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Global insights into scaling up a life science business

A Special Report from BIO International Convention 2017

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Growing a life science business involves big decisions and formidable challenges the world over. Access to the right kind of capital, scientific and business talent and a supportive political and regulatory environment are all important factors for achieving ambitions. At this year's BIO International Convention, held in San Diego, Mike Ward, Chief Content Officer for Informa Pharma Intelligence Insights Portfolio brought C-suite executives from a number of companies of differing focus and maturity together. They discussed how they have managed the challenges of scale up.

Dr Bill Newell, Sutro Biopharma, and Dr Jane Dancer, F-star Biotechnology

Given the attraction of creating highly paid skilled jobs, it is no surprise that the exhibition hall at the annual BIO International Convention is jam packed with many government and regional agencies extolling the virtues of why companies should either establish or relocate businesses in their life sciences cluster. Yet just what exactly do companies need to have in place to start up and then grow their businesses?

Access to capital is essential to get companies up and running. However, in the discussion, two issues around capital formation emerged: finance is not necessarily anchored to a particular location and it is important to attract the right kind of investors.

"The biggest challenge tends to be capital to allow us to do all the things we need to do," noted Dr Gil van Bokkelen, co-founder, chairman and CEO of Athersys, Inc. Founded in 1995, Athersys is a public clinical stage biotech, focusing on regenerative medicine. The technology underpinning the company's approach revolves around the development and use of an adult-derived off-the-shelf stem cell therapy called MultiStem. The company's lead program is about to start Phase III clinical trials to treat ischaemic stroke.

Indeed, the hardest challenge is to find investors that are willing to buy into a founding team's vision. "Part of it is to overcome the scepticism around something like stroke because Wall Street has heard that term many times over the past 20 years. Also [we have to] demystify some of the challenges that relate to a complex field like cell therapy or regenerative medicine. We would hear: 'We are not really sure what that means? And is it scalable? Or practical?'"

For Dr Laurent Levy, co-founder and CEO of Paris-based Nanobiotix SA, convincing potential investors to buy into a genuinely ground-breaking technology has been his biggest headache but it is getting easier.

"For us, the biggest challenge was to show the external world that we have a product that is different from anything they have so far seen. Before we had data from clinical trials to show what the product can do, it was difficult for people to imagine what we can do. We are now running several clinical trials in Europe, the US and elsewhere."

Nanobiotix is a public Paris-based biotech, with a US affiliate based in Cambridge, Massachusetts, that was incorporated in 2003 and is focusing on the potential of nanotechnology to create blockbuster cancer

Alderley Park, Cheshire, UK

medicines designed to treat millions of patients.

Raising money, however, is easier now the company has listed on the Paris exchange. "It took us 12 months to raise the first €700k while recently we raised €25 million in two hours," he noted. More importantly, he added, France offers companies generous R&D tax credits and conducting research is less expensive than other places.

Clearly, a politically supportive regulatory environment is a must-have but it is not sustainable on its own. Austrianova Singapore started life in Vienna, Austria as a classical drug development company. It had a candidate treatment for pancreatic cancer, based on its encapsulation cell therapy, that it was lining up for Phase III trials in the mid-2000s. Struggling to raise capital, the company's management revisited the business model and re-established itself as a biomanufacturing platform business underpinned by a proprietary stem cell encapsulation technology.

"We went out to Singapore because it was trying to do a big push in stem cells – which was not popular in Austria - and was giving incentives reimbursing 50% of what we spent which was a great help. We got a lot of support from the Singapore government for that Initially, we found Singapore was a good hub for getting things done. At that time costs were lower and it was a good place from which to communicate with the rest of the world," explained Professor Walter Gunzburg, founder, chairman and chief technology officer of Austrianova Singapore Pte. Ltd.

However, when the company wanted to scale up and start manufacturing, Singapore was not as attractive as it had once been. "It had become more expensive, the costs of renting facilities rose – they are very high now – and the money the government had to support businesses like ours ran out and it is pedalling back on what it is putting into biotech," he added.

Austrianova's choice was to look elsewhere in the region in Indonesia, Malaysia and Thailand for somewhere less expensive. The company opted for Thailand, which also offers incentives, to establish its new manufacturing facility.

Nevertheless, in hindsight, Professor Gunzburg cautions against the lure of incentives but argues it is probably best to locate in places that are more familiar with the travails of biotech. "You have to have people that understand the

Nanobiotix found fundraising easier once it listed on the Paris exchange

€700k

Raised in the first 12 months

€25m

Recently raised in 2hs

The participants:

Steve Bates
CEO, BioIndustry Association, UK

Dr Gil van Bokkelen
CEO, Athersys Inc

Dr John Burt
CEO, Abzena plc

Dr Jane Dancer
Chief Business Officer, F-star Biotechnology Ltd

Dr Chris Doherty
Managing Director Alderley Park

Professor Walter Gunzburg
Chairman, Austrianova Singapore Pte. Ltd

Dr Laurent Levy
co-founder and CEO of Paris-based Nanobiotix SA

Dr Steve McConchie
CEO, Aptus Clinical Ltd

Dr Bill Newell, CEO
Sutro Biopharma Inc

Mike Ward
Head of Pharma Scrip & Pink Sheet Informa Pharma News

Dr Danny Zurr
CEO of Quark Pharmaceuticals Inc

Research scientists at work in Alderley Park's BioHub

industry. In Singapore, investors understand IT, they can get their heads around software. Biotech is a closed book and don't want to invest in it because they don't trust it, there is no one to lead and that makes a big difference," he added.

Even companies in leading biotech nations such as the UK cannot take government incentives for granted. The UK's BioIndustry Association (BIA) continues to lobby the UK government to ensure it maintains an attractive business environment that is conducive to starting-up and growing a robust and vibrant bioindustry.

"Depending on the type of capital you [require] you do need to be integrated into the network that has access to that capital. If you have a lot of venture capitalists on your street, they know you and bump into you all the time, it is easier to form the trusted relationships that get you there. That is why you see a cluster effect and why it is easier to establish those relationships and build trusted networks if you are closer to big networks of people who are used to investing in this space," noted BIA's CEO Steve Bates.

There is plenty of evidence that capital will always flow to where the opportunities are, it does not matter much where they are located. While venture investors might like to be in close proximity to the companies that they are investing in, once a business gets past the early phases the questions potential financial backers will ask are: "Do you have access to the people you need? Do you have access to the infrastructure you need?"

Access to talent, for most of the roundtable participants, appears to be the most important driver for where to establish a business.

Thankful that he has not had to rely on venture capitalists, looking for early returns on investment, for financial support, Dr Danny Zurr, CEO of Quark Pharmaceuticals, Inc., a privately held company headquartered in Fremont, California with R&D facilities in Nes Ziona, Israel, explained that where a company recruits staff really depends on its stage of development.

"If you want to have a brilliant idea it comes from young people in the universities but to turn it into a real business, or an asset you can sell, then you need to have people with lots of experience developing a drug. If I am looking for someone to do pharmacovigilance I don't want to take a young guy that is learning the business. I want someone who knows the business and you can find those people easily in the Bay Area, in Cambridge, in Boston," he added.

Founded in 1994, Quark is a late clinical-

stage pharmaceutical company, focusing on the discovery and development of novel RNAi-based therapeutics. The company has two programs, QPI -1002 and QPI -1007, which are in global phase III pivotal clinical studies for Delayed Graft Function (DGF) and Non Arteritic Ischemic Optic Neuropathy (NAION), respectively. Novartis has licensed a globally exclusive option for QPI -1002. Quark has licensed QPI -1007 to RiboQuark, the company's Chinese joint venture company with Suzhou Ribo Life Science Co., Ltd for China and certain additional countries and to Biocon Limited for India and additional countries.

In its early days, the biotech industry was critically dependent on academic centres to provide the flow of talent and innovation, people living on the cutting edge in those institutions, but nowadays that dynamic has completely changed. Companies that have been started and which attracted the first wave of capital are not hiring people out of the academic institutions as much as they would have done 10, 15 or 20 years ago. Instead, they are hiring experienced practitioners from out of industry– from big pharma, big biotech to even small biotech depending on their organisational needs.

Accessing the right kind of staff was probably the major reason why F-star Biotechnology Ltd relocated from Vienna, Austria where it was founded in 2006 to Cambridge, UK. "What we struggled with, being based out there in Vienna - there was access to cash, we started out with grant funding - was getting access to the right kind of people. We needed people with a particular expertise in antibody engineering. That is why we set up the site in Cambridge to tap into that staff and we have done well," explained Dr Jane Dancer, F-star's chief business officer.

The company has a proprietary platform to make bispecific antibodies and is pursuing an asset-centric approach where it spins out new assets into separate companies that partners deal directly with. The approach not only enables F-star to provide near term returns on investment to its venture capital backers, it also ring fences the value of each asset created.

Indeed, access to experienced staff is one of the main reasons why clusters can prosper. This is especially true for businesses that require specialised skillsets not usually found in an academic environment.

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Dr Danny Zurr, Quark Pharmaceuticals

"For us, with a technology that started as a manufacturing platform, there are not a lot of people who are trained to do manufacturing outside of major biopharmaceutical hubs. Being in a cluster with a deep manufacturing tradition actually is a huge benefit for us otherwise I think it would have been meaningfully hard and challenging for us to be able to grow our manufacturing infrastructure," added Dr Bill Newell, CEO of Sutro Biopharma.

Sutro Biopharma is a private biotech based in South San Francisco, California that started out with a disruptive platform technology that involves cell-free protein synthesis but now has antibody-drug conjugates and immune-oncology focused bispecific antibodies in late preclinical development.

But it is not just the companies that benefit from co-existing in a cluster. Employees have better prospects should a company falter or the whole sector go through a temporary downturn. "It allows people to have security, they can move if something happens to the company. We don't have a particularly high turnover so we don't get people going elsewhere but there are benefits from having people moving between companies and bringing in different experiences," added Dr Dancer.

Sutro's Newell concurred: "I think, when the economy is down and investment dollars have dried up, it is really comforting to be in a cluster. It does not mean it is that much easier to get a new job but there are a whole lot more companies that you can go out to and talk to about getting a job. That is one more virtue in a downturn that clusters can provide a little more security."

The purchase of Alderley Park, near Manchester, UK, by property group Bruntwood in 2014 has created a potential nucleation point for the country's fastest growing biocluster. The site is being redeveloped and has been the subject of large scale investment.

"Working with Bruntwood's science subsidiary - Manchester Science Partnerships we are now re-developing the 400 acre site to establish Alderley Park as a national and international life science destination for small, medium and large CROs and service providers," said Dr Chris Doherty, Alderley Park's Managing Director.

"We have put a lot of

resource into the holistic and financial support around businesses that want to scale up. This ecosystem is about a broad spectrum of support but one of the real keys is having and making available a powerful mentor network - giving growing businesses access to industry professionals with specialist experience, expertise and other contacts that can unlock issues. That kind of resource can really make a difference when you are the CEO trying to raise funds or get over a big hurdle."

He added: "Generally we find that businesses welcome a culture of collaboration and support. Cyprotex, part of the Evotec group, for example, consolidated its UK operations at Alderley Park at the start of 2017. They have have already built relationships with many of the other companies at the site, some ofwhich now outsource business to Cyprotex."

Dr Doherty was responsible for the initiation of the on-site incubator, BioHub, which offers companies access to an investment fund to support business start up and growth. "We now have over 60 new start ups based here, two life science funds on site and there is a big talent pool in the area. These start-ups want to stay and grow."

"We also play a big part in the life science network within the UK, working alongside the Department for International Trade, the BIA and others. In the global context, the distances within the UK are small. We have a major international airport 20 minutes away and London within two hours."

Creating a cluster in the wake of a big pharma exit provides a great opportunity to build a fully functioning biopharma ecosystem from the start. Among the new start-ups are specialist services such as early stage clinical research organisation - Aptus Clinical which has grown from four employees three years ago to 12 now.

"We grew slowly but as the business has grown, the sales have improved and the client base has broadened we have started to bring in additional people. In first two years we operated with four people but in the past six months we have

THE UK'S LARGEST BIOSCIENCE CAMPUS

Alderley Park is an internationally-recognised R&D centre which is now home to 150+ businesses. The site is located in 400 acres of Cheshire parkland. It is 20 minutes from Manchester Airport, which has direct flights to the USA, Europe and China, and is two hours by train from London. As the home of the UK's largest bioscience campus, the site's Mereside campus boasts a wide range of bioscience capabilities, including state-of-the-art chemistry, biology and pathology labs with access to a range of shared scientific services.

The facilities include:

- 2 x High field NMRs – 700MHz and 500MHz
- Biobanking
- Tissue culture suites
- Open access laboratories
- High density fume cupboard chemistry labs

added another eight. The most important thing is access to intellectual talent and our companies are all built on that. For us it is very easy to access talent, due to the high concentration of skilled life science sector based employees in the region," noted Dr Steve McConchie, co-founder and CEO of Aptus Clinical Ltd.

Having access to both experienced talent and a customer base is a major attractant for service businesses. "We are seeing the benefit of that now because being based in Cambridge, Philadelphia and San Diego, which are three major clusters, we are close to a lot of the industry," added Dr John Burt, CEO of Abzena plc.

Abzena was created in 2014, following the 2012 and 2013 acquisitions by of Warwick Effect Polymers and Antitope, respectively, by PolyTherics, a predecessor company founded in 2001. It is a business to business provider of a number of biopharma services and technologies including protein engineering, cell line development, and antibody drug conjugate manufacturing technologies. Now headquartered in Cambridge, UK, the company also has facilities in San Diego, California, following the acquisition of PacificGMP, and in Bristol near Philadelphia, Pennsylvania, following the acquisition of TCRS, both in 2015.

"You need to be building companies of scale because it is in such companies that the staff will get the experience and training to develop as they are more valuable as they move onto smaller companies. That is what is needed – if the cluster only has small start-ups you are not in a position to train your staff – you want to be able to hit the ground running as soon as they walk through the door," added Dr Burt.

Interestingly, while San Francisco, Boston and San Diego are arguably the leading clusters it is worth remembering they have only emerged in the past 25 to 35 years and there is scope for new clusters to grow.

When the team that formed Athersys emerged from Stanford, it initially looked to start the company in the Bay Area. But even as recently as

Mike Ward, Informa; Dr Gil van Bokkelen, Athersys

1995, the Bay Area did not have incubators to help support new businesses.

"We recognised we were starting with a vision of what we wanted to build as a company. We didn't really have any intellectual property, anything tangible to speak of, we just had a group of people including several faculty members and some young entrepreneurial people that had this vision. We realised that we did not have access to any facilities, we didn't have access to any capital, any of the things you need to get started," explained Dr van Bokkelen.

Athersys ended up in Cleveland, Ohio – not one of the first places that comes to mind when thinking about biotech clusters – because one of the scientific cofounders was also a faculty member at Case Western Reserve University. The initial proposal was to do a deal with the university to get access to some of the laboratory facilities.

"The reason why we ended up staying in Cleveland, Ohio was that it gave us all the things that we could not get out here in the Bay Area – there were no incubator facilities at the time – and so the Cleveland Clinic and Case Western Reserve and the university hospitals and some of the other institutions said: If you guys are willing to entertain the notion of staying here we will build the infrastructure you need, the incubator facility that will actually give you a place to get started," he added.

More importantly, living in an emerging cluster has added benefits. "One of the things that I was able to point out to our early institutional investors, which came from all over the world, was that our operating costs having facilities in Cleveland Ohio were about 35% less than if we were located in the Bay Area or Boston or some other location. What that meant was for every $100 million we raised it would go 35% further than if we were spending it in a more expensive hub or location. That resonated with them," noted Dr van Bokkelen.

Dr Laurent Levy, Nanobiotix; Dr John Burt, Abzena plc

For Abzena's Dr Burt, it is less about access to capital and more about the absence of a return and so being in a lower cost environment is likely to boost profitability and enhance a financial backer's return on investment.

"Expectations for building a company of scale with hundreds of employees or a virtual business are going to be very different. For companies with significant number of employees it is about access to staff, are you going to be able to recruit the staff you need without having to pay over the odds? Either to get the staff to relocate or being in a very competitive environment where you might have to pay over the odds for staff with diminishing returns. It is always a challenge to get staff with appropriate skills," he added.

Chris Doherty, Alderley Park

Of course, executives building a business today have to future proof themselves.

"The question is, will, in thirty years' time, we see the same reasons for locating to Boston and San Francisco? I think the sectors that are developing today are different types of businesses from the past. San Diego is interesting because of its genomics focus and if you look at what you need in a big data environment or for different types of manufacturing, they have slightly different needs when it comes to skills and experience," concluded BIA's Steve Bates.

Professor Walter Gunzburg, Austrianova Singapore; Steve Bates, BIA