In Vivo

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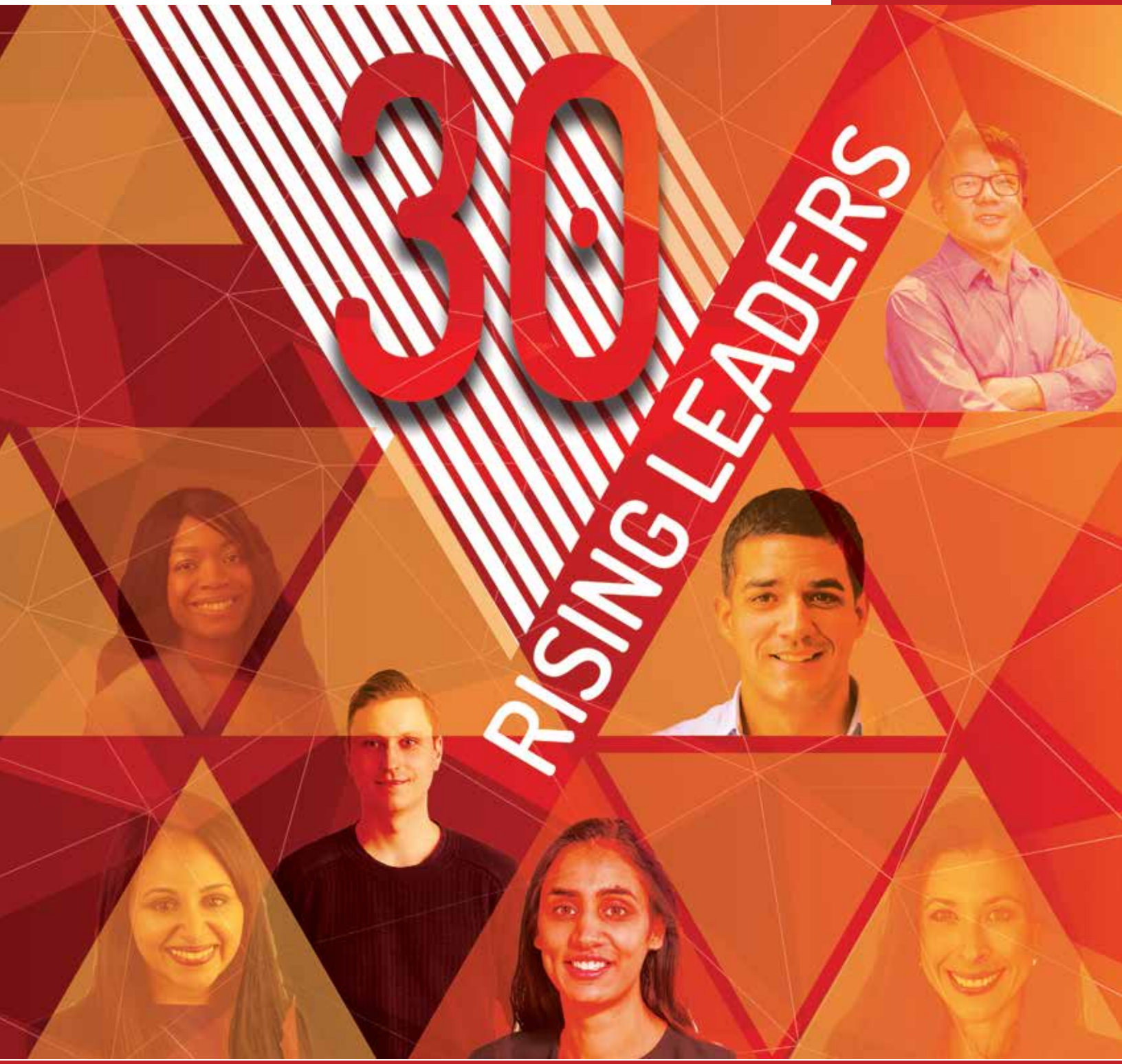

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Informa Pharma Intelligence

May 2020

Special Issue:

30 RISING LEADERS IN THE LIFE SCIENCES

– NICOLA REDFERN

In Vivo
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May 2020

DEPARTMENTS

EXCLUSIVE ONLINE CONTENT

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From The Editor

LUCIE ELLIS

Welcome to the special Leaders edition of *In Vivo*. This month we have focused on leadership qualities and career stories. For the first time, *In Vivo*'s editorial team has created a list of Rising Leaders, with a focus on entrepreneurs and innovators who represent the next wave of creativity in health care.

Also included this month are profile interviews with two of the 30 Rising Leaders: Bayer's Angeli Möller, who is responsible for the big pharma's digital transformation initiatives; and Christophe Bancel, CEO of French medtech innovator TISSIUM.

As part of this focus on leadership and mentoring, Anne Whitaker, CEO of Aerami Therapeutics, and Filippo Petti, CEO of Celyad SA, talk about their career journeys and how companies should be promoting and nurturing the next generation of top talent.

We will be continuing the Rising Leaders series throughout 2020, publishing interviews with each of the spotlighted innovators. Coming up in June, read more about Tim Guilliams, co-founder and CEO of Healx, an artificial intelligence company that has launched a Rare Treatment Accelerator program to establish partnerships with patient groups associated with orphan diseases.

Finally, in this issue you will find our annual Titans of Pharma infographic, which provides a snapshot of the compensation packages granted to the chiefs of the world's biggest pharma companies, along with key performance stats for the businesses they lead.

Join in the discussion online and follow our new LinkedIn Page: linkedin.com/company/in-vivo-pharma

Up-Front

SNAPSHOTS FROM MAY'S CONTENT

"It can be a difficult balance between fighting for a lighthouse case to get on its feet and being able to accept, if there are changes in strategy or issues, I have to be ready to pause or terminate a project."

PAGE 18

– Angeli Möller
VP and head of global data assets, pharma digital transformation and IT at Bayer

"I don't believe it will ever go back to the way it was," Brennan said. "There are too many things that have changed, and health care has progressed more in the last two months than it has in many years."

– Joseph Brennan
Moonshot Health Consulting

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$29.1m

Compensation paid to Daniel O'Day, CEO of Gilead Sciences, in 2019.

HTTPS://BIT.LY/2WU8FZB

CHRISTOPHE BANCEL'S THREE TOP TIPS FOR FELLOW START-UPS WHO ARE IN THE EARLY STAGES OF THEIR JOURNEY

1

In your technology-based company, the technology is key, but think about the team that you need. It is impossible to make it on your own.

2

If you have the good fortune of being able to select your investors, work with people who believe in you, and who are there not just to make money.

3

Enjoy what you do, as you'll be doing it a lot! Don't turn it into a prison.

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Around The Industry

Is Cardiometabolic Ripe For A Revival?

Opportunities in the cardiometabolic field are increasing, following a period of limited investment from larger biopharma players. Still, challenges remain, such as accessing funding at the earlier stages of development.

Investment in the cardiometabolic field has been flat over the past five years. The number of private financing rounds has fallen over that time, but the amounts raised have been steady. Interest in the field seems to be increasing though, with smaller companies finding gaps in the market for new mechanisms in niche indications.

A panel discussion chaired by *In Vivo* during the virtual BIO-Europe Spring conference in March 2020 looked at the rising profile of some cardiometabolic diseases (CMD) and how companies are targeting more niche indications within CMD. R&D companies in CMD have in the past been accused of being too conservative, particularly when it comes to the development of novel modalities, but approaches are evolving.

UNMET NEEDS

It is often suggested that diseases under the CMD umbrella are well served. Diabetes for example, has been manageable for some patients since the introduction of insulin therapy, for which Eli Lilly started large-scale production back in the 1920s. But gaps remain for better therapies that can provide greater benefits for patients and manage progression of the disease, while new treatments are sought for more niche cardiometabolic conditions.

Amanda Chaperot, a partner at the venture capital group Seventure Partners, highlighted diagnostics as a critical unmet need in CMD. She noted that better diagnostics are needed, not just for patient identification and stratification, but also to improve the understanding of how certain diseases progress. "We are looking at big indications and requiring enormous pools of patients to participate [in trials] … finding and identifying the patients that will give the cleanest and most interpretable results is challenging," Chaperot said, adding that this is an issue for trial recruitment and patient identification once a drug is on the market. Seventure has invested in both diagnostics and therapeutics for CMD.

Chaperot cited as an example Seventure's investment in Germany-based Humedics GmbH, a specialist for real-time and mobile measurement of liver function at the bedside of a patient. Humedics' LiMAx breath test-based diagnostic system allows clinicians to quantitatively determine the individual liver function capacity for a patient within minutes. The test enables better risk assessment of patients in liver surgery, allowing for more personalized surgery planning as well as more informed treatment strategies.

Tomas Landh, vice president of innovation sourcing at Novo Nordisk AS, agreed that diagnostics in CMD remained an unmet need. He added that Novo Nordisk was collaborating with others in this space. "One big focus in metabolic disease, in general, is of course new target identification. We are still lacking a good understanding of the biology … for that purpose we are collaborating with a large number of 'biobanks'," he said. Novo Nordisk is particularly focused on the better understanding of non-alcoholic steatohepatitis (NASH) and insulin resistance, which Landh called "a large unmet need leading to other cardiometabolic diseases."

Michel De Baar, executive director for business development and licensing, infectious diseases, vaccines, cardiometabolic, immunology and inflammation at Merck & Co. Inc., agreed that new targets are required to develop drugs that "really help patients." He highlighted NASH and non-alcoholic fatty liver disease (NAFLD) as newer indications that still need more work. "What we currently see is a very good start [in the treatment of NASH and NAFLD] but it is not yet sufficient." De Baar also noted the need for diagnostics to monitor both disease progression and therapeutic activity. He especially highlighted the need for biomarkers that can predict progression, for example the progression of fibrotic stages in NASH. This "holy grail" in NASH would identify which patients to treat to prevent progression of the disease to cirrhosis.

NICHE INDICATIONS

The CMD drug development field's biggest change in recent years has been a push into smaller indications – a trend

that is expected to continue. Niche indications "allow the opportunity to explore more aggressively and on a smaller scale," said Chaperot.

As an example, the disease hyperoxaluria has seen more investment recently. There are several types of hyperoxaluria, a condition that occurs when there is too much oxalate in the urine. This can be caused by genetic disorders, an intestinal disease or from eating too many oxalate-rich foods. Untreated, hyperoxaluria can eventually damage the kidneys.

According to TrialTrove, there are 11 trials ongoing in hyperoxaluria, nine of which started in the past five years. Chaperot pointed out that a number of companies were using new modalities, such as RNAi and microbiome-driven therapies, to treat this disease. Alnylam Pharmaceuticals Inc.'s lumasiran, a synthetic double-stranded siRNA compound, is expected to be approved in the US in the coming weeks for the treatment of primary hyperoxaluria type 1.

These niche indications that are attracting a lot of attention from small and mid-sized companies could also be seen as test cases for new modalities, Chaperot said. They can be used to reach proof of concept before a novel drug candidate is expanded into a larger indication – where much bigger budgets are needed to run studies.

Novo Nordisk does not have active development programs for the smaller or niche indications related to diabetes and obesity – its biggest portfolio areas in CMD – but it does have some discovery efforts ongoing. Nevertheless, Landh noted that Novo Nordisk had recently announced a refreshed biopharma strategy that included more emphasis on rare diseases. However, this trend toward fringe indications in CMD is seen by Landh "as a means for small biotech to take a small step in the arena for diseases like diabetes and obesity." While you can stratify diseases like type 2 diabetes, Landh said that the patient groups were still large even within that dissected patient group. He said there was more opportunity for stratification of patients in obesity.

Niche or orphan developers in CMD still require a line of sight to future development in larger indications. "If one modality can treat various orphan diseases, that would be acceptable, but we are not in the business of orphan drug development," said De Baar. "There are companies better suited to that type of commercialization." Merck is focused on processes and systems rather than indication and therapeutic area thinking, he said. In NASH for example, "there is the metabolic aspect, the inflammation aspect and the fibrotic aspect," he noted. "There is huge learning from inflammation of the liver in NASH, but also carrying that over to neuro or cardiac inflammation, as a general process."

At Novo Nordisk, the company has also shifted to a focus on pathway thinking and holistic biology. "These cardiometabolic syndromes are extremely holistic. If you take care of the liver, you have to think about what is happening to the kidney etc.," Landh said. "We have seen an increase in companies trying to understand this holistic view."

CMD PIPELINE GROWTH

CMD is a broad spectrum. But De Baar highlighted heart failure as a particular disease of interest, where "a lot of different modalities are being developed." He said there was more happening now in heart failure – monoclonal, small molecule and micro RNA approaches being but a few – that would "hopefully remove the conservative label" that is placed on CMD drug developers when it comes to the mechanisms of action that are being explored.

The CMD pipeline overall has seen an increase in players more recently, where the clinical studies used to mainly be led by a few big pharmas. Changes in regulations have made it easier for smaller companies to step into this area.

For example, the US Food and Drug Administration has released draft guidance for type 2 diabetes removing the requirement for a mandatory cardiovascular outcomes trial (CVOT). "This is positive from an investment point of view and for start-ups," Landh said. Phase III programs are still large and long for diabetes therapies, but the potential removal of CVOTs would cut the timeline down for late-stage trials and cut the costs.

Chaperot added that this draft guidance, with clarification, could give a boost to smaller companies and improve the risk profile for investors. Despite the possible regulatory relief, there are still hurdles for companies trying to bring novel diabetes products to market – like the high bar set by established treatments. De Baar also noted that with the level of generic competition already in diabetes and expected in the coming years as leading therapies lose exclusivity, a new treatment for type 2 diabetes would need to have "spectacular" added benefit.

INVESTMENT AND DEAL-MAKING LANDSCAPE

In parallel with regulatory changes potentially spurring more activity in areas like CMD, De Baar commented that investors were looking for promising assets away from the overcrowded oncology field.

However, Chaperot noted that while "there are always companies innovating in any field, it is heavily weighted to oncology; here there is an explosion of companies … that are able to demonstrate proof of concept quite early [in development]. This is something you rarely see in cardiometabolic," she said. "The number of deals in CMD is perhaps flat," Chaperot added, with the exception of liver disease.

The attraction for investment in CMD is in novel modalities and added benefit, Chaperot asserted. "We are seeing some new modalities coming in, such as the microbiome, using bacteria as potential therapeutics, and CMD lends itself to this," she added. When evaluating an investment prospect in CMD, Chaperot said, "We want to see strong preclinical data … we are really looking for safety because these are very likely to be chronically administered therapeutics."

According to data from Biomedtracker, cardiometabolic companies with active development programs raised approximately $8.8bn in private financing in 2019, from 56 transactions.

Landh noted that Novo Nordisk was in "active discussions" with around 25 companies at any time across four key therapy areas which included CMD, with two to three of those being later stage conversations for potential deals. Deal-making in the CMD space takes time, but he noted that Novo Nordisk "could move quickly" when it needed to.

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LUCIE ELLIS

COVID-19-Driven Regulatory Changes Put Telehealth On The Map

Adoption of telehealth services has skyrocketed during the coronavirus outbreak and US experts are expecting the trend to continue post-pandemic, fundamentally transforming health care.

The COVID-19 pandemic has pushed telehealth services to the forefront of health care and many expect its widespread use to continue far beyond the current crisis.

As of late-April, more than 3 million cases of coronavirus had been detected worldwide and the global death toll had passed 200,000, according to the US Centers for Medicare and Medicaid Services (CMS).

The fast-spreading virus has prompted the CMS and Health and Human Services (HHS) Office for Civil Rights to roll back major restrictions to telehealth services to protect health workers, which has led to skyrocketing demand.

BARRIERS TO TELEHEALTH REMOVED

Joseph Brennan, a telehealth consultant at Moonshot Health Consulting, highlighted key actions in the US that had removed barriers previously preventing the widespread use of telehealth. CMS's expansion of Medicare benefits under the 1135 waiver authority and the Coronavirus Preparedness and Response Supplemental Appropriations Act, has provided reimbursement for a variety of clinicians to provide telehealth services for Medicare beneficiaries. Prior to that announcement, Medicare was only allowed to pay clinicians for telehealth services, such as routine visits, under certain circumstances, and from a specific list of providers.

Now seniors can receive mental health counseling, preventive care screenings, physical therapy, occupational therapy and speech therapy, among other health services over the phone, which is a significant expansion. Prior to COVID-19, seniors also had to live in a rural area and travel to a local medical health facility for telehealth services. This can now be done from their own home, a nursing home or any other health facility.

> Brennan and Snyder agree that some telehealth restrictions may be reinstated after the initial pandemic eases, but that cannot stop the tailwind the industry is experiencing.

Another key change is the "enforcement discretion" on the Health Insurance Portability and Accountability Act (HIPAA), which allows patients to use online tools such as FaceTime, Google Hangouts and Skype to visit with doctors by phone or video conference at no additional cost. HIPAA-compliant telehealth platforms can be very expensive and not everyone can access them, Brennan explained. "Where that is really going to have the biggest impact is when you think about those two to three physician practices in rural communities, or the one- or two- doctor office in the urban settings," Brennan said. "They can now use the technology they already have in place to connect with patients."

A further expansion occurred on 16 March with the Drug Enforcement Agency (DEA) allowing DEA-registered practitioners to issue prescriptions for controlled substances to patients via telemedicine without a prior in-person exam. Practitioners must comply with both federal and state laws. Some states prohibit prescribing controlled substances via telemedicine while others allow it with some restrictions, such as only for treating psychiatric disorders or for treating chronic pain.

Brennan said the reimbursement for Medicare beneficiaries, the waiver of HIPAA requirements for technology use and the ability to prescribe controlled substances had really given telehealth momentum. "All of the barriers that we had before all started to fall and the last big one was the removal of the state-licensure requirement," Brennan said.

Before COVID-19, physicians had to be licensed in the state where the patient was located at the time of treatment. CMS also temporarily waived that requirement for Medicare patients, but recommended that physicians check with their state board of medicine or local department of health to ensure they are not violating state laws. As of last week, 48 states had waived the state licensure requirement to some extent.

Brennan said that the removal of the state licensure requirement was significant, because COVID-19 hit some areas more than others. In areas where there is a shortage of health providers, this removal allows health professionals from less impacted areas to provide care to those in need. He gave the example of his wife, an occupational therapist, who can now practice across state lines.

A guidance document, issued by the FDA on 20 March, also reduces the burden on health care systems during the current health crisis by allowing manufacturers of patient-monitoring devices to add or improve remote-monitoring features without first getting regulatory clearance.

On 13 April, CMS updated its guidance document on Medicare reimbursement to help health care providers plan for implementing a telehealth program.

DRAMATIC CHANGE IN THE MARKET

The removal of these barriers has led to a boom in the telehealth industry with several companies reporting unprecedented growth. Among them are US-based digital health companies Tyto Care and Eko Health.

Tyto Care markets a handheld device that allows for the remote examination

of the ears and throat. It can also listen to the heartbeat and lungs, and is used by health professionals and consumers.

April Radford, vice president of telehealth at Ochsner's CareConnect 360, said during a webinar hosted by Tyto Care on 22 April, that it had stepped up its virtual care services in response to the COVID-19 crisis. The system has trained thousands of providers to use video services and saw an explosive use of digital health tools such as TytoCare. Ochsner's home sales of TytoCare devices rose from 1,000 devices sold in 2019 to 2,500-3,000 devices sold in mere weeks since the crisis hit, speaking to the demand by providers and patients to use a virtual tool, Radford said.

In an interview with *In Vivo*'s sister publication *Medtech Insight*, Tyto Care's VP of provider solutions, David Bardan, said the company had seen an "unprecedented demand for their products across the board." *(Also see "Telehealth Sees Skyrocketing Demand Amid Regulatory Expansion, Hopes To Last Beyond COVID-19 Crisis" - Medtech Insight, 23 Mar, 2020.)*

Similarly, Connor Landgraf, CEO and co-founder of Eko Health, which markets a digital stethoscope with an AI-powered cardiac screening platform, said he had noticed "well over a 100% rise in orders" in three weeks – with the widest usage being on the front lines by clinicians who are using the technology to limit the spread of COVID-19.

Both company leaders said the waived restrictions on telehealth were major driving forces behind the sudden explosion of telehealth services and products. Bardan said the loosened restrictions on phones had greatly benefitted the company, because it allowed for asynchronous visits where a patient could collect health data and then forward it to the physician for later review. The elimination of the originating site requirement and ability to provide telehealth services in senior living facilities has led to new partnerships and the expansion of its product. He called the drop in the licensure requirement across state lines a "game changer."

In April, the US Food and Drug Administration has given Dexcom Inc. and Abbott Laboratories permission to bring their continuous glucose monitoring (CGM) systems into hospitals for the duration of the COVID-19 pandemic. Brennan considers this first introduction of CGMs in hospitals a big deal for two reasons. "One it allows that technology [CGM] to be used within the four walls of the hospital. Two, when that patient is discharged, they already know how to use the device, they're already comfortable with it. There is that continuity of care even after they are discharged from the hospital."

Health care workers will be introduced to Dexcom's G6 CGM and Abbott's FreeStyle Libre 14-day system to remotely monitor patients with diabetes, which helps minimize their exposure to COVID-19 patients and preserve the use of personal protective equipment.

CONTINUED PUSH

While it remains uncertain what post-COVID health care will look like, several industry experts expect that the wide adoption of telehealth by health providers and patients will create a fundamental shift in how patients and practitioners communicate.

Glenn Snyder, principal medtech practice leader for Deloitte Consulting LLP, expects social distancing and the inability to interact face-to-face will prompt all companies to rethink the way they do business. He advises companies to re-evaluate all of their processes and identify work that can be done virtually – from monitoring the performance of a product through its entire lifecycle to understanding the patient journey from start to finish, as well as points of engagement. He also advises medtech companies to work closely with hospitals to find solutions together in the future.

Brennan and Snyder agree that some telehealth restrictions may be reinstated after the initial pandemic eases, but that cannot stop the tailwind the industry is experiencing.

"What we've seen over the last four to six weeks is that all the barriers and rules as it relates to health care are being pushed to the side, so that we can bring the care that the patient needs in real time," Brennan said.

Many groups will be pushing to keep these new changes in place and the American Telemedicine Association is expected to lead the charge. Brennan does not expect reimbursement for telehealth to return to how it was before COVID-19, although privacy regulations are likely to be amended to make it easier for people to access telehealth. However, he does anticipate state licensure restrictions to be reinstated eventually.

COVID-19 has led to a huge demand for virtual care and triaging of symptoms. Both Brennan and Snyder expect that triaging patients in the future will continue its course of being digital, virtual and then physical. "Executives of health plans and hospital systems agree that that is the way the industry is going to permanently shift," Snyder said.

He expects patients will do a self-assessment using a mobile application or website with the next level of engagement being a virtual visit with the doctor, and lastly, a physical visit, if needed – for non-emergency cases. Snyder also expects certain services might permanently move out to freestanding centers or separate areas in hospitals to separate people who come in physically healthy from others that may be sick with an infectious disease. This continuation of social distancing within health facilities would help keep health care workers and the public safe from potential infection.

Brennan said the current crisis had led to an explosion of health chatbots and consumers' use of asynchronous care, relying on technology to make a diagnosis rather than talking to a provider. This trend is likely to continue.

More health systems will use chat bots as "health navigators" or first contacts to guide a consumer in the right direction. Examples of these are Ada Health, which uses a vast artificial intelligence-based database to check symptoms, or British company Babylon Health, which offers AI consultation based on personal medical history and live video consultation with a doctor. That may be followed by a video visit, and if needed, a physical visit.

"I don't believe it will ever go back to the way it was," Brennan said. "There are too many things that have changed, and health care has progressed more in the last two months than it has in many years," Brennan said.

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MARION WEBB

2020 TITANS OF PHARMA

CEO	ALBERT BOURLA	ALEX GORSKY	KENNETH FRAZIER	GIOVANNI CAFORIO	RICHARD GONZALEZ
					
COMPANY	PFIZER US	JOHNSON & JOHNSON US	MERCK & CO US	BRISTOL-MYERS SQUIBB US	ABBVIE US
Appointment Date	2019	2012	2011	2015	2013 *(at company inception)*
Previous Position	Chief operating officer, Pfizer	Chair, J&J Medical Devices	President, Merck & Co, Inc	Chief operating officer, Bristol-Myers Squibb	Head of Pharmaceutical Products Group at Abbott Laboratories
Background	Doctor of veterinary medicine, joined Pfizer in the animal health division in 1993 and moved to human health in 2010, occupying various leadership positions.	Began career as sales rep at Janssen Pharmaceutica, J&J. Defected to Novartis as head of pharma North America 2004-2008 before returning to J&J.	Legal: joined Merck in 1992 as general counsel.	Trained as a physician, held a number of roles at BMS since joining as Italy general manager in 2010; previously at Abbott Laboratories.	Spent 30 years at Abbott. Studied biochemistry but did not get degrees despite company filings claiming he had gained bachelor's and master's degrees in biochemistry.
Compensation[1]	$17.9m (-8.3%)[3]	$25.4m (+26.2%)	$27.6m (+32.1%)	$18.8m (-3.2%)	$21.6m (+1.6%)
Median Employee Compensation	$98,972 (+23.7%)	$76,000 (+1.3%)	$95,621 (+4.0%)	$123,365 (+10.0%)	$155,885 (+4.7%)
Compensation Ratio[2]	181:0 (244:1 in 2018)	334:1 (268:1 in 2018)	289:1 (228:1 in 2018)	152:1 (173:1 in 2018)	139:1 (143:1 in 2018)
Company Sales	$51.8bn (-3.4%)	$82.1bn (+0.6%)	$46.8bn (+10.6%)	$26.1bn (+15.5%)	$33.3bn (+1.5%)
Company Net Profit	$16.3bn (+4.6%)	$15.1bn (-1.3%)	$9.8bn (+58.1%)	$3.4bn (-30.6%)	$7.9bn (+38.6%)
Market Cap	$199bn (-12.6%)	$394.6bn (+4.9%)	$209.6bn (+2.0%)	$134.8bn (+75.7%)	$120.9bn (+4.2%)
R&D Head	**Mikael Dolsten**	**Paul Stoffels**	**Roger Perlmutter**	**Thomas Lynch**	**Michael Severino**
Appointment Date	2010	2009	2013	2017	2014
Previous Position	Head of Wyeth R&D, previously at Boehringer Ingelheim and AstraZeneca	Worldwide chairman, Pharmaceuticals, J&J	Head of R&D, Amgen	Chairman & CEO, Massachusetts General Hospital	SVP, global development and corporate chief medical officer, Amgen
Compensation[1]	$9.6m (+35.8%)	$14.1m (+32.8%)	$9.2m (+29.9%)	$8.3m (+17.8%)	$9.5m (+10.5%)

[1] Base salary, bonus & long-term incentives (including equity awards)
[2] Ratio of CEO compensation to median-paid employee 2019
[3] Percentage decrease is relative to 2018 compensation of predecessor, Ian Read
[4] From 1 Mar 2019, taking over from interim CEO Gregg Alton
[5] until 2 Aug 2019. No single CSO/R&D head appointed: Merdad Parsey joined as CMO (covering clinical development and medical affairs) on 1 Nov 2019, receiving compensation of $3,119,553; William Lee is EVP research since 2015 (covering research and preclinical programs)
[6] % increase compared with 2018 full-year pay for David Reese including $300k promotion bonus upon taking the role in July 2018
[7] Olivier Brandicourt retired on 31 Aug 2019, Paul Hudson joined on 1 Sep 2019

A snapshot of the industry's top leaders and the businesses they oversee

DESIGN: GAYLE REMBOLD FURBERT & JEAN MARIE SMITH

OLIVIER BRANDICOURT/PAUL HUDSON[7]	VASANT NARASIMHAN	SEVERIN SCHWAN	EMMA WALMSLEY	PASCAL SORIOT
				
SANOFI	NOVARTIS	ROCHE	GLAXOSMITHKLINE	ASTRAZENECA
FRANCE	SWITZERLAND	SWITZERLAND	UK	UK
2015/2019	**2018**	**2008**	**2017**	**2012**
Hudson: CEO, Novartis Pharmaceuticals	Global head of drug development and chief medical officer, Novartis	CEO Roche Diagnostics	CEO GSK Consumer Healthcare	Chief operating officer, Roche Pharmaceuticals
Hudson: Began career in sales and marketing at GSK and Sanofi-Synthélabo, held senior leadership roles at AstraZeneca.	Medical degree, master's in public policy. Joined Novartis in 2005 after working at McKinsey & Company.	Economics, law degrees, joined Roche as trainee in corporate finance in 1993.	Before joining GSK in 2010 was with L'Oreal for 17 years in marketing and general management.	Formerly CEO of Genentech, doctor of veterinary medicine and MBA holder.
Brandicourt: €7.1m[8] **Hudson:** €4.8m	CHF11.4m[11] (+15.3%)	CHF11.5m (-2.1%)	£8.4m (+42.1%)	£14.3m (+26.2%)
€76,930 (n/a)[9]	n/a	n/a	£68,200 (+4.7%)	£75,000 (+5.6%)
107:1[10]	n/a	**n/a**	**123:1** (90:1 in 2018)	**190:1** (160:1 in 2018)
€36.1bn (+4.6%)	$47.5bn (-8.5%)	**CHF61.5bn** (+8.3%)	**£33.8bn** (+9.7%)	**$24.4bn** (+10.4%)
€2.9bn (-34.1%)	$7.1bn[12] (-43.7%)	**CHF14.1bn** (+29.4%)	**£5.3bn** (+32.5%)	**$1.2bn** (-42.9%)
€106.1bn (+9.3%)	CHF194.4bn (-19.1%)	**CHF274.6bn** (+17.0%)	**£83.0bn** (+7.2%)	**£102.6bn** (+35.4%)
John Reed	**John Tsai**	**n/a**[13]	**Hal Barron**	**Menelas Pangalos**[14]
2018	**2018**	**n/a**	**2018**	**2019**
Global head of Roche Pharma Research & Early Development	Chief medical officer, senior vice president of Global Medical, Amgen	n/a	President, R&D at Calico	Executive vice president of the Innovative Medicines and Early Development Biotech Unit and global business development
n/a	CHF4.7m (-20.8%)	n/a	$6.3m (-3.4%)	n/a

[8] Olivier Brandicourt received €7.3m in 2018
[9] None provided in 2018
[10] Sanofi uses a figure of €8.2m for 2019 CEO compensation in calculating the pay ratio
[11] Vas Narasimhan assumed CEO post from 1 Feb 2018
[12] Net income from continuing operations, excluding $4.6bn gain from discontinued operations (distribution of Alcon to Novartis shareholders)
[13] No single R&D chief
[14] NB his R&D remit does not include oncology
[15] Average of all employees in Germany
[16] 2018 net sales restated to €36.7bn
[17] Kemal Malik's position was terminated at the end of 2019

SOURCES: *Company annual reports and DEF14a filings with the SEC.*

30 Rising Leaders In The Life Sciences

In this first edition of *In Vivo*'s "Rising Leaders" list, the focus is on entrepreneurs and innovators who represent the next wave of creativity in health care. Included are academics, CEOs of small and mid-sized companies, and rising employees in larger biopharma and medtech businesses.

There is no age restriction to being included, but all those named below have been recognized for bringing something new to the game. The list focuses on achievements, talent, creativity and strong leadership qualities. Look out for other features in this Rising Leaders series, including exclusive interviews with innovators and disruptors, alongside insights from more established industry executives.

In Vivo's 2020 Rising Leaders in the life sciences are listed in alphabetical order.

BY LUCIE ELLIS

Ali Afshar, Co-Founder and CEO

Cytera CellWorks

Ali Afshar has a PhD in printable inorganic photovoltaics from Imperial College London. His studies focused on developing a non-toxic, stable, efficient and flexible photovoltaic technology, designed to be cheap and quick to manufacture. He has co-founded two businesses: Vellum Devices and Cytera CellWorks.

Privately held Cytera, which was founded in 2016 by Afshar and Ignacio Willats and raised $1.8m in seed funding, is developing machines that can automate the growth of mammalian cells for biotech companies. Afshar describes himself as "a mixture between a scientist and an engineer, having solved challenges both using physics and chemistry, as well as through building hardware and software ... I see entrepreneurship as a tool to bring together strong teams and affect change."

As well as Cytera, in 2013 Afshar co-founded Vellum Devices, a hardware start-up that aims to recreate a paper-like experience in a new digital device.

Iraj Ali, CEO

Achilles Therapeutics Ltd.

Prior to becoming CEO of Achilles Therapeutics, Iraj Ali was a managing partner at Syncona Investment Management. During his time with the venture capital group, he was a board member for companies including Nightstar Therapeutics PLC (acquired by Biogen Inc. in 2019 for $800m), Blue Earth Diagnostics (sold to Bracco Imaging in 2019 for $450m) and Achilles Therapeutics.

Achilles is developing novel cancer immunotherapies targeting clonal neoantigens: protein markers unique to each individual that are expressed on the surface of every cancer cell. Achilles uses DNA sequencing data from each patient, together with a proprietary bioinformatics platform, to identify clonal neoantigens specific to that patient and enable the development of personalized cell therapies. Ali held the role of CEO at Achilles on an interim basis for some time before joining as the permanent chief executive in 2018.

Ali graduated from the University of Cambridge in 2001 with a PhD in biochemistry. Prior to his time at Syncona and Achilles, he was an associate principal at global management consulting firm McKinsey & Company.

Derk Arts, Founder and CEO

Castor

Derk Arts holds a PhD in decision support from the University of Amsterdam, and while studying epidemiology and medicine at the Vrije Universiteit, he realized there was no efficient application for simple and affordable data management. As founder and CEO of Castor, he developed the first version of its Electronic Data Capture (EDC) tool around 2011, as a cloud solution for capturing medical research data in clinical trials.

Castor's goal is to accelerate medical research by unlocking the potential of every byte of research data, tackling the issue that 85% of medical research data are never re-used. This is usually due to poor data quality, lack of standardization and the data being inaccessible to others.

Castor's EDC platform enables researchers to set up data capture forms, collaborate with colleagues, invite patients through questionnaires and import, export and analyze their data in a secure, compliant cloud environment, all without elaborate training or technical skills.

Christophe Bancel, Co-Founder and CEO

TISSIUM

Ex-Serono and UCB Group executive Christophe Bancel, co-founder and CEO of French medtech innovator TISSIUM, has made a career in various parts of the health care products industry, identifying business opportunities, founding, directing and leading ventures, and planning for contingencies.

TISSIUM is a medical device company developing disruptive surgical solutions for patients, based on a versatile platform of polymers developed at the Massachusetts Institute of Technology. The company launched in 2013 and started its first clinical program in 2016. It obtained its first CE mark in 2017 and started to build its manufacturing capabilities the following year.

Bancel holds a master's degree in molecular biology from the University of Tokyo, a master's degree in engineering technology from Ecole Centrale Paris and a bachelor's degree in engineering physics from Lycée Sainte-Geneviève. Prior to starting TISSIUM, Bancel also founded iBionext, an investment fund and start-up studio based in Paris, France.

Silvia Caballero, Scientist II

Vedanta Biosciences Inc.

At Vedanta Biosciences Inc., Silvia Caballero is striving to identify bacteria that can effectively control three potentially lethal bacterial strains often found in hospitals and nursing homes. Caballero's work led to the identification of a bacterial cocktail derived from human gut flora that can control all three types of bacteria. Vedanta expects to start clinical trials of this drug candidate in 2021.

Alterations of the human microbiome are increasingly recognized as a key factor in autoimmune, metabolic, infectious and many other diseases. Vedanta is developing a novel class of therapies that modulate pathways of interaction between the human microbiome and the host immune system. Vedanta was co-founded by PureTech Health and a group of world-renowned experts in immunology and microbiology.

The company's pipeline also includes a partnered Phase II program in *Clostridium difficile*, partnered Phase I programs in inflammatory bowel disease and cancer immunotherapy, as well as an in-house candidate being developed for food allergies.

Charlotte Casebourne, Co-Founder and CEO

Theolytics

Charlotte Casebourne is co-founder and CEO and co-founder of Theolytics, and a board member of the UK BioIndustry Association (BIA). Prior to this, Casebourne co-founded New Medicine Partners, a strategic consultancy supporting health innovators to translate advanced science and technology into effective practice. She graduated as a University of Cambridge Bioscience Enterprise M.Phil. scholar in 2016.

Founded in 2017, Theolytics is a preclinical-stage biotech using oncolytic viruses to combat cancer. The company is leveraging a convergence of emerging technologies within the viral therapy field – long-read sequencing, sophisticated bioinformatics and advanced genetic engineering – to accelerate discovery and development. It launched with £2.5m ($3.1m) in seed investment from Oxford Sciences Innovation (OSI), a £600m fund focused on commercializing ideas originating from the University of Oxford.

BIA is a trade association for life sciences in the UK, representing over 300 member organizations including bioscience and pharmaceutical companies, academic, research and philanthropic organizations, and service providers to the biosciences sector.

Virginie Buggia-Prevot, Senior Research Scientist

University of Texas MD Anderson Cancer Center

Through her work with the Neurodegeneration Consortium (NDC), Virginie Buggia-Prevot is driving novel research aimed at improving the lives of patients with neurodegenerative diseases. As a translational neurobiologist responsible for managing strategic alliances, she is a key member of MD Anderson's Therapeutics Discovery team – a drug discovery and development engine built within a leading US cancer hospital.

Buggia-Prevot is focused on early-stage target discovery in neurodegenerative conditions, including the neurotoxic effects of cancer treatment, with the goal of bringing novel therapeutics to the clinic.

In her present role, she serves as the liaison for the multiple academic institutions that make up the NDC, and manages research agreements with multiple strategic biopharmaceutical partners.

Additionally, Buggia-Prevot leads the Novel Targets team of the NDC, where she supervises a team of scientists focused on four main areas: neuroprotection, tau, neuroinflammation and ApoE. Her work on target validation data for one neuroprotective small molecule led to the launch of Magnolia Neurosciences, a company focused on the development of a new class of neuroprotective medicines. Additionally, data generated by her team led to a new strategic research agreement with Denali Therapeutics.

Buggia-Prevot completed her bachelor's and master's degrees at the University Joseph Fourier and received her PhD from the University of Nice-Sophia Antipolis.

Ryan Cawood, Founder and CEO

OXGENE

Ryan Cawood founded Oxford Genetics or OXGENE in 2011; it is a specialized contract research organization offering services to support the discovery, development and production of biologics, and gene and cell therapies.

The company believes it can address some of the most important and challenging questions in modern biology within gene therapy, antibody-based therapeutics and CRISPR gene editing. Its technologies enable precise and robust mammalian cell engineering. "Our automation and informatics driven approaches mean we solve the problems that no one else can to advance the delivery of new therapeutics," OXGENE says.

Cawood has been CEO of the company for nine years. He holds a PhD in oncology from the University of Oxford and a bachelor's degree in genetics from the University of Leeds.

César de la Fuente, Presidential Assistant Professor

University of Pennsylvania

César de la Fuente graduated from the University of British Columbia in 2014 with a PhD in microbiology and immunology. He is now a presidential assistant professor at the University of Pennsylvania, where he leads the Machine Biology Group.

The group aims to develop computer-made tools and medicines that will replenish the world's antibiotic arsenal. Current research projects being conducted in the de la Fuente lab include building artificial antibiotics, discovering new antibiotic molecules in biological information, generating technologies for microbiome engineering, developing tools for synthetic neuromicrobiology and engineering living medicines.

Raquel Deering, Associate Director, Immuno-Oncology

Regeneron Pharmaceuticals Inc.

While earning a dual doctorate degree in immunology from Harvard Medical School and biology from the Massachusetts Institute of Technology, Raquel Deering also had the opportunity to study the human genome at the Broad Institute. From there, she did a postdoctoral fellowship at Novartis AG where she studied the use of nucleic acids to develop novel infectious disease and cancer vaccines, and T-cell therapies.

Now, as associate director of immuno-oncology at Regeneron Pharmaceuticals, Deering leads a team of researchers focused on "outsmarting cancer." She is responsible for Regeneron's cancer vaccine development efforts, oncology clinical trial biomarker study design and analysis, and human tumor and immune cell sequencing and functional assay development.

Deering's team uses next-generation sequencing methods to extract information from patient samples that inform the design of more strategic therapies. They are also working to develop next-generation cancer vaccines and combine those vaccines with other immune-modulatory drugs to evaluate the potential benefits.

Deering was previously a consultant at venture capital firm Third Rock Ventures, eventually becoming head scientist at one of Third Rock's portfolio companies, Neon Therapeutics.

Thomas de Vlaam, Founder and CEO

Amylon Therapeutics BV

Thomas de Vlaam is founder and CEO of Amylon Therapeutics. He previously studied with the ambition of becoming a neurosurgeon, but a diagnosis of Scheuermann's disease caused him to forgo a medical career. De Vlaam instead turned to another career that would allow him to help patients – biotech.

He previously worked as head of CNS at ProQR, a company in the Netherlands developing novel drugs to treat rare orphan disorders. An expert in researching new approaches to treating amyloid disorders, de Vlaam started a new company in this space, Amylon Therapeutics.

Amylon, founded in September 2017, is developing RNA modulation technology to target rare genetic disorders of the central nervous system. The biotech has "high ambitions and wants to change the way the world looks at neurological disorders." Its most advanced asset, AT-01, is a first-in-class antisense oligonucleotide being developed for hereditary cerebral hemorrhage with amyloidosis Dutch type (HCHWA-D), also referred to as Katwijk's disease. HCHWA-D is a serious familial disorder characterized by the formation of amyloid-β, a toxic protein, which aggregates in the blood vessels of the brain and causes strokes in middle age.

De Vlaam holds a bachelor's degree in international medicine and global health from the University of Groningen.

Tomas de Wouters, Co-Founder and CEO

PharmaBiome AG

Tomas de Wouters is convinced that microbiome-based therapies will revolutionize medicine. An engineer with a PhD in biology, de Wouters' expertise in the microbiome resulted in the founding of PharmaBiome, where he established a platform technology for product development in the microbiome field.

PharmaBiome, based in Zurich, takes a bottom-up approach by engineering bacterial consortia based on their interactions. Its platform has provided new insights and allowed the development of new strategies for the development and production of multi-strain bacterial networks. The resulting microbiome therapies are function-based and can be tailored to specific indications.

The company is developing treatments for ulcerative colitis, cancer and graft-versus-host disease. There remains a high unmet need in ulcerative colitis that is not addressed by current therapies. "This is where a therapy that addresses the microbiome holds much promise. We have observed very encouraging results in preclinical models and are rapidly advancing toward the clinic," PharmaBiome says.

Cancer immunotherapy and colorectal cancer have been shown to have a direct link to the microbiome, while emerging research also points to an important role of the microbiome in graft-versus-host disease in transplant patients. These therapy areas are in earlier research phases for PharmaBiome.

Jason Foster, CEO and Executive Director

Ori Biotech

Jason Foster is CEO and executive director of Ori Biotech, a London- and Philadelphia-based innovator in cell and gene therapy manufacturing. The company's goal is to put "complex manufacturing challenges in the past." By fully automating and standardizing cell and gene therapy manufacturing in a closed platform, Ori offers developers the opportunity to scale from preclinical process development to commercial scale manufacturing. This addresses one of the biggest challenges still facing cell and gene companies, as more product candidates move through the pipeline.

Foster joined the company as CEO in June 2019. Prior to this role, he was managing director of the consultancy group Health Equity Consulting.

Foster says he helps to "build organizations that maximize the value of their products and services to improve health and achieve significant returns for investors."

Francesco Gatto, Co-Founder and Chief Scientific Officer

Elypta

Francesco Gatto holds a PhD in biomathematics, bioinformatics and computational biology from Chalmers University of Technology. He co-founded Elypta in 2017 with the goal of moving cancer diagnosis and treatment decision-making away from medical imaging. Elypta is focused on liquid biopsies for several types of cancer, in which a set of biomarkers make it possible to detect cancer at an early stage.

The molecular diagnostics start-up wants to improve the survival outlook of cancer patients by developing systems biology-driven biomarkers. He has invented a diagnostic and prognostic test for renal cell carcinoma based on an accurate liquid biopsy, one of the first based on cancer metabolism. Unlike other liquid biopsies that analyze the genetic material that flows through the blood (for example, pieces of DNA from tumor cells), Elypta detects a panel of 19 metabolites called glycosaminoglycans (GAGs). The level of these substances in the blood is an indicator for the detection of various types of cancer.

Tim Guilliams, Founder and CEO

Healx Ltd.

Tim Guilliams is a tech entrepreneur from the Cambridge Cluster, UK. He is passionate about using big data and artificial intelligence to accelerate treatments for rare diseases. Along these lines, Guilliams founded Healx Ltd., a tech company focused on treatment predictions for rare diseases.

Healx has developed the Rare Treatment Accelerator, a partnering program that gives patient groups and Healx the opportunity to work together to quickly discover and develop repurposed treatments for rare diseases using AI. The company has committed a total of $20m for finding new treatments – investing up to the value of $1m in AI and drug discovery resources per project.

"We collaborate with biotech partners to jointly progress new treatments toward the clinic and build each other's rare disease pipelines," Healx says. Its pipeline currently includes nine preclinical partnered programs in rare neurology, oncology and metabolic disorders.

Guilliams is also the co-founder and trustee of the Cambridge Rare Disease Network. He obtained a PhD at the University of Cambridge in the field of biophysics and neuroscience, developing nanobody technology for Parkinson's disease.

Anne Heatherington, Head of Data Science Institute

Takeda Pharmaceutical Co. Ltd.

Anne Heatherington, head of Takeda's Data Science Institute and a member of the R&D senior leadership team, earned her bachelor's degree in pharmacy from Queen's University Belfast, and her doctorate degree in pharmacokinetics from the University of Manchester.

At Takeda, Heatherington is tasked with ensuring the company is creative in how it brings its best people, technology and ideas together to build and infuse digital culture across R&D. This includes growing the company's informatics capabilities in research, pioneering new approaches to modeling and simulation, and promoting learning through artificial intelligence. To achieve these goals, she applies quantitative strategies in all aspects of drug development to drive innovation, efficiency and decision-making across the organization.

Before joining Takeda, Heatherington worked as head of clinical development at Summit Therapeutics PLC. She also spent 13 years at Pfizer Inc., where she held several executive leadership roles, including vice president and head of quantitative clinical sciences.

Patrick Hsu, Assistant Professor

University of California, Berkeley

Patrick Hsu is an assistant professor and faculty fellow at the University of California, Berkeley. His goal is to understand and manipulate the genetic circuits that control brain and immune cell function for the next generation of cell and gene therapies.

The Hsu lab aims to create new molecular technologies for genome and transcriptome engineering, perturb complex cellular processes at scale and develop next-generation gene and cell therapies. Recently, the Hsu lab discovered and developed novel CRISPR systems that expand the gene editing toolbox beyond DNA to RNA.

Hsu's work is supported by the University of California at Berkeley, the NIH Director's Early Independence Award and the National Institute on Aging, among others. He holds a PhD in biochemistry and biological engineering from Harvard University.

Michael R. Hufford, Co-Founder and CEO

Harm Reduction Therapeutics

Michael Hufford has spent 20 years as an entrepreneur, co-founding multiple pharmaceutical, medical device and mobile health companies across a wide range of therapeutic areas. He has raised money from both public and private markets, including VCs and angel investors.

An addiction researcher by training, Hufford received his PhD from the University of Pittsburgh and completed a clinical and research fellowship in the Department of Psychiatry at Harvard Medical School. Now he is co-founder and CEO of Harm Reduction Therapeutics, a non-profit company focused on preventing opioid overdose deaths by making low-price naloxone available over the counter.

"To succeed in getting naloxone into the hands of everyone who might benefit from it, money from non-profit foundations with an interest in public health and reducing the scourge of opioids must be combined with drug development expertise to bring naloxone to every drugstore in America," says Hufford.

Bhavna Hunjan, Head of Corporate Strategy and Development

C4X Discovery Holdings PLC

Bhavna Hunjan holds a master's degree in biochemistry from the University of Oxford. She joined C4X Discovery in 2016 as senior corporate strategy manager before becoming head of corporate strategy and development in 2017. C4X Discovery is an early-stage biotechnology company focused on small molecule drug discovery. At the company, Hunjan is responsible for a number of activities including business strategy, M&A, licensing-focused business development, alliance and partnership deal-making, as well as external strategic communications.

The company's DNA-based target identification platform Taxonomy3 utilizes human genetic data sets to identify novel patient-specific targets, which C4X hopes will lead to greater discovery productivity and increased probability of clinical success. Its near-term goal is to drive returns through early-stage revenue-generating deals with the pharmaceutical industry. Its in-house pipeline is primarily focused on inflammation, neurodegeneration and cancer (including immuno-oncology).

Prior to joining C4X, Hunjan was a senior strategy manager at Cancer Research UK, where she led several strategic projects and worked closely with the scientific community.

Rabia Khan, Chief of Translational Medicine

Sensyne Health PLC

Rabia Khan is chief of translational medicine at Sensyne Health, a health care technology company focused on accelerating the discovery and development of new medicines and improving patient care. This is achieved through the analysis of real-world evidence from large databases of anonymized patient data in collaboration with National Health Service Trusts in the UK.

Sensyne Health is listed on the London Stock Exchange's AIM and is based in the Schrödinger Building in Oxford Science Park.

Before her current role, Khan was vice president of systems medicine at Sensyne Health. She also previously worked for BenevolantAI as an associate director of strategy and planning.

Khan has a PhD in human/medical genetics from McGill University and a master's degree in business administration from Concordia University.

Jinxing Li, Postdoctoral Scholar

Stanford University

"It has always been a part of my approach to think about who outside of my lab might be able to help me think about my work in new ways."

Jinxing Li is a postdoctoral scholar in chemical engineering at Stanford University, who has designed rocket-like micromotors that run on gut fluids and biodegrade after use. He also holds a PhD in nanoengineering and bioengineering from the University of California, San Diego, and a master's degree in microelectronics from Fudan University.

Li has been developing "microrobots" to deliver therapeutics in the body. He has been working on loading antibiotics onto a microrobot for direct delivery to a bacterial infection in the stomach, a method he says has been six times more efficient in killing a bacterial infection than typical antibiotic capsules.

Recently, Li demonstrated that magnetically powered nanomotors cloaked in membranes from platelet cells could navigate through blood to remove toxins and pathogens without being cleared by the immune system.

Angeli Möller, Head of Global Data Assets, Pharma Digital Transformation and IT

Bayer AG

Angeli Möller has a PhD in molecular biology from the University of Edinburgh. She joined Bayer in 2016 as an IT business partner in the clinical sciences business, part of Bayer Pharmaceuticals. She has quickly risen through the ranks at Bayer. In 2018 she became head of IT business partnering research, followed by a promotion in 2020 to vice president and head of global data assets, pharma digital transformation and IT. Before joining Bayer, Möller worked as a data scientist for translational medicine at Thomson Reuters and as a researcher at Cancer Research UK.

Möller's role is two-fold: she co-leads Bayer's artificial intelligence work stream and is responsible for the research digital investment strategy. The scope of the AI work stream includes R&D, medical affairs, pharmacovigilance, commercial and product supply. The projects are run by teams working across Bayer's value chain and are supported by external partnerships.

As well as leading Bayer's digital transformation, Möller is co-founder and executive officer of the non-profit Alliance for Artificial Intelligence in Healthcare (AAIH).

Greg Mullen, CEO

Theragnostics

Greg Mullen was promoted to CEO of Theragnostics in January 2017, having held the position of chief operating officer since 2015.

Theragnostics is developing a complete portfolio of radiopharmaceuticals for the management and treatment of cancer patients: from initial diagnosis, to treatment planning and monitoring, to therapy.

Mullen is passionate about exploring the synergy between therapeutics and diagnostics technologies in drug development. Prior to joining Theragnostics, he was chief scientific officer for molecular imaging at Mediso Medical Imaging Systems. He was also head of vaccine formulation at the US National Institutes of Health, and holds a PhD in chemistry from the University of Kent.

"It has always been a part of my approach to think about who outside of my lab might be able to help me think about my work in new ways."

— Jinxing Li

Carlo Rivis, Board Member and CEO

Computational Life Inc. and InnovationDiscovery

Carlo Rivis holds a bachelor's degree in applied computer science and business management from the Free University of Bozen. He is CEO of San Diego-based InnovationDiscovery, a worldwide database of innovations that aims to promote, diffuse, acquire and sell innovative ideas.

Rivis has founded or co-founded several businesses, including Computational Life. The Delaware-based company's vision is to provide a Digital Avatar Platform (DAP) that simulates the human and animal body through modern mathematical models. Computational Life's software is able to concurrently simulate arterial and venous systems, heart dynamics, microcirculation, pulmonary circulation, cerebrospinal fluid and brain interstitial fluid.

Rivis says he is focused on creating companies that can provide "scalable technology solutions that align technology investments with business goals."

Nevada Sanchez, Co-Founder and Research Scientist

Butterfly Network

Nevada Sanchez is a graduate from the Massachusetts Institute of Technology. He co-founded Butterfly Network in 2011 as a digital health company with a mission to democratize health care, by making medical imaging universally accessible and affordable.

At Butterfly Network, Sanchez leads R&D efforts and contributes to product definition and system architecture. He leads the largest team in the company to design and implement powerful integrated circuits.

Powered by a single silicon chip on a handheld device connected to a smartphone, Butterfly iQ – the company's device – provides a complete diagnostic imaging solution that is less expensive than traditional systems.

Noor Shaker, Founder and CEO

Glamorous AI

Noor Shaker is a Syrian entrepreneur and computer scientist. She founded Glamorous AI to be able to apply innovative artificial intelligence tools to drug discovery. The London, UK-based start-up was incorporated in March 2020.

Previously, Shaker co-founded GTN, where she was CEO from April 2017 to August 2019. She also founded Phenogeneca, a privately held AI company that launched in November 2019. Phenogeneca is focused on the development of AI solutions and consultancy for AI, health care and life sciences businesses.

Shaker holds a PhD in machine learning, effective computing and computer games from the IT University of Copenhagen and a master's degree in artificial intelligence from KU Leuven. She is "passionate about changing the world through technological innovations" and is a "believer in the power of data and machine learning and their revolutionary impact on the future."

Lauri Sippola, Co-Founder and CEO

Kaiku Health

Lauri Sippola holds a master's degree of science, industrial engineering and management from Aalto University. Kaiku Health is a digital therapeutics company with a mission to improve quality of life through health data science. It was founded in 2012 by five software developers, including Sippola.

The company has built an intelligent platform for digital health interventions in cancer care, and its algorithms enable early interventions and personalized patient support. More than 50 European hospitals and clinics use the platform to better monitor patients, reducing manual work and allowing prioritization of clinical actions.

Kaiku Health is backed by Debiopharm Innovation Fund, TESI and Reaktor Ventures, along with other venture capital funds and private investors, and is supported by Business Finland, the Finnish Funding Agency for Innovation.

Jhaymee Tynan, Assistant Vice President of Integration

Atrium Health

"My passion is leading organizations to align strategy with execution and achieve positive results and outcomes."

Jhaymee Tynan is assistant vice president at Atrium Health, one of the largest non-profit health care systems in the US. Previously known as Carolinas HealthCare System, Atrium Health provides a full spectrum of health care and wellness programs throughout the Southeast region. Its diverse network of care locations includes academic medical centers, hospitals, freestanding emergency departments, physician practices, surgical and rehabilitation centers, home health agencies, nursing homes and behavioral health centers, as well as hospice and palliative care services. The group works to enhance the overall health and well-being of its communities through high-quality patient care, education and research programs, as well as collaborative partnerships and initiatives.

Tynan is also leading the way when it comes to advancing women of color in the health care industry. She has set a goal of sponsoring 100 women of color in health care by 2030. She hopes this sponsoring will help to advance the careers of the women she supports. Actions will include nominating women of color for industry awards to gain visibility, serving as an advocate for the next executive role to strengthen the talent pipeline, and celebrating the achievements of women of color in public and in private. "It means utilizing my network to make warm introductions to women of color that are making an impact in health care. Sponsorship means taking action and holding myself accountable for the results," she said in a February 2020 *Forbes* article.

Prior to joining Atrium, Tynan was manager of business model transformation at Deloitte. She holds an MBA in health care from Emory University, a master's degree in project management from George Washington University and a bachelor's degree in finance, insurance and business law from Virginia Tech.

Thomas Ybert, Co-Founder and CEO

DNA Script

Thomas Ybert co-founded DNA Script in 2014 to tackle one of the major challenges in the life sciences: being able to write DNA as fast and as simply as reading it. DNA Script's core R&D efforts have produced innovations in enzyme engineering, surface and nucleotide chemistries and instrumentation. The company has developed SYNTAX, a benchtop DNA printer powered by enzymatic technology.

In 2020, the SYNTAX prototype will be tested by public and private research teams in molecular biology and DNA Script plans to recruit 60 or more staff by the end of the year.

Ybert previously worked at Amyris Inc. and Sanofi. He has a PhD in biotechnology from Ecole Polytechnique, Paris.

Laura Soucek, Founder and CEO

Peptomyc

Founded in 2014, Peptomyc is a company focused on the development of a new generation of cell penetrating peptides (CPPs) targeting the Myc oncoprotein for cancer treatment. Laura Soucek is a leading figure in the Myc field and has pioneered studies on Myc inhibition since designing Omomyc when she was an undergraduate student.

Omomyc is a dominant-negative Myc inhibitor that shows therapeutic promise in a variety of cancer types. Peptomyc aims to further develop the Omomyc peptide – and improved variants – into clinically viable therapeutics for the treatment of cancer.

Since early 2011, Soucek has also headed the Mouse Models of Cancer Therapies Group at the Vall d'Hebron Institute of Oncology (VHIO), Barcelona, Spain. Her research at VHIO has been recognized through several national research awards and grants. In addition, she holds a PhD in genetics and molecular biology from Sapienza Università di Roma.

What Does AI Excellence Look Like In Big Pharma?

Angeli Möller, spotlighted by *In Vivo* as a 2020 Rising Leader, has quickly moved up the ranks at Bayer and is now spearheading one of its key initiatives to bring artificial intelligence and machine learning technologies into the pharma business.

BY LUCIE ELLIS

Angeli Möller is responsible for promoting the digital transformation of Bayer's pharmacuetical business.

The artificial intelligence workstream is part of Bayer's digital transformation core program. It is using "lighthouse cases" as stretch goals for the pharma division, to understand what the most impactful ways are to use artificial intelligence.

Möller is also co-founder of the Alliance for Artificial Intelligence in Healthcare, a not-for-profit that looks at the creation of policies, educational material and technical standards for the best practice use of AI in health care.

Angeli Möller joined Bayer AG in 2016 as an IT business partner in the clinical sciences unit, part of Bayer Pharmaceuticals. She has quickly progressed at the company. In 2018 she became head of IT business partnering research, followed by a promotion this year to vice president and head of global data assets, pharma digital transformation and IT.

Before joining Bayer, Möller, who has a PhD in molecular biology from the University of Edinburgh, worked as a data scientist for translational medicine at Thomson Reuters and as a researcher at Cancer Research UK.

Möller is "good at having lots of jobs to do." Her role at Bayer is two-fold: she co-leads Bayer's artificial intelligence (AI) workstream and is responsible for the company's research digital investment strategy. The scope of the AI workstream covers R&D, medical affairs, pharmacovigilance, commercial and product supply. Projects are run by teams working across Bayer's value chain and are supported by external partnerships. As well as leading Bayer's digital transformation, Möller is co-founder and executive officer of the non-profit organization, the Alliance for Artificial Intelligence in Healthcare (AAIH).

Global data assets at Bayer is a new "acceleration function" created for the pharma division to hasten its digital transformation. As head of this initiative, Möller leads three groups:

- the Science At Scale team, which includes platforms for machine learning, computer vision and advanced analytics for the whole pharma division;
- Global Data Assets, representing the collection, support and maintenance of Bayer's most valuable global data assets; and
- the Data Excellence Team, which is responsible for data governance, data stewardship and the application of the FAIR principles to ensure that data are findable, accessible, interoperable and reusable. This group focuses on the educational and governance

guidelines that are needed to gain full value from data.

The artificial intelligence workstream is part of Bayer's digital transformation core program. "We use 'lighthouse cases' from this workstream as stretch goals for the pharma division, to understand what the most impactful ways are to use artificial intelligence," she told *In Vivo* in an exclusive interview.

Möller has "always had this curiosity to go into science." She started her career as a molecular biologist, but with the global collaborations and automation seen in the lab, she very quickly moved into being a data scientist and informatician. "By the time I entered my post doc, I was already leading parts of consortia with 15 different groups worldwide to model the human chemical synapse, and that involved a high amount of data science and informatics." After her daughter was born, to balance having a small child and a research career, Möller became a full-time data scientist.

At that time, she joined Thompson Reuters as an external analyst for several pharmaceutical companies. "My two biggest clients were Roche and Bayer. After working on a Bayer project for nine months they offered me an internal position to be responsible for the digital transformation strategy for pharma co-metrics – that quickly expanded."

With having more of a leadership role at Bayer, and having been promoted most recently in January, Möller said one of the challenges is being able to demonstrate the impact she has on the business from a role that is not as hands-on. **"**For me, one of the challenges is how do I scale up my impact. If you are hands on developing an algorithm with a particular prediction, then it is very easy to point to it and show the influence it has had."

Her current roles at Bayer are more focused on "who should we be hiring, what is our talent strategy, what are the lighthouse cases we want to run, how do we choose our investment strategies for these?" To manage this change, "you have to be clear with yourself and with the executive team about what the true points of impact are throughout the year. While I won't be working hands-on all the time, I have a lot of areas of responsibility."

With her latest promotion, Möller's role has progressed to focusing on coaching, talent development and strategic frameworks. "It is about setting up the right space for other people to be hands-on and deliver on the project," she said. Having been in the data science and informatics fields for a long time, Möller feels she is able to articulate the needs of data scientists, particularly new graduates, as they enter a corporate environment. "I can relay what they need in terms of working culture and working environment to allow them to bring their best performance to the table."

> *"In product supply Bayer is developing AI tools to predict disruption. "We can proactively prevent disruption that could be caused, for instance, by defects in our machinery or by fluctuations in staff availability."*
>
> ANGELI MÖLLER

What Are 'Lighthouse Projects'?

The initiative for lighthouse projects at Bayer started in January 2019 and is part of a larger digital transformation program. "We run a series of AI lighthouse cases and each one is a stretch goal for the company, pushing the boundaries of what we are able to do," Möller explained. Usually the goal of these projects is to increase revenue streams, but they can also be targeted toward improving operational efficiency in the pharma division.

One example is the development of technology to identify patients with rare mutations to ensure the right medications are reaching them. "Currently, you need to do sequencing from samples from that patient. If they are very sick this sequencing can be quite a high burden for a patient who might already be having to give a lot of different samples," Möller noted. Also, the sequencing might be prohibitively expensive, meaning they might not be tested at all. "We are working on an approach using computer vision, a form of AI, to look at pathology images and then by analyzing the pathology images at high scale identify which patients are likely to have which mutations," she said. This approach is less invasive for the patient.

As another example, Bayer has a lighthouse case in trial for product supply. The company is using a machine learning approach to optimize its planning process for production. "We can anticipate and predict where we expect to see disruption in our production facilities. We can proactively prevent disruption that could be caused, for instance, by defects in our machinery or by fluctuations in staff availability because we can proactively predict when these things are likely to happen," Möller said.

Bayer has 10 lighthouse projects running across the pharma division, each targeting

different aspects of the industry. However, not all of these are expected to succeed. "When we put forward our proposal for funding to the executive committee, we said that we expected 50% of the projects to fail and that we would be constantly starting new lighthouse cases and embedding the lessons learned." This is how the group expects to grow its core capabilities.

As these are far-reaching goals for the company, changing the way it works in certain areas, Möller said it was inevitable that some of the cases would fail. "It can be a difficult balance between fighting for a lighthouse case to get on its feet and overcome possible challenges, and being able to accept that if there are changes in strategy or issues I have to be ready to say if a case should be paused or terminated."

The first step for assessing new AI technologies is a technical feasibility assessment followed by a business case evaluation. "We are looking at technologies that can impact the pharma P&L or change a time frame. If we reposition something within the division, the lighthouse cases must reflect these changes. We work closely with the pharma strategy team," Möller said.

Technology In A Time Of Coronavirus

At Bayer today, an algorithm is developed and trained on historical data. "We can use the technology to make predictions for the future based on what it knows about the past," Möller explained. However, when there is a new factor in play, like a virus that behaves differently from anything seen before, there are other options for using machine reading and learning technologies to advise decision-making. "You have the option to look at similar situations in historical data sets or you can look at collecting data to be able to quickly respond to sudden change."

Möller said it was important, in times like the current coronavirus global outbreak, to think about how to collect the right data now that would advise responses to events in the near-term and in the future.

Bayer has two key focus areas for its AI initiatives in 2020. "The first is how we can better leverage partnerships," she said. Bayer has a lot of external partnerships, for example with Genzyme and the Broad Institute. For 2020 it is looking at how to accelerate those partnerships and how to most efficiently co-create with its partners. "Data science is transforming the world and it is certainly transforming our industry; if we just tried through an internal training and hiring strategy to become major players in digital transformation we would most definitely fail," Möller said. As well as conducting retraining and hiring, Bayer has set up partnerships to build shared know-how with partners that can move faster. Möller points out "for instance, the Broad Institute, which uses the Terra platform that is also used by Verily."

Non-Profit Activities

Möller is co-founder of the Alliance for Artificial Intelligence in Healthcare (AAIH), a not-for-profit that looks at the creation of policies, educational material and technical standards for the best practice use of AI in health care. The organization includes a lot of start-ups but also some larger pharma companies, such as Johnson & Johnson and Bayer, and some big tech companies like GE Healthcare and Amazon.

"Bayer is very active in the technical standards committee. This is to make sure that we are creating interoperable technology standards and that we are able to have a shared understanding of what excellence looks like," Möller highlighted. Quality of the data and ensuring high-quality solutions for patients are key areas for the AAIH.

Bayer is also active in educational aspects of AI. Health care professionals are seeing more predictive algorithms in their day-to-day jobs. For example, radiologists are encountering a lot of predictive, machine learning tools in their workplace. "Health care professionals want to understand these tools better and be able to make the best choices for their patients. We see a lot of requests for training materials and workshops from the health care industry," Möller said. The group also recieves requests from policy makers for educational resources to help them better understand how to ensure quality, and for more information around how to use software to promote at-home treatments, and therefore cut costs.

Planning for the Alliance for Artificial Intelligence in Healthcare started in 2018 but it was officially launched in January 2019 at the annual J.P. Morgan Healthcare Conference. Through education and pilot projects, Möller wants the AAIH to "drive home low-cost care."

Some resistance remains around the wider use of AI and machine learning platforms for the delivery of health care. Just because something can be done with technology, should it be done? Möller said this is a valid concern, but the solution is about finding the right balance. "My background is in molecular biology. Earlier in my career we had very similar discussions about genetic engineering and stem cell research." She said that with any new technology, the best approach is to focus on the unmet need. "While I am excited by new technology, I focus on that high unmet need. You can have a measurable impact on the lives of patients."

Advice And Aspirations

Möller said the best advice she has received is to always ask the question: "What does good look like and what does excellent look like? "

"This question pushes you to think past what is the best Bayer can do now, or what is the best the pharma industry can do now, and instead think about what a full digital transformation of this space would look like. I ask myself this regularly when setting goals for my team, for the pharma division and for myself," she said.

Looking ahead at her career, Möller expects to continue working in the not-for-profit sector as well as big pharma, through the Alliance for Artificial Intelligence in Healthcare and the Pistoia Alliance. Pistoia is a global, not-for-profit alliance of life sciences companies, vendors, publishers and academic groups that are working together to lower barriers to innovation in R&D. "A key focus area for me is how you bring the right treatment to patients at low cost and how technology can contribute to this," Möller said.

At the same time, she sees growth for her career in the scaling up and industrialization of AI with big pharma. "What we have achieved in the last year and a half at Bayer are some impactful lighthouse cases, but what I want to focus on in the next three years is maturing these into enterprise-level transformations. Not just one-off cases, but technologies that are a part of daily life in the company."

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Nurturing The Next Generation Of Top Talent

Coaching and mentoring are important tools for the leaders of today to be able to foster the next generation of talent in the biopharma sector. While the routes into industry have not changed dramatically – most leaders hold a master's degree and/or PhD – the expectations of rising leaders have altered and the industry itself has become more collaborative.

BY LUCIE ELLIS

Anne Whitaker, CEO of Aerami Therapeutics, and Filippo Petti, CEO of Celyad SA, discuss their career journeys and provide pearls of wisdom for rising leaders in the life sciences.

They outline what the key skills are for emerging biopharma CEOs – and how these leadership assets have evolved.

Today's leaders must be flexible, they need to have a diverse CV with experience in different functions and they have to be able to reward risk.

In exclusive interviews, Anne Whitaker, CEO of Aerami Therapeutics, who is passionate about mentoring and is active in promoting higher education in STEM sectors, and Filippo Petti, CEO of Celyad SA, who recently shifted from a finance to chief executive role, talk to *In Vivo* about their career journeys, promoting top talent and aspirations for the future.

Petti started his career, after studying biochemistry and pharmaceutical sciences at degree level, with an internship at OSI Pharmaceuticals LLC, based in New York. "I had a family member who was diagnosed with cancer, someone who was very close to me, and that pushed me down the path of really wanting to make an impact on cancer treatments," he recalled. Petti's first project at OSI was working on a drug candidate that went on to become the non-small cell lung cancer treatment Tarceva (erlotinib) – one of the earlier epidermal growth factor receptor (EGFR) inhibitors to reach the market, which was co-commercialized between OSI and Roche.

Some of Petti's success at OSI was due to good fortune and good timing. The EGFR inhibitor project that launched his career was a compound returned to the company not long after Petti joined the business. Erlotinib had been licenced by Pfizer Inc. as part of a broader deal, but the big pharma returned the compound to OSI when it was in Phase I due to pipeline reorganization related to an acquisition. Pfizer acquired another EGFR compound in clinical development. "Pfizer was able to divest it [erlotinib] back to OSI very quickly and this changed the trajectory of the company to becoming a leader in oncological discovery and development," Petti said, adding that at the time, around 2000, "EGFR inhibitors were the hottest things" in development for cancer.

This kind of flexibility, which allowed OSI to change course quickly, is essential for biotech companies. "Flexibility is really inherent for success in the biotech sec-

tor. Being able to be nimble, changing focus, reading the key leads at the time and really predicting where the field is going, these are the greatest assets for a biotech organization as you try to build toward success."

Building Your Story

After his time at OSI, Petti moved through many other roles. He went from being a scientist to doing business development, then into equity research for biotech companies on Wall Street, before becoming a health care investment banker. Now he has come full circle back into biopharma, first as chief financial officer and then CEO of Celyad.

Belgium-headquartered Celyad is developing chimeric antigen receptor T cell (CAR-T) therapies aimed at treating severe diseases with poor prognoses such as cancer. It has two autologous therapies and one allogeneic candidate in Phase I trials, as well as other programs further back in the pipeline.

When it comes to building a team, Petti said that just as he had "traversed through my career," he wanted to employ people willing to get out of their comfort zones. "I was a scientist and then moved into the field of finance and business development." He said it was about "adding to the story, adding to the knowledge base you have."

Petti's advice to those thinking about the next step in their careers is to go for it. "Sometimes I regret not making the jump to Wall Street sooner, or at least going toward that financial, business development side a little bit sooner. Follow your gut feeling and don't be afraid to make the jump," he said.

Petti's aspiration is to "put Celyad on the map."

Working Up To The CEO Spot

Anne Whitaker, CEO of Aerami Therapeutics, started her career in pharma as a sales representative, having graduated college with a degree in industrial chemistry. After a short time in the lab, Whitaker found that she was better suited to a role with more human interaction. "My lab supervisor was afraid I was going to start talking to my beakers," she joked in an interview with *In Vivo*. "Although I'm an introvert, I really get my energy from people. I made the switch to pharmaceutical sales and worked my way up, moving in and out of marketing positions, all the way up to business unit head at GlaxoSmithKline." Whitaker held several business unit head roles at GSK, the last as head of the company's cardiovascular, metabolic and neurology business unit – where she oversaw around 3,500 people and $5bn in revenues.

"It is about "adding to the story and adding to the knowledge base you have."

Filippo Petti

While at GSK, Whitaker moved from the US to London, UK, to work closely with GSK's senior management team, including then-CEO Sir Andrew Witty. "[Witty] was really implementing culture change at GSK," Whitaker explained. When first in the UK, Whitaker was head of leadership and organization at GSK. "The position was transformative for me for a couple of reasons: I had the opportunity to really look at the entire business globally – I had 84 people around the world that reported to me – and I got to see every day what Andrew Witty's schedule looked like and what he was spending his time on. It was the first time I really had a view of the CEO job and what it entailed." This opportunity inspired Whitaker to pursue being a biopharma CEO as a career goal.

After moving back to the US, Whitaker eventually left GSK to join another European big pharma, France's Sanofi. She joined the company as CEO for the US and head of North America. In this role she led eight different business units worth around $12bn in revenues, and oversaw a staff of approximately 18,000. It was a "big change in scope and responsibility," she recalled.

It was a changing time at Sanofi, which had recently acquired Genzyme and, a few years prior to her joining the business, signed its major research agreement with Regeneron – a deal that has produced several leading brands for the two companies.

After three years, Whitaker took her first company CEO role, leading the public firm Synta Pharmaceuticals. Unfortunately, Synta – an oncology-focused drug developer – suffered a big setback when its leading program failed in Phase III. After this trickier time, Whitaker moved to Bausch Health to lead its branded pharma business, which included recently acquired businesses like Salix and

Dendreon. "That was a good experience, an interesting experience; it was quite a volatile time at Bausch Health," Whitaker said. *(Also see "Bausch Health Rises From Valeant's Simmering Ashes" - Scrip, 8 May, 2018.)*

Whitaker's path to chief executive of Aerami Therapeutics took a few more turns, one of which saw her set up a company from scratch based on technology from the University of North Carolina. She also added several board positions to her resume and is still on the boards of Mallinckrodt and Vectura today. She took on the role of Aerami CEO in October 2018, tasked with the job of expanding the company's strategy and diversifying the business.

The Skills For Success

"What is important for leaders and people aspiring to senior roles is that they do work in a variety of different functions that are critical for the business," said Whitaker. "If someone starts in a scientific area, I think it is important for them to have experiences outside of R&D, whether that's in business strategy, in commercial or elsewhere."

Petti notes that being a CEO means broadening your thinking. It is about "strategically thinking about how the pieces of an organization fit together for the greatest success." He added that daily the job is about "quickly making decisions and leveraging the management team. It's not all on me, it's also about building the support staff, having confidence and trust in my executive team and the board."

Looking at the role of a biopharma CEO today, Petti said the "profile or phenotype has certainly changed." Petti himself has followed an unusual route into the job and does not have an MD or PhD. "Along the way I've been able to gather a perspective and a lens into the industry that has allowed me to really color many aspects of this role."

He said the sheer number of biotech companies today, and the pace of scientific achievement, has revealed opportunities for aspiring leaders. "Even if you dial the clock back just 10 years, someone such as me probably wouldn't have had as many opportunities to become a CEO [in this industry]." While there are many more companies in terms of volume of biotech business, there is a shift occurring in the skills that are desired in a would-be CEO. "Folks are coming from different angles to be able to help lead an organization such as Celyad, and other biotech companies of our size and shape. As I was going through the ranks you could typically say I wasn't a traditional health care investment banker given my background in science and equity research, and I think that's probably the case as well as a CEO."

"Being able to build the right team is always going to be critical. CEOs must be able to assemble a high-performing team that fills the necessary skills for the business."

ANNE WHITAKER

Petti believes that having a different background means leaders like him bring to companies an "edge" and a fresh point of view.

Whitaker's advice to rising leaders in biopharma is to be "authentic." She explained, "the best advice I received was to really show up fully, to be comfortable in my own skin." Whitaker said this advice, to be authentic, was transformational as she realized that leaders do not know it all. They have to build strong teams to have collective success. "Being able to build the right team is always going to be critical. CEOs must be able to assemble a high-performing team that fills the necessary skills for the business. Leaders today, in pharma in particular, have to be driving innovation. We have learned so much with regard to the achievements in human genome [research] and as far as manufacturing complex products, be it small molecules or biologics. It's a matter now of visionary leaders being able to really define and drive for innovation to bring new therapies to market."

Whitaker added that CEOs needed to think holistically about their organizations and to do this requires experience with system thinking. "This connects to the point that I made that people need a variety of different experiences in functional areas before rising to the senior level. We cannot have silos in businesses." To be successful, biopharma companies need to be connected across the various functions, which can be achieved via project teams that include members from different areas of a business, for example. "CEOs really have to have vision and drive to build an organization in this way."

Leaders today have to be able to recognize the different expectations of employees from different generations. "They

need to build performance systems that will motivate different employees, and this will help them to retain key talent across different generations," Whitaker said. She noted, for example, that the youngest generation in the workforce, those in their twenties, expects to see incentives for short-term achievements. While the previous generation was happy working toward longer-term goals and rewards.

Finally, Whitaker highlighted that leaders must be able to reward risk. "Leaders need to create a culture where it's OK to fail because that's the only way we are going to be able to innovate. The goal is an agile workforce that is willing to push for innovation, fail quickly and learn fast. Each of those experiences is really important."

Mentoring And Diversity

Whitaker has been involved in mentoring programs since joining GSK in 2003, and praises one of her early mentors, Lou McCloud: "She had quite an impact on me." Whitaker highlighted that McCloud was one of the only female sales reps at GSK at the time, having come into the company with a background in nursing. "I'm very fortunate to have had Lou as a mentor because she shaped my leadership style. She helped me to be comfortable in my own skin, to be a more authentic female leader and to demonstrate what is quite natural for me – which is connecting with people, being empathetic and using my intuition." After her own experience, Whitaker was committed to mentoring other women in pharma.

Whitaker is also a member of the board for the science, technology, engineering and mathematics (STEM) focused high school, North Carolina School of Maths and Science. She was surprised on joining the board that while 50-60% of students at the junior and senior school are female, by the time they get into the workforce only 25% pursue STEM careers. Often, "young females move away from STEM careers because they don't see other female leaders in those roles," Whitaker said. "I started getting involved with mentoring individual high-potential young female scientists and have really stayed active with that in the North Carolina area."

Aerami's CEO believes the issue of diversity at the top in biopharma persists in part because there are no clear paths for aspiring leaders. "You want to look up and see that there is a pathway, that other people have gone there. Also, the people who are hiring for those top positions are still largely males who are looking for people like them. That is at the board level and at the CEO level. There needs to be more work done to get more women on boards." She added, "it is often these subtle, micro biases that people don't recognize they have. There needs to be more emphasis across the board for people to become aware of these issues."

Always Aspiring

Whitaker expects Aerami to move more than one of its product candidates into the clinic over the next 18 months, an opportunity for her to grow the business into a full-scale biopharmaceutical company. She will be looking to hire the right team and "have the experience of coaching and shaping future leaders that I hope will have impact in the industry curve in many years to come."

Looking to the future, Petti said he would not want to be working in any other industry and that biopharma would be "the most exciting place" for the next century. "The biotech industry will just continue to drive health benefit, not only for current patients but future patients too, and it will build a better, healthier kind of environment for the world."

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Comments:
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Stick To The Plan – But Be Ready To Change

CHRISTOPHE BANCEL

Know your strengths, surround yourself with experts and ensure your solution "does what it says on the tin." These are among the guiding principles of Christophe Bancel, co-founder of France's biopolymer innovator TISSIUM, a health care start-up on the cusp of commercialization.

BY ASHLEY YEO

If leadership is many things, one important element is knowing what you do not know and having the ability to assemble the experts who can give the necessary guidance on innovation.

It is not simply focusing on the immediate project at hand, but also about working on below-the-radar innovations, bringing investors along on the journey, and being keenly aware of timings.

And as TISSIUM's CEO Christophe Bancel demonstrates, it is knowing how far to take products in-house and when to opt for partnerships.

Without a vision, unmet clinical needs do not get turned into products. But without the right support for original concepts that can be turned into solutions, the vision often dies before it has had time to take root. Importantly, before any of that happens, the unmet need must be defined.

That was the thought process that led Christophe Bancel and colleague Jeff Karp, from the Brigham and Women's Hospital, to form TISSIUM (formerly Gecko Biomedical) in 2013. Their remit was to tackle one of the biggest medical challenges since the inception of surgical procedures: the reconstruction of damaged tissue and the restoration of natural function.

The technology they used was created jointly by Karp and Massachusetts Institute of Technology (MIT) professor, Robert Langer. TISSIUM has developed the technology to the point where, in April 2020, the company received CE marking for its first sterile biodegradable sealant in a pre-filled syringe for use in vascular reconstruction. Before this, it gained a CE marking in 2017 for the vascular sealant, Setalium.

In the field of tissue reconstruction, the challenge is to ensure the tissue can live inside the body in an effective way. That has yet to happen, in Bancel's view. The technologies designed and invented to date have largely been based on repair techniques that work on inert or on non-biological materials; they are nailed, sewn or stapled, i.e. methods used to fix non-living materials.

"Apply those to the living body, and they will not react the same. It is a living environment," said Bancel. With Karp and the company's chief innovation officer Maria Pereira, Bancel decided that, to repair tissue effectively, the living environment must be taken into account. That prompted the company to develop its biomorphic polymer.

"This is why we believe our materials are better designed for certain procedures," Bancel told *In Vivo*. Sutures and staples are not about to disappear, although in certain cases, like peripheral nerve repair, sutures can be detrimental, inducing inflammation or neuroma, he said. For this usage, TISSIUM is designing a connector into which the nerve can be slid, thereby protecting it. "We fix it to the nerve with our own adhesive, and get around the damage and limitations of standard suture repair."

The Market

There are many potential applications for the company's polymer. This has made for complexities when explaining the solution to different stakeholders, said Bancel. Four applications are underway, each with its own sub-market:

- the first, in the vascular/cardiovascular space (Setalium Vascular Sealant), addresses a $300m market;
- the second application, for peripheral never repair, is in a $1.2-1.3bn market;
- the third market that will be addressed, hernia mesh repair, is valued at $2bn; and
- the fourth – but not to be the last – is in the ENT submarket of chronic sinusitis, a $3.95bn market.

These four markets represent a target opportunity of some $7bn. TISSIUM is expected to follow its CE marking for Setalium some 2.5 years ago with the filing later this year for an IDE with the US FDA.

Need For User Case

Getting momentum behind the concept and growing users' awareness called for a user case. This became the basis for building the company. The user case was selected to be around vascular/cardiovascular applications. This established with stakeholders that TISSIUM's core technology is the polymer. But surgeons buy final surgical solutions, not substances. "We had to demonstrate that our polymer from MIT could be developed for clinical use," said Bancel. "We also had to show that it could be assembled into a product with the right accessories."

The challenges at the beginning were that the polymer was a completely new concept, and it was targeting the market share of established technologies. There was also lot of uncertainty on the regulatory and clinical fronts, Bancel admitted. "Taken altogether, that was too much uncertainty at once, so we said we should balance the risk, and pick an indication where we knew that, if we were successful, we would have an approved product."

It was not the biggest market, but having settled on the cardiovascular indication as the user case, TISSIUM saw that it could use all the work that was derisked at this first stage of product development and redeploy it very quickly for second, third and fourth products, etc.

So while it had taken four to five years to bring one product to market readiness, the ensuing 18 months yielded another two or three. "It was a snowball effect, and to have that, you need to invest from the get-go in your platform," said Bancel. "We were very fortunate to have investors who believed in our strategy and were able to give us the financial resources and the time," he said, alluding to a key entrepreneurial quality common in leaders – the ability to attract funding.

Seen in another way, two years of the company (2014-2015) were spent on scaling the product and making it a "safe version" of what had been developed in the academic phase. The next two years were a period of validation from a clinical and regulatory point of view of the first use case. "But in parallel, we were starting to expand already and deep dive into new indications," said Bancel. "Now we have reached the stage where we are capable of running projects one after another."

Clinical trials of the peripheral nerve repair product are expected to launch in summer 2020, however the company isstill finalizing this schedule in light of the COVID-19 pandemic. The hernia repair product will enter clinical trials in early 2021; and the ENT product, for chronic sinusitis, which is a mix of a drug and a device, is being prepared for a Phase I clinical trial in late 2021/early 2022. "With a new trial every six to nine months, we are at the stage where the platform is going at full pace," said Bancel.

Manufacturing – A Trump Card

Not so common among medtech start-ups, TISSIUM, a company of 55 staff, owns its manufacturing facilities, in Roncq, northern France. Bancel's logic is clear. "If you don't have your own manufacturing capabilities, with such a technology, you are not able to produce technical batches for regulatory purposes or clinical batches for clinical indications. You're simply stuck."

The strategy at TISSIUM was always to plan for leveraging the effort on the first product for ensuing solutions. A proprietary manufacturing plant is key to Bancel's strategy. "If I had to rely on subcontractors or suppliers for my polymers, I would be extremely dependent on others." The way TISSIUM has set itself up, it can expand programs when it needs to, and focus on the priorities it identifies.

"It's a huge leverage," Bancel said, adding that the crucial element for the company was getting investment from day one. One of its investor partners is Sofinnova, whose Antoine Papiernik sits on the TISSIUM board. "They believed in our vision and have been supporting us." Bpifrance Investissement's Jean-François Morin and CM-CIC Capital Innovation's Karine Lignel are other investors on the board.

"The challenge has always been: how to do work for tomorrow, but prepare for what comes after tomorrow at the same time." It was a balancing act, said Bancel, who added that the company needed to be fully hands on. "I always keep in mind thoughts around, 'If we are successful, how do we move this forward in an accelerated manner?'"

Efficient business planning has provided breathing space. "From idea to first-in-human, we can now do things in 12-18 months; what we didn't want was to take three years to get to the first product, and the same for each product thereafter.

TISSIUM is now churning its R&D activities to develop new applications. Three years ago, the company restructured internal R&D into two parts. One led to the formation of an Innovation Hub, to devise ideas inspired by unmet needs and develop them to prototype. That division is led by CIO Pereira. The second was the Group Development Factory, where products are industrialized and prototypes are rapidly made into commercial products.

"From top to bottom, the processes are all fully integrated. It's one of the reasons we did a pretty decent job," said Bancel, allowing himself a rare moment of self-

congratulation. "I am convinced we will be successful moving forward because of just that – we have integrated and can control everything."

Market Focus

TISSIUM chose to focus on the US and EU markets first, and later bring China and other parts of Asia into the business plan. In the EU, the change of regulation from the Medical Device Directive (93/42/EC) to the Medical Device Regulation (EU 2017/745), recently delayed by COVID-19 to 26 May 2021, has led to a lot of uncertainty in the air.

"We made a decision not to be dependent on those changes," said Bancel. "At the end of the day we can have limited impact on those changes, so we decided to leverage certain geographies where first in human could be done in an effective manner. For instance, in the US for early feasibility studies, and in Australia, where we can get those early data, and then go on to do pivotal trials in the US."

He added, "Until we have visibility back in Europe, which won't be the case for the next few years, we cannot put ourselves in uncertain situations. We may set up centers in Europe, but the design of studies would in future be aimed towards FDA approvals first."

Thus the pivotal trial for an expanded indication of the already CE-marked vascular sealant (Class III) will be in the US. In the US, it will be expanded into a cardiovascular product, with a change in the polymer formulation to tap the broad $300m market. But the plan here is to be able to partner on the product. "This cardiovascular asset is, we believe, something that should belong to a portfolio within a large medical device company that targets a broad audience."

Bancel explained that the original polymer formulation used as a vascular filler has been evolved into a resin that can be used for 3D printing. It has an enhanced design in terms of adhesion, allowing more pressure to be withstood and greater medical application. "We now have polymers for adhesion and fixation, and for use as a resin for 3D printing, both from the same family."

TISSIUM's ongoing products in development will all be based on the resin, PGSAA, with all of the finished product polymers provided sterile and pre-filled. "We tailor the kits to the surgical procedure – this is something quite unique to us; we don't sell polymers, we sell surgical solutions," said Bancel. "What we do is provide the full solution."

This was a function of the company's capacity to internalize all its programs and processes, Bancel maintained. "My team wants to define both the unmet need, and the right accessories," he said. "This makes for simplified surgery for doctors, more consistent for outcomes for patients, and greater efficiencies for the health care system, as there is not much variability in how the product is used and costed."

This is where TISSIUM offers elements of personalization, tailoring products to individual fields for better surgical solutions for the patient, including the right accessories. "Whatever we bring to the market is better and simpler for the surgeon – we tailor it for the surgical approach, rather than the individual patient."

In peripheral nerve repair, the technology should allow TISSIUM to make two to four products, with options of either designing the first product and commercializing it within a subspecialty field; or building the portfolio to become a leader in the peripheral nerve repair area.

It is an example of the flexible business ethos Bancel is overseeing. If a product is more "standalone," the idea is to partner it with a company that has an existing portfolio, as in the example of the cardiovascular product. But if it can be expanded into a portfolio, Bancel wants to develop the position internally and build standalone business area leaders.

The vehicle for these decisions will be a new body, Tissium Ventures. "We have plans for single asset companies and multiple assets in a field. For some, we will partner, for others, we will provide finance or go direct in the field."

Funding Needs

Bancel said he was fortunate to have investors, co-founders and team members around him who understood that TISSIUM had a unique product, and that realizing its full potential meant taking a somewhat longer view. Other key elements are the right supply of materials and a total understanding of where the product can create the most value.

In late 2019, TISSIUM announced the completion of a series B funding round of €38.75m, which has given the company the means to develop all four of its programs currently underway. Later, it will go back to the market for funding for full commercialization operations.

Alongside these programs, TISSIUM has been doing other development work away from the public view. These projects are appraised by the group of experts who review the clinical needs, market potential and the ability and suitability of TISSIUM's technologies to provide clinical solutions. "When all these intersect, we define a program, create a new business plan, and, if it is robust enough, we invest internally. We already have the top four, but the list is quite long."

And the pipeline is flowing. In February, the company announced an early collaboration with the Crohn's and Colitis Foundation's IBD Ventures funding mechanism, to accelerate the discovery and development of novel research-based products targeting perianal disease, including anal fistulas. What is certain is that any design proposition must bring value to the multiple stakeholders involved: the patient, the person who benefits; the surgeon, who implements it and is accountable for execution; and the payer, either through tax or insurance, who funds it. "Design propositions need to factor in the integration of all three," he noted.

But the emphasis differs, depending on the product type. In the more generic product areas, payers are more central; in chronic care delivery, the patient has more of an influence in the use of one product over another; and in acute care cases, the surgeon and payer are central in decisions of which solutions are used, and why. For the company's cardiovascular and nerve repair solutions, a lot of decisions are driven by the surgeon.

Value Of Clinician And Provider Partners

Using the skills and expertise of clinicians and providers is an important element in TISSIUM's design-for-innovation processes. "It is hard to be an expert in everything. We are experts in our own material and how to develop it into products," said Bancel.

TISSIUM does not always know all the clinical subtleties, he admits, so once an idea is identified, a team of experts and practising surgeons is assembled. They create a scientific and surgical report for that specific field, after which the company identifies the R&D experts to use. "We share the vision with them, and they work with us to validate and innovate products until we are ready."

Later, in clinical trials, the decision-making moves to focus on geographies and regulatory issues – seeking the routes that are faster and/or most favorable. It requires a mix of clinical knowledge and regulatory awareness. "Essentially, it's about surrounding ourselves with the best surgeons for the innovation in question." Bancel described it as a co-innovation effort: "It's us in the lab when it comes to chemistry, but it's not us in the lab when it comes to making a product." At the root of it all, if you want to make the right product, you need to spend time with people who know the unmet need and who the surgeons are.

R&D-based health care companies have long since not designed products that are country specific – unless it is a very big market. TISSIUM has its operations in France, is headquartered in Paris, and has stronger connections in Europe than in the US. But the technology on which its products are based originated in the US, where it has a subsidiary (Boston), and the industry is global.

"Our strategy at the start was to develop the business with both the US and Europe – the core markets – in mind. Later, when entering the stage of commercialization, we would look to prioritize locally," said Bancel. That includes factoring in the complexities of national reimbursement, where solutions are all viewed differently, depending on the product. "It is hard to make a general rule, which means we are really looking at every single case individually."

But as a general rule, from the earliest stages of an innovation, the company has already assessed its reimbursement dynamics – whether existing codes can be used, or if a new code must be created. The latter points to a major slow down on entering commercialization.

China is also on the TISSIUM road map. It is not a key market yet, but will be in two to three years. "We are still at the business case design stage there, educating ourselves and how we can make a difference."

Going Public?

TISSIUM has not sought to go public through the IPO route, but it has completed funding rounds. "It's a balance," said Bancel. "Financing at the end of the day for the entrepreneur is a means to an end, not the goal in itself." The need is both to finance the project in advance and ensure the right return for investors will be delivered down the line.

Going public as a single asset company was extremely risky, said Bancel. That is because the market seeks motion. "It needs news flow, information and a dynamic picture. If a company is at a stage where it is delivering its key milestones at certain stages, then it is probably not ready," he explained. But if a company has scale, production and innovation, it is more in tune with what the market seeks. "In that case, the market can judge you in a fair manner. Whether you are successful or not is a different matter, but at least you are compatible with those requirements."

TISSIUM seems to tick those boxes, but Bancel is cautious. "My core belief is that going public too early can be very dangerous. TISSIUM has been trying to remain private to achieve the right breadth. Eventually, when we are ready to fit that kind of dynamic, we will do it."

Bancel anticipates that the company will be generating revenues in 2021, but at present it is content to pick up the plaudits for its innovation. La French Tech picked TISSIUM as one of its 120 French innovators to watch in 2020, labelling it as a fast-mover and interesting innovator. This kind of validation is humbling, in Bancel's view, but it shows that the company is going in the right direction. "We were proud to be selected last year in a competition to identify 'future potential unicorns' in France." TISSIUM was in fact selected two years in a row.

"Designing solutions for health care is a very long road, but we aim to be proactive and we are getting the right traction," said Bancel. "We tend to do what we say we'll do, and there is growing confidence in and around the team now." Back at the company's origins, the leaders made a commitment to expand what it saw was a great material in multiple directions for the benefit of patients. "We have recently begun to deliver on that."

That is due in no small part to the realistic take on business success and failure that the TISSIUM CEO brings to bear. His guiding principles include being honest from the start and be ready to change tack. "It's a combination of bold options, strong pragmatism, and a twist of paranoia," as Bancel puts it. "And you have to deal with all three. The pragmatism is there for when you have a bad day: you have a plan B, so you can come back strongly the next day."

Useful Advice For Start-Ups

Elsewhere, Bancel has advice for fellow start-ups: the highs are indeed high, but the lows are very low, and companies need to be prepared for that. Is TISSIUM a role model in this respect? If so, Bancel would not say as much, but he does make himself available. "I am open to sharing my experience; I don't need keep it all to myself. I am always happy to talk with peers, but I ensure they know that mine is just one opinion. And they need to start from somewhere."

Bancel, also a founder and venture partner at the Paris-based iBionext health care technologies growth platform, has three top tips for fellow start-ups who are in the early stages of their journey:

1. In your technology-based company, the technology is key, but think about the team that you need. It is impossible to make it on your own. Once you are sure you have a good technology, it is all about the people. The journey will be very hard in some cases, so surround yourself with people who can complement you.

2. If you have the good fortune of being able to select your investors, work with people who believe in you, and who are there not just to make money. In fact, they will anyway, but the point is that you want them to be part of the journey.

3. Enjoy what you do, as you'll be doing it a lot! Don't turn it into a prison; have fun along the way.

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Comments:
Email the author: *Ashley.Yeo@Informa.com*

Leading The Dawn Chorus

NICOLA REDFERN

Spearheading discussions with NICE, bluebird bio's UK general manager Nicola Redfern has been central to efforts to introduce fresh reimbursement models within the health technology assessment process and commercial framework. Success could change the way cell and gene therapies are assessed and affect the outlook for many patients living with rare diseases.

BY JOANNE SHORTHOUSE

When bluebird bio's gene therapy Zynteglo launched in Germany this year it was first time the product had been commercially available.

The collaborative discussions that led to that first launch will pave the way for future entries into other markets.

Nicola Redfern, who is leading UK market access activities for Zynteglo, talks to In Vivo about how the process is evolving. Although there is an awareness at NICE that innovative therapy assessments need to be revised, more emphasis is needed from UK government and the NHS to spur improvement.

Nicola Redfern has been in position as bluebird bio Inc.'s UK general manager for less than two years, before that heading up UK market access from 2017. In that time, there has been an increased interest in the curative possibilities and market access challenges of cell and gene therapies, Britain's exit from the European Union, and bluebird bio's first drug approval.

Redfern's new role at bluebird came at a pivotal time for its European operations. With its gene therapy Zynteglo (autologous CD34+ cells encoding βA-T87Q-globin gene) for transfusion-dependent beta-thalassaemia (TDT) approved in the EU in June 2019, the European team is testing the landing ground for pricing talks with payers in the continent's patchwork of reimbursement bodies. TDT is a genetic, inherited blood disease characterized by reduced or absent production of hemoglobin, which leads to decreased red blood cell production. The most severe form of TDT requires regular blood transfusions to enable survival.

In June 2019, the European Commission (EC) granted Zynteglo conditional marketing authorization in Europe, with the German launch in January this year the first time Zynteglo was commercially available. The collaborative discussions that led to this launch will pave the way for future entry into other markets.

With a price tag of €1.575m, the company is pushing its outcomes-based payment over time model, which asks for five payments of €315,000 ($356,000) over five years contingent on Zynteglo's ability to eliminate TDT patients' needs for blood transfusions. In Germany the University Hospital of Heidelberg has been set up as a treatment center, with other hospitals starting to get set up. Now all eyes will be on country heads in Italy, the UK and France to bring back equally successful negotiations to the bluebird nest.

While the German reimbursement picture looks to be a successful blueprint, Redfern has the unenviable job of leading the discussion about this innovative payment model with England's Department of Health and Social Care (DoH), the health technology

assessment institute NICE and NHS England (NHSE).

NICE To Meet You

Redfern said in a February 2020 interview with *In Vivo* that the company is "deep in conversation" with NICE and NHSE, with NICE in the process of reviewing the dossier. Bluebird has a "very good rapport" with NICE, she said. It engaged very early with the HTA and NHSE, was a pilot for the Office for Market Access, and has engaged with NICE scientific advice for future research. Redfern said that the "big discussion point" is, inevitably, around outcomes-based payment over time and how to shape that within the UK environment.

"The outcomes piece brings certain hurdles and challenges because you have to have good registries and data sets to track those patients. I also think our proposal about payment over time is resulting in lots of discussions because it may need Treasury and accountancy rules to change in order to facilitate those separate invoices and payments. It's getting complicated," Redfern told *In Vivo*.

There has been engagement, she says, in some "very open conversations" with NICE and NHS England on bluebird's aspiration to introduce this type of model. Some of these conversations have been taken forward to the DoH and the Treasury, but Redfern admits that "where that will land, we don't yet know."

This topic has been discussed in the industry holistically, with the NHS and NICE pondering how to bring forward new payment models and introduce new innovations for many years. For cell and gene therapy companies, these conversations are imperative. "There are multiple products coming through over the next decade, many of which have highly prevalent populations and from an affordability point of view, although its perhaps not an issue now, it could be an issue in the future," said Redfern. Bluebird is determined to ask how it can recode the system. "How do we make sure it is fit for purpose for the future?" she asks. "Not only from a bluebird bio point of view, but for the industry as a whole, so as those new innovations come through, we don't hit future hurdles or delays based on affordability."

Gene therapies are able to come to market quite quickly, based on data from relatively small patient numbers in the clinical trials. From a health economics perspective, the bluebird models lifelong benefit but with a limited duration of follow-up after treatment. "That inherently brings uncertainty to the table and the company feels that we have an obligation to underwrite some of that uncertainty and take joint responsibility," Redfern explained. "It's about how we take some of that risk on and how we can share that risk with the NHS. Resulting in the NHS only paying if the patient benefits, and again that is a different model."

She added, "I don't think we anticipated the discussions would be quick, there's a lot of stakeholders it impacts on," she said. The concern for Redfern and bluebird is that a pathway might not be found. Could that result in patients not being able to access new innovations in the UK? "Does it make the UK less attractive to cell and gene therapy companies? Are we going to continue to struggle to launch new innovations here, especially post-Brexit? And what does that mean for a family living with the disease?"

Methodology Review

The planned NICE Methodology Review marks a huge opportunity for cell and gene therapy companies to engage. Former NICE CEO Sir Andrew Dillon, on announcing the review, said that "NICE is undertaking this review at a time of unprecedented change in the health care system, where developments such as personalized medicine, digitalization of health, and use of cell and gene therapy, mean products are becoming ever more challenging to evaluate." There is a shortlist of topics considered in the review and for each, a case for change will be explored, and proposals presented for public consultation in late-2020. The review will cover NICE's single technology appraisals (STA), highly specialized technologies (HST), medical technologies and diagnostics assessment programs.

"There are opportunities within the methodology review to rebalance how NICE look at rare diseases, because I think it is widely recognized that there is a gap currently between the STA and HST programs and orphan diseases often fall between that gap," said Redfern. "The opportunity is there now to reshape it." For example, she said, bluebird bio would like to see the discount rate revisited as part of the methodology review. Generally NICE requires a 3.5% annual discount rate on costs and health outcomes, but Redfern notes clear guidance from the UK Treasury Green Book, stating that "Discounting of resources relating to health and life issues is carried out using the appropriate standard discount rate of 3.5% declining after 30 years. The value of VPFs, SLYs and QALY* effects should be discounted at the health rate of 1.5%, declining after 30 years."

Additionally, the NICE Report, *Exploring The Assessment And Appraisal Of Regenerative Medicines And Cell Therapy Products* acknowledges that "the discounting rate applied to costs and benefits was found to have a very significant impact on analyses of these types of technologies." In Redfern's view, "this confirms that further consideration should be made to the use of the 1.5% discount rate for such therapies."

There are more questions up for discussion, she says:

- Are there other areas that specifically require or would lend themselves to having a higher threshold, such as the severity of a disease?

- Should something that has lifelong benefit be treated differently?

- Is rarity something that should be treated differently because it is more difficult to research?

There is certainly a need for joined up thinking. Although there is an awareness at NICE that innovative therapy assessments need to be revised, it needs the UK government and the NHS to express an aspiration for improvement for NICE to embrace those changes. To some extent all the key stakeholders are independent, and although NHSE and NICE work very closely together, if NICE puts something into place that makes higher prices viable, NHSE must pick up the bill.

"There has to be aspiration expressed at government level to treat cell and gene therapies differently. We want to deliver

them to the UK population quickly and we recognize the long-term benefits these things might have that today aren't fully quantifiable, but by embracing that innovation now, you open up those choices to families and individuals and attract more investment into the UK," said Redfern.

Career Flight Path

Redfern has a long history of working with NICE. She was involved as a marketeer of one of the first drugs that NICE assessed, Eloxatin (oxaliplatin), a Sanofi colorectal cancer drug. Her varied career in pharma started in 1989 in sales and has since seen her work for 10 different companies during that time. In 1997 Redfern moved into the oncology field, and since has focused on cancer and rare disease.

With both her mother and grandmother working as nurses, she was already familiar with the possibility of health care as a career. A psychology degree led to a role in a children's hospice in 1987. Here, Redfern witnessed the the reality of not having any solutions to genetic disease. This, plus her 30-year pharma career, led her to bluebird bio, a firm she admired for its cultural makeup as well as its groundbreaking science.

"I like a really good balance between on-the-edge science, innovation and something that's very patient-focused. Gene therapy is innovative, changing the way we approach medicine holistically. And potentially is giving life-long benefit," she said. "It is completely changing the way we think about treating a patient."

Aside from the culture of the company, Redfern appreciated that it was engaging early with multiple stakeholders. "Even before I joined, which is nearly three years ago, the company had already started to engage with NICE and NHSE in some of the discussions. The aspiration to collaborate and partner with multiple stakeholders in the payer world is very much at the forefront of the way the organization works," she explained.

Redfern became UK general manager in 2018, and access and reimbursement remain a top priority. "If we can't come to some arrangements and get reimbursement it means patients can't access that treatment and they don't have that choice. On a day-to-day basis reimbursement is still very much at the forefront of everything we're doing," she stressed.

The Brexit Effect

Britain has repeatedly heard since the 2016 UK referendum result, in which the public voted to leave the European Union, uncertainty is the only certainty when planning for a post-Brexit world. Redfern questions how the UK Medicines and Healthcare products Regulatory Agency (MHRA) will treat orphan diseases. Whether it is still going to recognize conditional approval, at what speed it expects submissions in, and can it do things more quickly? ("Which would be potentially great for UK plc," she said.)

"My caution is, we can aspire to get things through the MHRA earlier, but if we don't have the right methodology for NICE, we're still going to hit reimbursement challenges later. Doing bits of the puzzle quickly is not necessarily going to solve patient access," Redfern said. One thing she is certain of is that Brexit is already having a tangible impact on her working life. She recalls a meeting in which bluebird was engaged with the EMA and European HTA bodies for joint scientific advice on a registry. NICE was actively supportive, she says, but post January 31st was told it could not continue to take part. Bluebird is engaging with NICE separately. "It does create re-work," she said. "Rather than have the one meeting with all stakeholders around the table, we're now looking at separate discussions. Although it is too early to necessarily know how things are going to work moving forwards, we're already starting to see things impact."

Feathering The Nest

Redfern made the decision a long time ago to remain UK-based, she told *In Vivo*. The creation of her UK team, and finding opportunities for those individuals to develop was important, she said. Equally, the R&D that bluebird is currently doing will benefit patients with ultra-orphan diseases "more like the children I'd have worked with at the hospice," she said, remarking on how "it'll be really exciting to see those come through."

With other therapeutics in clinical trials for severe genetic diseases such as cerebral adrenoleukodystrophy and sickle cell disease, activity and excitement levels around the biotech is ramping up. The Cambridge, MA-based firm also has oncology assets, such as idecabtagene vicleucel (ide-cel; bb2121), a chimeric antigen receptor T-cell therapy targeting B-cell maturation antigen (BCMA) in the treatment of relapsed or refractory multiple myeloma, developed in partnership with Bristol-Myers Squibb Co.

At the end of March 2020, the companies submitted their Biologics License Application to the US Food and Drug Administration for patients who have received at least three prior therapies, including an immunomodulatory agent, a proteasome inhibitor and an anti-CD38 antibody.

Redfern commented that with these other assets in the pipeline, "it'd be great to stick around and see them come through." If the Zynteglo NICE negotiations are successful, with more products needing the same country knowledge, bluebird could not afford to let this UK bird fall from the corporate nest.

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Editor's Note: Following up on our earlier interview with Redfern, it is clear that Covid-19 brings a new level of uncertainty to every aspect of society, including bluebird bio's operations. The team is continuing to support the clinical and patient community where appropriate, but some of the conversations that were underway have now been delayed. Discussions with NHSE and NICE will resume later in 2020 but patient access to this innovation will undoubtably push later into 2021.

** valuation of a statistically prevented fatality (VPF), statistical life-years (SLY) and Quality Adjusted Life Years (QALYs)*

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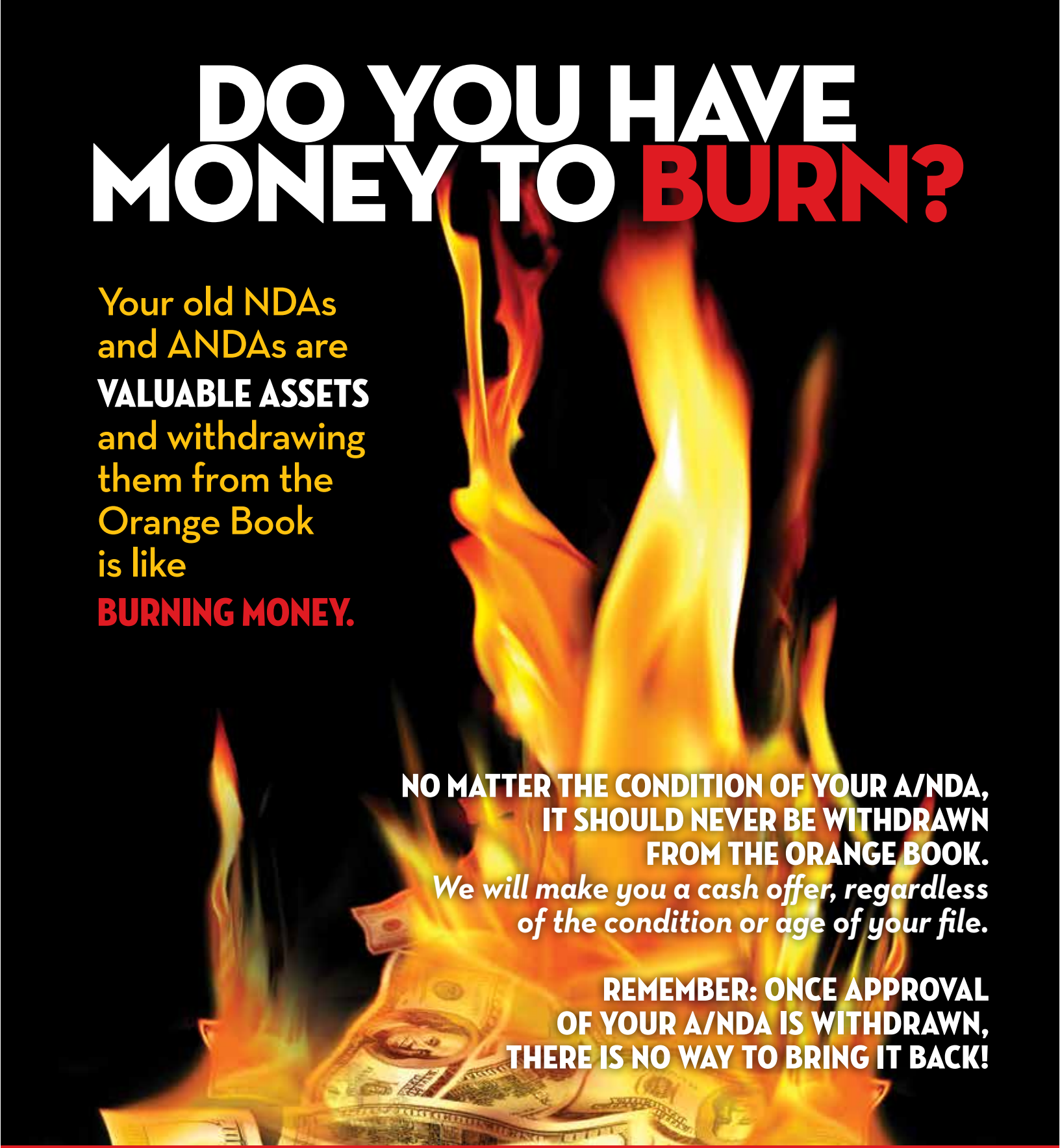

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Recent executive appointments in the life sciences industry

DEBRA BARKER

RUSSELL ELLISON

JONATHAN FREVE

COLIN GODDARD

COMPANY CHANGES

EXECUTIVE	TO COMPANY	NEW ROLE	FROM COMPANY	PREVIOUS ROLE	EFFECTIVE DATE
Anders Gaarsdal Holst	Acesion Pharma	Chief Medical Officer	Novo Nordisk AS	Senior International Medical Director	5-May-20
Mark Adams	Adaptive Biotechnologies	Chief Technical Officer	SVB Leerink	Managing Director, Healthcare Advanced Analytics	9-Apr-20
Jennifer Creel	ADC Therapeutics SA	Chief Financial Officer	Celgene Corp	Chief Financial Officer and Corporate Vice President, Global Finance and Business Planning	21-Apr-20
Arndt Schottelius	Affimed Therapeutics AG	Chief Scientific Officer	Kymab Group Ltd	Head, Research and Development and Executive Vice President	1-Apr-20
Thomas Karalis	Antengene Corp	Head, Asia Pacific Regions	Celgene Corp	General Manger, Celgene East Asia and Vice President, General Manager, Celgene Australia and New Zealand	13-Apr-20
Shawn Cross	Applied Molecular Transport	Chief Financial Officer	JMP Securities	Managing Director and Co-Head, Healthcare Investment Banking	21-Apr-20
C. Greg Guyer	BioMarin Pharmaceutical Inc	Chief Technology Officer and Executive Vice President, Global Manufacturing and Technical Operations	Bristol-Myers Squibb Co	Senior Vice President, Operations	4-May-20
Andrei Stoica	BioTelemetry Inc	Chief Technology Officer	IQVIA	Senior Vice President, IT Systems Development	7-Apr-20
Ken Reali	Bioventus llc	Chief Executive Officer	Clinical Innovations llc	Chief Executive Officer and President	30-Apr-20

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ANDERS GAARSDAL HOLST

D. MARK MCCLUNG

GAIL MCINTYRE

ROLAND WANDELER

COMPANY CHANGES

EXECUTIVE	TO COMPANY	NEW ROLE	FROM COMPANY	PREVIOUS ROLE	EFFECTIVE DATE
David Setboun	BrainStorm Cell Therapeutics Inc	Executive Vice President, Chief Operating Officer	Life Biosciences	Vice President, Development, Strategy and Business	1-Apr-20
Tim A. Benner	Endologix Inc	Chief Commercial Officer	Abbott Structural Heart	General Manager and Division Vice President, US	14-Apr-20
Thomas Civik	Five Prime Therapeutics Inc	Chief Executive Officer, President and Director	Foundation Medicine	Chief Commercial Officer	14-Apr-20
Julie Krop	Freeline Therapeutics	Chief Medical Officer	AMAG Pharmaceuticals	Chief Medical Officer	1-Apr-20
Jonathan Freve	Galecto Inc	Chief Financial Officer	Spring Bank Pharmaceuticals	Chief Financial Officer	27-Apr-20
Harpal Kumar	Grail Inc	President, Grail Europe	Johnson & Johnson	Senior Vice President and Head, Innovation, EMEA	10-Apr-20
Anila Lingamneni	Haemonetics Corp	Chief Technology Officer and Executive Vice President	Baxter International	Vice President, Research and Development	1-Apr-20
Christina Brattström	Idogen AB	Chief Medical Officer	Bayer AG	Medical Director, Scandinavia	1-Apr-20
Gigi Feng	I-Mab Biopharma	Global Head, Corporate Communications and Vice President	Amgen	Japan Asia Pacific Regional Head, Corporate Communications	20-Apr-20
Edgardo Baracchini	Imago BioSciences	Chief Business Officer	Xencor Inc	Chief Business Officer	16-Apr-20
Essam Farouk	Julphar Gulf Pharmaceutical Industries	Chief Executive Officer	Elkendi	Chief Executive Officer	5-Apr-20
Roland Wandeler	MorphoSys	Chief Commercial Officer	Amgen Inc	Corporate Vice President and General Manager, US Bone Health and Cardiology	21-Apr-20

COMPANY CHANGES

EXECUTIVE	TO COMPANY	NEW ROLE	FROM COMPANY	PREVIOUS ROLE	EFFECTIVE DATE
Debra Barker	Polyneuron Pharmaceuticals AG	Chief Medical Officer	Polyphor	Chief Medical and Development Officer	7-Apr-20
Michael Greco	Rallybio	Head, Legal Operations	SpringWorks Therapeutics	General Counsel	7-Apr-20
Shingo Iwamoto	Sandoz International GmbH	Country Head, Japan	Aspen Japan KK	President	1-Apr-20
D. Mark McClung	Sangamo Therapeutics Inc	Chief Business Officer and Executive Vice President	Amgen Inc	Vice President, General Manager, Global Oncology Commercial	17-Apr-20
Jay M. Moyes	Sera Prognostics	Chief Financial Officer	Achieve Life Sciences	Director	2-Apr-20
Lisa von Moltke	Seres Therapeutics Inc	Chief Medical Officer and Executive Vice President	Alkermes	Senior Vice President and Head, Clinical Development	6-Apr-20
Anne-Francoise Nesmes	Smith & Nephew plc	Chief Financial Officer	Merlin Entertainments	Chief Financial Officer	3-Aug-20
Achim Plum	Sphingotec GmbH	Chief Commercial Officer and Managing Director	Curetis Group	Chief Business Officer	16-Apr-20
Lisa Rojkjaer	Viracta Therapeutics Inc	Chief Medical Officer	Nordic Nanovector ASA	Chief Medical Officer	1-May-20
Robert Pietrusko	Vor Biopharma Inc	Chief Regulatory and Quality Officer	Voyager Therapeutics	Senior Vice President, Regulatory Affairs and Quality Assurance	7-Apr-20
Shawnte M. Mitchell	Zogenix Inc	General Counsel, Executive Vice President and Secretary	Aptevo Therapeutics	Senior Vice President, General Counsel and Corporate Affairs	20-Apr-20

PROMOTIONS

EXECUTIVE	TO COMPANY	NEW ROLE	PREVIOUS ROLE	EFFECTIVE DATE
Bittoo Kanwar	Applied Molecular Transport	Chief Medical Officer	Senior Vice President, Clinical Development	21-Apr-20
Gail McIntyre	Aravive Inc	Chief Executive Officer and Director	Chief Scientific Officer	9-Apr-20
Randy Shultz	Arcadia Biosciences	Chief Technology Officer	Head, Research and Development	1-Apr-20
Chad D. Costley	BlueWillow Biologics	Chief Medical Officer and Director	Director	22-Apr-20
Scott A. Kelly	CytoDyn Inc	Chairman, Chief Medical Officer and Head, Business Development	Chairman	13-Apr-20
John Davis	Magenta Therapeutics	Head, Research and Development and Chief Medical Officer	Chief Medical Officer	17-Apr-20
Joshua Allen	Oncoceutics Inc	Chief Scientific Officer	Senior Vice President, Research and Development	3-Apr-20
Lee Schalop	Oncoceutics Inc	Chief Executive Officer	Chief Operating Officer	3-Apr-20
Russell H. Ellison	Rockwell Medical	Chief Executive Officer, President and Director	Director	20-Apr-20

PROMOTIONS

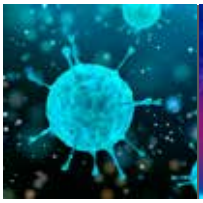
EXECUTIVE	TO COMPANY	NEW ROLE	PREVIOUS ROLE	EFFECTIVE DATE
Tim Watts	Shield Therapeutics	Chief Executive Officer	Chief Financial Officer	22-Apr-20
Robert W. Duggan	Summit Therapeutics plc	Chairman and Chief Executive Officer	Chairman	14-Apr-20
Hiroshi Nagumo	Terumo Corp	Chief Executive Officer and President, Terumo Americas Holding Inc	Senior Vice President, Blood Center Solutions, Terumo BCT Holding Corp	1-Apr-20

DIRECTORS

EXECUTIVE	TO COMPANY	NEW ROLE	EFFECTIVE DATE
Brian Pereira	Abeona Therapeutics Inc	Executive Chairman	21-Apr-20
Jean Stéphenne	CureVac AG	Chairman, Supervisory Board	2-Apr-20
Samir R. Patel	CytoDyn Inc	Director	20-Apr-20
Timothy P. Walbert	Exicure	Chairman	7-Apr-20
Colin Goddard	FoRx Therapeutics AG	Executive Chairman	22-Apr-20
Charles Bancroft	GlaxoSmithKline plc	Director	1-May-20
Michael Coyle	Haemonetics Corp	Director	17-Apr-20
Bob Baltera	Imago BioSciences	Independent Director	22-Apr-20
James C. Borel	Neogen Corp	Chairman	10-Apr-20
Raymond Wong	Oncoceutics Inc	Chairman	3-Apr-20
Chris Nolet	PolarityTE Inc	Director and Chairman, Audit Committee	6-Apr-20
Suzanne L. Bruhn	Retrophin Inc	Director	9-Apr-20
Elisabeth Bjork	Rocket Pharmaceuticals Inc	Director	22-Apr-20
Bob White	Smith & Nephew plc	Non-Executive Director	1-May-20
Karen L. Ling	TherapeuticsMD Inc	Director	22-Apr-20
B. Kristine Johnson	ViewRay Inc	Director	14-Apr-20

ADVISORS

EXECUTIVE	TO COMPANY	NEW ROLE	EFFECTIVE DATE
Raymond L. Benz	Cereno Scientific AB	Scientific Advisor	2-Apr-20
Justin Stebbing	Heat Biologics Inc	Covid-19 Advisory Board Member	1-Apr-20
Lanying Du	Heat Biologics Inc	Covid-19 Advisory Board Member	1-Apr-20
Natasa Strbo	Heat Biologics Inc	Covid-19 Advisory Board Member	1-Apr-20
Raymond Pickles	Heat Biologics Inc	Covid-19 Advisory Board Member	1-Apr-20
Sheila Copps	Hemostemix Inc	Advisory Board Member	7-Apr-20
Timothy C. Chang	Hemostemix Inc	Advisory Board Member	21-Apr-20
Abhijit Patel	NuProbe Inc	Clinical Advisory Board Member	22-Apr-20
Amir A. Jazaeri	NuProbe Inc	Clinical Advisory Board Member	22-Apr-20

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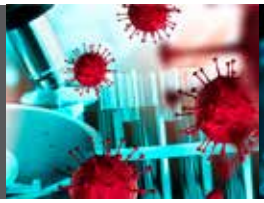
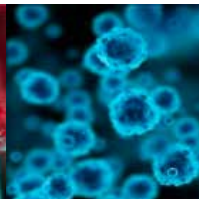

STRATEGIC INSIGHTS FOR LIFE SCIENCES DECISION-MAKERS

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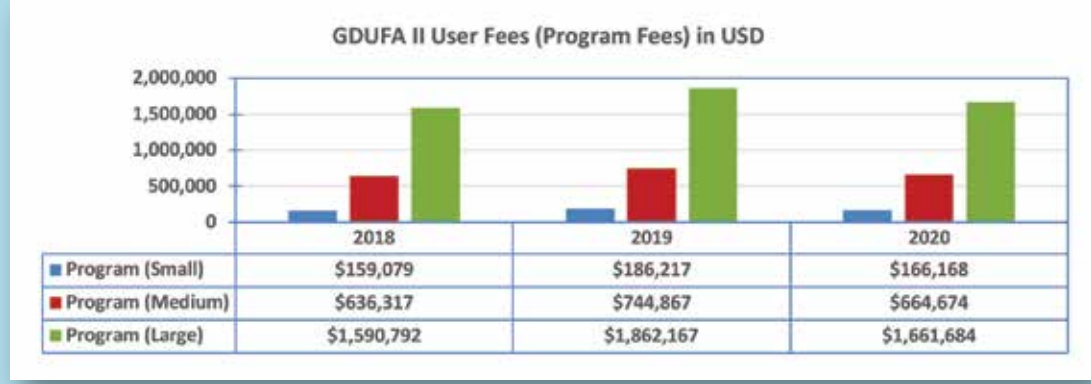
Park Unused ANDAs Here

For GDUFA II Program Fee Relief

GDUFA II User Fees: They Saved Paradise and Put Up a Parking Lot

The Generic Drug User Fee Amendments ("GDUFA") payment due date has just passed — the first business day on or after October 1st of each year — and companies are trying to plan ahead now in 2020 to see if there's a way to reduce costs and save money. Fees can be dramatic and impactful just to keep the assets you own already and worked so hard to develop or acquire.



	2018	2019	2020
Program (Small)	$159,079	$186,217	$166,168
Program (Medium)	$636,317	$744,867	$664,674
Program (Large)	$1,590,792	$1,862,167	$1,661,684

This is true especially for a company in the small and medium size operation tiers—and perhaps one or two in the large size operation tier — seeking a way to potentially save significant program fees. A few years ago, a system dubbed "ANDA Arbitrage" was introduced by a company called **ANDA Repository, LLC** in an effort to help companies potentially decrease annual user fee liability under GDUFA II.

Imagine a parking lot. The owner of a car that is not being used on a daily basis needs a parking space for that car. In exchange for that parking space (and an annual fee) the car's owner transfers title of the automobile to the parking lot owner. The former owner of the car can, with appropriate notice, take back ownership when he decides he wants to use the automobile again. Provided the parking lot owner has enough cars in the lot, this can be a beneficial venture for all of the parties involved.

In the imagery above, the automobile owner is an ANDA sponsor (typically with a discontinued, but not withdrawn approval, ANDA), and the parking lot owner and attendant is **ANDA Repository, LLC**. As a "large size" operation, ANDA Repository, LLC pays a flat GDUFA II ANDA Holder Program Fee regardless of how many ANDAs are owned. In exchange for its services, ANDA Repository, LLC charges an ANDA sponsor an annual fee, which is significantly less than the ANDA Holder Program Fee the ANDA sponsor would otherwise pay as a small or medium size operation.

If you're interested in the program, please reach out to ANDA Repository, LLC soon. The mechanism to communicate to the FDA a transfer in ANDA ownership well prior to October 2020 is relatively painless. Also please check with us before WITHDRAWING your ANDAs. There were 388 ANDA Withdrawals last fiscal year, which is like burning your own assets. Unless mandated to do so, **ANDA Repository** is a far better option, and we may be interested in purchasing them from you outright. Contact us NOW!!!

Phone: +1-570-261-1901 | Email: info@andarepository.com