, "This process continues to this day, as we continue to improve our understanding of the complex, living biomaterial that is clot, and evolve our test models to reflect this. Having these accurate stroke simulation models enables us properly assess the effectiveness of different design solutions without putting patients at risk and has been key to the successful development of the EmboTrap device."

More than four out of five people who experience a stroke have an ischaemic stroke, which is when a blood clot blocks an artery supplying blood to the brain. The EmboTrap device represents a major breakthrough for mechanical retrieval of such clots, improving outcomes for patients around the world.

Device design: Making lasers work for medtech

Dr David Gillen founded the company in 2006 to develop and manufacture dedicated, highly accurate, laser micromachining equipment to be used to process materials for use in advanced manufacturing generally.

"The type of technology we use is not something you can just go out and buy. It must be developed from scratch from first principles. Without research and development we wouldn't be where we are now; it is core to what we do," says Gillen.

"Design is based on customer requirements and you have to be flexible. We work very closely with customers to determine what they require and each has a different roadmap. Flexibility can lead to mistakes, so we applied for the Quality Management Systems ISO 9001 and the standard for medical device quality management systems ISO 13485. Within these



Disruptive innovation

standards, there are very tight procedures around how we handle the development of new devices and products. It allows us to formalise the process and stick to it very closely."

In 2011, Blueacre Technology was approached by medtech companies which weren't looking to machine components, but rather wanted to use lasers to probe them and see what was inside.

"This led us to working with companies to develop laser-based cancer microscopes. These devices use laser light into the cells of a biopsy. The laser light interacts with the cells in different ways, allowing scientists to analyse cells which are pre-cancerous or cancerous," says Gillen. "This experience showed us that there was more to the company than what we had set it up to do. We could see there was a lot more we could do with lasers and were more than just machine builders."

About three years ago, Gillen saw the opportunity to use lasers to manufacture components in-house. "Instead of building a machine for a client and selling it to them, we decided to hold onto the machine and use it to manufacture parts for

the client. This enabled us to control the machines and be a lot more accurate in terms of what they do. The largest part we would machine would be 1 millimetre in size. We would tend to machine features of those parts down to a thousandth of a millimetre, which is not visible to the naked eye. Clients could struggle to maintain the type of accuracy required if they are not experienced with lasers."

Blueacre Technologies has grown the contract manufacturing side of the business to the extent that 95% of its output in this area is medtech. "Ireland has a lot of contract manufacturers for medtech, but we are the only company to use purely laser-based processing. This has led to significant growth in revenues and capability for us," notes Gillen.

Blueacre works with customers right through the medical device lifecycle – from early product development and process validation prior to during clinical trials, through to large-scale production and ongoing product revisions and process re-validations.

One of the significant capabilities Blueacre Technology has developed has been in the manufacture of microneedle moulds. Less

than a millimetre tall and the width of a human hair, instead of being in a metal tube, these needles themselves are the drug which then dissolves into the body. "We are one of the only companies in the world that can use lasers to manufacturer the moulds for these products," notes Gillen.

Last November, Blueacre Technologies was one of the first companies to be awarded under the €500 million Disruptive Technologies

Innovation Fund, which is part of the Project Ireland 2040 plan. It is partnering with Trinity College Dublin on a three-year micromachining project called DEFINE-AM. It aims to develop an innovative machine tool with 5-axis of motion that addresses the challenges of post-processing 3D-printed metallic parts, ie parts produced by the Laser Metal Deposition additive manufacturing technique.

Olivia Gillen and David Gillen



The unifying voice of design

Design thinking can make a good idea a great idea. Novel technologies must be user friendly to encourage uptake by clinicians and patients. Designers and strategic partners can make functional products emotionally resonate, whether it's with digital and connected health elements that empower patients or improving usability to ensure effective use. Design has helped manufacturers become more consumer-focused.

Brainstorming for success

Design for life is about designing medtech products for the widest range of end users, including patients, nurses and clinicians, whether they are eight or 80 years old, according to Sean McNulty, founder and director of Dolmen Design.

"With design for life, you're not just looking at the functional aspects, but also the emotional issues and triggers associated with a product. The aim is to establish what will create a good outcome for people and give them trust and confidence in that product. The physical aspect of the product is important, but is only part of an integrated experience for the end users. This has become all the more relevant as devices incorporate multiple services, digital platforms and smart technologies," he says.



“ We are there from the get-go with medtech clients, conducting interviews with surgeons, feeding into brainstorming and ideation sessions and helping them to generate patentable ideas.”

McNulty founded Dolmen Design in 1991, and since then has witnessed a mindset change in medtech product development involving a new focus on doing things in the right order. “When I started out, for the first ten years I was told what to do by clients. Now, 80% of successful medtech products are driven by customer-centric, design-driven innovation aligned with the objectives of the business,” he says.

As a product design and research and development (R&D) partner, Dolmen helps businesses to transform their innovation pipeline by creating award-winning and intellectual property rich products. In the medtech sector, it mainly works with multinationals, but also SMEs and early stage startups from product concept right through to design for manufacturing. The company

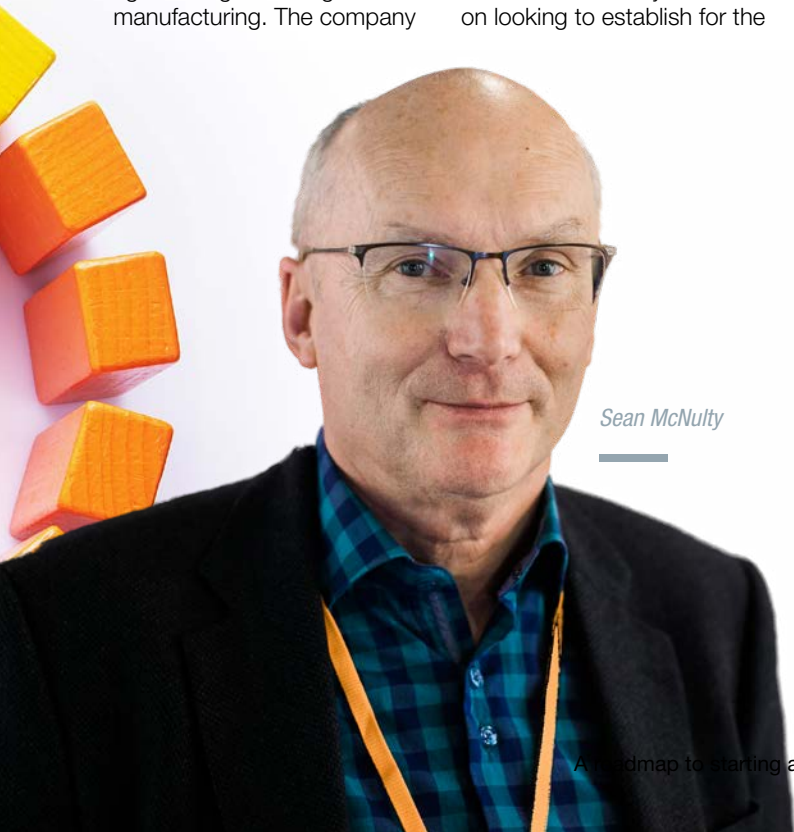
is based at the DCU Alpha innovation campus in Dublin.

“One of the main reasons companies work with us is that it adds value as we have a different way of looking at things. Medtech companies are brilliant at what they do but being truly innovative requires lateral thinking that can be pulled in from other industries. We are there from the get-go with medtech clients, conducting interviews with surgeons, feeding into brainstorming and ideation sessions and helping them to generate patentable ideas.”

Dolmen’s structured three-phase design thinking process “Discover, Develop and Deliver” creates an innovation framework which can be dropped into the existing R&D process within a company. “Part of innovation is failure. Much of our activity is focused on looking to establish for the



Frances Mitchell



Sean McNulty

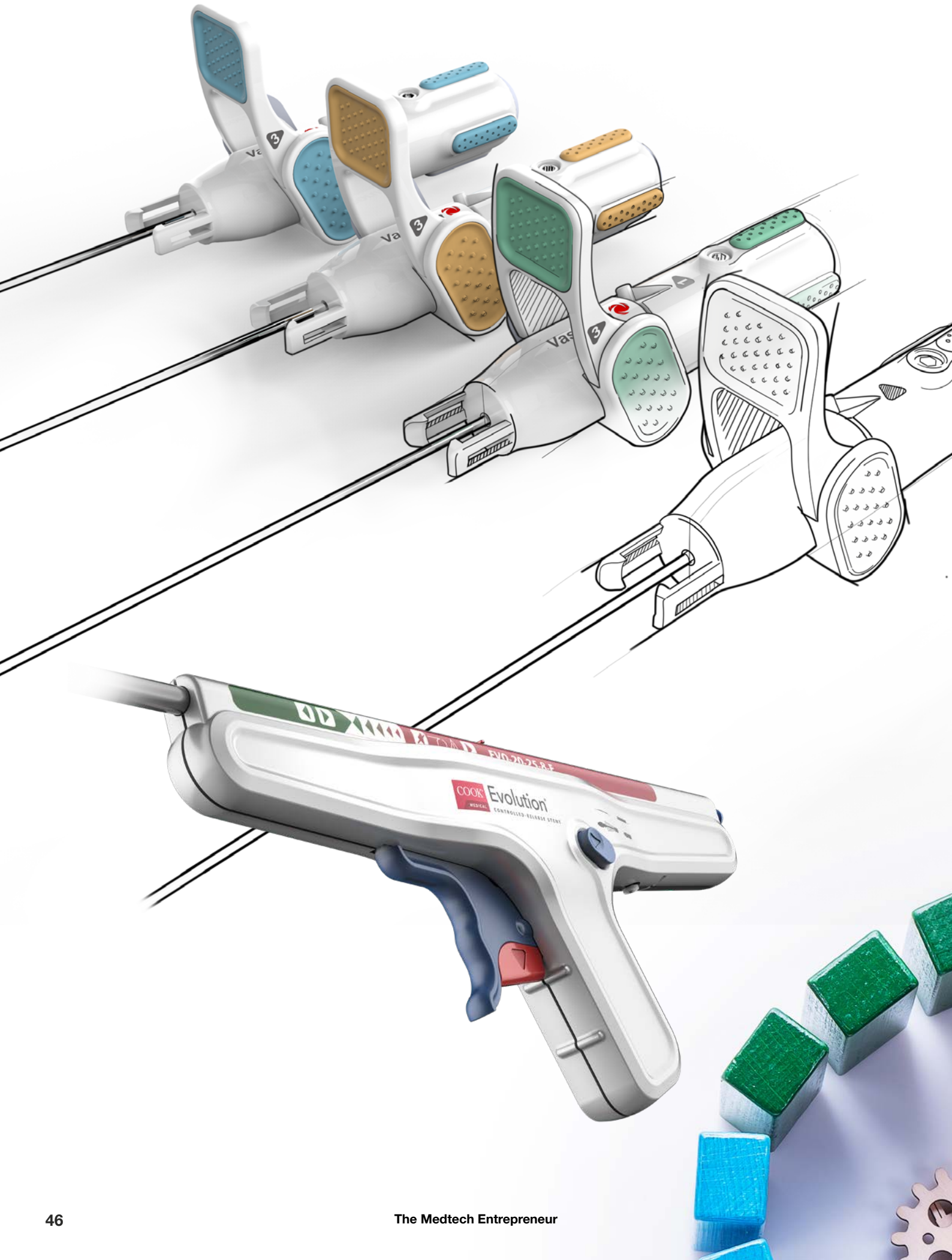
CEO what ideas will and won’t deliver so that resources can be maximised accordingly,” says McNulty.

As Dolmen’s director of business development Frances Mitchell explains, most of the time it works between the R&D and marketing functions within a client’s organisation. “We sit between the two and make sure technical excellence and marketing insights are combined to the best effect,” she says.

“For example, we user-

tested one product and found that it was bigger than it needed to be, as human beings didn’t need it to be that size. There was no issue in relation to regulation so this could literally be changed. This led to significant savings in terms of material usage right down to the number of units that could be stored on a pallet in a hospital. Small insights such as this can make a big impact.”

Design thinking can help set global standards for medtech, she adds, “During





Brian Stephens

ethnographic research into oesophageal stent delivery for Cook Medical we discovered that sometimes surgeons would like the opportunity to retract the stent, so we helped develop the world's only reversible stent delivery system."

When products are user-tested in this way right through the full development cycle, the solution can get incredible buy-in from end users, she adds. "It means risks are mitigated up-front and the time to market can be accelerated. The biggest risk

a medtech company faces is bringing the wrong idea to market by not understanding deeply enough the problems its customers have. Everything we do is based on what is meaningful for the end user."

Design thinking in medtech

Brian Stephens, CEO of Design Partners in Bray, Co Wicklow, believes that without question, the right application of design and design thinking results in safer and more effective medtech products.

"Incorporating design as an end-to-end process means you have a full design file showing the history of how the product evolved and a controlled, measurable record of how the team made the right design decisions based on monitored testing with users," he says. "It takes a lot of the guesswork and personal bias out of the process and makes product development more rigorous and objective."

Established in 1984, Design Partners is a strategic product and interaction design consultancy. It is focused on growing brands by designing "exceptional product experiences that make life better".

"Design thinking is the application of design principles and creative methodology to tackling both strategic and product related issues. It is

about being empathetic to the users needs and having a coherent process to creatively experiment, prototype and iterate effectively. This makes perfect sense in the medtech sector where the user's needs are quite specific and where safety and performance really matter. Design, at its best, is a kind of glue between the original innovative concept and the precise needs of the user. Because design is a multidisciplinary process, it considers all sorts of factors but especially the users physical and psychological needs," says Stephens. "Because we work across a broad range of categories beyond medtech and apply this knowledge to everything we do, I believe our solutions are as progressive and as thought through as they possibly can be. We strive to always see the big picture, to understand and represent all the stakeholders needs and interpret these in a creative and actionable way."

Design Partners has worked on medtech projects for big names as well as start-ups. Recent projects include exciting new products for international clients such as Abbott and Shire Pharmaceuticals and Irish start-ups HealthBeacon and ProVerum. . The consultancy is focussed on five categories: surgical and interventional devices, diagnostic equipment, connected health products, patient experience design and capital goods.

"Point-of-care diagnostic equipment is an area where design thinking has become extremely important. It speeds up the process of providing an accurate diagnosis at point of care rather than having to send samples to a lab," says Stephens.



Five years ago, Stephens recognised that if Design Partners wanted to provide a tailored service to medtech clients, it needed to build the right expertise in-house and develop this as a core competence. This involved upskilling existing staff members with relevant postgrad degrees and training and hiring people with a medtech background. "To provide the highest standard of expertise to our clients, we also set up a purpose-built lab for user testing, observation and prototyping and we invested in 3D printing capability using technology specially developed for medical applications," notes Stephens.

"As a company, mechanical engineering has always been fully integrated into our creative work, we have always designed for manufacture and for mass production. Human factors engineering is an integral part of our process for the last five years. We have been evolving it and applying it as a process for all our medtech development projects and beyond."

As Stephens points out, users of medtech devices are well informed users who are digital natives with the same expectation from a medtech device as they would of their mobile phone. "Digital design is a lot about clarity and simplification. An increasingly important part of our design

work is making sure that both the digital and the physical product experience are one and the same and are both fully integrated into the whole product experience"

Putting the user first

CEO of Synecco in Galway, Tony Doherty agrees that there is now a push towards bringing a consumer-grade edge to medtech device design, particularly when devices are being used in home-based settings.

"In hospital, medtech devices are deemed as being medical, but at home they are simply products that should blend in with home life. Patients don't want to draw attention to the fact that they have an ailment. They want their inhaler to look as appealing as their iPhone," he says.

Based in Ballybrit, Co Galway since 2004, Synecco saw the need to add a design function to its contract manufacturing operation in 2009. Nowadays, its Irish operations include a 20,000 sq ft facility in Galway with a dedicated design and development centre, and a 60,000 sq ft manufacturing site in Clare.

"Our core focus is on designing and manufacturing products with polymers. Increasingly, we're working

with medtech clients all the way through from initial product design through to manufacturing," says Synecco CEO Tony Doherty.

Usability engineering is now a key pillar which has been built into the team and programme of activity at Synecco. It has been aligned with design, process development and validation. "Designing a medtech product with usability in mind has become as important as designing with manufacturing, cost and regulatory requirements in mind. The industry wants products that are intuitive to use, safe and effective. Human factors is so

prevalent now and a key focus of regulatory submissions to comply with the standard for medical devices IEC 62366" says Doherty.

He gives the Ez-Tract Stent Delivery System as an example of Synecco's application of design and human factors engineering expertise to solve an unmet user need, namely the need for a better, more user friendly way to deliver stents, with the solution presented in an intuitive and aesthetically pleasing form factor.

"We consider usability throughout the product life cycle right the way through to packaging, manufacturing and



Tony Doherty

“ We carried out research with nurses and patients and eventually reconfigured everything around the product; packaging, messaging, training materials and elements of the product itself. It was marketed on the back of the research and design we did.”

sometimes how the product will be destroyed or reused.”

“The development cycle for medtech devices is relatively long because of regulatory approvals. This makes identifying risks in relation to how devices could be used so important early on. If this kind of road testing is left until the device is finished, companies may have to re-loop back into the cycle all over again.”

Connecting people

Henry Poskitt worked in OSA a general product design and innovation company before becoming a Director at Frontend, which was Ireland’s first dedicated user experience design agency. For over 20 years now, it has specialised in shaping how people interact with a broad spectrum of new technologies and services.

Frontend’s path into medtech started with a design discipline called ‘out of box experience’. “We had been working with companies like HP and O2, all of which had a common problem: they had a complicated technical product in a box which needed to be set up by somebody who wasn’t trained,” Poskitt explains. “The first medtech company that found us was Roche Diagnostics, which had a similar problem with a blood glucose meter. It came in a box and had to be set up by a nurse who wasn’t always familiar with the product.

“We carried out research with nurses and patients and eventually reconfigured everything around the product; packaging, messaging, training materials and elements of the product itself. It was marketed on the back of the research

and design we did.”

The agency increasingly got involved in developing mobile apps for clients in sectors such as financial services. It wasn’t long before life sciences companies approached it to create companion apps for their products, including monitoring and digital therapeutic treatments.

“Now, most of our medtech work is in the area of connected health, focused on the design of interfaces to improve patient engagement with a therapy. It is still the same fundamental challenge that we started out with – a person with a piece of technology and the relationship between the two.”

The most recent medtech project Frontend worked on which went to market was a companion system developed

by Merck Serono for children with growth hormone deficiency. A connected auto-injector sends messages back to a server to indicate a pattern of adherence and the solution encourages the patients to stay on their treatment using electronic messaging.

In Poskitt’s experience, product design, whether physical or digital, hinges on a deep understanding of a problem and looking at it dispassionately from multiple viewpoints. “The real gems in the process are when you uncover new opportunities within those problems. A lot of the time, it is really about open-minded assessment, finding a genuine need for end users and coming up with a novel solution that is both commercially viable and improves lives.”



Henry Poskitt

Spinning out

While entrepreneurs may have a DIY attitude, spinning out from academic institutions can give them a head start. You can get your technology investor ready faster by engaging with key opinion leaders and research experts to help you set a clearer path for market access and success.



John Gleeson

The academic advantage

SurgaColl Technologies' novel tissue regeneration products for the surgical treatment of disease of the bone and cartilage tissue are based on biomaterial technologies developed by the Tissue Engineering Research Group (TERG) at the Royal College of Surgeons in Ireland over the last decade, headed by Professor Fergal O'Brien.

Founder and Chief Technical Officer of SurgaColl John Gleeson was lead researcher within RCSI Tissue Engineering Research Group (TERG) and managed the development of the technologies from 2007 until 2012. He then decided to set up a spin-out company with O'Brien after identifying a clear and enduring unmet need for these regenerative products that could be commercialised from their research.

"I am a big believer in the potential of medtech companies spun out from academia. There are significant advantages in terms of early commercial supports and business validation, given the extensive sector expertise within Ireland and the local angel and VC

investment community" says Gleeson. "Startups can leverage a large amount of regulatory expertise and get rapid feedback, directly from product end-users such as clinicians and potential partners/exit targets with top global medtech manufacturing companies having a major presence in Ireland. The biggest advantage for SurgaColl was the regulatory-compliant, early product development work completed within RCSI (as part of Enterprise Ireland's Commercialisation Fund supports).

"RCSI had the commercial foresight to complete early safety and biocompatibility assessments prior to spin out. This gave us a technology that was investor ready and a clear route to market, allowing early investment to focus on manufacturing setup and product builds for clinical use."

SurgaColl's two products are bone, HydroxyColl, and cartilage, ChondroColl, graft substitutes. The strength of these products is that they are orthobiologics, that is implant materials that use naturally derived biomaterials to form a scaffold to encourage rapid regeneration. The implants biodegrade as healing

progresses, which means a faster healing process and the implant is ultimately replaced by the patient's own new healthy tissue over 12-18 months.

HydroxyColl received CE Mark approval in early 2016 and in the same year was used to rebuild a thoroughbred mare's jaw. The technology has netted the Company and Gleeson numerous publications and awards such as, The Royal Academy of Medicine in Ireland Bioengineering Division Bronze Medal, Best Emerging Company InterTrade Ireland Seedcorn all-island business competition, and more recently a Royal Academy of Medicine in Ireland award at the Irish Bioengineering Conference. At this conference, in January 2019, his paper highlighted the successful regeneration of a challenging horse jaw defect.

Turning to human studies, SurgaColl now has clinical data available for HydroxyColl on over 35 Irish patients through its work with plastic surgeon Dylan Murray at Children's University Hospital, Temple Street and 10 lower limb trauma cases with Mr Mike Risebury in Basingstoke Hospital in the UK. "Our

bone graft has been used in young adult jaws for facial augmentation, trauma-related defects, addressing poor development of the jawline, as well as helping relieve knee arthritis pain through joint alignment procedures” says Gleeson.

“The key thing we are seeing from our early-stage clinical and research work is that our products can facilitate more rapid healing and produce better regenerated tissue. After 12 months the implants are absorbed as part of newly healed tissue. Most importantly, the quality of the tissue we’re seeing, formed by the implants, appears to be significantly better our products can regenerate tissue that is as good as the original healthy bone or cartilage that the patient had before the injury.”

In 2012, SurgaColl raised €2 million in seed funding from four main investors, including Enterprise Ireland and AIB Seed Capital Fund. It closed the 1st part of an ongoing Series A funding round in January 2018, raising £3.1 million in total and led by Catapult Ventures in Manchester in the UK.

“The funding we have secured has allowed us to complete our early stage clinical validation, giving us early market feedback based on the positive early clinical data for both products. HydroxyColl will be approved for use in the USA later this year and current fundraising activities aim to repeat this process with our lead product, ChondroColl, for the repair of joint cartilage damage through to early regulatory approval and commercialisation. The cartilage market is very exciting and extremely attractive to investors,” says Gleeson.

With R&D and manufacturing based at the Invent Centre at Dublin City University, SurgaColl employs 13 people and their recent clinical achievements led to recognition winning the

‘Spin-out Company’ award for SurgaColl at the 2018 Knowledge Transfer Ireland Impact Awards, presented to RCSI’s Office of Research and Innovation.

Spinning out to get your product out

Having lived in the UK for ten years, biomedical engineer Olive O’Driscoll returned to her native Cork to take on the role of Technical Project Manager at Cork Institute of Technology’s Medical Engineering Design and Innovation Centre (MEDIC) in 2009.

“My job at MEDIC involved working with surgeons and companies on medical device solutions from the idea stage, designing devices, conducting market and regulatory assessments to the final stage of getting the product to market,” she says.

Together with John Vaughan, Product Development Engineer at MEDIC, O’Driscoll spent four years working on technology to develop a device which would enable the quick and simple insertion of ear grommets in children without the requirement of general anaesthesia or operating rooms.

Their innovative product, the Solo Tympanostomy Tube Device (Solo TTD), is an all-in-one ear tube placement device. The handheld device is pre-loaded with its own ear tube at the tip enabling the surgeon to safely place the tube into the child’s ear in just a few seconds, with just one click of the button.

“The Solo TTD allows procedures to move out of the operating room and into new settings, such as a procedure room. The operating theatre is the most expensive room in the hospital. It is so much more cost effective to treat patients in other settings. Our product saves time, is less invasive and reduces costs to the healthcare provider while



Olive O’Driscoll

also providing a better patient experience,” says O’Driscoll.

Securing an Enterprise Ireland Commercialisation Fund grant enabled the pair to develop and manufacture the device so that it was ready for clinical trials...

“From research we knew there was a good market for our device, we were confident of our product and its value and were eager to spin out the company and take it to the market ourselves,” says O’Driscoll.

“Throughout my career in the medical device arena I made a number of great clinical connections internationally and was fortunate to be in a position to reach out to a them who in turn introduced me to their ear, nose and throat colleagues. Right from the start we developed strong relationships with a number of surgeons and their input was invaluable. The feedback helped us to make sure our device was meeting all of their requirements and we

could show good usability on the bench in the 3D printed ear models we created and cadaver testing..”

After this process, O’Driscoll and Vaughan developed a business plan and spun out as a company, AventaMed, in 2014.

AventaMed won the “Best Overall Early Stage Company” in the InterTrade Ireland Seedcorn competition that same year, winning €100,000.

“As well as the fantastic financial boost the Seedcorn competition granted us, it also really helped us to focus and define our business plan and strategy, and ultimately accelerated interest and commitments from investors,” says O’Driscoll.

Currently employing a team of six at its base in the Rubicon Centre, Cork, AventaMed announced a second round of funding worth €1.8 million from the Halo Business Angel Network and Enterprise Ireland in October 2017.

Investing in medtech

Finding the right medtech investor is a lot like matchmaking. You need to get to know each other before entering into a relationship, you need to have clear expectations and meet at the right time.

From seed funding, business angels, and venture capital, to research grants, as well as mergers and acquisitions, there's a different source of funding for different stages. First, to attract an investor you need to be able to tell your story to help them understand your idea, the market and the role of your management team in linking the two. But if you find the right investor, you won't just benefit from an injection in funding, you can tap into advice on strategy, regulatory pathways and even mentorship.



Dr Brendan Boland

Growing together with investors

Co-founders of Loci Orthopaedics Dr Brendan Boland and Gerry Clarke got to know their investors over an 18-month period before closing their seed fund round – something which has been beneficial in more ways than purely financial

In July 2018, NUI Galway BioInnovate spin-out Loci Orthopaedics closed a seed funding round of €2.75 million to enable it to achieve key regulatory, clinical, and commercial milestones over a 24-month period for its “InDx Implant” to treat thumb-based arthritis.

The funding was provided by Enterprise Ireland, the Western Development Commission, the investment arm of KU Leuven University in Belgium and a number of industry veterans.

“Most entrepreneurs trying to raise or close finance, particularly seed finance, know how challenging it can be in terms of timelines. You do have to spend quite a period of time building relationships with potential investors. They need to get to know you, but equally you need to get to know them,” says co-founder of Loci Orthopaedics Brendan Boland.

“The first time we met the people who were going to be our investors was 18 months before we closed the seed round. They got to monitor our progress and how we managed the process and we, in turn, were able to understand their needs and expectations.”

The investment group that formed for Loci Orthopaedics’ seed round has been very supportive, adds Boland. “They are very knowledgeable about the product and the company and have been doing their own research into the market. We have been able to ask for their advice and input on business strategy and regulatory approvals.”

“This is an endorsement for us, but also means we can tap into the Western Development Commission’s knowledge and

Top three tips for VC

Co-founder of stroke care company Neuravi, David Vale believes venture capitalists generally look at three things when considering investing in a medtech startup: “big market, great technology and strong team”.

“The commercial opportunity has to be big for sure, but it is the way these three elements link together that matters. A medtech startup has to be able to tell a good story about how it is going to gain and retain a decent share of a large, and growing, market and explain how it is going to prevent a competitor doing the same or better,” he says.

Differentiation and protection, ideally through a strong patent portfolio, should be core elements of this story. The credibility of the business plan is also key, and depends to a large extent on the perceived competence of the team, which can be a challenge for startups, especially those with a young and/or inexperienced team. Neuravi was lucky in that the founding team had a strong track record, but we still had to demonstrate how we were going to attract top talent into key areas such as Regulatory and Clinical.”

Vale continues: “At the same time, there is no point telling a wonderful story over and over again to investors who aren’t qualified to invest. You have to do careful screening to make sure you focus your efforts on those with sufficient knowledge and experience of your space to properly perform their due diligence, who have money available to invest, and ideally who have sufficient term left in their fund to be able to follow their money in a future round.

When Neuravi went looking for Series A funding, it had a good working prototype and had done an animal study. “We had some evidence that our device was likely to work and two Irish venture capitalists agreed to back us [Fountain Healthcare and Delta Partners]. We raised €5.2 million in 2012 to take us to CE mark approval with support from the Western Development Commission.”

In 2015, Neuravi’s Series B investment round raised a further €19 million. It was led by Dutch private equity firm LSP, and Fountain Healthcare, Delta Partners and the Western Development Commission returned as investors. “We might wish to have had international investors at an earlier stage, but it is unusual for an international VC to invest without an Irish one. LSP and Fountain have since partnered in other Irish investments, which is great to see,” says Vale.

Neuravi used the Series B funding to perform a clinical trial to get FDA approval to sell into the US market and roll out the device on a commercial basis across Europe. In 2017, Neuravi was acquired by a Johnson & Johnson company for an undisclosed sum, believed to be in the hundreds of millions of euros.



David Vale

skill base,” notes Boland. The participation of the investment arm of KU Leuven represented the first time it had been convinced to support a medtech startup outside its own boundaries. “It was a great achievement to get this investment across the line,” says Boland.

Depending on the length of the regulatory approvals process, Loci Orthopaedics hopes to do its first clinical trials in early 2020 and to roll out to the market towards the end of that year.

“We expect a large demand for InDx. Our primary market will be the US, followed by the EU, dependent on regulatory timings. Worldwide, 120 million people are affected by ongoing pain in their hands caused by thumb joint arthritis. The same proportion of the population (5%) has thumb joint arthritis as hip arthritis, yet there are 400,000 hip implants in the US a year compared to only 70,000 thumb joint procedures due to the sub-optimal outcomes associated with current treatment options for thumb joint arthritis. The InDx Implant is the first evidence-based solution to be developed to meet this huge unmet clinical need and under-penetrated market.”

Guided by angels

In 2016, Signum Surgical in Galway closed a €2.6 million Series A funding round, with €1.1 million of this coming from the Halo Business Angel Network’s (HBAN) MedTech Syndicate.

A spin-out from the BiInnovate Ireland programme, Signum Surgical was set up by Eoin Bambury and Moshe Zilversmit to address a colorectal condition called anal fistula. Signum Surgical’s solution is designed to encourage healing, prevent reinfection and protect patient continence.

Having been granted commercialisation funding from Enterprise Ireland, the pair left NUI Galway after a year and began talking to potential investors including angels, individuals, groups and venture capitalists.

“What we ended up with was a mix of a number of angel groups, some private individuals, along with Enterprise Ireland and the Western Development Commission,” says Bambury.

“It was an interesting round of funding in that it was really led by the angel groups. The availability of investment is constantly in flux. It is important for any medtech



Tom Fleming

startup now to establish who has the kinds of funding suitable to the investment round they are seeking. They need to prioritise the groups they are most suited to.”

Many members of the medtech syndicate have specialist experience in the industry, which they are sharing with the co-founders, along with their extensive network of contacts. Declan Quinn of the medtech syndicate is a Non-executive Director on Signum Surgical’s board.

“The mentorship we are receiving from the angel investors is of huge value to us as a company. Moshe and I have both previously worked in startups, but as first-time founders we really appreciate the fantastic experience and wide network of contacts

available through the angels, many of whom have started, run and sold companies themselves,” says Bambury.

In December last year, Signum Surgical received a €2.3 million Horizon 2020 grant and a €1.3 million grant under the Government’s new Disruptive Technology Innovation Fund. The latter involves a partnership with Galway based Anecto Ltd.

“We will be one of the first companies to use Anecto’s planned medtech innovation centre, which will incorporate clean rooms for early stage companies to use. The grants will help us to get through the finish of our design and testing and to our first clinical in-man study later this year in Budapest,” says Bambury.

Investment after the seed round

Tom Fleming worked at Boston Scientific for 21 years before being appointed as Chief Executive Officer of 4TECH Cardio in 2018. One of his roles as General Manager at Boston Scientific was to work with its business development groups to look for potential investments or acquisitions.

“This was how I knew about 4TECH Cardio, as we had looked at the company as a potential strategic investment,” he says. “It is very common that very early stage medtech companies such as 4TECH Cardio funded through the angel network. Angel investors in medtech play an important role in funding medical device startups.”



Angel Investors are many times the preferred route to finance a company beyond the seed round with friends and family. Angels can be individuals and increasingly we are seeing networks of Angels, ie, Halo Business Angel Network, formed that can place multiple bets and reduce their overall risk through a portfolio approach.

“When the company founder is a physician, a group of people interested in the clinical area concerned tend to form naturally. This extends out to physicians, supporting angels who are analysing potential business deals, and then to a broader circle, attracting capital from people who may or may not have experience in the particular field. The opportunity for angel funding is there, it all comes down to your idea, the market you’re focused on, and your management team.”

Fleming believes there is a good network of potential angel investors in Ireland, who are tied in with different physicians across Europe and into the US. The need for Healthcare is global, and while Western countries have been more advanced in technology adoption in the past, Asia has the potential to eclipse current markets in the future. Access to partners who have a global perspective can only help in guiding a company in the development stages.

Dedicated to developing a minimally invasive transcatheter solution for the treatment of functional tricuspid regurgitation, 4TECH Cardio has been located in Galway since 2011. Its initial group of angel investors came through connections with its four founders, who were based in Israel, Italy, Belgium and Switzerland.

Some of the original angel investors took part in its Series A round and were joined by venture capital firms which traditionally step in when rounds exceed €5 million or more. The total amount raised by the company to date is around €35 million.

As with all startups, there can be highs and lows. I think it is important to have the right investors in each round. Early investors should understand

that risk will be high. As you move to future rounds, some risk should be taken off the table but there will still be bumps in the road. Looking for investors that have capability to add funds if needed is a smart move. Investors familiar with your market can also bring their experience and contacts to help support the inevitable decisions and strategic adjustments as the company matures. We will look towards a Series C round towards the end of this year,” says Fleming.

Achieving milestones

Formed in Dublin in 2012, NeuroTronik Limited is a development-stage, venture-backed medtech company

pioneering a unique approach for the in-hospital treatment of acute and advanced symptomatic heart failure patients. The therapy approach is cardiac autonomic nerves stimulation (CANS).

The achievement of key milestones has been central to NeuroTronik’s venture capital journey. The company was initially financed by a Series A investment round in 2013 of US\$13.1 million. The Series A milestones were met, including the major deliverable, the Human NeuroCatheter™ Study by late 2015. During a somewhat protracted Series B fundraising process, the company continued to make project progress, including an interesting study during 2016 in which NeuroTronik CANS Therapy® demonstrated a positively differentiated acute treatment effect versus that of dobutamine.

In April 2017, NeuroTronik landed its Series B funding, US\$23.1 million, tranching according to project milestones. “We continue to achieve our project milestones during this Series B timeframe. Project-to-date, the amount of risk that has been retired is impressive,” says CEO Fred McCoy.

“Our most recent deliverable was the NeuroTronik CANS Therapy Study. We treated 12 target patients in the target clinical situation for the target duration



Fred McCoy

“ We founded NeuroTronik with the Ireland domicile, and went ahead to establish the broader corporate structure to potentiate growth and value. While we have pursued early development via a team located in the US subsidiary, Ireland operations figure to be important as we develop.”



Daniel O'Mahony

Medtech, worth investing in

Based in Dublin, Seroba Life Sciences invests in breakthrough technologies that promise to improve lives and transform healthcare. Currently with €200 million in funds under management, it closed its third fund in 2016 and to date has invested in three medtech companies based in Ireland as part of this, Endotronic, Atlantic Therapeutics and Medlumics, Seroba Life Sciences Partner Daniel O'Mahony tells us.

"If a company has the right product, management team, mission and strategy it can certainly be successful in raising venture capital funding. Companies at a later stage in technical development, commercialisation and seeking FDA approval are probably finding it easier to fund-raise right now. Those at the prototype or design freeze stage are under more pressure."

Seroba Life Sciences made five investments in medtech with its second fund. As part of this, in 2011, it co-led the Irish medtech Novate Medical's Series B funding round which raised €8.7 million. Novate was acquired by BTG in September 2018 in a deal worth up to \$150 million. With its second fund it also invested in the medtech Veryan Medical which has a significant operation in the Galway medtech cluster; Veryan was also acquired by the Japanese company Otsuka in 2018. Its medtech investment portfolio company Apica Cardiovascular was acquired by Thoratec in 2014; Apica was spun-out of Emory University, Atlanta, USA by its founder and CEO Jim Greene and was headquartered in the Galway medtech cluster hub. Jim is now CEO of Medlumics which works closely with various research teams in Ireland.

In O'Mahony's view, the journey time to mergers and acquisitions for Irish medtech startups is longer now than it was five years ago. "Startups need to be planning to bring products through regulatory approvals, have more financing and innovative, disruptive technology to be considered by the investor community," he says.

of therapy. The results were mighty encouraging – even better than we had expected."

The next milestone is now on the horizon: a multi-centre new clinical study designed to achieve CE Mark and to attract a desirable Series C Preferred Stock financing, structured financing, or acquisition.

NeuroTronik's named institutional investors are Hatteras Venture Partners, Synergy Life Science Partners, Mountain Group Capital, Lord Baltimore Venture Capital Partners and Sovereign's Capital, all based in the United States. Additional equity funding has come from strategic and individual sources.

NeuroTronik is a spin-out of Synecor, a business accelerator based in the Research Triangle Park, North Carolina USA.

"We founded NeuroTronik with the Ireland domicile, and went ahead to establish the broader corporate structure to potentiate growth and

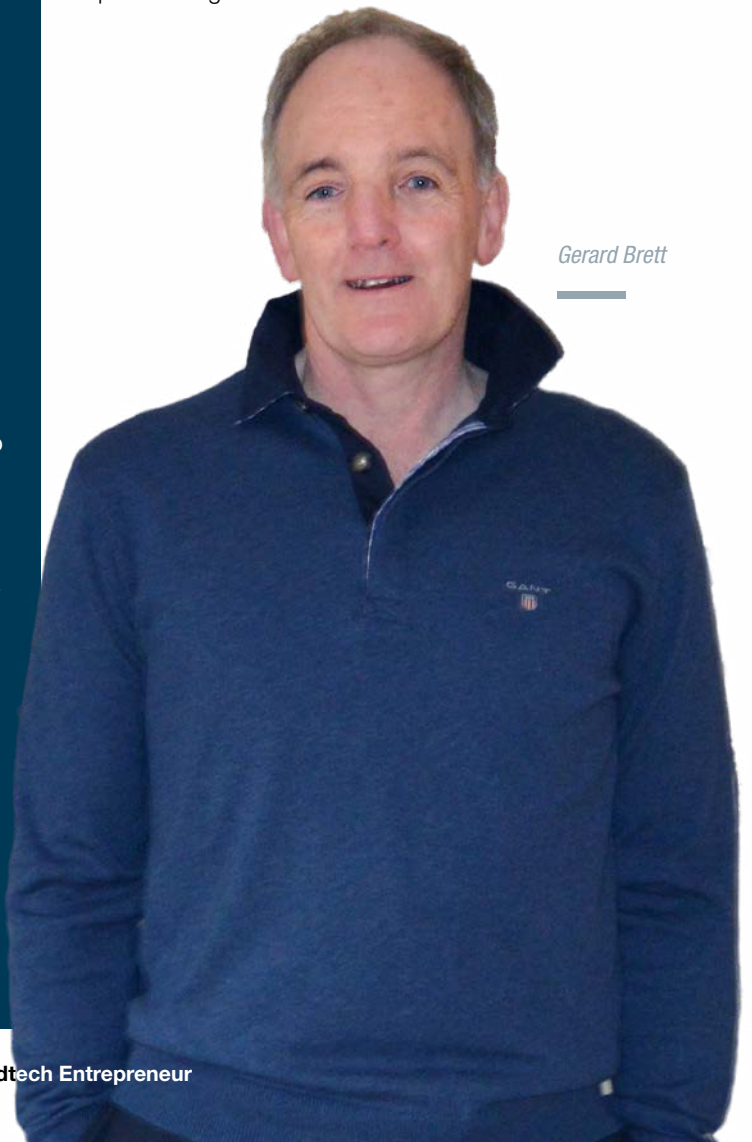
value. While we have pursued early development via a team located in the US subsidiary, Ireland operations figure to be important as we develop," commented McCoy. "This next clinical study will land us at the door of extraordinary market opportunity."

A fountain of support

Vivasure Medical is pioneering fully absorbable technology for percutaneous large-hole vascular closure.

In Ireland, Dublin-based Fountain Healthcare Partners has been Vivasure Medical's anchor investor, leading its Series A and Series B funding rounds with two US venture funds, and returning for Series C, completed in 2016, raising €16.2 million.

The Series C funding round was led by Life Sciences Partners of the Netherlands, and co-led by Evonik Venture Capital (Germany) and Panakes Partners (Italy).



Gerard Brett

Brett also co-founded Zerusa, which was acquired by Vascular Solutions in 2011 and is now under the Teleflex umbrella (further to Teleflex acquiring Vascular Solutions in 2017).

"We had built up a significant network of physicians, business and venture contacts in the US through Zerusa. When looking for funding for Vivasure, we talked to some of our Irish venture capital groups and Fountain Healthcare was happy to back us," says Brett.

"Fountain Healthcare has been a core part of our company from the beginning. We expanded our funding base in Series C, adding some European venture capital groups, so we now have a dynamic mix of Irish, European and U.S. funders."

The latest round of funding is supporting the European commercialisation of Vivasure's PerQseal® technology, as well as the execution of a US FDA regulatory study.

In Brett's view, there are increasing opportunities for venture capital investment in Irish medtech startups. But, he says, they need to be at a certain stage of development for venture investors to become interested.

"I'm seeing medtech startups looking to alternative routes to fund early validation milestones — demonstrating the clear market need and market potential, and completing proof of concept for their technology — *before* attracting venture investors," he says.

"As you build these early value points, you must also consider your management team. The individual who came up with the idea may be a technical genius, but may not be the right person to be the CEO," says Brett. "Getting the management team right is significant when going after venture funding. People invest in people."

Dr Ross O'Neill



Bringing it together with investment

Ross O'Neill, founding CEO of Neuromod Devices, has also found Fountain Healthcare to be a great partner. "We were the first company that they invested in from their second fund. Fountain Healthcare's Managing Partner Dr Manus Rogan led our Series A investment round, which raised €5.5 million in 2015, and he joined the board as our new Chairman," he says.

"We talked to Fountain Healthcare very early on but we were at too early a stage. When we met Fountain again, we were of very much the same mindset that to really crack the tinnitus market, Neuromod would need to come from a position of scientific strength and clinical credibility."

On that basis, Fountain Healthcare agreed to go make the investment that would allow Neuromod to work with the top scientists in the tinnitus space and conduct some of the largest-scale and longest-term device trials ever done in tinnitus with more than 500 patients.

"Enterprise Ireland was a critical partner at the very early stages, both when we were developing the technology at Maynooth University and when we spun the company out to commercialise the

technology. Robert Moffett, who is a highly successful entrepreneur and co-founder of the company Combilift, has been and continues to be a fantastic investment partner and mentor to the business," says O'Neill.

"The Series A funding really changed everything for us. It was a single moment of coherence where everything came together. We were able to bring big names on board, including Prof. Hubert Lim of the University of Minnesota as our Chief Scientific Officer and Professors Berthold Langguth, Sven Vanneste, Deborah Hall and Rich Tyler onto our Science Advisory Board. We also brought Chris Smith, former CEO of Cochlear onto our board and Deborah Arthur, a renowned regulatory specialist, onto the management team"

Research funding breathes life

Cork-based PMD Solutions received €4.2 million in Horizon 2020 funding in November 2015 to commercialise a new respiratory monitoring device which will revolutionise the way healthcare providers measure patient breathing.

"Horizon 2020 is highly competitive but a huge opportunity for startups to leverage shareholder friendly

capital to grow their business. It takes a lot of time to articulate the proposition and its potential impact in Europe. For us, it was very important to present a proposal which aligned with where we wanted to bring the business anyway — as opposed to delivering lip service to get investment capital. That's why we focused on demonstrating our knowledge of the market, our ambition to be a market leader and our plans for implementing our strategy," says PMD Solutions founder Myles Murray.

"You need tenacity and to keep going back if you're rejected. We were turned down twice, but took the feedback on board and refined our proposition while still staying true to our vision. Getting the right message across takes time and refinement. We were successful after a year with our third attempt."

PMD's product 'RespiraSense' is the world's first continuous and motion tolerant sensor that measures the 'mechanics of respiration', ie a sensor that measures the chest and gut movement during breathing.

This gives medical staff the earliest signs of possible patient deterioration from conditions such as respiratory compromise, increasing severity of sepsis, worsening

Myles Murray



pneumonia, and oncoming heart attacks. The device, a discrete wireless sensor, is placed on the patient's chest at admission and worn continuously until discharge to deliver highly accurate measurements.

"The global standard of care is for nurses to manually count breaths per minute and watch a patient's chest. This is prone to human error much like placing your hand on a patient's forehead to

estimate temperature; hot or cold akin to identifying fast or slow breathing. Our technology objectively measures this sentinel vital sign, which in itself, by only a difference of 3-5 breaths per minute, is the single earliest and most sensitive indicator of oncoming patient deterioration," says Murray.

"We have clinical evidence to demonstrate that objectively measuring the respiratory rate using our technology allows

healthcare providers to identify patient deterioration six to 12 hours earlier than by using manual counting techniques. Every 30-minute delay in administering antibiotics to treat sepsis increases the risk of mortality by 11%."

The Horizon 2020 funding allowed PMD Solutions to engage with health care professionals to ensure usability, develop clinical evidence to demonstrate the technology was usable

and improved outcomes, roll out a dissemination and communication strategy and helped Murray to identify key markets to enter. Most importantly, though, it meant the company could develop the product so it was ready for commercialisation. "It was a lot of money. We are delighted to be able to deliver what the company needed to reach this value inflection milestone," says Murray.

"We have clinical evidence to demonstrate that objectively measuring the respiratory rate using our technology allows healthcare providers to identify patient deterioration six to 12 hours earlier than by using manual counting techniques. Every 30-minute delay in administering antibiotics to treat sepsis increases the risk of mortality by 11%."



David Gillen and Olivia Gillen

R&D as a pillar in startup's strategy

Since the very early days of the company's founding in 2006, R&D has been central to the strategy of Blueacre Technology. As a company whose growth has been largely organic, to carry out meaningful R&D, Blueacre needed to access external funding for R&D.

Enterprise Ireland R&D supports were an early source of advice and funding for R&D, helping to ensure that the company could build and develop its own proprietary technology in-house. This early investment in capability was key in helping the company establish its distinctive competitive edge in the marketplace. Blueacre Technology provides precision laser micro machining to the medical device industry.

In 2015, Blueacre moved into a whole new league of R&D projects, as a participant

in the "Openmind" project under the EU's Horizon 2020 R&D funding scheme. This was one of the biggest Horizon 2020 projects, involving 100% funding and partners right across Europe, ranging from Germany's prestigious Fraunhofer Institute to specialist technology firms in Northern Italy, Spain and beyond.

The project's ambitious aim was to develop the next generation of medical devices which could be customisable to individual patients' requirements. Blueacre developed advanced laser processes that were integrated into a series of production steps, powered by new software and AI.

David Gillen, founder and CEO of the company gives the following advice to other medtech startups "Don't be daunted by the paperwork

Reaching expectant mothers worldwide

Another Cork-based medtech startup, Metabolomic Diagnostics, also took a number of attempts to secure Horizon 2020 funding and learned the importance of having a clear story supported by the marketplace in the process. In May 2018, it was awarded €2 million under the Horizon 2020 SME Instrument, which received a total of 1,280 applications from all over Europe.

It is using the money to commercialise its breakthrough product PrePsia, a simple blood test taken in early pregnancy, which can identify women who are at increased risk of developing preterm preeclampsia. Metabolomic Diagnostics are building on their work to date with a commercial strategy that helps them engage with key groups for early adoption, from clinicians and labs to patient groups, build and increase awareness of the disease, present their work internationally at conferences and meetings, as well as gather further market intelligence.

PrePsia has the potential to transform prenatal care by allowing clinicians to administer effective treatments early that can dramatically reduce the incidence of the disease, thus improving pregnancy outcomes while lowering healthcare costs for treating the disease.

"We went to the EU with our story that we had identified a way of measuring biomarkers in the blood but the work we needed to turn this in to a commercial product was expensive," says CEO Charles Garvey. "We needed the money to help fund the cost of bringing the technology to market. Phase 2 Horizon 2020 grants are generally for companies that have products at the prototype or near-market stage to help them bridge that final gap to get them out there.

"With this EU support we believe that PrePsia has the potential to become part of pregnancy screening programmes worldwide. The Horizon 2020 award was recognition by the EU of the huge progress we had made and the enormous societal benefit that our innovative test will bring to expectant mothers and their babies all over the world," says Garvey.

Speaking about the future, Garvey adds "Our long-term vision is to be able to provide each woman a personalised risk profile of her pregnancy, so that her clinician can tailor her care to her specific needs and help her avoid complications."

Metabolomics Diagnostics was previously supported by the EU through FP7 funding, as well as private investors, SOSV, Enterprise Equity, AIB Seed Capital Fund and Enterprise Ireland.



and administration involved in R&D funding applications: as long as you are clear about the outcomes you want to achieve, and the roadmap to get you there, you will have the basis for a sound grant application”.

The company's R&D footprint continues to grow, Blueacre has a long-standing partnership with Manchester University's Laser Processing Research Centre, and has recently been awarded funding under the Government's Disruptive Technologies Innovation Fund (DTIF) for a collaboration with Trinity College Dublin (TCD) on new 3D printing technology.

“This marks a new departure for the company” says Olivia Gillen Blueacre Technology's Commercial Director, “this new R&D initiative will support us in building out our strategy beyond laser processes, which have been our core capability to date.”

Aiming for an exit

Novate Medical and Veryan Medical had exit strategies from the start, and last year were both acquired by large global companies which recognised their market potential

Two medtech companies Paul Gilson has been involved in were acquired in 2018 – Novate Medical in September by BTG in a deal worth up to US\$150 million and Veryan Medical by Otsuka Medical Devices in December for an undisclosed sum.

In both cases, the companies' financial backers invested with a view to wanting an exit or trade sale. Founded in 2006, Novate Medical raised an estimated total of US\$22 million in funding since 2007, with its backers including Act Venture Capital, Seroba Life Sciences, Omnes Captial, Crédit Agricole and Enterprise Ireland.

“Novate Medical was primarily venture capital funded by Irish VCs and there was some French funding in there. From the get-go, we

prepared the company for an exit. We worked towards establishing intellectual property for our product; then went towards CE Mark and FDA regulatory approvals,” says Gilson. “All the different elements were built in as milestones to be reached to have the product ready to go on the market. We appointed a banker to run the process.”

Novate has developed Sentry, the first bioconvertible inferior vena cava (IVC) filter for the treatment of blocked arteries, pulmonary embolism (PE), which was granted 510(k) regulatory clearance in the US last year. Sentry's 12-month clinical trial data demonstrated no new symptomatic pulmonary embolism and no evidence of device migration, tilt, fracture, perforation or embolization – complications which have been associated with other IVC filters. The unique bioconversion feature eliminates the need for an additional procedure to retrieve the device.

“The US represents 80% of the world market for the device developed by Novate. It is now on the market there. We had identified funding if we were going to take it to the market ourselves and did not find a trade sale. You always need to have a dual strategy,” says Gilson.

Gilson and Chas Taylor were Novate's co-founders. In 2007 they were appointed as Chief Scientific Officer and Chief Executive Officer of Veryan, three years after it had spun out from Imperial College London. The company has raised an estimated US\$66 million in seven funding rounds, with backers including Imperial Innovations, Seroba Kernel, Oxford Capital Partners Limited and Nesta.

Veryan has designed, patented and developed a highly innovative stent technology, the BioMimics 3D Vascular Stent System, which is based on the link between vessel geometry, blood flow mechanics and vascular disease. “When Chas and I came on board, we brought Veryan in a different direction and onto the pathway it ended up being on. It started out developing vascular grafts in the early years, but now is focused on vascular stents, which is a much bigger market,” notes Gilson.

“The story with Veryan was similar enough to Novate. The desire of our VC funders from the start was to go for a trade sale. We brought the product through pre-market approval, achieved CE Mark approval and launched it Germany, The

Netherlands and France. We established an ability to sell the products in Europe.

“In a small number of sites, key opinion leaders (KOLs) carried out clinical trials under controlled conditions. These KOLs presented these clinical data at international conferences – which again was about us achieving a trade sale.”

Otsuka is a large Japanese company, which was beginning to build a portfolio in medical devices having mostly been focused previously on pharmaceuticals and nutrition. “Entering the medical devices market was a new strategic direction for Otsuka. It had acquired a medtech company in the US two years previously and the second element of that was to add an innovative stent system,” says Gilson.

“One of the general trends now with companies acquiring technologies is that they tend to want to see some market performance. You are much more likely to see M&As of technologies what have achieved market penetration. Compared to years ago, M&A is happening at a much later stage once a medtech startup has clinical data, marketing information and a sales history.”



Paul Gilson

Demonstrating patient benefits and safety

Don't be afraid to reach out to the regulator early. Getting regulatory approval takes time and money. Early engagement can help you save on both by setting clear expectations of what the regulator expects for your technology to get approval and gain market access.

Early meetings support success

Olive O'Driscoll, CEO and co-founder of AventaMed in Cork, has found that engaging with the notified body for the CE Mark in Europe for its product helped to streamline the approval process. In AventaMed's case, this was the British Standards Institute (BSI).

"Early interactions with the regulators are really important to establish what regulators are looking for. It is a rigorous process and you need a lot of time and money to get through it, for AventaMed, we had to provide a lot of biocompatibility data," she explains.

AventaMed's innovation, the Solo Tympanostomy Tube Device (Solo TTD), is an all-in-one ear tube placement device, which enables the quick and simple insertion of ear grommets in children. It took the British Standards Institute three months

to review the company's paperwork in order to process and grant CE Mark approval, which happened in 2016.

CE marking is a certification mark that indicates conformity with health, safety, and environmental protection standards for products sold within the European Economic Area. In order to put the product on the market in Europe, AventaMed's product and quality management system required approval also

"We spent one year setting up and implementing an ISO 13485 accredited system for the company. The notified body visits the company and carries out two audits to approve this. Also, a technical file for the product must be reviewed separately after the audit, it is a challenging but necessary and important process," explains O'Driscoll.

AventaMed had a limited launch of the Solo TTD in Europe. It has been used to successfully treat over 100



Olive O'Driscoll

“It is really important to have these [FDA] meetings before embarking on clinical and biocompatibility testing as this is a very expensive process and can take many years of work. It is imperative you know up front what data the regulator expects to see and what clinical outcomes are expected for FDA clearance.”

patients in three different countries. Most recently, it has been used to effectively treat patients outside the operating theatre in outpatient procedure rooms.

In October 2017, AventaMed raised €1.8 million from the Halo Business Angel Network, which has partly been used since to cover testing required for Food and Drug Administration (FDA) clearance. “We are currently completing a clinical study as part of the clearance process and anticipate achieving FDA clearance by the end of this year,” says O’Driscoll.

“Similar to Europe, we engaged with the FDA early on before testing our product in pre-submission meetings. Our team met with them in their headquarters in Washington DC to demonstrate the Solo TTD product, explain the features and functions and how patients will benefit from it. I have found that it is much better to have a face-to-face meeting. You have the opportunity to ask questions, clarify anything and debate back and forth about what your plan should be.

“It is really important to have these meetings before embarking on clinical and biocompatibility testing as this is a very expensive process

and can take many years of work. It is imperative you know up front what data the regulator expects to see and what clinical outcomes are expected for FDA clearance.”

Achieving approval

Founded in Galway in 2008, Vivasure Medical is pioneering fully absorbable patch-based technology for percutaneous vessel closure, with a focus on arterial and venous closure devices.

Chief Executive Officer and co-founder of Vivasure Medical Gerard Brett previously co-founded Zerusa, which was acquired by Vascular Solutions in 2011 and is now under the Teleflex umbrella (further to Teleflex acquiring Vascular Solutions in 2017).

Zerusa, which developed hemostasis valve technology to minimise blood loss during cases with multiple catheter exchanges, achieved both CE Mark approval and US-FDA 510(k) clearance, opening up distribution channels in both Europe and the USA.

Today, Vivasure Medical is on a similar path. “We have an active R&D programme looking at other opportunities for our fully bioabsorbable platform technology. In our current devices, the patch goes on the

inside of the blood vessel to seal the hole,” explains Brett.

Brett says Vivasure’s experience with the US-FDA has been very positive so far. “We have found the FDA to be very helpful, interactive and clear about what they want. If, as a startup, you provide them with what they want, they will reciprocate by helping you to achieve the type of approvals you’re looking for,” he says.

Vivasure Medical’s product is classified as a Class III device in the EU and the USA. These devices usually sustain or support life, are implanted, and are more high-risk. Examples include coronary stents and implantable pacemakers. Approximately 10% of medical devices fall under this category.

“The bar is high for Class III devices, particularly with bioabsorbable implants for vascular applications. We have to complete a lot of testing, verification and validation activities to demonstrate the device is safe to use in clinics and has a future as a marketed product,” says Brett.

“We have completed this work and have been granted a CE Mark in the EU. We continue to work with the US-FDA and plan to initiate our pivotal study later this year.”



Gerard Brett

The regulator, supporting innovation

Supporting innovation was identified as one of the Health Products Regulatory Authority's (HPRA) key priorities for the period 2016 to 2020. It applies across all health-related products, but is particularly pertinent for medtech, according to Dr Niall MacAleenan, Head of the Medical Devices Department at the HPRA.

"One of the key initiatives undertaken as part of our focus on supporting innovation has been to establish an innovation office. This is a central point within the organisation where innovators of any health product can receive advice and support. Requests for information will be managed and dealt with by the appropriate product regulators. A lot of medtech queries come through this route," he says.

The HPRA team is happy to meet with medtech product developers from academia and small companies at any stage in the product development process. There are two types of meetings. Preliminary meetings happen at a very early stage when people have a concept or idea and want to learn about the regulatory system, understand how they might interact with it and meet the regulatory requirements during the product development phase.

"Our key piece of advice here is that while regulations may seem a bit daunting, start as early as you can to understand how to apply them to your product. It is best to look to meet the different

requirements as you go along the development phase for your product, rather than having to backtrack later. It's also a lot more scientifically robust."

The second type of meeting offered happens further down the line in the product development process when innovators are preparing to submit applications to conduct clinical research for non-CE Mark devices in Ireland which require HPRA approval.

"At these pre-submission meetings we discuss the requirements of the regulations

and the assessment process we operate, so potential applicants are clear on what to submit, how and to know what to expect during the assessment. We find that this type of practical discussion advice helps to ensure submission of a robust application," says MacAleenan. "It is very useful engagement for us and means that when it comes to the assessment of applications, things are as predictable as possible for the innovators."

MacAleenan notes that it approves applications for about 15 new pieces of clinical



Dr Niall MacAleenan

research for non CE Mark devices each year and the HPRA meets twice or three times that many developers at different stages.

"When it comes to supporting innovation, it always comes back to our role as a regulator. This is to protect and enhance public health. It is not about reducing any regulatory expectations, but rather to support innovation through clarity of the requirements and proactive compliance."

The HPRA runs innovation workshops at academic and clinical centres interested in clinical research, such as the Health Innovation Hub and Cúram in Galway. "We bring a team for the day and deliver a practical workshop about our role and the processes around clinical research. The events are well supported and we know from those taking part that they welcome the opportunity to engage with us at the pre submission stage," says MacAleenan.

"Sometimes innovators may be wary about sending us in a query as they are concerned it might affect a future regulatory submission. This is not the case as we're not looking to apply regulation earlier than is necessary or be more stringent. It is really about trying to anticipate the regulatory requirements and building blocks in a way that suits the product development process. Ultimately in my view, this helps to both support effective product development and ensure that public health is protected with people enrolled only in clinical investigations that are safe and scientifically robust."



Top tips to avoid common pitfalls

1. Do not underestimate the amount of time required for a notified body review of the technical file
2. Keep your technical file up to date with high quality data
3. Do not rely on another manufacturer's data unless you have full access to their technical file and you can demonstrate equivalence – technically, biologically and clinically
4. All classes of devices require a robust clinical evaluation

A guiding hand to get to market

The National Standards Authority of Ireland (NSAI) CEO Geraldine Larkin explains the role of the NSAI as HPRA designated notified body and how startups can engage early with this important part of the medtech ecosystem to ensure medical technology safety and avoid common company mistakes.

The NSAI carry out conformity assessment of medical devices, active implantable devices and in vitro diagnostic devices to ensure the devices conform to the requirements within the relevant European directives. The organisation also audits the medical device manufacturers to ensure compliance with the quality management standard

for medical devices ISO 13485:2016.

Larkin notes that, "We are one of only 14 recognised auditing organisations under the medical device single audit programme MDSAP. This programme allows a single regulatory audit of a medical device manufacturer that satisfies the regulatory requirements of regulatory authorities participating in the program such as: Canada, Brazil, Australia, Japan and the United States of America."

She adds "It is the duty of NSAI as a notified body to ensure that devices which bear our CE mark are safe and perform as intended under the relevant directives. NSAI is also seeking designation under new medical device and

in vitro diagnostic regulation which have been transposed into law."

NSAI encourages startup companies to engage early, "As a notified body we cannot consult but we can provide information based on the current directives, guidance documents and standards. This information can be a crucial part of the early stage development for a startup and can inform the startup of the regulatory needs which can drive the funding model," Larkin explains.

"Once initial contact has been made, we encourage the manufacturer to keep the lines of communication open with us through our Industry Engagement officer," Larkin concludes.



Geraldine Larkin

Identifying and breaking into strategic markets

There are different routes to commercial success, some companies expand organically across markets by aligning with key players, while other proactively identify influencers to help position themselves as industry leaders. While there's no right way to break into new markets, identifying clear market pathways will help set expectations for market access and opportunities to maximise market share.



Transforming care in the NHS

PMD Solutions successfully enrolled onto the NHS Innovation Accelerator (NIA) Programme in 2017. This was a significant step on its internationalisation journey which it identified while mapping out who the key decision makers and influencers are.

NIA is an NHS England initiative delivered in partnership with England's 15 Academic Health Science Networks and focused exclusively on identifying and partnering with only the top leading healthcare pioneers in the market.

According to PMD Solutions founder Myles Murray, participation in the NIA programme represented the culmination of a lot of hard work and dedication in developing RespiraSense, the world's only continuous, motion-tolerant, respiratory rate monitor.

Murray founded the company in 2011, having identified a clinical need in the emergency department of Cork University Hospital. He was on a work placement at the Medical Engineering Device and Engineering Centre at Cork Institute of Technology at the time as a mechanical engineering undergraduate.

"To get onto the NIA programme, each applicant is reviewed by the highest level of executive leadership at the NHS in terms of clinical safety, healthcare economics and clinical guidelines," he says. The strength of PMD's clinical evidence and market readiness of its technology convinced NHS England to engage with them.

"The UK market is strategically important for us if we want to change the standard of care, globally. Success in changing everyday practice of the measurement of respiratory rate in the UK could propagate across Europe and into North America."



Fred McCoy

In Murray's view, the global healthcare market can be pretty much attributed to four key markets: Europe, North America, China and Japan. PMD Solutions has filed for protection of its inventions in each territory. Last year, it achieved patent approval in Japan. China is due this year and patent approval is pending in Europe and North America.

"Our priorities at the moment are to focus on the innovation and marketing of our technology and to establish a thought leadership position in the industry. RespiraSense has centres of excellence across the UK and Europe with world-leading opinion leaders in the field of vital signs and patient deterioration," says Murray.

Last October, PMD Solutions received the 2018 Visionary Innovation Leadership Award for the best non-invasive respiratory market at the Frost & Sullivan Best Practices banquet in London. The award recognises how this leadership position enables a market participant to deliver highly competitive products and solutions that transform the way individuals and businesses perform daily activities.

An Irish startup with a US subsidiary

Founded in 2012, NeuroTronik Limited is headquartered in Dublin and has a US subsidiary in Durham, North Carolina. It is developing a device to treat acute heart failure syndrome for patients who go to hospital for treatment of worsening symptoms.

"The therapy is cardiac autonomic nerves stimulation to produce increased cardiac output without raising the heart rate," explains NeuroTronik CEO Fred McCoy, who is based in Durham, but regularly visits and works from Ireland.

"The effect of that is a rebalancing of hemodynamics in the patient. It means patients should feel better sooner, spend less time in intensive care, be able to leave the hospital sooner and come back to the hospital for follow-up treatment less frequently."

NeuroTronik is a spin-out from Synecor, a business accelerator based in the Research Triangle Park, North Carolina. "The concept of having a US subsidiary came from the fact that we needed to quickly pull a team together with the relevant experience in electroactive therapy and percutaneous procedures," says McCoy.

"These people are present in a few places, one of which is the US. As the company came out of Synecor, we felt North Carolina was the place to pull together the team that could achieve the early work of this project."

There are currently 12 people based in the US subsidiary, NeuroTronik, Inc. The team based there is focused on the development of NeuroTronik CANS Therapy®. NeuroTronik is funded by a syndicate of US venture capital, strategic, and individual investors. With experience now in over 170 human cases, NeuroTronik is now working to finalize the system and conduct a clinical study that, among other objectives, is designed to achieve CE Mark.

"When we started out, the pathway to the US market was unclear, and the pathway to the Europe market was clear. Over these few years, the converse has developed. Consequently, we are fortunate to have remained somewhat at equipoise," says McCoy.

"Our objective is to achieve the relevant clinical and regulatory milestones. With success, that will lead naturally to expanded operations. Ireland is a terrific place from which to do business in medtech as well as to stage

global operations. On the plus-side of the ledger, the deep and rich talent pool would allow us to expand, and our view is that Europe continues as an important initial market for us.

"Most of the large, global medical technology companies have significant operations in Ireland. That NeuroTronik Limited is in Ireland could be advantageous when one or more of them decides to pursue us in earnest."

From Dublin to New York

Leveraging its experience of partnering with hospital systems in the US in the past few years, i360medical signed a collaboration agreement with EIT Health last December, which has expanded its footprint in Europe.

EIT Health has a network of 140 universities, industry and other healthcare organisations across the EU. The EIT Health Innovation Projects programme provides comprehensive support for innovations that show the potential to have a positive impact on healthcare. The most promising ideas are developed into commercially viable products through a multi-disciplinary approach, involving business, medicine, IT and other fields of knowledge.

Originally housed within the Royal College of Surgeons in Ireland, and following a partnership agreement signed by Enterprise Ireland in 2016, i360medical went on to become effectively a one-stop-shop for outsourced medtech R&D. It takes clinicians' ideas from the very earliest stage and assesses their potential. If promising, it progresses these ideas, builds prototypes, further develops and puts them

through regulatory rigor before presenting them as a commercially acquirable devices.

i360medical's role in the EIT Health partnership differs in that it provides objective and independent feedback on initial project proposals and, where potential exists, to coach and mentor the project teams to strengthen their proposal.

"In collaborating with EIT Health, we ultimately wish to leverage all we have achieved in the US where there's an openness to taking risks and driving innovation, using exactly the same model as we have introduced at Northwell Health across all of Europe – finding ideas, qualifying to determine if they can go forward and helping to commercialise them," says Derek Young, founder i360medical.

Northwell Health was the first big hospital system partnership secured by i360medical in the US. It is one of a small number of Irish medtech companies to build a relationship with the healthcare provider.

New York State's largest healthcare system, Northwell Health comprises 23 hospitals, 68,000 employees and around 14,000 affiliated physicians.

President and CEO of Northwell Health, Michael Dowling is a Limerick native, he's supporting the strategic partnership with Enterprise Ireland. He is enabling Enterprise Ireland client companies to work with Northwell Health to commercialise their new medical technologies, secure joint ventures and provide platforms to integrate with US healthcare companies.

"Northwell Health was like a Greenfield site for us – we had to implement our process, formalise and normalise it, and make it open to everybody from the clinical community

in 23 hospitals across the State of New York. It was a big task," notes Young. "Not every clinician is a researcher or believe themselves as an inventor. What makes us different is we connect with nurses, clinicians and surgeons all doing their day jobs, but with no inkling of working on the R&D element of an idea. Our people look after that.

"We found ways of getting clinicians into groups, set up brainstorming sessions and developed an online portal so they could easily interact with us. Face-to-face time is critical and our Irish team goes over once a month to sit down and spend time with the inventors to work on their ideas. They need a lot of guidance in terms of what to look out for when developing a product. We have taken them on that journey by building personal relationships."

i360medical has replicated its way of working with other healthcare systems in the US, including HSS in New York and Baptist Health South Florida and others.

"We had to educate the market and our clientele in the beginning, but healthcare providers in the US have been willing to allow us to dovetail into their system and run the innovation function, with their tech transfer offices and research centres supporting us. We have become the outsource element for R&D and the commercialisation of their medtech intellectual property."

To date, i360medical has helped inventors from US healthcare systems to progress five different devices to the point of commercialisation. They are in the areas of cardiovascular, general surgery, transplants, orthopaedics, urology, neurology, vascular, obstetrics and gynecology.

Connemara's international reach

Having a strong senior management team and expanding to two facilities in County Galway has allowed Complete Laboratory Solutions (CLS) to scale for international growth.

"Many of my senior management team have been with me for 21 years, including Director of Microbiology, Anne O'Donnell, Validation Engineer, Sonia O'Dwyer, our Director of Environmental Services, Caecilia Terloh and my brother Colin O'Toole, who joined in 1999 and in 2007 became our Director of supplying trained analysts on contract," says founder and CEO of CLS Evelyn O'Toole.

"Once the core leadership team was in place, crucial support functions including finance, human resources and sales were added including our IT Director, Ken Hennessy, Chief Financial Officer and Operations Excellence, Caroline Clancy, and Human Resources Manager, Tom McAvinchey – senior quality appointments and specialist technical sales executives were added to complete the team. We've also had several colleagues return to us over the years to continue their career development. With everyone's work CLS has become the largest privately-owned contract laboratory in Ireland."

The premises O'Toole started out with in Ros Muc, County Galway in 1994 has doubled in size since and CLS has extended its footprint in Galway City also by 60% with a second facility dedicated to medical devices and pharmaceuticals called CLS MedPharma.

Currently CLS achieves 12% of annual turnover from overseas which has been a result of working with existing clients, representation in



Evelyn O'Toole

Europe and attending trade missions to the United States.

“Our overseas work is a combination of contracts with our multinational client’s sister operations abroad. Much of the work has been with Europe based predominately in Norway and Denmark, as well as California in the US. We have supplier approvals that allow us to bid for work overseas, the majority being project based, new market studies and validations. We also get frequent requests from international companies for our sterile barrier testing as

we are one of a few suppliers who can do this,” says O’Toole.

CLS achieved international recognition for a test it developed for the first system on the market for cancer cell containment with US FDA approval. “The company developed the new system that could contain the cells, but they weren’t able to prove it worked. They got us on board to prove that it could work which involved us carrying out simulations and creating a false uterus to test the new system on.

It was successful and was subsequently submitted to the FDA and was approved.”

In 2017, O’Toole was the first woman in Ireland to win the EY Industry Entrepreneur of the Year award, which increased the company’s profile further. “We have seen an increase in enquiries since, most recently they have included contract manufacturers from the UK seeking laboratory support for their new facilities here (in preparation for Brexit) and we are advancing how we can collaborate and support

them to take on their non-core requirements so they can work on their core activity.”

“We have a proven track record and many years of expertise and this definitely helps with our international sales plan. Ireland is a great launching pad for growth, for us we are moving to become more commercially focused, increasing our sales resources and refining our messaging to target more project based work and non-core testing.”

“ We had to educate the market and our clientele in the beginning, but healthcare providers in the US have been willing to allow us to dovetail into their system and run the innovation function, with their tech transfer offices and research centres supporting us.”

How collaboration is driving innovation

From building parts to finished products, Ireland's contract manufacturing base and strategic partners are helping their customers by reducing work and adding value. Now as we look to the future of medtech not only are they helping realise sophisticated product concepts, they're supporting a new age in manufacturing from the internet of things revolutionising modern manufacturing to physical devices that include add-on services with connected platforms to meet changing user needs.

Medtech partners take the lead

As an independent test laboratory, Anecto's role as a partner to the medtech sector is to make sure products are tested appropriately so they reach clinicians as required, as well as supporting manufacturing with testing requirements.

The Galway-based company offers a full range of services that support medtech companies in their efforts to increase reliability and reduce the risk of failure throughout the product lifecycle. Last November, Anecto's testing services business became part of Steris Laboratories as an add-on to Steris Group's global lab capability.

"Over the past four years, we have become more focused on supporting medtech clients on the complete journey from start-of-concept through to commercialisation," says Anecto Chief Executive Donal Devery. "On the one hand we are tuned into customer needs, the types of products they are working on and the

supports required to complete their testing. The other aspect is to understand what regulatory authorities need and specifically what is called for in terms of standards for different devices."

Testing can happen at various points along the medtech product lifecycle, the level of which will vary depending on the standards

Helping to make ideas stick

At Zenith Adhesive Component's (ZAC) innovation centre in Athlone, Co Westmeath, medtech clients can look at and touch a wide range of materials from 100 different suppliers around the world to figure out what will work best for their product designs. These include adhesive, wicking and absorption, shielding, bonding, gasketing and filtering materials. ZAC will then make the components desired to the client's specification from the materials selected.

"We always focus on value-add materials and partner up with companies that make interesting materials, for example breathable membranes for use in anything from headphones to ostomy bags. We don't offer or accept exclusivity to partners, as we want to make as many options as possible available to our clients," explains Pat O'Neill, who founded ZAC in 2012.

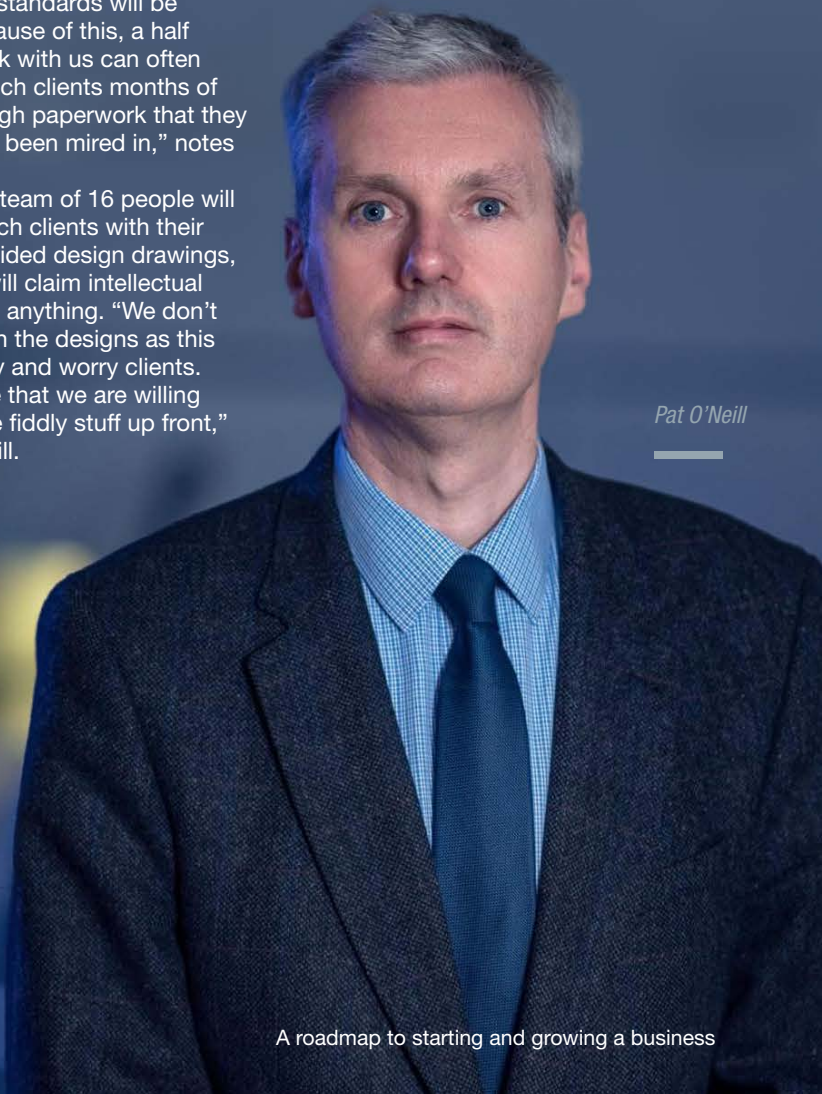
"Clients can sit down at the design table, cut shapes out and leave the building with a sample of exactly what they want. They usually don't know what they want until they see the materials – for example, they might have a device idea, but don't know how to stick it to the body."

"This can be anything from breathable adhesives for sticking drug delivery systems to the skin, catheter or feeding tubes retention to the body, inert seals for use in diagnostic kits, bonding within device assemblies, to wicking and absorption of fluids in diagnostics and T.E.N.S. patch sub-components using electrically conductive adhesives.

About one third of ZAC's business is now medtech, generally Class C components with varying levels of complexity. It counts Teleflex, Hollister and Boston Scientific among its client base and looks after one or two brand new Irish medtech companies every six months.

In all cases when ZAC is making medtech components, medical grade materials suited to skin contact and only those that have been thoroughly tested by certified laboratories to show compliance with the biological evaluation of medical devices ISO 10993 standards will be used. "Because of this, a half a day's work with us can often save medtech clients months of going through paperwork that they would have been mired in," notes O'Neill.

The ZAC team of 16 people will help medtech clients with their computer-aided design drawings, but never will claim intellectual property on anything. "We don't want to own the designs as this would delay and worry clients. People love that we are willing to do all the fiddly stuff up front," notes O'Neill.



Pat O'Neill

required. Anecto will look after every type of testing from the prototyping stage through verification and validation planning, technical file reports for regulatory approvals and finally testing manufacturing processes. Anecto testing ranges from specific component testing to full product testing including a vast range of testing required for packaging and transportation of the product.

Originally established in 1994 in Galway as a test facility for the electronics industry, Anecto started to develop testing capability for medtech in the early 2000s. "We are an approved vendor for 85-90% of all medtech companies in the world, ranging from startups to multinationals," says Devery. "To be a leader in this space, a track record, skills, competence and experience are important. You have to have a great understanding of medtech. Our independence is critical and having the product or packaging testing carried out by an independent laboratory is of value to our customers."

In general, over the past 20 years Devery has observed how medtech in Ireland has changed. "The sub-supply companies have evolved from manufacturing and building parts and sub-assemblies to building final products," he says. "The next step is happening now, where some sub-contractors are engaging earlier in the design cycle, setting up manufacturing processes, validating them and ultimately supplying the product." This is a model that Anecto test services has also engaged in within the test cycle required for new products and re-certification of existing products.

Navigating medtech manufacturing

Founded in 2006 in Spiddal, Co Galway by Barry Comerford and John Farragher, Cambus Medical is now the 2nd largest global

provider of Hypotubes in the Medical Device Industry.

Currently employing 140 people in picturesque Connemara, Cambus Medical has almost quadrupled in size since its joint venture with Freudenberg Medical in 2012 and is on a path of continued growth, with Comerford expecting a 20% increase in annual turnover going forward.

“We have achieved this growth and market position, through our strategy of partnering with startups and/or Original Equipment Manufacturers (OEMs) and together; creating, developing, manufacturing and supplying hypotubes and related micro-component solutions for minimally invasive medical devices” Comerford says.

Cambus Medical's products, services and technologies are focused on 'Minimally Invasive Surgical Devices' or MIS for short. “We provide critical components for these devices, which are then used in many different interventional procedures, including but not limited to areas like: cardiology, endoscopy, peripheral arterial disease, neurology, ENT, electro-physiology, structural heart, 'Smart Guidewires' and other products that use any vascular of natural pathways to reach a disease or therapy site” explains Comerford.

In order to support this global OEM and startup



Barry Comerford

customer base, Cambus Medical developed and branded a process which it calls Navigate®. It is a design and development process, where Cambus' team takes the lead in process development and material technology, thus allowing the customer to focus on their core product innovations. “This approach speeds up the program of work for both parties, in-turn, reducing costs and saving time” says Comerford. “More recently, the Navigate® Team's resources have been further enhanced with additional dedicated manufacturing processes, space, and test equipment”.

“Our team spends a lot of time with customers as they are developing their next generations of products or components, bringing them from concepts and ideas all the way through to product validations and on to higher volume manufacturing,” explains Comerford. “The Navigate® area sits right in the heart of our manufacturing space. By opening our processes to our customers, we are helping them to try things out 'in-real-time' and to get instant feedback. In addition, by working with our sister sites; VistaMed, and Freudenberg Medical, we are able to deliver a fully finished product if required.”

Getting smart on the factory floor

Five years ago mechanical engineer Brendan Sheppard had an idea for data gathering for medtech manufacturing. He had spent 20 years installing data collection systems in the fast-moving consumer goods sector for the likes of multinationals such as Proctor & Gamble.

Sheppard's commitment to continuous process improvements, lean manufacturing systems and real-time data visualisation, underscores the vision behind his company SmartFactory, which he launched in 2017.

“I could see the opportunity in medtech as there has been huge innovation in product development, but very little around the process of gathering data from production lines, which was being done manually,” he explains. “I came up with the idea of using high-tech wireless sensors and the whole area of industrial Internet of Things (IoT) and applying this to medtech manufacturing.”

Sheppard agreed partnerships with Siemens for networking and industrial computers and Banner Engineering, for wireless sensors and IoT gateways. Together, they developed a software platform which allows machines to be connected

“The Navigate® area sits right in the heart of our manufacturing space. By opening our processes to our customers, we are helping them to try things out 'in-real-time' and to get instant feedback.”



Brendan Sheppard

happened before a crash, video downtime analysis uses integrated video hardware to enable you to see what happened 30 or 60 seconds before an incident on the production line such as a robot crashing.”

At present, Smart Factory is working with clients in Ireland, Switzerland and the USA including Boston Scientific, Stryker, Medtronic and Teleflex. Sheppard’s intention is to target all 17 of the world’s top 25 medtech companies with operations in Ireland. “The world leaders in manufacturing recognise the business value in digital transformation, he says. “Those who don’t will get left behind.”

to wireless sensors and data to be captured from manual operations. The beauty of using wireless sensors is that they can be rapidly implemented and re-validation avoided.

SmartFactory is based in the Nexus Innovation Centre on the University of Limerick campus. Working with the CONFIRM centre in UL and a group of researches in gamification in CIT, they worked to make the visualised data as impactful as possible for operations.

“We were able to bring all of this data together to make it really engaging. How you present the data is very important. It has to resonate with the viewer, who might be an operator, manager or R&D engineer,” Sheppard explains.

SmartFactory’s first step with a medtech client is to identify how this technology can be used to create real business value, within their manufacturing process, in a secure way.

“One of the biggest challenges at morning

meetings on the factory floor is that engineers are looking at historical data which they have no ability to influence. Our solution provides them with real-time actionable data, to optimise operational performance. It also allows us to introduce clever things like ‘pick to light’ and digital workflows,” says Sheppard.

“Every medical device has a standard operating procedure (SOP) on how it is built. Converting that from paper to a digital workflow means criteria defined in the SOP can be checked and verified, in real-time. This ensures that every product is made consistently to the same standards, helping to make every operator your best operator. Pick-to-light tells the operator which components to pick next using a series of lights, which makes this process accurate and efficient.”

Another feature of the Smart Factory solution is video downtime analysis. “Similar to the way a dashboard camera in a car allows you to see what

Garrett Coady





Accelerating to connected health

Founded by Garret Coady in Dublin in 2007, BlueBridge Technologies provides technical and regulatory development support to enable its clients to accelerate their connected health and digital medical device solutions. It allows companies to navigate the regulatory and technical pathways and combine them to address user needs in connected health.

Soon, all modern medical devices will have a “brain”. Bluebridge Technologies strength is developing and managing intelligent components for all parts of the connected medical-device ecosystem. They make adaptive, regulated software and hardware that manages chronic conditions such as cancer, diabetes, Parkinson’s, respiratory and heart disease.

From mechanical engineering to data science, the expertise is in developing networked medical-device technology effectively and securely.

This is a rapidly-changing sector in terms of the patient

needs it addresses, the technology it uses and the regulatory environment in which it operates. BlueBridge Technologies is particularly adept at responding quickly to those changes.

The current and potential client base is made up of global medtech and pharma companies that demand all products and services supplied to them meet very exacting standards. Our current client list includes Novartis, Roche, Medtronic and Boston Scientific.

“BlueBridge Technologies is a key strategic partner to medtech and pharmaceutical companies which are trying to crack this complex connected health nut,” says CEO Garret Coady. “A lot of the large multinationals are struggling to marshal the blended interdisciplinary skillset required to do this. We have all the individuals needed on our team to develop the solutions and we work with strategic vendors to pull everything together.”

The BlueBridge

Technologies team of 25 people is a mix of engineers, scientists and industrial designers with a lot of experience in a variety of industries. Coady himself originally worked in the automotive industry, which has given him a keen insight into what is coming down the line in medtech.

“We have already seen the infusion of software and technology in cars on the journey towards autonomous vehicles. The medtech sector is at the early stage of this type of journey. There are a lot of parallels with the automotive sector, but it may not happen in exactly the same way,” he says.

“The automotive industry had to respond to the need to layer services on top of mechanical high volume manufacturing using sophisticated electronics and software systems. The whole business model was interrupted. If medtech companies are going to migrate into services companies this has to be done

by connecting the physical devices so they can overlay services. The emergence of resilient business models underpinned by the new technologies is the part a lot of companies struggle with.”

An example of BlueBridge’s work in the medtech space was the development of a medical mobile app for a Class III diabetes management system that monitors and manages patients in a home care setting. A sensor on the glucometer worn by the patient interfaces via medical-grade Bluetooth Low Energy with the app in accordance with medical device software standard IEC 62304. The resulting data is sent over GSM to the cloud.

“Our mantra is ‘Lean compliance with uncompromised quality’. We help to navigate the compliance area but always deliver high levels of innovation,” says Coady.

Ireland's medtech community

From the clinical to the commercial, Ireland's startup ecosystem offers a wider range of supports to help entrepreneurs realise their ambition. Medtech startups can test innovative solutions by tapping into the health system here, benefit from experts in smart medical devices and connected health, map commercial pathways and even access funding from Europe's lead investor in startups. You just need the right guide to navigate you through the startup community.

Bringing innovation into the health system

Health Innovation Hub Ireland (HIHI) was officially established as a national entity in 2016 with the aim of driving collaboration between the health service and enterprise, leading to the development of new healthcare technologies, products and services.

Supported by Enterprise Ireland and the Health Services Executive, HIHI incorporates University College Cork, where its central base is, Cork Institute of Technology, NUI Galway and Trinity College Dublin and all of their associated hospital groups.

HIHI has three pillars of activity: Industry, healthcare and education. The first is geared towards companies with innovative solutions that can impact the healthcare system.

"Ireland is an innovative country, we know that from the various innovation rankings, and many of these innovations are focussed on healthcare, from disease related issues, to improving processes, keeping our older population at home for longer or indeed, keeping our young population healthy.

The voice of Irish medtech

“The Irish Medtech Association is Ireland’s largest and most influential trade association representing both major FDI multinationals and innovative startups in the medtech industry as part of Ireland’s leading business group Ibec,” says Irish Medtech Association Director Sinead Keogh.

The Irish Medtech Association aims to:

- Promote a business environment that supports growth
- Support job creation and upskilling as well as industry investment
- Build awareness of the value of medtech to people and the economy
- Propose and support policies as well as strategy nationally and internationally
- Facilitate interaction with strategic growth sectors such as ICT and biopharma

“Our growing membership have access to a range of services including, lobbying, networking opportunities including must-attend conferences, industry foresight, PR opportunities, worldclass self-assessment tools, subsidised and industry-led training,” Keogh adds.

“We are led by a Board of Industry CEOs and business leaders who implements its strategy with working groups and taskforces in key areas such as Quality and Regulatory Affairs, Commercial, Connected Health, Public Relations, Operational Excellence and Advanced Manufacturing, Employer Relations as well as Leadership Development,” Keogh explains.

“The group has steadily expanded over the past two decades to help the industry realise its ambition. We welcome both large and small companies in our membership and give them a voice as part of Ireland’s global medtech hub, she concludes.

To find out more about getting involved and membership, you can email membership@ibec.ie.



Irish Medtech Association
Ibec



Dr Tanya Mulcahy

Irish companies have created innovative solutions to many health problems. We need these solutions to deliver change in the way health is delivered globally. However, the value of a solution is only truly known when it is validated in a real scenario and our experience is, that companies can have difficulty accessing the healthcare system. They might find it hard to contact the right clinicians, unit or ward, or even understand the procurement and buying process within a hospital,” explains Dr Tanya Mulcahy, National Manager, HIHI. “We link companies with the right healthcare location or person so they can test, validate and get feedback on their products.”

HIHI issues annual calls for new innovative solutions from industry but they also operate an ‘Open Door’ policy and will consider applications at any time outside the call window. There is a rigorous review process from which companies are selected. To date, over 237

companies have contacted HIHI about their innovations, many of these are small Irish companies. HIHI has provided valuable guidance to about 150 of these companies and 59 of these have developed into active projects running in clinical locations around the country.

“Once a company is accepted, we help to manage the project from start to finish. We identify what they need to do, set up a plan, identify the location and get the clinical team on board. We produce a report at the end, which is valuable to the company in terms of feedback, a reference site and validation but this report is also informative to the healthcare system,” explains Mulcahy.

The second pillar of HIHI’s activity involves identifying innovations and entrepreneurs within the healthcare system itself. “People at the coalface working with patients, our doctors, nurses, carers, health experts, encounter problems on a daily basis- we call these clinical ‘needs’ They see

the problem and many have developed the solution in their head, some may even have doodled it on a napkin. However an idea is nothing unless you do something with it. Those with the desire to develop their ideas into products can come to us," says Mulcahy.

"We give advice on protecting ideas, identifying those with potential and what to do to bring them further on the commercialisation journey. When your focus is delivering care, it can be difficult to know how to get information on the market, on the regulatory landscape, design processes etc so we point them in the direction of the Irish Medtech Association, Enterprise Ireland the Local Enterprise Offices and other support within the ecosystem that is open to them. We map out the commercialisation pathway for them and where products have significant potential, we link them with the expertise needed to deliver the end product, this often comes from within the academic community or existing industry in Ireland.

So far, 128 ideas have come into HIHI via this strand of activity. HIHI has followed up and given valuable advice

Abhay Pandit



to 105 of these and 31 have been developed into a technology assessment process.

New centre supports smart medtech research

With ten academic partner institutions and 30 industry partners, CÚRAM is establishing a global hub of research expertise in medical device technology from its base at NUI Galway. CÚRAM represents investment of €107.5 million by Science Foundation Ireland and industry to 2020.

The centre's vision is to develop affordable, innovative and transformative device-based solutions to treat global chronic diseases. The research is focussed on six main clinical areas: respiratory, neural, cardiovascular, musculoskeletal, renal and urology and soft tissue.

There are 187 researchers at CÚRAM working on projects with a view to designing and manufacturing the next generation of 'smart' medical devices and implants to improve health outcomes and enhance quality of life for patients with chronic illnesses.



Pauline O'Flanagan, Paul Healy and Sinead Keogh

Driving competitiveness with learning and upskilling

The Irish Medtech Skillnet is the national learning network for medtech businesses of all sizes to share best practice and to respond to their business needs. "This successful network has already delivered 46,000 training days and over 8,900 trainees have completed their programmes in a broad range of key areas from Quality and Regulatory Affairs to Lean Leadership and Operational Excellence," Irish Medtech Skillnet Manager Network Manager Pauline O'Flanagan remarks.

The network provides strategic responses to emerging opportunities and challenges with industry-led, specialised education and training for the medtech industry. Training is government subsidised and offered at a competitive rate.

O'Flanagan explains "The Irish Medtech Skillnet can help you identify skills needs, programme design as well as development, customised training programmes, advice on gauging the effectiveness of training, access to a network of business leaders, and events including conferences, masterclasses as well as both certified and uncertified courses."

Membership of the networks is open to all private sector enterprises within the sectors in the Republic of Ireland. To find out how the Irish Medtech Skillnet can help you succeed, email Michelle.Reinecke-Quain@lbec.ie.

“Our research has been looking at devices that will last longer in the body and interface better with the body. We have expanded our remit so that this doesn’t only cover implants but also external sensing devices,” says the centre’s director Professor Abhay Pandit.

One of the exciting pieces of work at CÚRAM is an implant to treat myocardial infarction (heart attack) which is injected into the body. Scar formation reduces and the heart performs much better. “We have a large pre-clinical study to demonstrate this and the next phase will be to scale up to a large animal study,” notes Pandit. “Another technology coming up is a treatment for back pain – a gel that can be injected into the back to relieve pain symptoms for a considerably long time.”

Already after only four years there are signs of commercial activity coming from CÚRAM’s work. To date, 35 patent applications have been filed, three patents have been awarded and 10 licences granted. Thirty-seven contracts have been signed with industry partners amounting to €3.75 million in value.

“Industry is central to drive the translation of research into the next generation of medical devices and implants,” says Pandit. “CÚRAM is showing that academia is not the only career option for people when they finish their PhD. They can work in a large company or startup to gain experience. Our researchers are encouraged to file patent applications so that innovation becomes embedded in their research.”

Ireland’s ambition for clinical research

Health Research Board Clinical Research Coordination Ireland (HRB-CRCI) was set up in 2015 to bring more clinical research to Ireland while at the same time supporting the pharmaceutical and medtech communities (both commercial and academic) in conducting multi-centre clinical trials across the country.

More and more clinical trials need participation from more than one site to ensure that enough participants can be recruited, and to show that the effect of a trial (or lack of an effect) is not localised in a particular region or country. In the past, this could sometimes prove to be tricky. HRB CRCI is addressing this bottleneck while also providing the link to ‘Ireland’ as a partner in multinational trials.

“Our vision is that Ireland is internationally recognised for conducting innovative, high quality clinical research,” says Dr Fionnuala Keane, Chief Operating Officer HRB-CRCI.

HRB-CRCI is funded by grants from the HRB and Enterprise Ireland, supported by the six largest Irish universities and hosted by Clinical Research Development Ireland in Dublin. It coordinates eight research facilities around the country, which are affiliated to the universities.

“CÚRAM is showing that academia is not the only career option for people when they finish their PhD. They can work in a large company or startup to gain experience. Our researchers are encouraged to file patent applications so that innovation becomes embedded in their research.”



Dr Fionnuala Keane



Ronan Furlong

“There are a lot of interesting projects going on at the various research centres, including studies on asthma and tinnitus. However, Ireland could do an awful lot more. A lot of trials and studies are exported to the Netherlands or Germany and we should be providing those services here,” says Keane.

“A large part of what we do at HRB-CRCI is to support individual investigators and entrepreneurs. Our dedicated Clinical Industry Liaison Officer, funded by Enterprise Ireland, is there to advise people in the medtech area on the pathway through product development and clinical trials – things to look out for, the regulations they need to adhere to and matching them up with the right research centres and clinicians who will provide access to suitable patient cohorts to work with for their studies. HRB CRCI is the connecting piece between the entrepreneur, the clinician and the patient.”

A collaborative cluster

DCU Alpha is a commercial innovation campus that promotes the growth of research-intensive businesses that are creating the technologies and services of tomorrow. Repurposed and reopened by Dublin City University (DCU) in 2014, the site had played a pivotal role in innovation and scientific research over its 70-year history, having previously served as headquarters for Enterprise Ireland. The main DCU academic campus is 800 metres away.

“The aim with DCU Alpha was to create a cluster of like-minded innovative companies that want to collocate and tap into the research activities and talent networks within DCU,” says Ronan Furlong, Executive Director, DCU Alpha. “The companies that have come here are looking to tap into specific capabilities or competencies in the university – specifically arenas in which

DCU is best placed to lead – such as connected health, artificial intelligence, sensor technologies and wearable devices. The technological flavour of the cluster in DCU Alpha, is primarily around the Internet of Things and data analytics in particular.”

There are currently 100+ companies employing 750 staff between them at DCU Alpha. Around one fifth of these are operating in the medtech space. A situation has naturally evolved where companies are not only linking up with academic researchers at the university, but also collaborating with each other.

“We’re seeing that this type of intra-company collaboration is just as compelling as the links established by companies with the university,” notes Furlong. “For example FIRE1, one of the medtech enterprises based here, is developing a remote heart monitoring product, which will naturally require antenna technologies and data analytics capabilities. On the

floor above them, antenna design company Taoglas is developing new ‘machine to machine’ technology, so an interesting collaborative conversation has sprung up between them. Meanwhile, Dolmen Design, which is on another floor and was already working with FIRE1, is now partnering with numerous other DCU Alpha companies in various other hardware sectors, off the back of their medtech product design work.”

Furlong adds that DCU Alpha is neither an incubator nor an accelerator for medtech or connected device startups, and is more of an innovation platform or enabler for these companies. “We don’t make bets on whether companies will make it or not. We don’t try to take equity. We simply try to catalyse these businesses by connecting them to the right people and skills – be that in the university or within the cluster of companies itself.”

A new model for startups

Turning clinical problems into medtech solutions lies at the heart of the worldclass BioInnovate Ireland programme. By combining skillsets, bringing clinicians, engineers and business leaders together they build super teams to identify and address global health needs.

Identify, invent, implement

In 2010 an Irish Government and medtech industry delegation travelled to the US to explore the area of medical device innovation with a view to creating a new immersive educational experience in the Irish Higher Education Sector.

“The focus of our visit was to ensure that we continued to nurture and grow our medtech industry in Ireland through exogenous growth but to also seek more opportunities to grow indigenously thus creating a robust ecosystem from both an educational and industry perspective,” says Faisal Sharif, Director, BioInnovate Ireland.

In considering international models of innovation, the Stanford Biodesign Programme was selected as both a best practice and a best fit model to adopt in Ireland. The programme established in 2000 had at this point significant outputs, clinical engagement and embodied many of the values important to the medtech delegation including its core principles of ‘Identify’, ‘Invent’ and ‘Implement’.

The Biodesign programme at Stanford was a first of its kind postgraduate programme which trained biomedical technology innovators this needs led

BioInnovate in numbers:

- Over 150 hospitals accessed and 1,000 physicians interviewed
- 81 Fellows graduated from the entrepreneurship programme
- 130 people from established industry trained on the intrapreneurship programme
- One startup acquired (Embo Medical acquired by CR Bard subsidiary Clearstream in 2015)
- Seven high potential startups formed, 22 potential startups in the pipeline
- 15 patents filed
- 18 clinical areas investigated

process for developing technologies and delivering patient and practitioner based innovators to meet unmet needs. A core value of the programme is that innovation is a process that can be learned, practised and perfected.

BioInnovate Ireland is led by NUI Galway as a national programme with partner universities since its inception in 2011. The programme is designed to facilitate the collaboration and development of entrepreneurship in the medical technology sector. What makes the programme unique according to Sharif, is the fact that it combines multidisciplinary skillsets and perspectives. Over a ten-month period, teams of four high-performing individuals, experienced Fellows from clinical medicine, engineering, business development, industrial design and project management work together to identify clinical unmet needs and align them with market opportunities.

“An engineer may want to develop a new device, but will not necessarily know where to start or what the problem is, while a doctor might know the problem, but not know how to build intellectual property or come up with a business model,” he explains. “True success in terms of developing an innovative medtech startup comes from combining these skillsets.”

The multidisciplinary teams focus on one specific clinical area and continuously receive mentorship from industry, clinicians, venture capitalists, domain experts and academics with stipend support from Enterprise Ireland.

“Once the clinical area has been identified, the domain experts in that speciality host the team who make clinical observations in hospital settings. Their job is to translate these into problems, and the problems into a single unmet need. Everything about that unmet need has to make it a commercially viable option,” says Sharif.

This is the first phase of the programme, the ‘identify’ phase. It is followed by the ‘invention’ phase, which involves figuring out what the concept will look like and whether it is possible to do it in terms of intellectual property. The teams also look at regulatory risks and business models and sometimes prototype around their solution direction”. “The ‘invention’ phase is all about further cementing the unmet need. If the Fellows are in any doubt, they can always look at a different unmet

need. They usually have a top five,” says Sharif.

The ‘identify’ and ‘invention’ phases usually take nearly the full ten months, and that is when the really important phase happens, according to Sharif. Successful teams are granted a commercialisation fund through a highly competitive process from Enterprise Ireland to help them to go through the implementation phase over an 18-month period.

“This Enterprise Ireland support is the key differentiator between our programme and any other medtech programme full stop,” says Sharif. “It enables the companies to get the pre-seed funding necessary to build prototypes and finalise their proof of concept before they start to look at manufacturing capability and do pre-clinical work and clinical trials.”



Dr Faisal Sharif

A national medtech accelerator

Eight medtech companies are currently immersed the second BioExel programme, which is Ireland's first-ever medtech accelerator aiming to bridge the gap between technology de-risking and raising investment.



Dr Sandra Ganly

Still in its pilot phase, BioExel offers €95,000 in seed funding to successful applicants along with six-months of intensive training, mentoring, lab space and supported interactions with potential investors. The programme allows participants to build and commercially validate their technologies by working with existing entrepreneurial networks, mentors and management teams.

BioExel is managed by Medtech Director, Dr Sandra Ganly, also a co-founder of BioInnovate Ireland and Senior Research Fellow in NUI Galway, and Fiona Neary, Commercial Director and co-founder of BioExel, and Innovation Operations Manager at NUI Galway. It is a partnership programme funded by Enterprise Ireland, Galway University Foundation, the Western Development Commission and Bank of Ireland Seed and Early Stage Equity Fund.

“Back in 2016 there was a competitive call by Enterprise Ireland for regional-based accelerators, as a key action under the Action Plan for Jobs 2016, targeting an increase in the number of and quality Irish startups that can create regional employment and economic impact. In collaboration with colleagues at NUI Galway and in partnership with key regional and sectoral stakeholders, together we could see an opportunity to develop a medtech-dedicated accelerator, a gap in the existing supports for medtech startups, We decided to give it a shot and see if adding a medtech-specific accelerator to the existing ecosystem supports would make a difference” says Ganly.

While housed in the heart of Galway's medtech cluster, BioExel shares resources and training with BioInnovate Ireland and other entrepreneurial initiatives to offer this important national accelerator programme. With access to 64 expert mentors, it has held 112 training events over the past year.

“Our job is to be complementary to other programmes, not to duplicate anything. While BioInnovate Ireland is an intensive programme to allow multidisciplinary teams to identify unmet clinical needs worth solving, BioExel is a mentor-centric programme to allow existing companies to accelerate to the next stage of their commercial journey,” Ganly explains.

Ganly and Neary wanted to test the theory that if companies are brought together, irrespective of their stage of development, learning from each other will be equally as important as disseminating domain expertise.

“The six-month programme is a deep dive on their business, getting under the hood of the technologies and addressing commercial milestones and fundraising requirements. We have shown so far that being together in a dedicated space creates a sense of community and helps to expedite opportunities for the companies involved,” says Ganly.

There were six companies in the first cohort of the BioExel programme, which finished in June 2018. Three of these companies have already secured seed funding.

“The technologies in the first cohort ranged from a wound care solution right up to a neuro regenerative product using cellular therapies and biomaterials for spinal cord injury. Our remit is not to bring these technologies to market but to move the dial along so they reach the next inflection point to trigger investment,” explains Ganly.

“The constant supports over a six-month period have helped the company CEOs to avoid certain pitfalls. What the participants learn from each other is astounding – even when they have very different technological offerings, they may have similarities in terms of business models or routes to market.”

Thumbs up for innovative implant

Co-founders of Loci Orthopaedics Dr Brendan Boland and Gerry Clarke were matched up in 2013 as part of a four-person team on the BioInnovate Programme. They believe that the “InDx Implant”, the new thumb implant they have developed, has the potential to completely disrupt how painful thumb joint arthritis is treated.

Boland’s background is in medicine, having graduated in 2006 and then practised as a doctor for seven years. Meanwhile, medical technology engineer Clarke has over 35 years’ experience in the medtech sector.

“I had a broad understanding of medical devices, but my knowledge of product development was minimal. My original intention was to up-skill by doing a Master’s in medical device innovation and then return full-time to clinical practice,” says Boland. “However, at the end of the BioInnovate programme I changed my mind as I saw an unmissable opportunity to continue with our project. We had identified a massive unmet clinical need and a potentially huge market for our product. Also, I thought, where else would I find an engineer with 35 years’ experience to do a startup with me?”

The clinical area Boland and Clarke’s BioInnovate team focussed on was orthopaedics. “We were dispatched to orthopaedic operating theatres and spent hundreds of hours observing current clinical practice, as well as meeting

sports medicine experts, physiotherapists and occupational therapists,” says Boland.

The team zoned in on thumb joint arthritis and spent a lot of time looking at current treatment options and the failure modes and mechanisms of other implants and devices. “This is one of the good things about BioInnovate – that you learn from history what went wrong and don’t make the same mistakes,” says Boland. “We found that devices had failed because of the materials used or the biomechanics of the design. We decided our USP would be based on the biomechanics of the joint as we were reassured that materials such as cobalt chrome and polyethylene were well known and proven for such implants.”

A key point came for Boland and Clarke in 2015 with the publication of a research paper by two hand surgeons, Dr Peter Weiss from Brown University and Dr Amy Ladd from Stanford University. It focussed on using high resolution 3D CT scanning to map the micro-motions of the thumb joint, which hadn’t been done before.

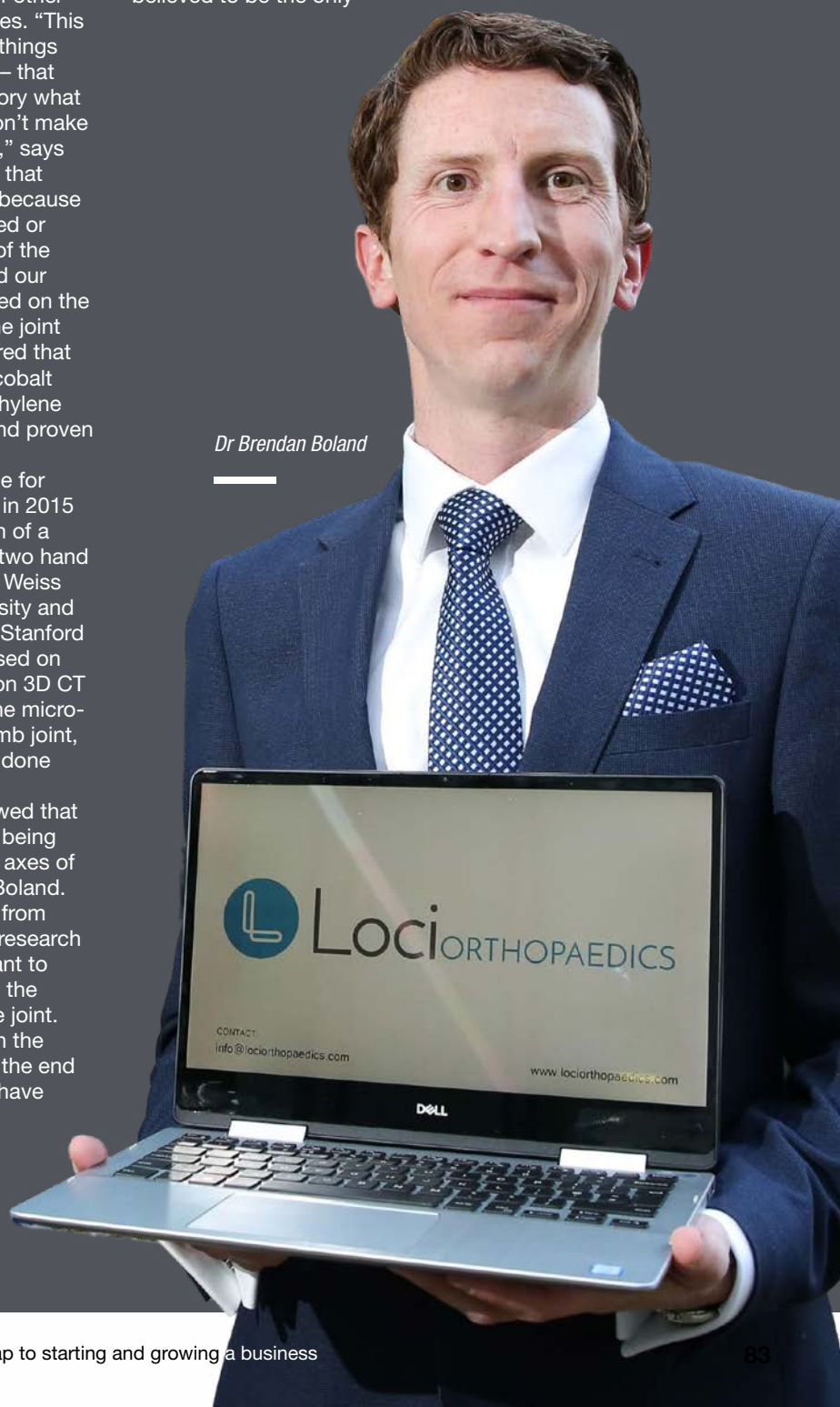
“The paper showed that instead of the joint being uniaxial, it had two axes of movement,” says Boland. “We used the data from this core scientific research to design our implant to make sure it meets the requirements of the joint. Gerry came up with the concept and since the end of BioInnovate we have

been working closely with Peter, Amy, and Prof Filip Stockmans at KU Leuven. It has been great to have such eminent hand surgeons as advocates of our product. They are a core part of the project and design team.”

The InDx Implant is believed to be the only

implant that successfully mimics the complex motions of a healthy thumb joint, as it provides two points of rotation that can move concurrently and independently, while enabling the joint to move in all six degrees of freedom.

Dr Brendan Boland



A nose for a good idea

In 2014 a four-person team including Brian Shields and David Townley were assigned ear, nose and throat (ENT) as their clinical area to focus on as Fellows in the BioInnovate Ireland programme.

“We clocked up around 1,000 hours in direct exposure to the care givers, who were largely surgeons and audiologists and got to see how they interacted with patients in every setting,” says Shields. “We were given huge access across theatres, outpatient units and on ward rounds. It was excellent to be able to follow patients through the system. Positioning a solution in the correct patient setting is an integral part of a successful commercial opportunity”

The team identified rhinitis treatment as a significant unmet clinical need and had a few ideas about how to tackle it. “We travelled to the US and approached a lot of different health systems and surgeons as we wanted to validate that this was a genuine global need which was recognised by surgeons,” says Shields. The founders believed that the needs led approach to their innovation was critical to driving the commercial feasibility of their technology.

Being successful in their application for a commercialisation grant from Enterprise Ireland allowed Shields and Townley to go through a two-year commercialisation assessment process while based at NUI Galway. “We spent a lot of time validating the science that underpins the theories we rely on and built enough value into the proposition so that we reached a point where we could speak to potential investors,” says Shields.

The company they spun out, Neurent Medical, has developed a minimally invasive, hand-held radio-frequency device which ENT surgeons will be able to use to treat patients with rhinitis in an office setting. They aim to remove complications and costs associated with alternative treatments.

In May 2018, Neurent Medical raised €9.3m in a Series A financing round led by Fountain Healthcare Partners with participation from Atlantic Bridge Capital, the Western Development Commission, Enterprise Ireland and a syndicate of Irish and US medical device veterans.

“Ireland is brilliant for medtech startups as there is a deep skillset here, however there is a lot of competition for resources” said Shields. On raising capital, Shields commented that “money is becoming increasingly more difficult to access for early stage companies, however finding the right investors is paramount in maximising the value that can be achieved with the invested capital.

Champions for enterprising startups

Innovation is the key force that drives this growth and particularly so in the Medtech sector.

“With 15 of the top global 20 medtech companies in the world located in Ireland, people may not realise that 60% of the industry here are indigenous Irish companies. We have a dynamic group of established companies with a strong track record in innovation,” says Deirdre Glenn, Director, Lifesciences & Food Commercialisation and Manager of Lifesciences Sector Market Department, Enterprise Ireland.

The indigenous medtech cluster is comprised of medical device, diagnostic and digital health companies as well as hugely innovative and competitive engineering and component manufacturers Ireland has a vibrant medtech startup ecosystem. In addition to the established players, Ireland is being recognised as a vibrant hub for medtech startups, said Glenn. “They are among the best in the world in terms of new technology, processes and services. They are going to define the future of healthcare globally,” she contended.

The commercialisation agenda is very important when it comes to Enterprise Ireland’s support of medtech startups. “We are the leading agency for the commercialisation of research out of third-level institutions. Our Commercialisation Fund gives innovative teams in academic institutions and clinical communities funding to validate the technical and commercial viability of ideas and products supporting the creation of new technology startups.” In 2017, nine of the thirteen lifesciences high potential startups (HPSU’s) supported by Enterprise Ireland were HPSUs from research.



Brian Shields



Medtech sales worldwide are forecast to reach €530 billion by 2024

Medtech is the most innovative sector in Europe with 13,795 patents filled with the Europe Patent Office



Connected health is forecast to have sales of €15.7 billion by 2024

Ireland is home to 10 of the top 10 biopharma companies and 10 of the top 10 tech companies



“Ireland is truly seen as a leading innovative medtech nation. Not only are we very competitive and offering high quality, we can deliver something unique to customers internationally, ultimately contributing to jobs and economic growth in Ireland.”

Enterprise Ireland are co-funders of the Bioinnovate Ireland programme, a National programme which supports innovation and “design thinking” in the medtech sector. A significant number of Alumni Bioinnovate Fellows of the have been successful in creating new HPSU’s from research in recent years.

Enterprise Ireland is the biggest seed investor of startups in Europe, having invested €23 million into startups across the board in 2018, including 82 high potential startups (HPSUs). In February, it announced the first call for expressions of interest from seed and venture fund managers under its new

€175 million Seed & Venture Capital Scheme (2019-24).

Since the Seed & Venture Capital programmes commenced in 1994, the investment provided through Enterprise Ireland commitments has leveraged substantial additional external funding and as a result over 500 Enterprise Ireland clients have received in excess of €900 million in investment.

“An important part of our efforts is to try to work with others to find alternative ways for startups to gain access to the funding they need. We have been successful in filling that gap,” notes Glenn. “For example, our medtech HPSUs have been particularly good at drawing down the Horizon 2020 SME funding instrument.”

Enterprise Ireland supports Health Innovation Hub Ireland, BioExel and HRB-CRCI, all of which are covered elsewhere in this report. Its international network of 35 overseas offices provides companies with access to people on the ground who understand the local culture and way of doing business.

“Ireland is truly seen as a leading innovative medtech nation. Our startups are focused on building global partnerships, growing scale and expanding into new export markets. Not only are we very competitive and offering high quality, we can deliver something unique to customers internationally, ultimately contributing to jobs and economic growth in Ireland,” said Glenn.



Deirdre Glenn

Local supports for business growth

One of the central roles Local Enterprise Offices (LEOs) play is to provide a one-stop-shop to anyone seeking information and support on starting or growing a business in Ireland.

“It can be confusing for entrepreneurs to navigate the range of services State and other bodies provide. The staff at the 31 LEOs around the country are very much in tune with the programmes on offer and can fast-track people into the support services that are right for them,” says Oisín Geoghegan, Chair of the network of LEOs.

“Funding is often the first thing people ask about. If someone has a medtech idea that needs to be explored and is not fully validated or tested, LEOs can help them to ascertain if it is viable. If the business proposition does qualify for funding, the team will encourage applications and explain the different funding mechanisms. Feasibility study grants are usually the most common type initially for new medtech ideas.”

In the past year, Enterprise Ireland’s Agile Innovation Fund was opened up to LEO clients. Offering fast-track approval and a streamlined online application process, this fund allows companies to access up to 50% in support for product, process

or service development projects with a total cost of up to €300,000.

Throughout the LEOs, there is an abundance of different programmes and activities to help entrepreneurs or aspiring entrepreneurs to move forward. These range from start your own business programmes through to one-to-one mentoring.

“We often find with medtech companies that the promoters don’t necessarily have the commercial expertise needed to progress and we will help them to identify what management skills they need to develop,” says Geoghegan.

LEOs play an important role in promoting entrepreneurship generally in Ireland, for example through Local Enterprise Week and the Student Enterprise Programme. In addition, they have been running the Ireland’s Best Young Entrepreneur programme for the past four years, with each LEO having a share of the overall prize fund totalling €2 million. “A good number of medtech entrepreneurs have emerged through this process in the past couple of years, including Kevin Kelleher of Ostoform, who has created a breakthrough surgical seal system for patients with colostomy bags,” says Geoghegan.



Oisín Geoghegan

A lending hand

For medtech entrepreneurs there are a number of startup reliefs and schemes you can tap into. There are opportunities for unemployed people take a chance on themselves by founding a company that they can believe in and funding for entrepreneurs to test the waters with feasibility studies or to achieve technical and commercial milestones. Entrepreneurs can also get a lending hand to grow their business with low cost loans, tax relief and share options to help them compete for talent. But access to venture capital remains one of the most important elements of the startup formula for success.

Back to Work Enterprise Allowance

The Back to Work Enterprise Allowance scheme is designed to encourage the long-term unemployed to take up self-employment opportunities by allowing them to retain a reducing portion of their social welfare payment, plus secondary benefits in certain circumstances, over two years.

The objective is to support the unemployed to commence self-employment in order to generate new enterprises and increase employment.



Capital Gains Tax Relief

Capital Gains Tax (CGT) is a tax charged on the capital gain (profit) made on the disposal of any asset. It is paid by the person making the disposal. CGT relief is designed to encourage business people to re-invest the proceeds of previous asset disposals into new business ventures.

You may claim relief from CGT if you made gains from disposing business assets. There is a lifetime limit of €1 million on the gains that you can claim relief on. If you can claim this relief, you must pay CGT at the rate of 10% on gains from the disposal of business assets.

Competitive Start Fund (CSF)

The purpose of Enterprise Ireland's Competitive Start Fund is to accelerate the growth of startup companies that have the capacity to succeed in global markets. The fund is designed to enable those companies to reach key technical and commercial milestones.

Applicants to the fund should ideally be able to demonstrate the following: that product or service has reached MVP stage, has demonstrable customer validation with (trial and/or paying) customers, a proposition addressing a clear gap in the market, evidence of innovation as well as export potential and employment capacity, with a clear execution plan outlined.

Credit Guarantee Scheme

The purpose of the SME Credit Guarantee Scheme is to encourage additional lending to SMEs, not to substitute for conventional lending that would otherwise have taken place.

A State guaranteed loan constitutes De Minimis State Aid. The aid attributable to the Scheme loan facility is calculated individually for each facility, but is typically around 20% of the value of the loan facility. Businesses seeking to avail of the guarantee scheme can approach a participating bank, such as Ulster Bank, Bank of Ireland and AIB.

Employee share option schemes

Employees can avail of certain share options from their company that may be 'tax free' or 'tax efficient'. There are 3 main ways in which an employee can benefit from shares in the company: Approved Profit Sharing Schemes, Share Options, and Key Employee Engagement Programme (KEEP)

Generally, gains arising from various types of share schemes are chargeable to the Universal Social Charge (USC) and Pay Related Social Insurance (PRSI). However, gains arising from the KEEP programme on the exercise of qualifying share options will not be subject to income tax, PRSI or USC at the date of exercise. The gain will instead be subject to Capital Gains Tax on a future disposal of the shares.

Employment Incentive and Investment Scheme

The Employment & Investment Incentive (EII) allows individual investors to obtain income tax relief on investments made, in each tax year, into EII certified qualifying companies. Eligible SME activities must fulfil at least one of the following conditions: they have not been operating in any market, they have been operating in any market for less than 7 years following their first commercial sale. The cumulation limit on EII investment is now €15 million as defined under the General Block Exemption Regulation (GBER). The cumulation rules set out in the GBER may apply to other State Aid received by the undertaking where the total State Aid received by the undertaking exceeds €15 million.

High Potential Startup Feasibility Study Grant

The aim of Enterprise Ireland's High Potential Startup (HPSU) Feasibility Grant is to assist an early stage company or individual entrepreneur to investigate the viability of a new export orientated business or proposition. The objective of the study is to provide the necessary information to enable the promoter, and Enterprise Ireland, to reach firm conclusions regarding the project's viability and set out investor ready plans and financials associated with developing and commercialising your innovative product or service on international markets.

Typical elements involved in carrying out a feasibility study include; market research, business plan development, technical research, and/or prototyping.

Innovation Vouchers

The Enterprise Ireland Innovation Voucher initiative was developed to build links between Ireland's public knowledge providers (ie higher education institutes, public research bodies) and small businesses. Innovation Vouchers worth €5,000 are available to assist a company or companies to explore a business opportunity or problem with a registered knowledge provider.

The Innovation Vouchers initiative is open to all small and medium-sized limited companies registered in Ireland.

Microfinance Ireland

Microfinance Ireland provides small loans through the Government's Microenterprise Loan Fund. The purpose of the fund is to help startups and established businesses to start up a small business or expand your existing business. It helps these businesses by providing unsecured business loans of €2,000 to €25,000 for commercially viable proposals.

Microfinance Ireland works closely with all partners, including Local Enterprise Offices, the Irish Local Development Network, as well as all the major banks to provide viable businesses with the support they need to get started or to grow their business and create jobs.

Research and Development (R&D) Tax Credit

If a company spends money on research and development activities, these activities may qualify for the R&D Tax Credit. The credit is calculated at 25% of qualifying expenditure and is used to reduce a company's Corporation Tax (CT). Where a company has offset current and previous years' CT liabilities, it may apply for a credit payable in instalments.

A company may qualify for the R&D Tax Credit if: it is within the charge of CT in Ireland, it carries out qualifying R&D activities in Ireland or the European Economic Area (EEA), the expenditure does not qualify for a tax deduction in another country.

Start Your Own Business Relief

If you have been unemployed for at least 12 months and set up a qualifying business, the Start Your Own Business scheme provides an exemption from income tax up to a maximum of €40,000 per annum for a period of two years.

Start Your Own Business Relief only applies to income tax payable on the profits from your business. It does not extend to PRSI and Universal Social Charge (USC) so you will be liable to pay PRSI and USC on any profits earned in your new business.

Short-Term Enterprise Allowance (STEA)

STEA gives support to people who have lost their job and want to start their own business. To qualify you must be getting Jobseeker's Benefit. There is no qualifying period, which means you do not need to have been getting Jobseeker's Benefit for a certain period of time. However, you will not qualify if you are getting Jobseeker's Benefit and working part-time.

The Short-Term Enterprise Allowance is paid instead of your Jobseeker's Benefit for a maximum of 9 months. It ends when your entitlement to Jobseeker's Benefit ends (that is at either 9 or 6 months).

Startup Relief for Entrepreneurs (SURE)

SURE is a tax relief that provides a refund of income tax that you paid in previous years. You can claim the relief if you are starting your own business and you are: an employee, an unemployed person, a person who has recently been made redundant.

The general conditions for SURE are that you must: establish a new company carrying on a new qualifying trading activity, have mainly Pay As You Earn (PAYE) income in the previous four years, take up full-time employment in the new company as a director or an

employee, invest cash in the new company by purchasing new shares, keep the purchased shares for at least four years.

Strategic Banking Corporation of Ireland

The Strategic Banking Corporation (SBCI) was established in 2014 to make low-cost credit available to Irish SMEs. Credit will be provided through on-lending institutions who, in turn, will lend directly to SMEs.

Funding for the SBCI has been provided from KfW (the German State Development Bank), the European Investment Bank and the Ireland Strategic Investment Fund (a new fund to which the assets of the National Pensions Reserve Fund were transferred). The NTMA assigns staff and provides business and support services and systems to the SBCI. Responsibility for the discharge of the SBCI's functions is a matter for the SBCI Board.

Tax relief for new startup companies

If you have started a new company, you may be able to apply for tax relief for startup companies. This tax relief is a reduction of your Corporation Tax (CT) for the first three years you trade. The relief can be applied to the profits from your new trade and on chargeable gains made on assets used in that trade.

You may be entitled to relief if your CT due is €40,000 or less in a tax year or partial relief if your CT due is between €40,000 and €60,000. Tax relief for startup companies also depends on the amount of employer's Pay Related Social Insurance (PRSI) you pay. Since 2013 it may be possible for your company to carry forward any unused relief from your first three years trading. Certain restrictions may apply and they are outlined in this section.

Venture Capital

Venture capital is vital for startups to get to market and grow with more than €3.5 billion raised by medtech companies in the first half of 2017 alone. However, for more than five years there's been a steady decline in the number of VC deals while the size of deals increased. VC to Irish technology firms fell by over 40% in to €196.8 million in the first quarter of 2019 in Ireland, but lifesciences startups dominated the deals made accounting for 47% with all five investments that exceeded €10 million being in the sector.

About Ibec

Ibec is Ireland's largest lobby group representing Irish business both domestically and internationally. Its membership is home grown, multinational, big and small, spanning every sector of the economy. Together they employ over 70% of the private sector workforce in Ireland. Ibec and its trade associations lobby government, policy makers and other key stakeholders nationally and internationally to shape business conditions and drive economic growth. It has over 230 professional services staff in seven locations including Brussels and has 38 different trade associations in the group.

SFA+ Medtech

If you are a small business in the medtech industry (1-5 employees) SFA+ Medtech membership will give you the full benefits of SFA membership along with essential sector insights from the Irish Medtech Association.

Membership of SFA+ Medtech gives you:

- Access to the Irish Medtech Association community via member only invites to regular member networking events, including the Annual Medtech CEO Forum and Awards, Medtech Brew and the Founders Circle
- Irish Medtech Association electronic updates on key sectoral developments and international trends
- Cost-effective subsidised "member rate" training in the areas such as innovation, lean, quality and management for the Irish medtech sector
- Profile your company via Ireland's largest Annual Medtech Industry Awards
- Profile your company news via the Irish Medtech Association's digital newsletter
- Advertise your jobs on the Irish Medtech Associations website
- Access to member only Quality & Regulatory and Sterility Forums
- Access to Irish Medtech Associations Code of Ethical Business Practice (Compliance) website and training materials

You can find out more by visiting www.sfa.ie/medtech or calling 01 605 1664.





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