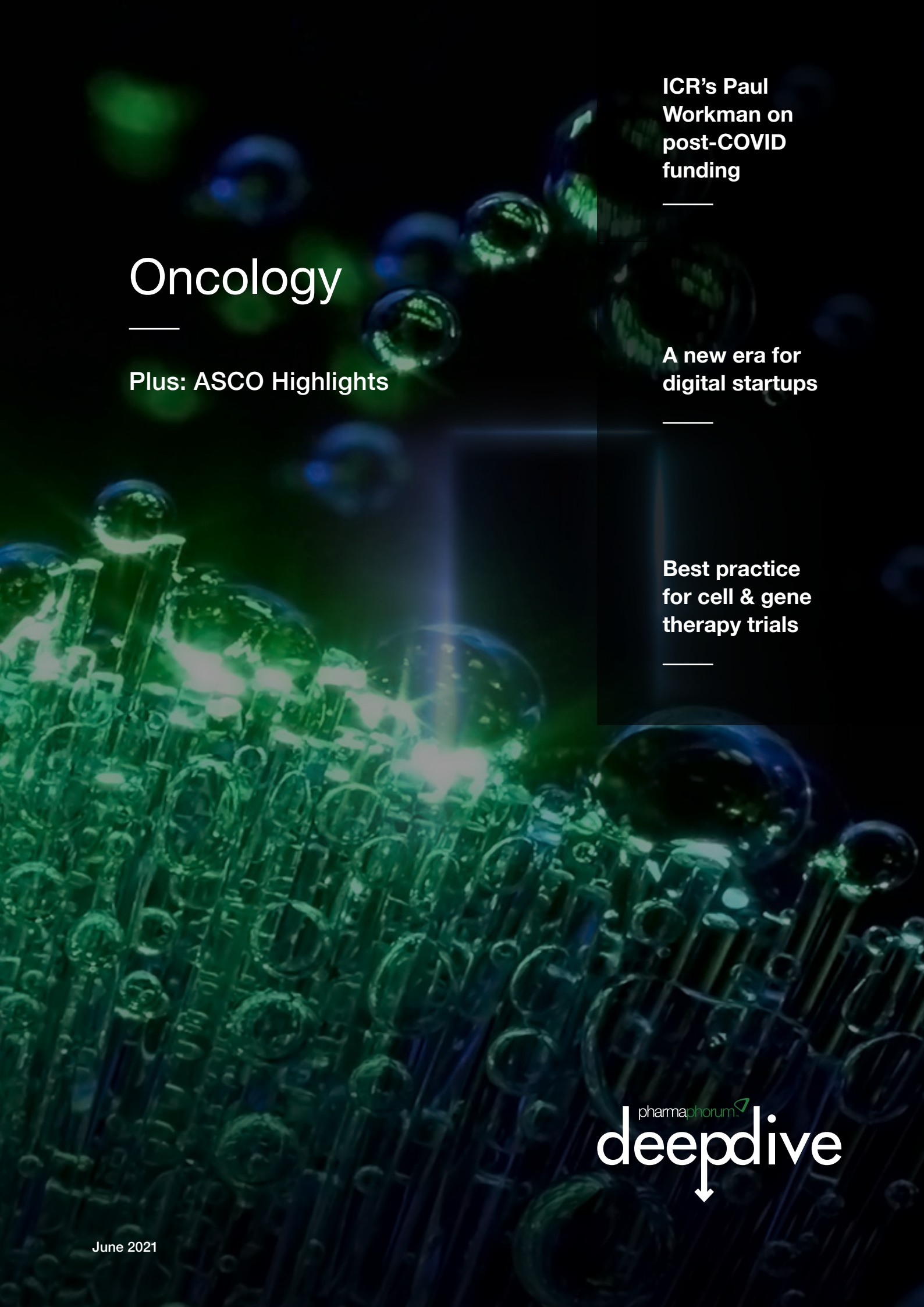

Oncology

Plus: ASCO Highlights

ICR's Paul Workman on post-COVID funding

A new era for digital startups

Best practice for cell & gene therapy trials

pharmaphorum deepdive

June 2021

Deep Dive: Oncology 2021

This has probably been the toughest year for cancer researchers in memory.

As experts from the Institute of Cancer Research, Lucid Group, and Syneos Health discuss in this issue, funding gaps, paused trials and patients' health anxiety will have reverberations impacting outcomes for years to come.

But it's perhaps a testament to the sector's strength that even among these challenges, all of our contributors see the huge potential for cancer research going forward. In this year's ASCO roundup we look at the next generation of exciting cancer immunotherapies, Olivia Kersey from Prime Global tells us how patient insights can vastly improve oncology research, and speakers from ICON demonstrate how cell and gene therapy trials are becoming ever more sophisticated.

Looking more broadly, Healthware's Kristin Milburn and Debiopharm's Tanja Dowe discuss trends in digital health start-ups, and we highlight several digital companies shaking up healthcare and research – including Ampersand Health, Within3 and BrightInsight.

As long as all healthcare stakeholders can come together to build innovative solutions to post-COVID challenges, we can be confident there's a bright future ahead for oncology research and the cancer patients it benefits.

George Underwood
Editor, *Deep Dive*

Next issue:
Communications & Commercialisation (September 2021)
Plus:
• Launch excellence
• Data-driven sales & marketing

Catch up on recent issues:

Market Access – April 2021

R&D – February 2021

Patients & Partnerships – December 2020

Digital Health Innovation – October 2020

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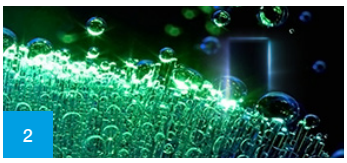

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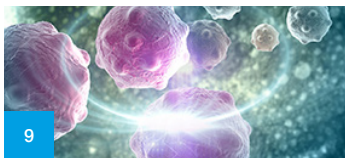

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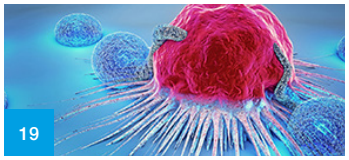
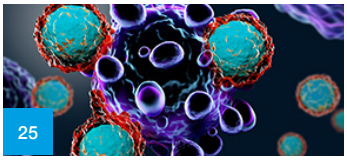
We roundup the biggest stories from this year's conference, giving us a glimpse into the exciting future of oncology



Oncology and a year of COVID: lessons for the future
COVID's impact on cancer care and oncology research has been devastating, but the pandemic has also opened up opportunities to take learnings and create long-lasting change in research, practice and education, says Lucid's Frances O'Connor



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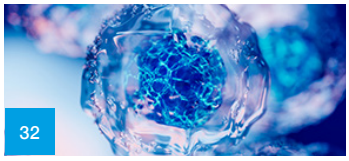
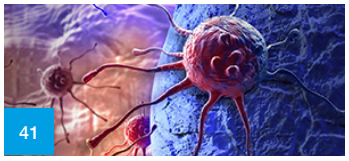
The explosion in immuno-oncology therapies over the last few years shows no signs of slowing down. As the field becomes more crowded, digital tools may be critical for improving outcomes, says a new whitepaper



Lessons from the first generation of cell & gene oncology trials
Advances in cell and gene science are paving the way for transformative cancer treatments, but there are still many complexities in delivering clinical trials for these therapies. ICON's Tamie Joeckel and Brandon Fletcher take us through best-practice approaches to CGT studies



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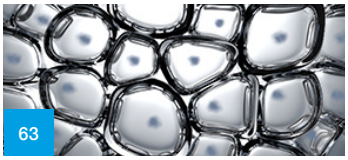
How pharma, regulators, payers and patient groups can collaborate for deeper and earlier patient engagement

How digital pathways are changing healthcare
Digital health is no longer experimental. Ampersand Health has been working in the space since 2015 and has seen it evolve from a niche approach with limited acceptance to widespread acceptance and deployment across disease areas

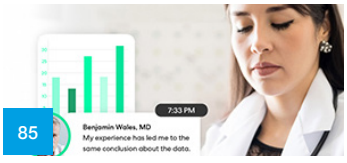
A new investment era for digital start-ups
Healthware Lab's Kristin Milburn explores how digital health start-ups can harness the huge potential for the sector in a post-COVID world and the paths they need to take to grow their business



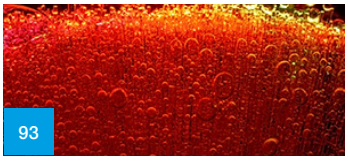
Enabling healthcare's digital future
Debiopharm Innovation Fund's Tanja Dowe on investing in digital health start-ups and supporting them on their rollercoaster rides to improve patient outcomes

Why pharma shouldn't forget about sites in a post-COVID world
The pandemic forced massive changes to oncology sites to ensure patient safety and research continuity – but we must recalibrate and work with sites to understand the value proposition of the technologies and methodologies adopted, says Syneos Health's Angela Hirst

Surprise pandemic lessons for pharma
IQVIA's John Proctor looks at what the pandemic has taught pharma when it comes to adapting its commercial model



How hybrid virtual engagement is accelerating oncology communication
COVID has revolutionised the way pharma engages with healthcare stakeholders – but to be truly successful, digital engagement needs to move away from an overreliance on real-time meetings, say experts from Within3



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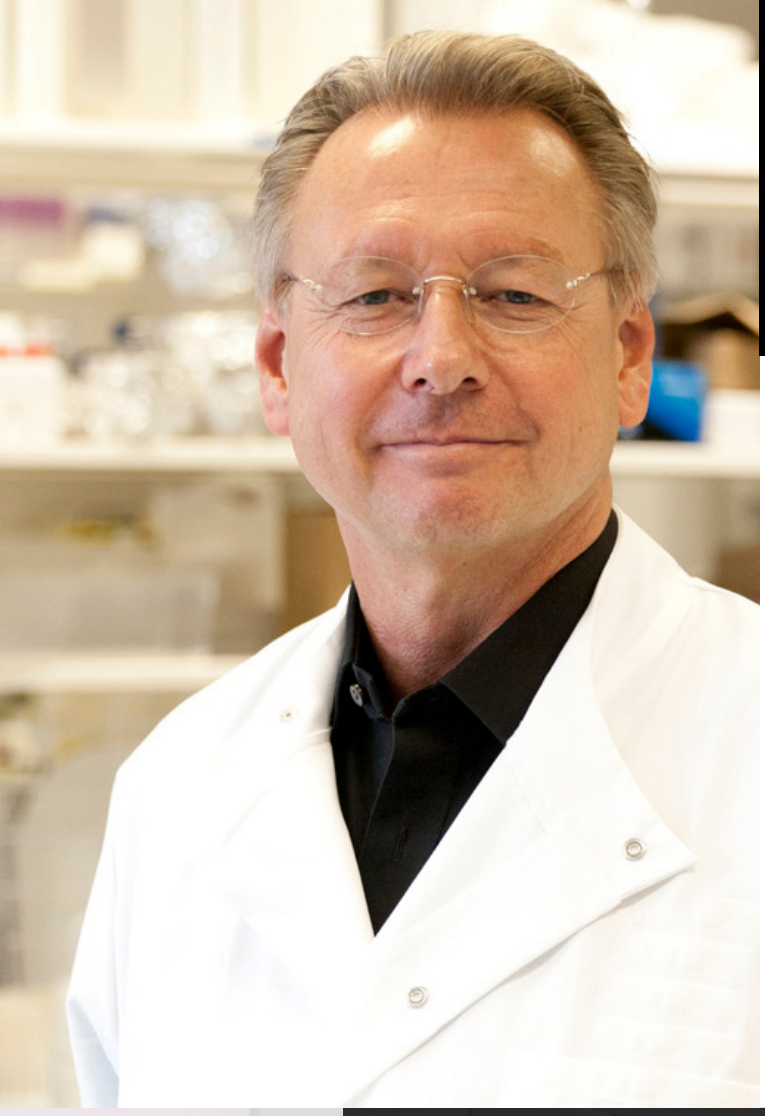
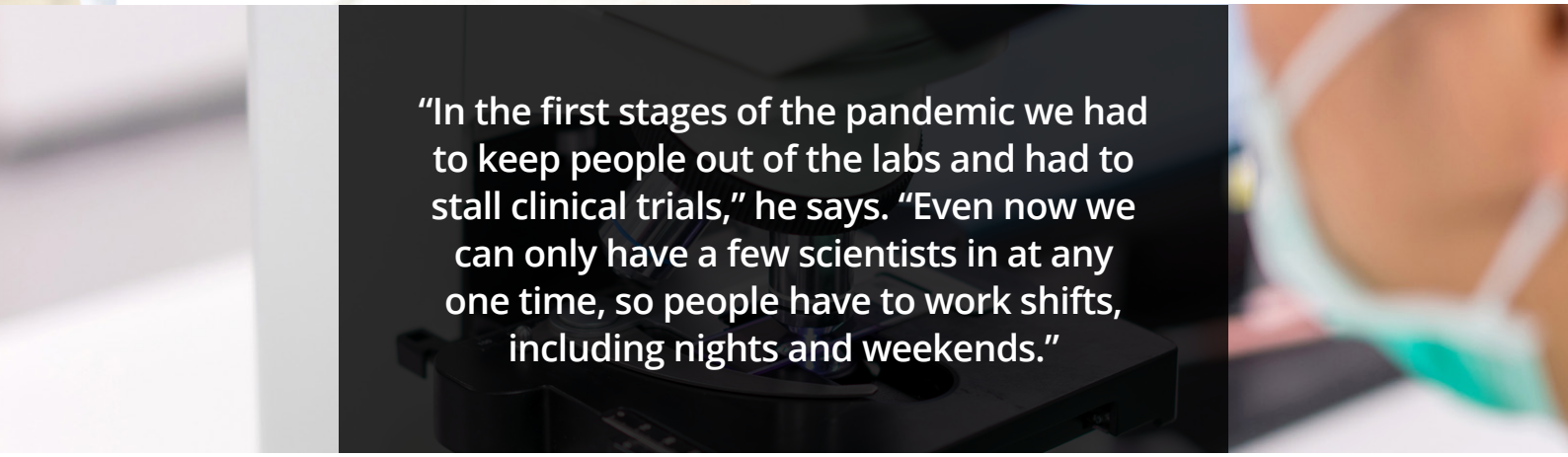


Cancer research faces uncertain post-COVID landscape

There's a bright future ahead for cancer research in the UK, but only if the government is able to implement a clear plan for funding and development going forward, says The Institute of Cancer Research, London's Paul Workman.

Cancer research in the UK risks facing a "perfect storm" of stalled work and reduced funding that could "capsize" the sector.

That's according to Professor Paul Workman, CEO of the Institute of Cancer Research (ICR), who says that COVID has delayed advances for cancer patients by at least 18 months.



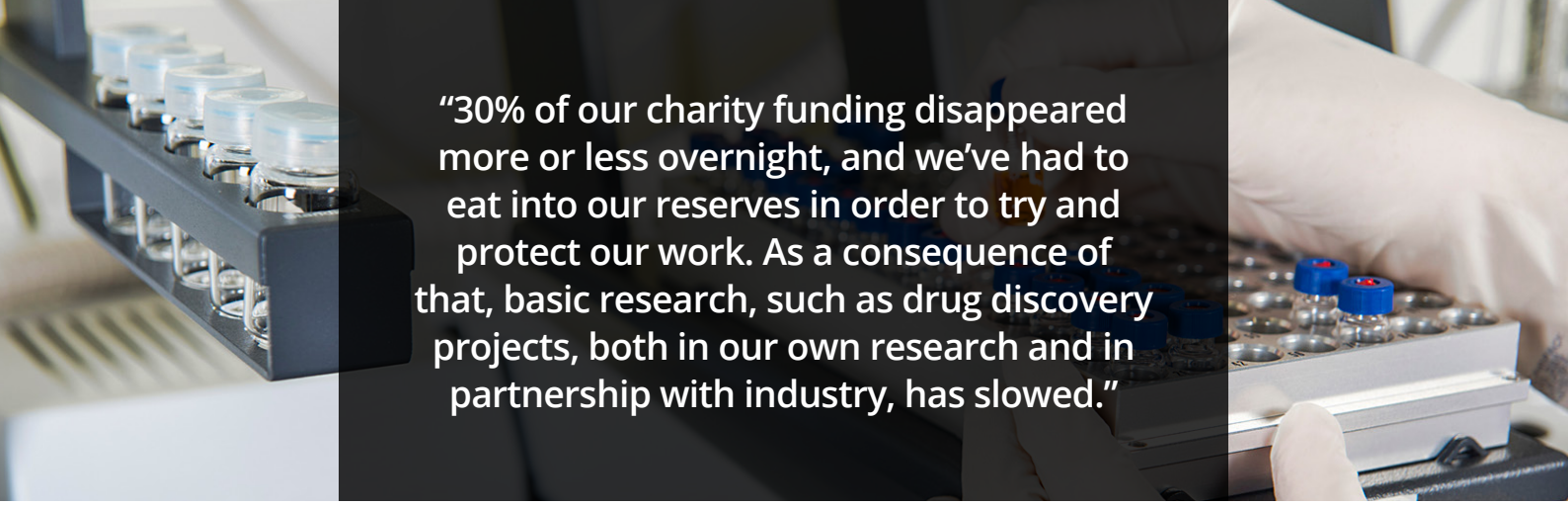
"In the first stages of the pandemic we had to keep people out of the labs and had to stall clinical trials," he says. "Even now we can only have a few scientists in at any one time, so people have to work shifts, including nights and weekends."

On top of reducing output, this is impacting scientists' morale.

"We have passionate researchers who are frustrated that they can't get into the lab and do their work," says Workman. "They're missing the buzz of having the institute full, and the resulting creative interaction that can spark new ideas."

But a more tangible threat to cancer research in a post-COVID world are the funding blows the sector has had to endure.

Workman says that charity funding – which accounts for 50% of all publicly funded medical research and over a quarter of the ICR's funding – "fell off a cliff" when medical charities had to close their shops and cease fundraising events.



"30% of our charity funding disappeared more or less overnight, and we've had to eat into our reserves in order to try and protect our work. As a consequence of that, basic research, such as drug discovery projects, both in our own research and in partnership with industry, has slowed."

Thankfully industry collaborations and commercial income are one area that has largely held up, Workman says.

"The pharmaceutical and the biotech industries and related funding are quite buoyant. Pharma companies have not suffered from the same acute cuts as medical charities."

Workman says his biggest worry is that the capacity will not fully build back up after the pandemic is over.

"Government intervention will be required to stop that. If the government invests now to fill the gap that has been created, then we will build back to full capacity.

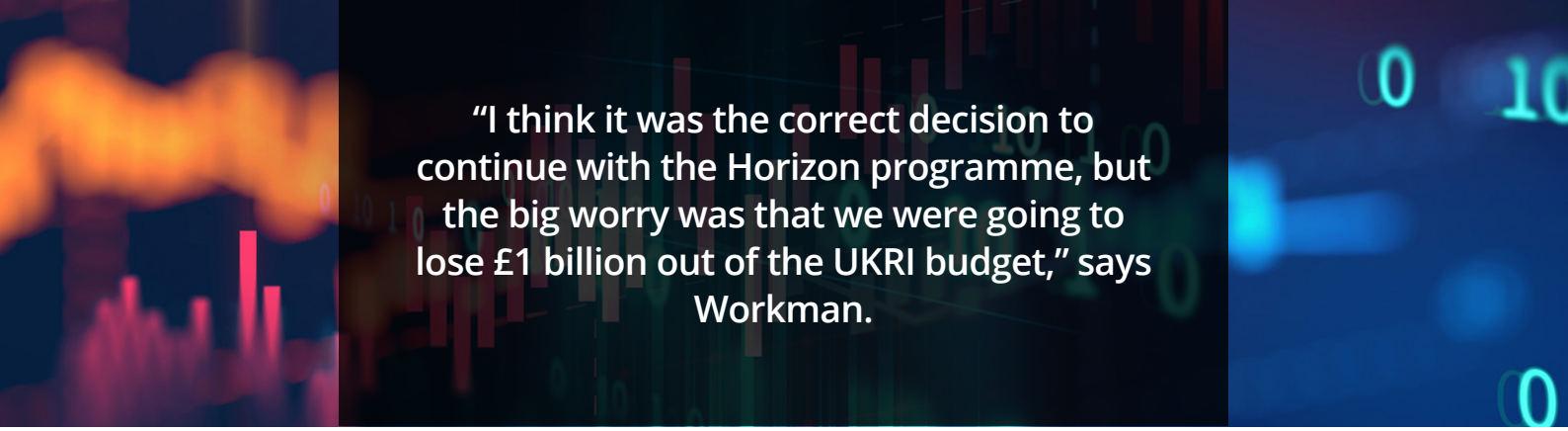
"If not, everything will be delayed – from the next biological paper in Nature through to the next drug discovery project and, ultimately, those new drugs benefiting patients."

Perfect storm

For a time it seemed that the government would actually be cutting funding to UK research – because it was unclear where funding for the European Commission's research and innovation programme Horizon 2020 would be pulled from. There was speculation that the UK Research and Innovation (UKRI) budget might have been used.

Around 18% of the ICR's income comes via UKRI, and the cuts could have reduced that by as much as a fifth.

In a statement the ICR said the cuts could have a massive impact on cancer research as a whole.



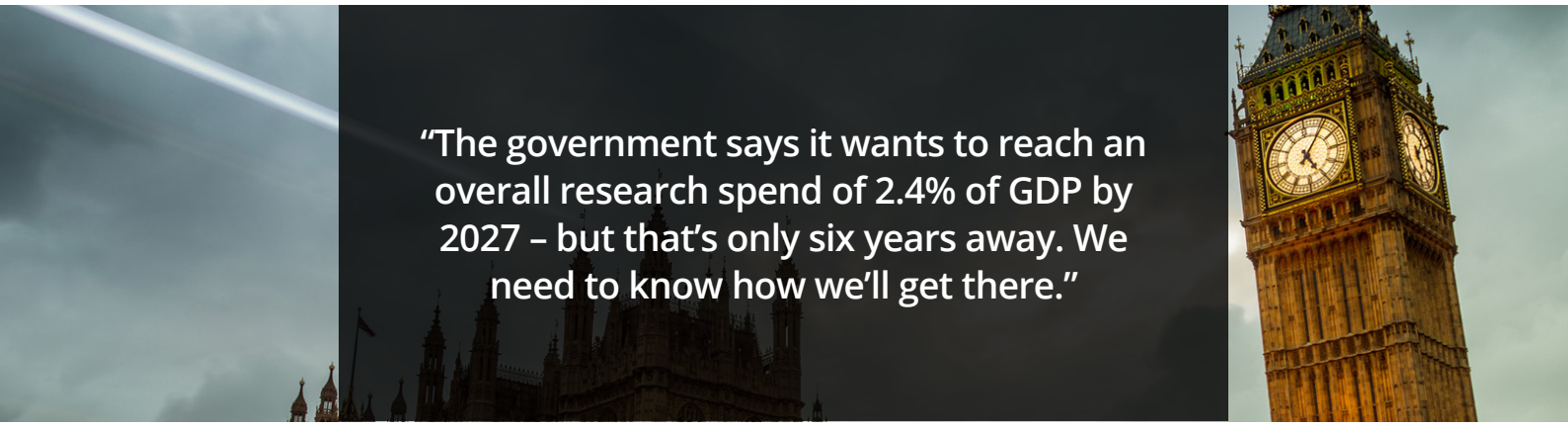
"On top of COVID, that would have been a sucker punch from which the sector probably couldn't have easily recovered."

Pushback from the ICR and other academic leaders eventually led to the government finding funding elsewhere – but Workman says the danger is far from over.

"All we've been reassured about regarding UKRI funding is that this year's £1 billion contribution to Horizon 2020 is now covered and won't impact the existing research budget. Next year, and every year after, the cost of being involved in the Horizon 2020 project will be £2 billion. We have not been told where that £2 billion will come from."

Workman says there is a "joint plea" from academia and UK research companies for the government to provide certainty in terms of planning and investment.

"We need a clear, transparent, ambitious funding plan for UK research.

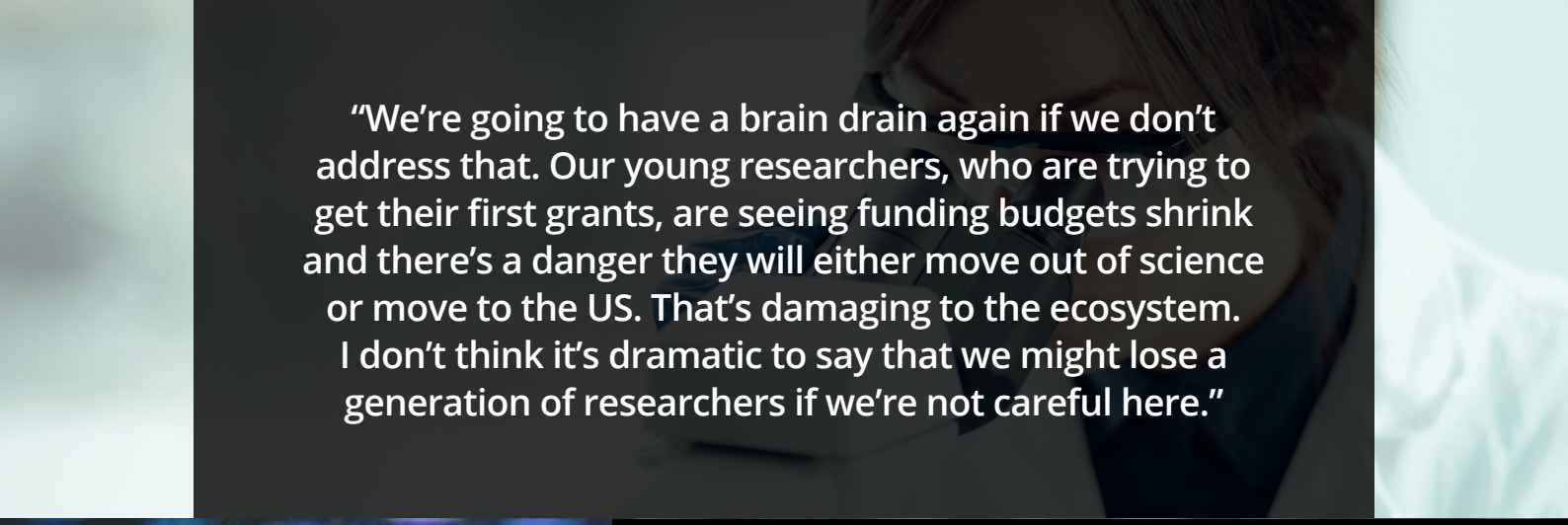


The sector also needs to know how the government will plug the gap from loss of charity funding, he says.

"It has been estimated that the cost to the charity sector will be £1 billion over the next three years, and that it will probably take us longer than that to fully recover from COVID.

"In the grand scheme of things of our industry and what the government has put into other schemes, that doesn't seem like too much of a spend if it plugs the gap for institutions like ours. That would allow us to get back up to speed quicker, and further help us to reach that 2027 vision."

He contrasts the UK situation with the US under president Joe Biden, where the National Institutes of Health (NIH) has recently been promised a $51 billion funding boost.



"We're going to have a brain drain again if we don't address that. Our young researchers, who are trying to get their first grants, are seeing funding budgets shrink and there's a danger they will either move out of science or move to the US. That's damaging to the ecosystem. I don't think it's dramatic to say that we might lose a generation of researchers if we're not careful here."

A bright future

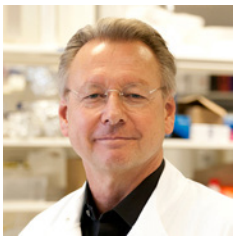
The upside is that if it is able to secure this certainty, Workman is "absolutely convinced" the sector will bounce back, and that the UK will remain among the top places in the world for cancer research.

"We've never had a better understanding of the biology of cancer, new molecular targets for drug discovery, liquid biopsies, DNA sequencing, tests to select patients who benefit from drugs, or the ability to predict the evolution of cancers and how they become resistant. In the next 10 years, all of that will make a huge difference to the survival gap.

"More than half of cancer patients now survive for more than 10 years, and we also expect to see big improvements in harder to treat areas such as pancreatic cancer and brain cancer.

"There's an enormous amount of things to be positive about. That's almost part of the frustration our researchers have – we have all of this incredible knowledge and we know we can make a difference, we just need to be certain that we're able to do it."

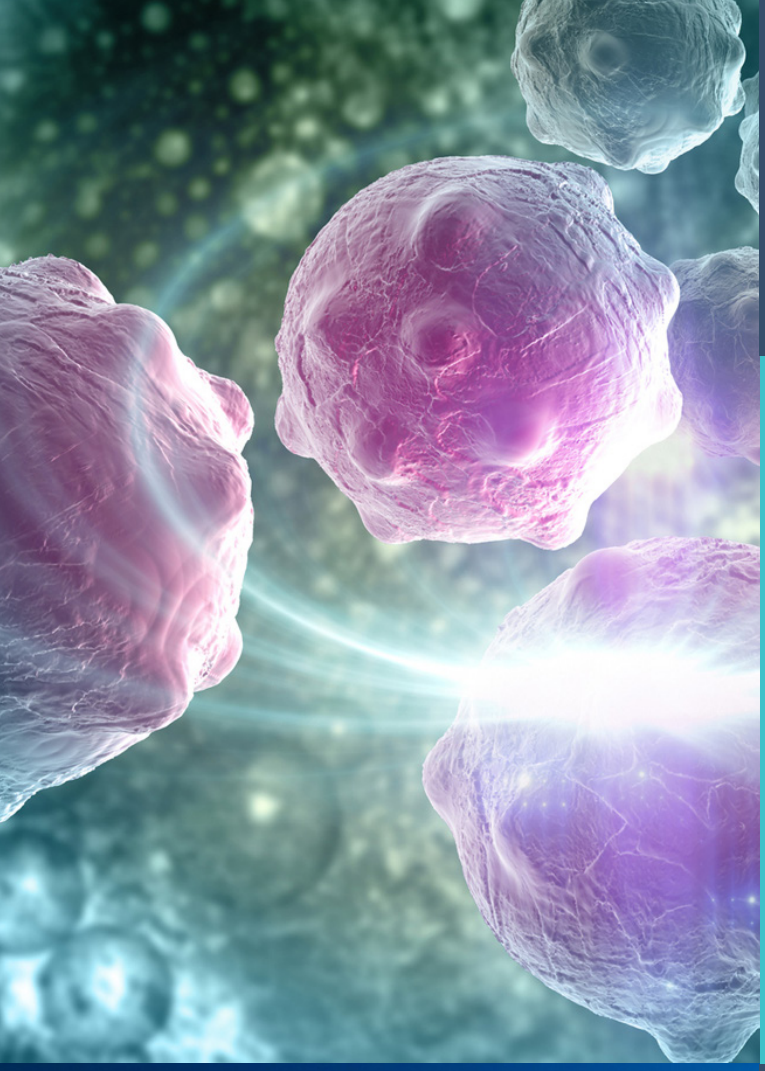
About the interviewee



Professor Paul Workman FMedSci, FRS is chief executive and president of The Institute of Cancer Research (ICR). He is a passionate advocate of personalised molecular medicine and is an enthusiastic practitioner of multidisciplinary cancer drug discovery and development approaches to 'drugging the cancer genome'. Professor Workman has successfully built a series of multidisciplinary drug discovery and development teams in the academic, large pharma and biotechnology company sectors. He has been responsible for the discovery of a number of drug development candidates, including in particular pathfinding inhibitors of the HSP90 molecular chaperone and the PI3 kinase family of signalling enzymes.

About the author

George Underwood is the editor for pharmaphorum's Deep Dive digital magazine. He has been reporting on the pharma industry since 2014 and has worked at a number of leading publications in the UK.



ASCO highlights: the next generation of cancer therapy

For the last two years, the American Society of Clinical Oncology (ASCO) conference has been a reminder that even when COVID dominates headlines, amazing advances are still being made in cancer therapy – including in diseases previously thought almost-untreatable. Here we round up the biggest stories from this year's event, giving us a glimpse into the exciting future of oncology.

Next-gen immunotherapies take centre-stage

Bristol-Myers Squibb and Merck & Co have long been arch rivals in the immunotherapy space with their competing PD-1-blocking drugs Opdivo (nivolumab) and Keytruda (pembrolizumab) – and the competition shows no sign of letting up after both companies presented data from the new class of LAG-3 drugs at ASCO.

Lymphocyte-activation gene 3 (LAG-3) and programmed death-1 (PD-1) are two distinct inhibitory immune checkpoints that are often co-expressed on tumour-infiltrating lymphocytes (TILs) – white blood cells that migrate to tumours attempting to kill them.

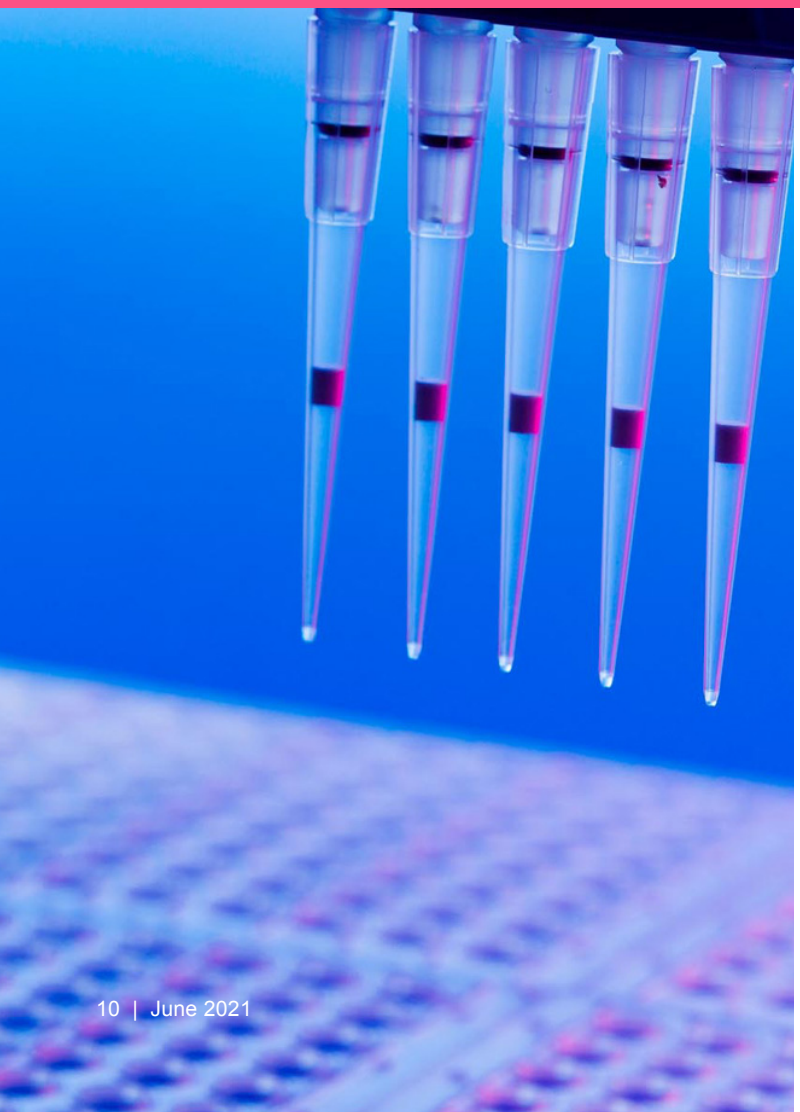
Tumours fight off the attack by stimulating LAG-3 and PD-1, causing the white blood cells to become exhausted.

The combination activates T-cells, beefing up the improved immune response and promoting tumour cell death.

Bristol-Myers Squibb made a splash ahead of the conference with results showing a single infusion of its LAG-3 blocker relatlimab and Opdivo improved progression-free survival in advanced melanoma compared with Opdivo alone.

Not to be outdone, Merck & Co countered with results from its LAG-3 favezelimab, with phase 1 data showing a combination with Keytruda could have potential in metastatic colorectal cancer.

BMS said that this is the first regimen showing a statistical benefit over PD-1 monotherapy such as Opdivo in metastatic melanoma, which has become established as standard of care in the indication in the last decade or so.



Results come from the phase 2/3 RELATIVITY-047 trial in patients with metastatic or unresectable disease.

In those receiving the combination, the median progression-free survival (PFS) was significantly longer at 10.12 months compared with 4.63 months in those receiving Opdivo.

The PFS benefit of the fixed-dose combination was observed early, at the time of the first scan, and was consistent over time.

In exploratory, descriptive analyses, the combination of relatlimab and nivolumab extended PFS regardless of pre-specified subgroups and stratification factors, BMS said.

Safety-wise no new signals or types of clinically important events were identified with the fixed-dose combination therapy when compared with Opdivo monotherapy.

However there were more grade 3/4 drug-related adverse events – 18.9% in the combination arm compared to 9.7% in the Opdivo arm.

Discontinuation rates were higher in the combination arm (14.6%) compared with 6.7% seen in the Opdivo arm.

BMS said that results will be used as the basis for filings with the FDA and other regulators.

Meanwhile, Merck & Co's data from favezelimab comes from a small group of patients with metastatic colorectal cancer, showing it shrank tumours in five patients (6.3%), with one seeing their tumours clear completely.

PFS was a median of 2.1 months and overall survival was around 8.3 months, according to the trial.

PD-1 inhibitors have a low response rate in this form of cancer, working in only around a fifth of patients as their tumours aren't easily targeted by the immune system.

MacroGenics (tebotelimab) and Novartis (LAG525) are among around 20 other companies that are researching LAG3 drugs.

Adjuvant therapies make waves

Both Opdivo and Keytruda also showed promising results in adjuvant settings at ASCO. Adjuvant Opdivo provided "clinically meaningful efficacy" in updated results of phase 3 trial of patients with esophageal cancer (EC) or gastroesophageal junction cancer (GEJC).

The study's primary results, which were published earlier this year, showed that the median disease-free survival doubled with nivolumab versus placebo — 22.4 months and 11 months, respectively.

New data at ASCO 2021 showed that distant recurrence was lower with nivolumab versus placebo (29% and 39%, respectively), as was locoregional recurrence (12% and 17%, respectively).

Meanwhile, Keytruda was shown to significantly improve disease-free survival when given to renal cell carcinoma (RCC) patients following surgery, according to results from the phase III KEYNOTE-564 study.

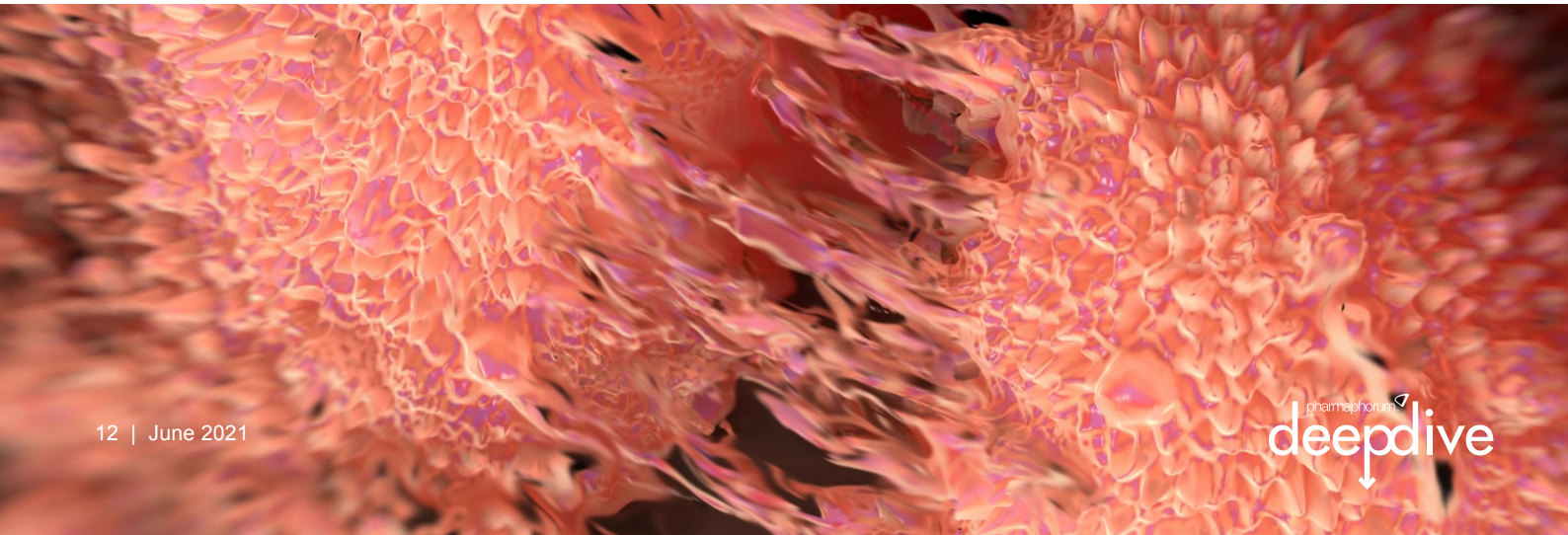
The addition of the drug as adjuvant therapy led to a 32% reduction in the risk of disease recurrence or death compared with placebo.

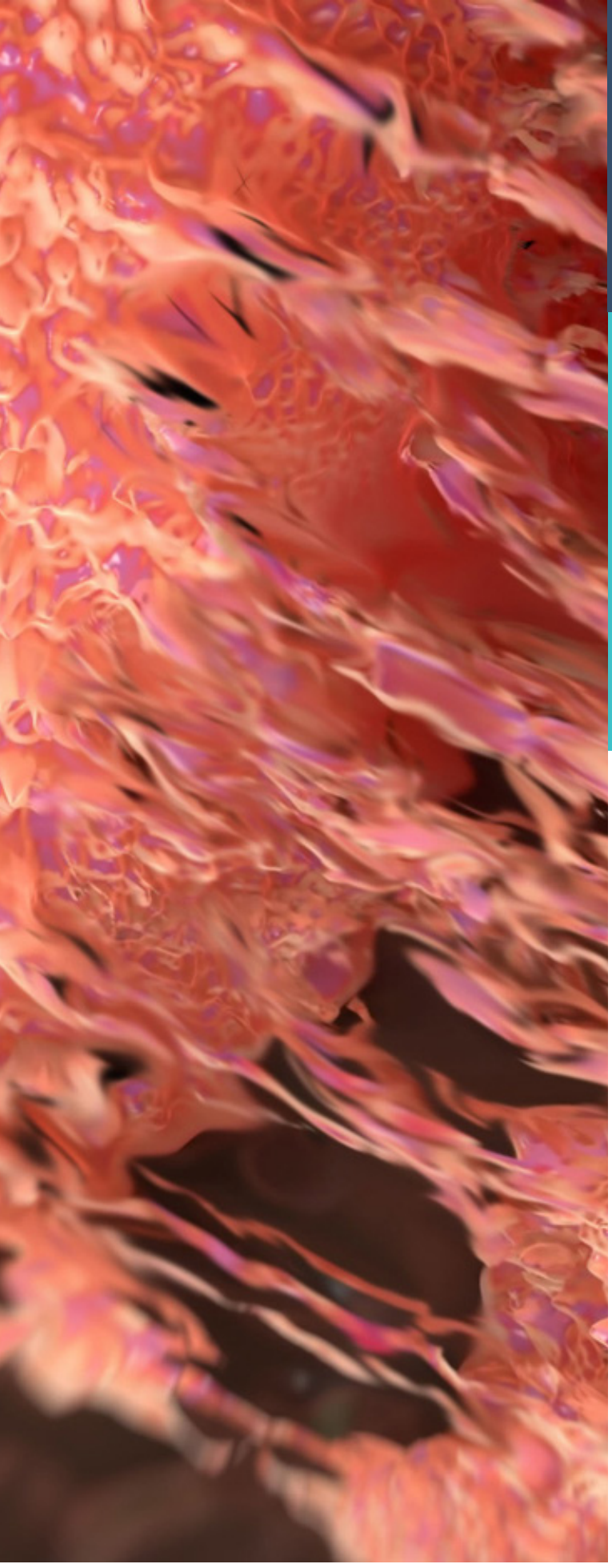
Adjuvant therapy seemed to be something of a theme at this year's conference, with Roche's PARP inhibitor Tecentriq (atezolizumab) also showing that it could improved disease-free survival by more than one-third in people with PD-L1-positive resectable early-stage lung cancer, if administered following surgery and chemotherapy.

Meanwhile, AstraZeneca and Merck & Co's Lynparza is primed for even wider use in the treatment of breast cancer after a phase 3 trial showed it could extend the time for the cancer to return when used as adjuvant therapy.

Giving Lynparza (olaparib) to women with BRCA-positive, HER2-negative breast cancer straight after chemotherapy and surgery to remove the tumour reduced the risk of recurrence, secondary cancers or death by 42% compared to placebo after 2.5 years of follow-up.

Lynparza is already the most widely-used drug in the PARP inhibitor class, and the new results extend its lead over rivals like Clovis Oncology's Rubraca (rucaparib), GlaxoSmithKline/Tesaro's Zejula (niraparib) and Pfizer's Talzenna (talazoparib).





CAR-T: Novartis, Gilead, Allogene and J&J ready for a tussle

Novartis' Kymriah has had the CAR-T therapy market for acute lymphoblastic leukaemia (ALL) to itself so far, but Gilead Sciences' Kite subsidiary is now looming in the rear view mirror – armed with new data for its already-filed rival Tecartus.

Results of the phase 1/2 ZUMA-3 trial of Tecartus (brexucabtagene autoleucel) reported at ASCO revealed a 71% complete response rate with the CAR-T in heavily pre-treated adult patients with B-cell precursor ALL.

The median response duration was 12.8 months, while overall survival was more than 18 months for all patients in the study and had not yet been reached for complete responders.

Kymriah (tisagenlecleucel) was approved for relapsed/refractory ALL in 2017, but its label covers use in children and young adults aged up to 25, who account for the bulk of cases of the blood cancer.

Gilead/Kite have taken a different approach with Tecartus, going after an adult patient population initially, but there will be overlap between the two therapies in the young adult category. Around 40% of ALL cases occur in adults, although most occur in people aged under 20.

Kymriah achieved a complete response rate of 81% in its relapsed/refractory ALL trial – called ELIANA – with 95% of patients MRD negative.

But Novartis has an opportunity to fight back and muscle into territory held by Gilead's other approved CAR-T Yescarta (axicabtagene ciloleucel), after hitting the mark in the phase 2 ELARA trial in relapsed or refractory follicular lymphoma (FL).

The ELARA trial revealed a 66% complete response rate and 86% overall response rate with Kymriah in this form of non-Hodgkin's lymphoma (NHL), which accounts for around 22% of all cases of the cancer.

Yescarta was only approved by the FDA for FL in March, adding to its earlier green light in B-cell lymphoma, and Novartis now says it intends to file for approval of Kymriah in FL later this year.

However, both Novartis and Gilead may have to watch their backs in the coming years, as relative CAR-T newcomer Allogenemoves forward with its "off the shelf" rival therapy.

Tecartus is also being tested in paediatric and adolescents patients with previously-treated ALL in the ZUMA-4 study, which would put the two therapies in direct contention. However results from that aren't due to read out until 2023, according to the entry for the study in the clinicaltrials.gov database.

Tecartus is already approved to treat relapsed/refractory mantle cell lymphoma (MCL), becoming the first CAR-T for that indication in mid-2020, and made sales of $31 million in the first quarter of this year.

It was filed for the adult ALL indication in the US in April, and has a priority review from the FDA, with a verdict due in October.

"Outcomes in adults with [ALL] are poor relative to what is observed in children, with less than half of people over 20 years of age expected to survive the illness," said Bijal Shah of Moffitt Cancer Centre in Florida, who led the ZUMA-3 study.

Importantly, most of the responses seen with the CAR-T were associated with undetectable minimal residual disease (MRD), he added. Undetectable MRD is associated with longer remissions – and potentially longer survival – in ALL and other blood cancers.

Allogene was founded in 2018 by the former leadership team from Kite Pharma, on a mission to outdo the CAR-T therapies they had just sold to Gilead for $12 billion with drugs that could be cheaper and easier to use.

Currently-approved CAR-T therapies are autologous, meaning the the patient's T cells are harvested and genetically modified to include a new gene that helps then target and kill lymphoma cells, and the modified T cells are then infused back into the patient.

It's a process that can take at least a couple of weeks, and carries a risk of side effects including cytokine release syndrome (CRS), which can cause fever and flu-like symptoms and can be life-threatening. Around a quarter of patients treated with Tecartus had a severe immune reaction, and there were two deaths in the trial.

Allogene's allogeneic or "off the shelf" cancer cell therapies, however, are derived from a bank of cells and can be manufactured and administered in bulk like drugs.

In phase 1 results released in the run-up to ASCO, the ALLO-501 lead candidate showed an overall response rate of 75% and a complete response rate 50% in a group of patients with large B-cell lymphoma (LBCL) and follicular lymphoma (FL) who had not previously received CAR-T.

The complete response rate was 36% in CAR-T naïve patients with LBCL, data described by a team of analysts at Jefferies as "solid".

They noted that it "checks all the boxes for a compelling profile versus its autologous peers" adding that the safety profile of '501 seems to be "clean".

Overall key opinion leaders viewed the safety profile as "very tolerable and don't see any outstanding risks over autologous CAR-Ts".

Another considerable advantage of allogeneic CAR-T products is that they can be administered with a second booster shot, something that is not possible with autologous CAR-Ts.

The Jefferies analysts noted that across two studies, four patients were converted from a partial response to a complete response with the ALLO647 booster shot.

In its analysis Jefferies noted that when asked about the relative importance of attributes for non-Hodgkin lymphoma treatments, doctors prioritise efficacy and patient access.

"In comparison to autologous CAR-Ts, allo-CAR-Ts have a unique advantage in broader patient access through addressing issues such as undesirable wait time, manufacturing failure, and high production cost," said the team led by equity analyst Kelly Shi.

In a separate note Jefferies analyst Michael Yee said that the strong data from the allogeneic therapies will prompt Gilead to expand the cancer cell therapy infrastructure it built following the acquisition of Kite.

A move into cell therapies for solid tumours, which marketed CAR-Ts cannot tackle, could be next, although continuing research into next-generation CAR-Ts could be an option.

However he added: "That said, Yescarta will also always have much longer durability (over 3 years now) and follow-up, more data and safety."

Led by former Kite execs Arie Belldegrun and David Chang, Allogene partnered with French firms Cellectis and Servier to develop allogeneic CAR-Ts, after buying out Pfizer and taking over its role in an R&D collaboration.

The BCMA boom

Also entering the ring with its own CAR-T therapy is J&J, whose multiple myeloma therapy ciltacabtagene autoleucel (cita-cel) – developed in collaboration with Legend Biotech – demonstrated a 98% overall response rate, 80% stringent complete response rate and 66% progression free survival rate at 18 months with no new safety signals in the Phase 1b/2 CARTITUDE-1 study

The drug targets B-cell maturation antigen (BCMA) – making it part of an increasingly crowded category.

Other drugs targeting BCMA include GlaxoSmithKline's antibody-drug conjugate (ADC) Blenrep (belantamab mafodotin) and Bristol-Myers Squibb/bluebird bio's Abecma CAR-T therapy (idecabtagene vicleucel).

GlobalData reckons that therapies targeting BCMA now account for approximately 10% of all immuno-oncology drugs in phase 1 to 3 development, but it's worth noting that most patients diagnosed with myeloma will relapse over the course of their disease and there is some evidence that patients who fail one BCMA-targeting therapy may still gain benefit from another.

At ASCO J&J also highlighted results for another myeloma drug, bispecific antibody teclistamab, which targets CD3 on T-cells as well as BCMA.

Updated results from the MajesTEC-1 study of teclistamab in myeloma patients treated with five prior lines of therapy showed some impressive figures, including a 40% complete response rate and 58% VGPR, that suggest a deepening effect of the drug over time.

There were also no side effects that resulted in dose cuts with teclistamab in the study, which could point to a safety advantage over rival BCMA-targeting bispecific drugs like Pfizer's elranatamab and Amgen's pavurutamab, which have both had studies paused this year due to toxicity concerns.

J&J also reported updated results from the phase 1 MonumenTAL-1 study of talquetamab, another bispecific antibody.

Talquetamab also binds to CD3, as well as GPRC5D, a novel multiple myeloma target

After around six months' follow-up, talquetamab achieved an overall response rate (ORR) of 70% in the 30-patient trial, which recruited subjects who had on average received six prior lines of the therapy for their myeloma.

A sizeable chunk of J&J's oncology pipeline is dedicated to bispecific antibodies. Like the recently-approved Rybrevant (amivantamab), alquetamab and teclistamab have arisen out of the fruitful collaboration between J&J's Janssen pharma division and Danish biotech Genmab, which also generated its $4.1 billion myeloma blockbuster Darzalex (daratumumab).

Other highlights

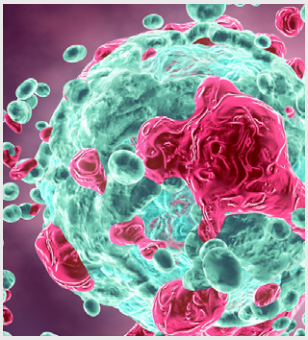
AstraZeneca threw down the gauntlet to AbbVie and Johnson & Johnson with new data for Calquence in chronic lymphocytic leukaemia (CLL) that it says show a safety advantage over Imbruvica – currently dominating the BTK inhibitor market.

In the ELEVATE-RR study, Calquence (acalabrutinib) matched Imbruvica (ibrutinib) when it came to keeping adults with previously treated, high-risk CLL alive without disease progression at a median follow-up of 40.9 months.

Both drugs achieved a progression-free survival (PFS) of 38.4 months, but Calquence was associated with a lower rate of atrial fibrillation.

AZ needs Calquence to deliver financially, as it has invested a lot in the drug. It was originally developed by Acerta Pharma, a company in which AZ bought a majority 55% stake for $4 billion in early 2016.

Novartis' big investment in radiopharmaceuticals for cancer seems to have paid off, after lead candidate 177Lu-PSMA-617 helped men with advanced prostate cancer and few treatment options live longer in a phase 3 trial.



New data from the VISION study showed that 177Lu-PSMA-617 on top of standard care reduced the risk of death by 38% compared to standard care alone in men with PSMA-positive metastatic castration-resistant prostate cancer (CRPC) who had progressed after three or more anti-androgen and prior chemotherapy regimens.

Novartis has been investing heavily in the radio-oncology category, with its Endocyte acquisition followed by other deals including recent licensing deals with iTheranostics and Artios Pharma.

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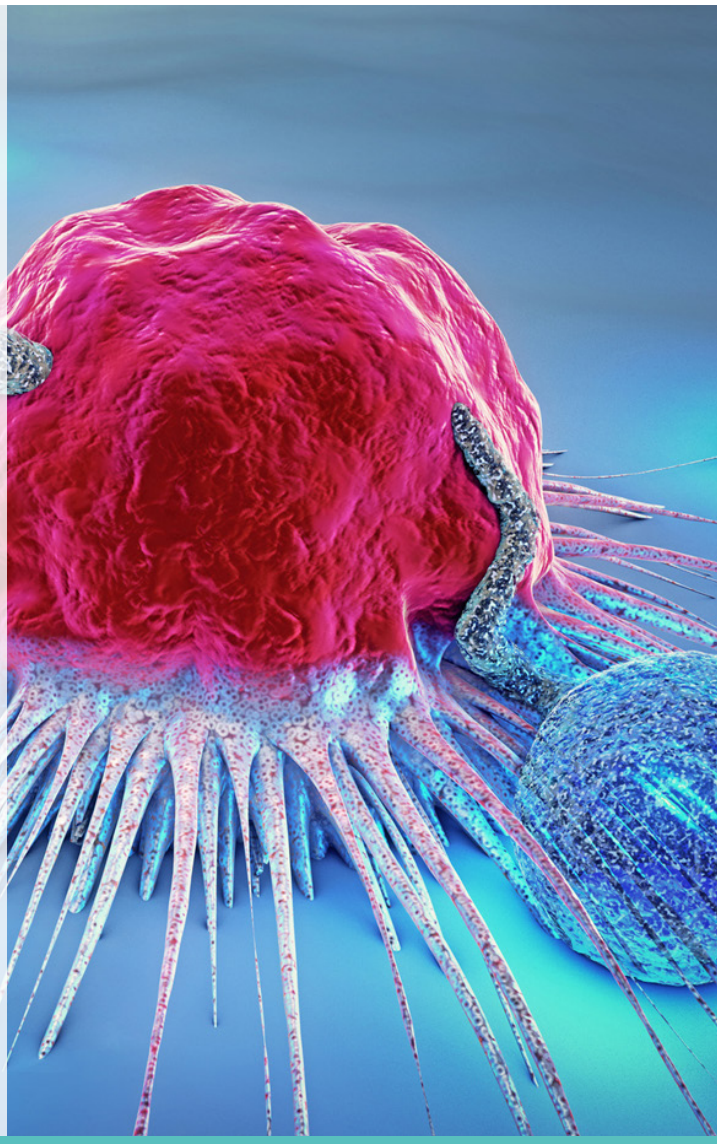
Oncology and a year of COVID: lessons for the future

COVID's impact on cancer care and oncology research has been devastating, but the pandemic has also opened up opportunities to take learnings and create long-lasting change in research, practice and education, says Lucid's Frances O'Connor.



The COVID-19 pandemic might finally be in its latter stages after a year and a half of disruption, but its impact on oncology is likely to last much longer – with potentially devastating effects on long-term survival.

These 'lost years' in cancer care are a result of many cumulative factors – we've seen diagnosis delays, treatment delays, missed scans, missed face-to-face appointments and detrimental changes in treatment and pathway changes; for instance those with slower growing cancers being put on watch and wait regimens instead of treatment to avoid clinic time. As we look to the future, collaboration is key on many levels.

Collaboration in clinical research

The last 18 months have seen some incredible scientific leaps directly tackling the pandemic, brought about by unprecedented alliances seen between pharma companies and between academia and pharma. However, the impact on many other areas of research, including cancer, cannot be ignored. According to the ICR, cancer research has faltered due to the closure and restrictions placed upon labs, redirection of resources to COVID research as well as trial enrolment issues and sample collection challenges. They also note that the livelihood of researchers has been impacted profoundly given the changes and even terminations of some research programmes.

Data collection is a real issue due to many patients shielding because of their immunocompromised status. Treatment approvals have, and will, be impacted where registrational trials were undertaken in this time with many deviations from the set out statistical analysis plan. It is of paramount importance to get our trials back on track – perhaps the more extensive collaborations we have seen during the pandemic could be a way to regain some of the 'lost years', and it's time for a much more egalitarian or revolutionary approach to oncology research. The American Society of Clinical Oncology (ASCO) has published an extensive report outlining learnings from the pandemic and setting out key pillars for future research and delivery of care.

Using innovative, collaborative, digital randomised trials in oncology is one such bright idea. The super-smart COVID-19 Recovery trial is a successful example of a platform trial, which has shown us how large clinical studies can be run in an agile way and be set up much quicker, evaluating several interventions against a common control, pooling datasets and minimising the data that each clinical team needed to collect about each patient, keeping it as fast and straightforward as possible.

In cancer, where there are lots of combinations to be tested in late-line therapy, a trial that can adapt as the treatment paradigm evolves comes with a lot of advantages – there is an opportunity here for bigger, more efficient multisponsor studies.

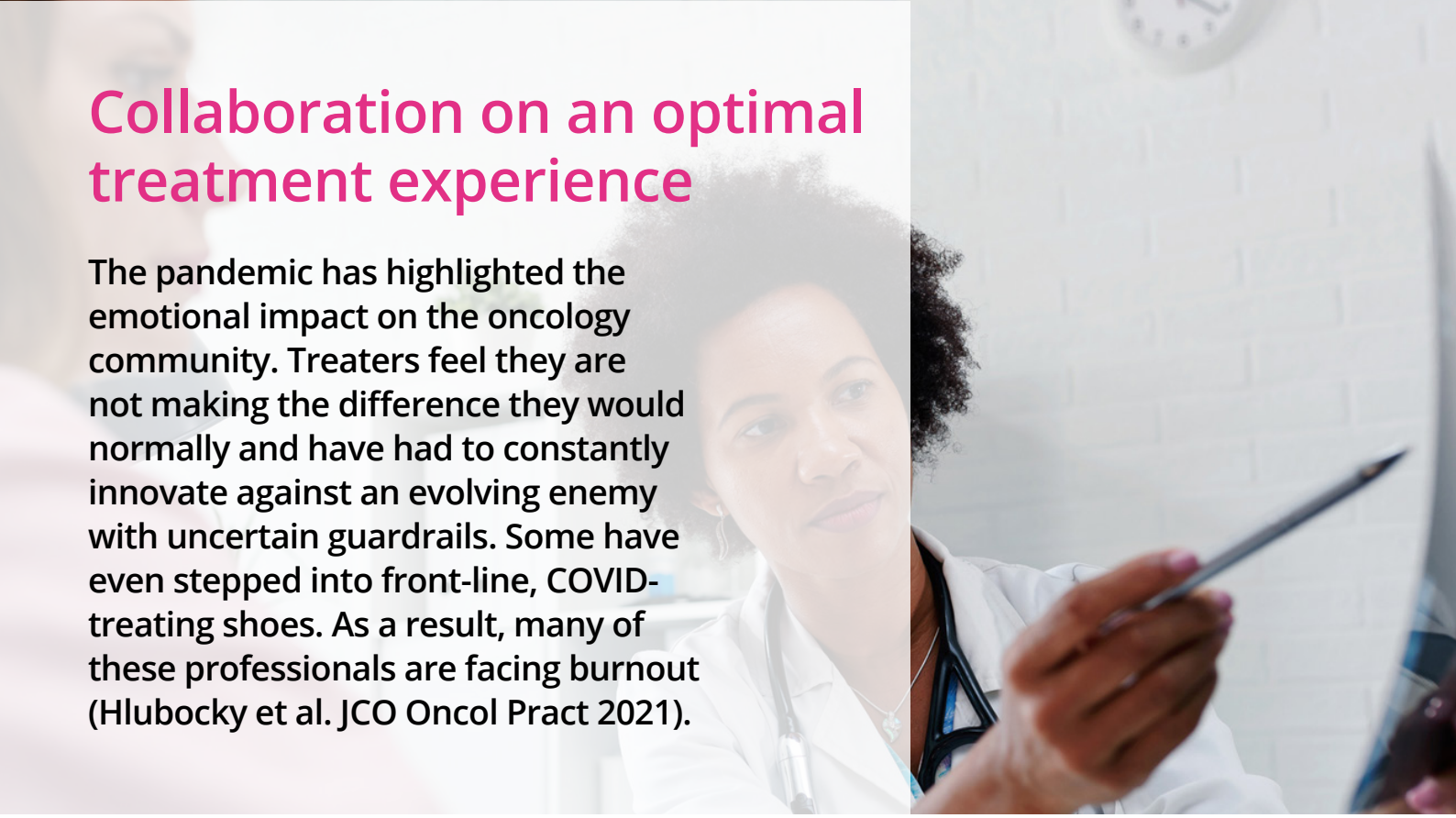
With the continued difficulties researchers face, virtual, decentralised approaches, where a patient never has to go to a research site for assessments are a good option to keep the pace, and perhaps speed up, continued research.

Collaboration on real-world evidence

When it comes to revolution, one clear positive is that the pandemic has magnified the value of real-world evidence (RWE) in oncology and the community is giving this topic the focus it deserves – so much so, that there was significant discussion at ASCO 2020 surrounding telemedicine, accounting for missing data, obtaining laboratory tests and images locally, using remote informed consent procedures, and additional considerations for continuing ongoing clinical trials and initiating new ones.

With the very real concern that we are on the cusp of entering an endemic world, RWE is important in a world with constantly changing goalposts where we need to understand the impact on our patients now and in the future. Partnerships like that between Roche and Flatiron Health will help to develop even further robust approaches allowing this evidence to feature more in regulatory decision making

Collaboration on an optimal treatment experience



The pandemic has highlighted the emotional impact on the oncology community. Treaters feel they are not making the difference they would normally and have had to constantly innovate against an evolving enemy with uncertain guardrails. Some have even stepped into front-line, COVID-treating shoes. As a result, many of these professionals are facing burnout (Hlubocky et al. JCO Oncol Pract 2021).

Where appropriate, there are opportunities for pharma to collaborate and support oncologists with wider 'soft skills' training such as resilience and mindfulness or by offering support networks through their field force.

Cancer patients are enduring treatment changes and setbacks which have the very real potential to shorten lives. We have an ageing population dealing with isolation from family support, who are often the protagonists of appointments, calmers of health anxiety and nullifiers of healthcare avoidance, and these issues are leading to later presentation, and the potential for more advanced disease and worse outcomes overall.

It's a challenging time for all, with systems and processes put in place to manage the risk of COVID which threaten the empathy of care. Our social distancing regulations have, for most, not allowed family members to accompany loved ones to appointments to support them, and coupled with the rise in telemedicine, have highlighted the many communication/education challenges we face. Companies such as ourselves exist to support healthcare professionals and patients by employing strategic problem solving to these challenges.

Sometimes, it's the simple things that make the patient experience better – video calling a relative, recording (where this is possible) the diagnosis chat to refer back to, use of plain language summary documents etc, all of which is challenging when under the additional stresses of operating in a pandemic. Through our educational programmes, we have supported oncologists to understand motivations using MI techniques, we've encouraged deeper and more insightful conversations as well as thinking about overall aims, belief shifts and behaviour changes that are needed to help oncologists bring true value to their patients – but this value has sometimes been harder to achieve in a more remote world.

Collaboration in oncology medical education

It has been mooted that remote consultation is, in part, here to stay. Coupled with the continual changes in practice, we will need to consider what best practice looks like, how we design education to support the changing environment, the different patient-physician interactions and how the changes in the status quo affect behaviour-driven considerations to keep improving patient outcomes.

We have ensured we allow more timepoints for collaboration with our steering committees and insight gathering when designing educational programmes throughout the pandemic, thus allowing us to pivot quickly to address changing needs and fix the healthcare problems within the community we are addressing – rigorous outcomes measurement has been crucial to this agility.

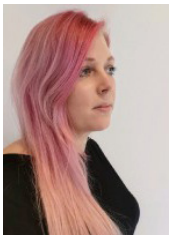
Insights gained from our oncology programmes throughout the pandemic have included the need to be laser-focussed on impact, understanding what is relevant, what is evidence-based and what is practical, and avoiding what is too ethereal or full of conjecture at the same time. Sometimes less really is more.

Hope for the future

A more fundamental lesson from COVID is the importance of getting bigger, more diverse groups of people to talk to each other more, breaking down silos, working for the best interests of the patients, and a singular focus on the task at hand. Some amazing networks have arisen over the pandemic – some as simple as WhatsApp groups of immunologists from multiple countries, who discuss what they're seeing as the situation evolves.

To harness that and bring together people from different vistas would be such a positive learning to take from the pandemic – and it is something pharma could really help facilitate. More joint working across industries, geographies and disciplines coming together to solve the 'big questions', embarking on a journey to find the best way forward together on our journey to cure cancer – wouldn't that be really something?

About the author



Frances O'Connor has 15 years of medical communications experience. She started her career in contract research organisations giving her a good grounding in clinical development. During her career, Frances has been responsible for the strategy and delivery of global and regional, pre-launch, peri- and post-launch communication programmes for many assets with oncology featuring in her top three therapy area specialism. Frances is passionate about storytelling and innovation. She is fanatical about insight, understanding behaviours and decision making, and engaging groups of very special individuals who want to be and want to deliver the very best they can as part of a high performing team creating the best outcomes for the patients we serve.

About Lucid Group

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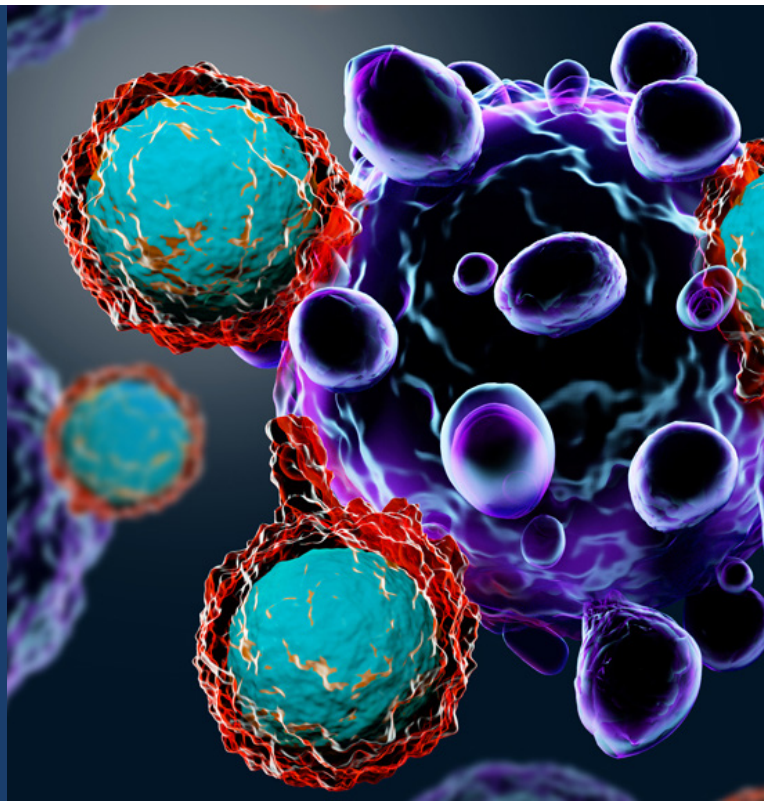
Digital tools key to immuno-oncology's future: report

If ASCO 2021 proves anything, it's that the explosion in immuno-oncology therapies over the last few years shows no signs of slowing down. As the field becomes more crowded, digital tools may be critical for improving outcomes, says a new whitepaper.



The whitepaper, 'The Role of Digital Health in Immuno-oncology Therapy Development and Adoption' from BrightInsight, highlights the many ways in which digital can realise and accelerate the impact of innovative immuno-oncology (IO) therapies.

It says that the growth in treatment options is making it more difficult for oncologists to match patients to the right therapy – but there are many ways in which digital tools can help address this by leveraging data.

"Increasing the accuracy of patient matching – by getting the right patient the right therapy and maximising adherence – could have greater impact on clinical outcomes than more primary innovation with new therapies," the authors point out.

Companion digital diagnostics and clinician support tools – aided by predictive AI algorithms – can help doctors sort through data and decide which IO medicines will work best for a particular patient, ultimately allowing for more precision treatment.

And after a patient has been matched to a treatment, data gathered from companion apps and remote monitoring tools such as wearables can optimise outcomes, both through assessing how well a treatment is working and by flagging potential adverse events.

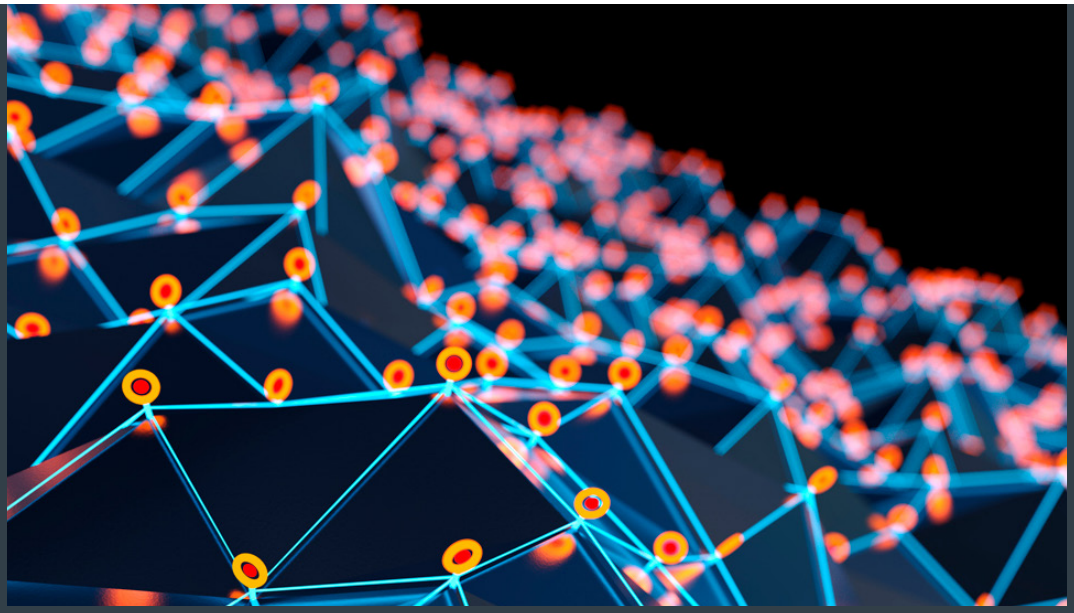
Digitally monitoring a patient's body temperature, for example, can help physicians predict and mitigate cytokine release syndrome (CRS) in CAR-T patients, an early indication of which is fever.

But with increasingly large volumes of data on IO drugs and cancer patients being generated every year, it is becoming more difficult for stakeholders to parse out insights that are actionable and valuable.

"A wide variety of IO combination therapies are gaining approval for the treatment of a wide variety of conditions," the whitepaper says. "As the datasets for each combination become smaller, especially in late-stage clinical trials, validating results with sufficiently powered studies becomes more difficult."

This, too, is an area where digital can make life much easier for pharma companies and clinicians.

"All of these datasets are incomplete and disconnected," says BrightInsight's chief commercial officer, David Matthews. "None of it is coming together in one simple way for clinicians making treatment decisions.



"Digital infrastructure, combined with informatics and predictive sciences, offers us an opportunity to bring that disparate data together and get the most out of it."

One issue is that many health IT systems and biopharma companies run on proprietary software that does not integrate well with others, while data silos exist between biopharma and diagnostic companies.

The whitepaper therefore recommends that companies invest in a common underlying digital infrastructure that enables interoperability and integration across systems.

"A regulated digital health platform enables transferring, processing, and analysing data to support therapy development, making the data more accessible," it says.

Expanding access

Remote monitoring and the real-world data it produces can also address another major challenge with IO drugs – their costs.

IO therapies often have price tags in the range of hundreds of thousands of dollars, and therefore manufacturers are increasingly being asked to show unequivocally improved outcomes in real-world data to continue and expand reimbursement from payers.

"With digital, you can measure how well immuno-oncology drugs are working in a real-world setting in a more reliable way," Matthews says. "If you can demonstrate who gets the most benefit out of a particular therapy, payers may be more likely to reimburse these treatments.

"This enables pharma to take advantage of reimbursement trends that favour outpatient over inpatient treatment, as well as a trend towards value-based care systems in which payers only reimburse drugs that are demonstrably effective."

Digital can also improve access by making clinical trials more accessible to more patients, the whitepaper adds.

Clinical trial enrolment is an expensive and time-consuming process, and currently only 8.1% of oncology patients participate in clinical studies.

The whitepaper notes that AI can assist in the patient matching process by structuring patient records for ClinicalTrials.gov and comparing inclusion and exclusion criteria. Meanwhile, in-depth protocols reduce rejection rates by applying machine learning to pre-screen information against protocols.

From there, remote monitoring can enable more home-based treatment and participation, allowing for patients with more limited resources and difficulties in travelling to participate in studies.

"These applications of digital health have the potential to significantly reduce the costs associated with clinical trials, increase patient enrolment and expand clinical trial coverage," the whitepaper says.

The right path for adoption

Matthews says that these benefits of digital tools are already clear to IO manufacturers – and that the question isn't "whether" they should adopt them, but "when and how".

"Over the next five years digital is going to become essential to the clinical and brand strategy for every type of therapy, and digital will be considered from the outset of IO drug discovery, through to clinical trials and commercial launch."

Matthews says a key decision these companies need to make early on is what to build in-house and what to build in partnership with dedicated digital organisations.

“Digital is such a massive undertaking, and it can present many challenges to a pharma company that does it all by themselves.

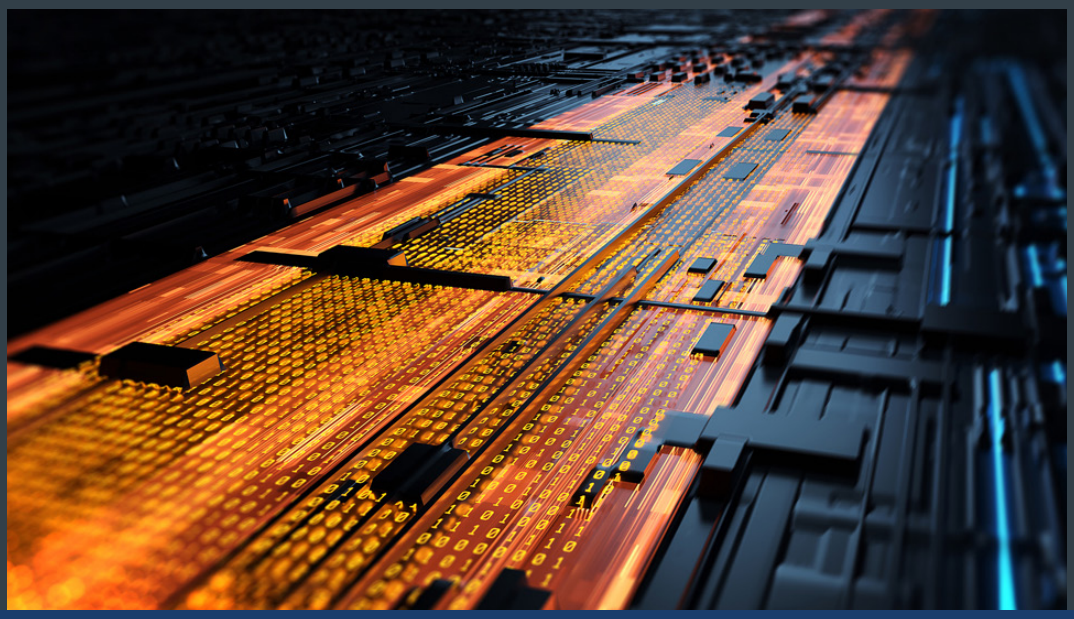
“We see pharma companies going further and faster by partnering rather than trying to build solutions entirely in-house.”

Through this, he says, companies can bring in a common digital health data infrastructure that will underlie every digital solution they create, allowing them to build regulated solutions more quickly

Using a common platform for every digital tool can also pre-empt issues with “app overload,” Matthews says.

“If all these digital tools that pharma creates are not interconnected – e.g., there’s a different app for each treatment or each stage of the patient journey – we run the risk of patient and clinician fatigue.

“That problem becomes even more pertinent in combination IO treatments, when there might be different tools for each drug in the combination.



“Pharma can provide more value by connecting disparate data across every engagement point and facilitating the flow of the patient journey through a common ecosystem.”

And if that underlying infrastructure has regulatory considerations built in, Matthews says, it can help minimise the time and administrative burdens associated with regulatory approval.

"Getting regulatory approval for a digital device can be a huge endeavour; there's a massive volume of accreditations and certifications that are necessary just to begin building these tools.

"In cases where a digital tool is actually making a clinical decision based on the measurement – such as a temperature sensor warning of the risk of CRS – regulatory bodies will want to be heavily involved and have a lot of oversight on what is produced.

"Because of that, we strongly encourage companies to think about the regulated nature of their digital endeavours or digital ambitions from the very beginning."

Beyond this, he says that the biggest remaining barrier to ensuring widespread adoption of digital tools in immuno-oncology is awareness among doctors and patients.

"We need to make sure clinicians recognise that solutions like clinical decision support tools are not designed to replace them, but instead can help them do the best job possible.

"Likewise, the purpose of these tools for patients is not to make their life revolve around a treatment plan, but to enable them to have a better life because their treatment is managed more effectively through digital.

"The awareness piece has to focus on how digital can demonstrably make the lives of patients and clinicians better from an experience and outcomes perspective."

Asked what he hopes people can take away from the whitepaper, he says that companies working in immuno-oncology should recognise that digital transformation is already happening, whether or not they are ready for it.

"We have ample evidence to show that it's valuable and may improve outcomes – so the question then becomes, what is pharma going to do about it?

"The best answer is to get involved and provide digital solutions, apps, connected devices, and algorithms to the patients and clinicians who are using immuno-oncology treatments in order to generate the best possible outcomes."

To read the full whitepaper, 'The Role of Digital Health in Immuno-oncology Therapy Development and Adoption', visit BrightInsight's website.

About the interviewee

David Matthews, PhD, has 15 years of experience in pharmaceuticals, medical technology, and medical research. Before joining BrightInsight, David was a partner in the Healthcare, Commercial, and Corporate Finance & Strategy Practices at Boston Consulting Group (BCG), where he helped lead the West Coast Medical Technology business. He was selected as an Ambassador to BCG's internal thinktank, the Henderson Institute, where he designed and published on new economic models for biopharma products, including building the Netflix model for curative therapies. Prior to his time at BCG, David was a computational neuroscientist, with more than 20 publications and conference proceedings across machine learning, bioinformatics, brain imaging, neuroanatomy, and health economics. David holds a PhD in Computational Neurobiology from The University of California, San Diego and the Salk Institute, where he was a National Science Foundation (NSF) Research Fellow and NSF Center for Theoretical Biological Physics Fellow; and a Bachelor with honors in Molecular Biology, and minors in Bioengineering and Neuroscience, from Princeton University.

About BrightInsight

BrightInsight

BrightInsight provides the leading global platform for biopharma and medtech regulated digital health solutions. When speed matters, we help companies accelerate time to market for regulated digital health offerings across therapeutic areas, including apps, algorithms, medical devices, connected combination products, diagnostics, and Software as a Medical Device (SaMD).

BrightInsight replaces the need for lengthy and complex 'build from scratch' implementations by offering configurable software modules and a proven platform built under a Quality Management System to support global security, privacy, and regulatory requirements. When building digital health products on the BrightInsight Platform, compliance is future-proofed as intended use changes scale across geographies.

Lessons from the first generation of cell and gene oncology trials

Advances in cell and gene science are paving the way for transformative cancer treatments, but there are still many complexities in delivering clinical trials for these therapies. ICON's Tamie Joeckel and Brandon Fletcher take us through best-practice approaches to CGT studies and discuss what the future could hold for this exciting area.

Cell and gene therapies (CGTs) might be showing amazing promise in tackling cancers that were previously thought almost-untreatable, but their novelty and complexity mean the industry is still working out how best to run trials for these therapies – which have some key differences from 'traditional' studies.

ICON was one of the first CROs of scale managing CGT trials, and Tamie Joeckel, the company's global business lead for their cell & gene therapy center of excellence, says they have learnt from first-hand experience what does and does not work.

"When we first started working in the earliest CAR-T programmes, there was definitely an overall lack of awareness of how these trials are different from traditional studies," she says. "We were literally learning alongside our sponsors.

"As research in the area has grown, we do see more discussions and participate with various organizations on the work around defining standards – but there are still gaps."

She adds that there is not a "one size fits all" approach to these studies, and that working with clients on CGT programmes often present unique challenges, requiring detailed reviews of workflows, communication plans and strategies.

"In the past, very few companies seemed to grasp just how different CGT trials can be from standard trials," adds Brandon Fletcher, cell and gene therapy principal at ICON. "Every trial, therapy, mechanism of action etc. is vastly different – therefore so are the processes, the skillsets, the knowledge and even the resources required."

Nevertheless, Fletcher and Joeckel note that there are a few common challenges and best-practice solutions that apply to the majority of CGT studies.

A complex supply chain

One major difference between CGT trials and traditional studies is in how the supply chain needs to operate – Joeckel says the term "orchestration" is more appropriate here than in any other area.

"This is the most complex supply chain in medicine. When we come to the table to discuss requirements, we're often talking to groups who don't understand the nuances of working with 'living therapies'. Cell therapies require ultra-cold temperatures, micro-managed timelines, rigorous quality standards and coordination of an extremely complex ecosystem that involves sites, service providers and the patients," she explains.

"Chain of custody and chain of condition is of the utmost importance as shipments and storage are both time and temperature sensitive. In autologous programmes, the patient's own cells are used to manufacture a batch of a single dose, so the chain of identity must be tracked from the point of cell collection through multiple handoffs from manufacturing to final dose administration.

"We spend a significant amount of time working with sites to integrate their specific procedures with the IP and sponsor's cell therapy manuals and protocols. We routinely hold dry runs with mock shipments with each site to document and train site personnel."

Finding the right site

Site capabilities in general are a key concern for CGT programmes. Especially in rare diseases, these sites need to be highly specialised – requiring unique and extensive resources that go beyond therapeutic expertise and patient population such as availability of validated apheresis units, cell therapy labs, storage availability or liquid nitrogen storage.

Joeckel says there is often competition for the most desirable sites.

"We also have to research and consider the CGT competitive programmes that can overlap," she says. "Site selection requires robust feasibility with detailed patient population assessment. Strong site relationships and leveraging patient advocacy groups are key. ICON has made significant investments in building global site intelligence databases that allow us to 'think outside the box' to expand site selection when necessary."

Likewise, Fletcher says that sponsors need to conduct deep due diligence regarding site resources.

"You also need to know your centres and their capacity. Don't assume the key centres with the greatest experience will have the capacity for another trial, as CGT trials are exhaustive and drain the system."

A related challenge is data management.

"Data in a CGT trial does not follow the standard linear curve as seen in standard trials, where data accumulations slowly build over time," says Fletcher. "Roughly 80% of study data collected in CGT trials is in the first few weeks, from screening to post infusion. This significantly impacts the site entering the data, the clinical monitoring, and the risk of not obtaining expedient exposure of potential safety information – thereby compromising the ability to extrapolate critical information for forward protocol and safety decisions.

"Not to mention the site impact, those providing both the clinical care and the data, this nuance adds to the already diminishing site resources and the overtaxing of clinical site collaborators."

Fletcher says that sponsors and CROs need to optimise tools and techniques used to manage high volumes of data.

"This might include: Lab Sample Work Flow, which clarifies the optional paths of lab samples; Positive Lab Reconciliation, which provides seamless reconciliation with the specialty lab from the start; Data Cleaning Plans, which define review by role, thus eliminating gaps; or batch cleaning early and often to facilitate cleaning of bolus of data collected in the first six months of a trial."

The regulatory environment

All these factors are coupled with what Fletcher says are "intense and multi-layered" Regulatory Affairs and Regulatory Submissions processes.

"The labelling of CGT therapies and any related products as genetically modified organisms adds multiple layers of reviews, considerations, red tape etc. They also require heavy involvement of institutional biosafety committees (IBCs), and often other oversight entities – which can, and often do, bog the study down.

"Meanwhile, aspects like extensive, mandated long term follow-up – sometimes up to 15 years – raise their own, entirely new sets of complications.

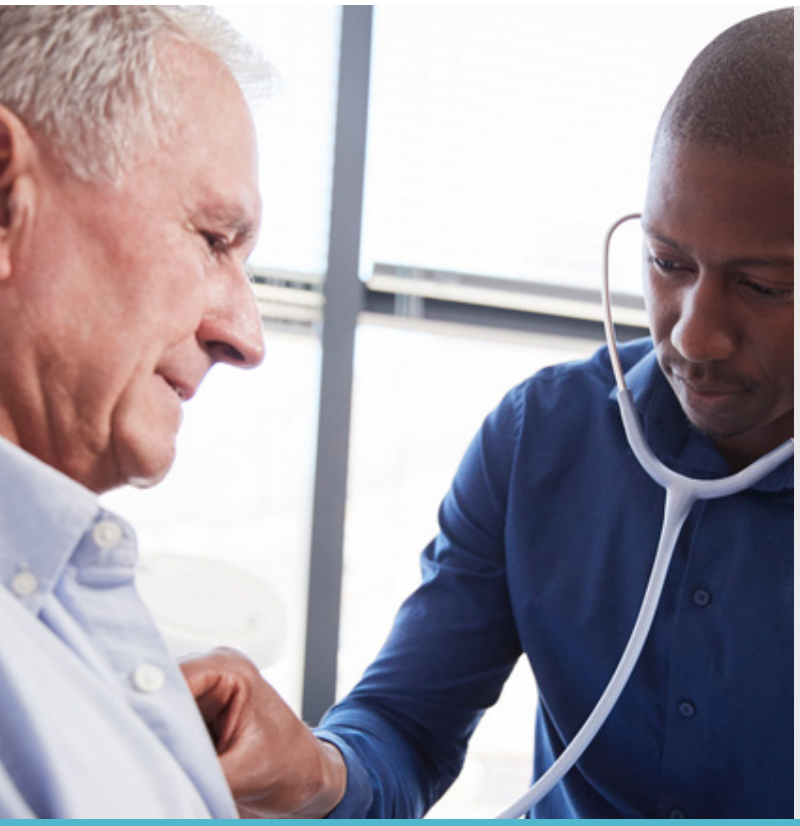
"We also have to account for unique and complex serious adverse events. Non-CGT trials do not typically require intense understanding of cell therapy related syndromes such as CRS, immune effector cell-associated neurotoxicity syndrome, etc."

Fletcher therefore stresses the importance of managing long term follow up strategy early, having it in place before study launch, and also engaging early with the FDA and the CRO.

Patient engagement

At the centre of these concerns, though, are the patients themselves.

"In CGT trials, patient centricity isn't just a term or concept – many times the patient is the product and the process!" says Joeckel. "That means the patient engagement continuum is critical.



"Beyond the operational execution excellence that's required, it's also important to remember we're dealing with patients and families who are frightened, who have probably failed standard treatments and are running out of options.

"While there are strict rules around informed consent that dictate how the risks are communicated to the patient and their caretakers, the often incomprehensible technical documents can be daunting. Having a clear, concise and coordinated communication plan that's understandable and transparent about what to expect is critical."

Once the patient journey begins, the coordination of concierge services such as travel planning and coordination is a huge value add to the process, says Joeckel.

"At ICON, for example, we also work with our sponsors to include other conveniences such as inclusion of home health services wherever possible. This was a great help during the pandemic to address site access changes and patient fears."

Another factor is that there are often more eligible patients available than slots for manufacturing.

"Often there is only one drug, made specifically for one patient being made at a time – literally a batch of one," Fletcher explains.

"Expansion of this scalability limitation is underway, and many modalities can now produce cell product volume, but this is not often the case, especially in the earlier, phase I and autologous arena.

"This complicates the patient experience and the ethical care of patients, as waiting for slots and manufacturing at a critical juncture in the patient's journey must be central to design and care decisions."

She says that sponsors should ensure they have clearly defined how patients will be managed around drug manufacturing constraints, and how that fits in with preconditioning, safety management and prophylaxis – especially where there are multiple cohorts in dose/cell load escalation and dose finding phases.

Best practice in CGT trials

Overall, Fletcher says it's important that companies remain flexible and expect to make adaptations during the CGT trial process. Planning and foresight are of utmost importance in programme design and management.

"There is no 'one size fits all' approach.

"You also need to be careful to not bite off more than you can chew," she says. "Delays are costly and you can always expand as you go if necessary."

She adds that sponsors should spend the time and money to fully vet the competitive landscape.

"Some indications are exploding with potential therapies and the competition is broader than just cell therapy trials, including many other targeted approaches such as antibody therapy, BiTES, oncolytics, viruses, vaccines etc."

When preparing for any trial, Fletcher says that sponsors should ensure they have clearly vetted and defined the optimal end points, as well as the biomarkers for secondary or exploratory endpoints.

"For combination treatments, ensure you define whether to go sequential or parallel," she adds.

"Also consider necessary companion diagnostics for both the trial and further marketing ease and co-develop them if necessary."

Finally, Fletcher says that sponsors should be engaging with KOLs as much as possible.

"They add intelligence and credibility to the project."

To navigate all of these potential challenges, from mapping out a strategic regulatory roadmap to fully understanding the manufacturing scale and constraints, Joeckel agrees that strategic planning is "vital", and that it's important to have a "keen focus" on documenting workflows and training – and having the tools and technology to provide ongoing re-training.

"Training isn't a 'one and done' process in CGT trials," she says.

Much progress has been made in finding the best ways to run trials while ensuring efficiency and keeping patients safe – but there are many factors that mean the space will continue to rapidly evolve, and companies will need to stay on their toes and continue to learn.

"Our increasing genome knowledge is likely to continually impact the CGT space," says Fletcher. "We know the genome quite well now and this knowledge expands daily.

"Meanwhile, with roughly 1,000 companies developing in the regenerative medicine space, more brains are dedicated to the development of life altering, potentially curative modalities.

"Sharing this knowledge is our next challenge, though most agree and actively practice sharing the knowledge for overall elevation of the field."

The success of existing CGTs is increasing confidence across the board, which means the pace of change will likely only increase.

"The data is pretty impressive, with some therapies showing 100% response rates, and the management of known toxicities is strongly improving," says Fletcher.

"The CGT space is evolving every second."

Within this context, Fletcher believes we will see more trials directed towards outpatient and early first line settings, especially in slow growing disease and multiple myeloma – as well as a predominance of solid tumour settings now that we can better understand the tumour microenvironment.

"I also expect to see more allogeneic, off-the shelf approaches and more combination therapy trials."

She adds: "Soon we won't need to just rely on the one patient, one patient-specific T cell therapy process. We now are experimenting with other cell types – even cells that we can manipulate to differentiate to anything we want, or can be produced in volume, ready and waiting on the pharmacy shelf.

"This will broaden both the patient availability and also minimise the risk of waiting for the treatment, thus appealing to more caregivers and patients."

And, of course, lessons from COVID-19 will be vital to improving research going forward.

"I need not remind anyone what we have seen and learned from streamlined and accelerated processes created, or leveraged, during COVID-19 drug development," says Fletcher.

"I believe we have seen how we can cut the fat safely, and hopefully this will take hold more broadly, especially for these promising drugs for incurable diseases."

One thing that won't change is the clinical need that CGTs can help address – and Fletcher says that the sector's current trajectory means that there are plenty of reasons to be optimistic about the future across therapeutic areas.

"We are guessing less, hoping less and are now leading with confidence. We are starting to get this down, and as a result we're encountering fewer bumps in the road to slow us down."

About the interviewees

Brandon Fletcher, cell and gene therapy principal, ICON

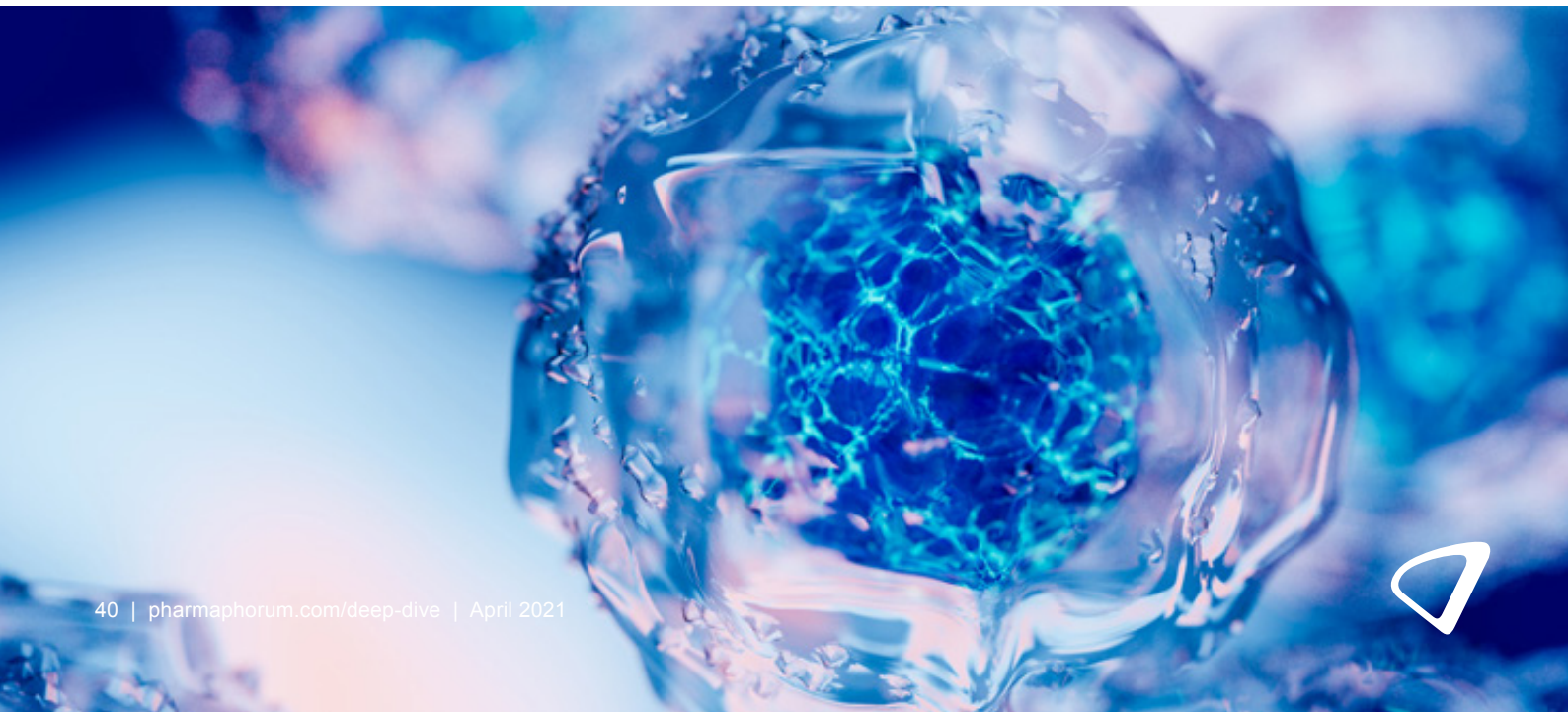
Brandon is a biochemist and cancer immunologist with roughly 30 years of research experience, specialising in haematology-oncology, rare disease and infectious disease. She has held roles in broad immune-oncology and cell and gene therapy research within academia and industry. Brandon is a collaborator with NCI's origination of cancer CGTs and co-founded a global immune-oncology research training and support organisation.

Tamie Joeckel, cell and gene therapy global business lead, ICON

Tamie has over 25 years of experience in commercialising specialty biologics and has worked in cell and gene therapies for the last 8 years in global cryologistics and operations. As a former senior executive at one of the largest drug distributors, she specialised in commercialisation, patient hub services and reimbursement support for plasma derived drugs and therapies for oncology and rare diseases. At ICON, she is a member of the Cell and Gene Therapy Centre of Excellence and supports ongoing strategy and innovation across therapeutic areas and is very active in industry groups focused on developing standards for the regenerative medicine sector.

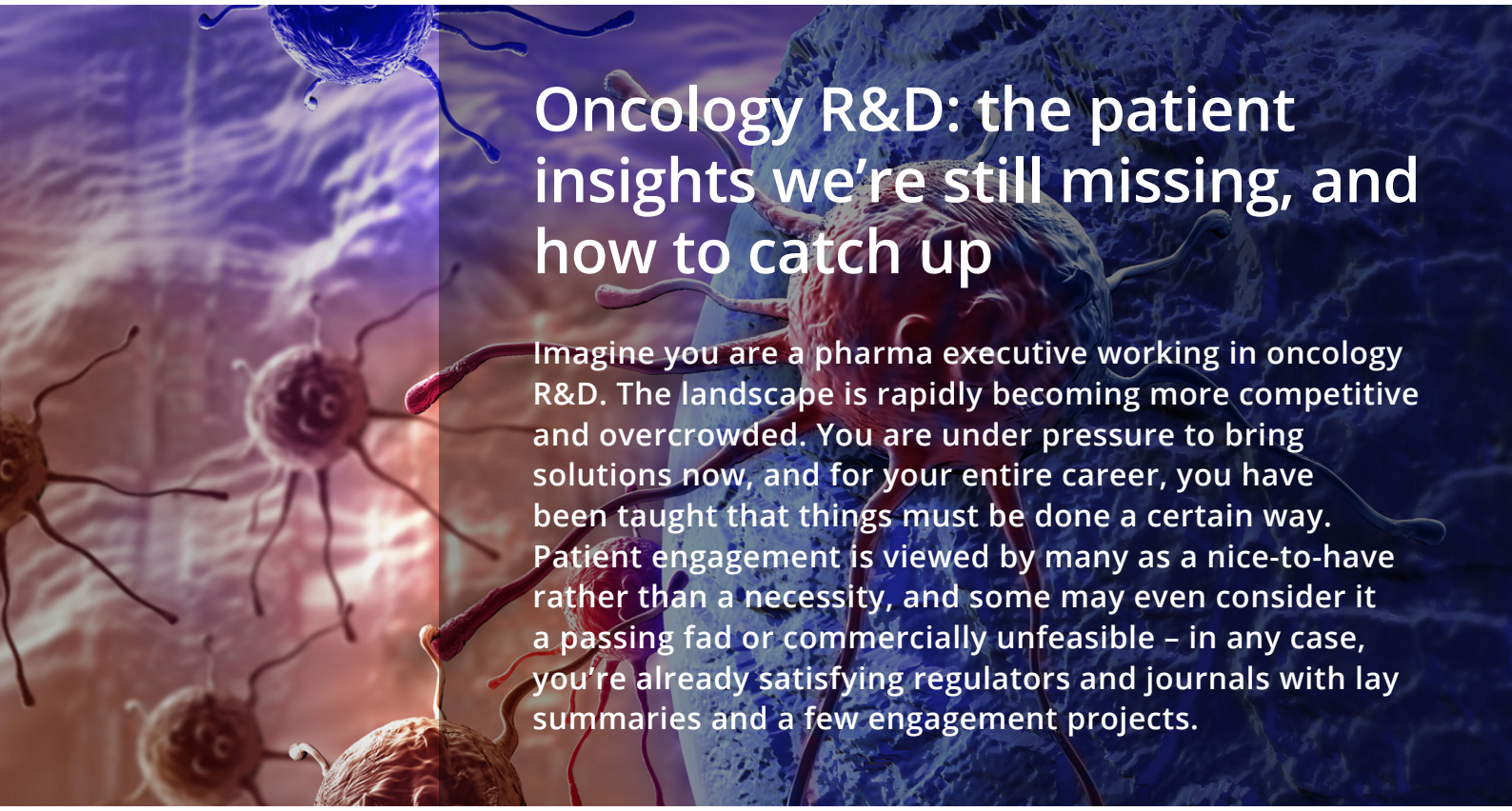
About ICON

ICON is a global provider of consulting, and outsourced development and commercialisation services to pharmaceutical, biotechnology, medical device and government and public health organisations. ICON's focuses on the factors that are critical to clients – reducing time to market, reducing cost and increasing quality – and its global team of experts has extensive experience in a broad range of therapeutic areas. ICON has been recognised as one of the world's leading Contract Research Organisations through a number of high-profile industry awards. With headquarters in Dublin, Ireland, ICON employs approximately 15,250 employees in 94 locations in 40 countries. Further information is available at www.iconplc.com.



PRIME PATIENT

Prime Global Patient Center of Excellence



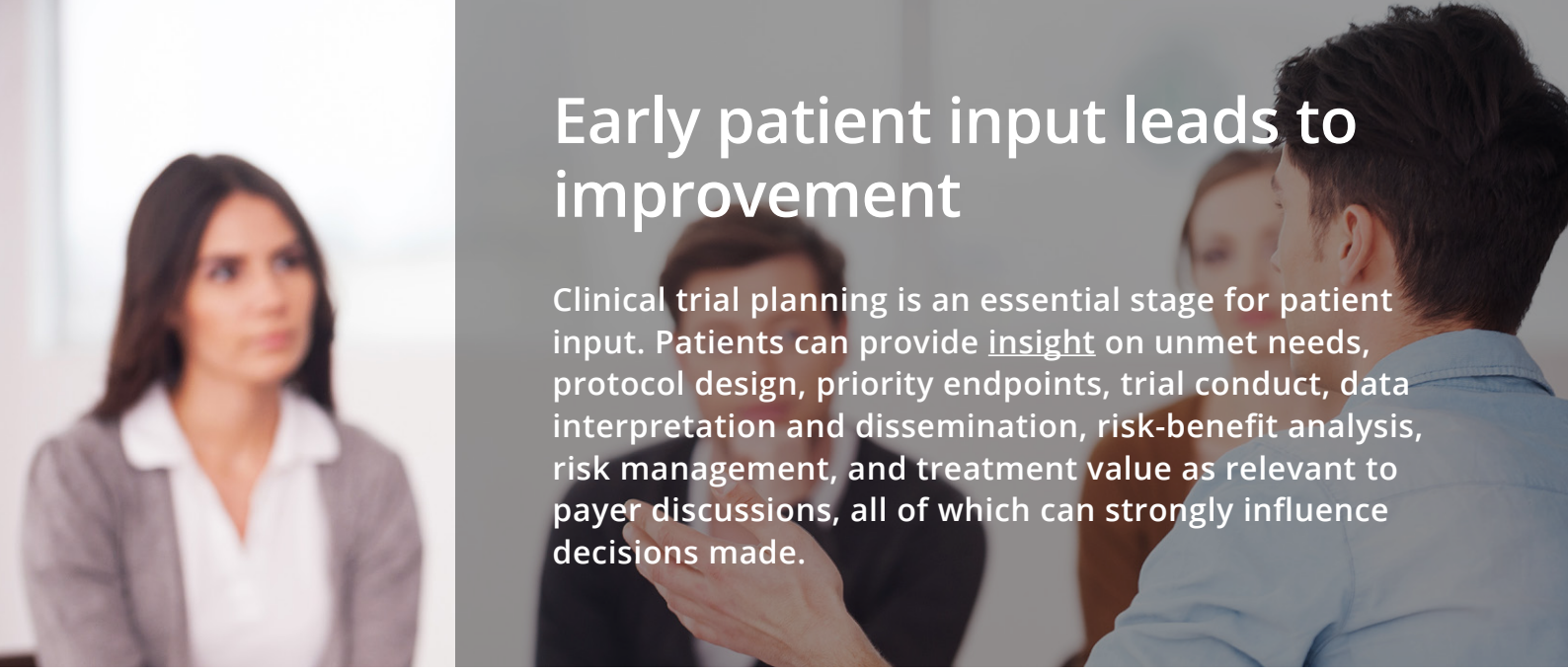
Oncology R&D: the patient insights we're still missing, and how to catch up

Imagine you are a pharma executive working in oncology R&D. The landscape is rapidly becoming more competitive and overcrowded. You are under pressure to bring solutions now, and for your entire career, you have been taught that things must be done a certain way. Patient engagement is viewed by many as a nice-to-have rather than a necessity, and some may even consider it a passing fad or commercially unfeasible – in any case, you're already satisfying regulators and journals with lay summaries and a few engagement projects.

In this pressured environment, are you going to be drawn towards taking a risk by giving patients more power to influence trials? Some may say yes, but many would feel more inclined towards traditional, comfortable R&D methodology. After all, pharma are the experts in getting drugs through trials and onto the market, right?

In fact, the old way is dying out. Evidence shows that, despite historical success, the oncology R&D pipeline is unsustainable, not only becoming increasingly difficult and costly, but also fast approaching relative stagnation. The numbers are striking – in just the 13 years following 2003, R&D costs were estimated to have doubled, and with failure rates as high as 90% and time to market stagnating at ~12 years for the past three decades, the R&D innovation need is urgent. Healthcare systems and patients are suffering the consequences, as drug prices and times to market increase, and access to treatments is consequently hindered in the context of an ageing population carrying an ever-rising chronic disease burden. Indeed, increasing costs pose pharma's biggest R&D challenge today.

Luckily, the tools required to escape from this downward spiral already exist – enter patient engagement. However, despite R&D being the area of pharma most widely accepted as benefiting from the patient voice, few trials are truly patient-centric. Fortunately, patients can provide valuable input across the drug development process, and the costs of accommodating this are low within the scale of investment required for R&D overall. If drug developers, regulators, payers and patient associations can collaborate to arrange deeper and earlier engagement that is structured, well-defined and consistently applied, a triple win for pharma, patients and society is certainly achievable.



Early patient input leads to improvement

Clinical trial planning is an essential stage for patient input. Patients can provide insight on unmet needs, protocol design, priority endpoints, trial conduct, data interpretation and dissemination, risk-benefit analysis, risk management, and treatment value as relevant to payer discussions, all of which can strongly influence decisions made.

Patients who have participated in previous trials can also point to pros and cons of prior studies, which provides a useful benchmark for new trials. Patient input on protocol design is particularly vital, as the design of a trial may exclude target patients before the study has even begun. For example, sponsors may not be aware that the energy levels of patients with long-term fatigue may be strongly affected by the time of day, and thus the time of study appointments (or lack of predetermined clarity around this) may make the trial inaccessible.

There is no substitute for asking patients directly. Both sponsors and physicians have been shown to identify different desired outcomes to patients, and while outcome preferences may overlap, oftentimes patients will suggest a key outcome that was not previously suggested by any other party. Notably, some patients may prioritise quality of life over the typical endpoints of progression-free or overall survival. While some may consider patient perspectives as easy to imagine or simply common sense, researchers do not know what they do not know, and unexpected revelations are far from incidental.

As well as engaging with patients directly, it is also critical that companies sustain long-term relationships with these patients and clearly communicate steps taken in response to insights provided. Not only does this protect against engagement appearing tokenistic, but it also embeds a sense of purpose for the patient, rewarding them for sharing their personal perspectives and encouraging further engagement with industry.

Incorporating the patient voice at early stages brings numerous benefits to R&D. These can be immediate, such as higher chances of ethical approval, and also longer term. In 2017, AstraZeneca hosted a clinical trial simulation to facilitate patient input prior to study commencement. Consequently, 60 recommendations on how to improve the experience were provided by patients, which saved AstraZeneca significant time and costs compared to if those amendments had been made further down the line. In addition, the trial was less of a burden on patients, which would make the trial design more appealing to patients approached for recruitment if it were to be adapted for future studies.

Expanding beyond the AstraZeneca simulation, patient insights can be included in study planning for as little as €10,000 – a very low cost compared to that of running a multicentre trial. Indeed, this is a small price to pay for the protection these insights afford against errors which could delay a trial by several months – not to be sniffed at considering the harshly competitive nature of the oncology pharmaceuticals market.

Furthermore, it is in pharma's interest to engage with patients to ensure they are health- and trial-literate so the most informed insights as possible can be provided. With a third of older adults in England shown to struggle with comprehending basic health-related information, only 12% of Americans possessing health literacy, and various studies demonstrating patient misunderstanding of research aspects including trial aims, side effect risk, and likelihood of personal benefit, the need for pharma to step up on patient education is evident. Furthermore, if patients enter a trial with unrealistic expectations, they are more likely to become disappointed or frustrated and consequently drop out.

Sponsoring attendance to the European Patients' Academy (EUPATI) Expert Training Course, which educates patients and patient advocates in medical R&D to the level of becoming qualified partners in drug development, is a gold-standard intervention, but solutions can be more low-key. Building a simple platform through which lay health and (particularly) trial information may be efficiently shared with patients by HCPs and using literacy screening findings to inform targeted patient education content would greatly complement existing patient trial materials. By investing in patient education, pharma can expect to see returns in the depth of insights gained from involving patients in study design.

Overall, consulting with patients is essential in ensuring that trials are relevant and beneficial to them, while also refining treatment value, reducing later-stage protocol amendments, and saving time and costs.

Greater success from recruitment to product launch

Evidence suggests that if clinical trials enrol patients at higher rates, the speed of treatment evolution and corresponding improvements to cancer population outcomes increases. Unfortunately, 80% of trials face difficulties with recruiting the target number of participants, and approximately 30% of patients who are recruited drop out. However, by making trials more comfortable for and relevant to patients, implementing patient insights can speed enrolment (and thus time to regulatory submission) and improve retention.

One study found that integrating patient centricity into oncology trials resulted in an average recruitment time saving of 37% (reduced time = reduced costs), also noting that interestingly, given the significant benefits of innovation in cancer therapy, oncology trials appeared to be less commonly innovative (with innovative trials defined as patient-centric, adaptive, precision medicine- or RWD-based) than trials in neurology or rare disease.

Patient centricity will become an even more valuable asset to trial enrolment in future, as recruitment pressures are projected to rise with the advent in precision medicine and consequent shrinkage of patient pools. Recruitment competition is already high, with 38% of all compounds in the visible 2019 preclinical pipeline being oncological (an increase from 23% in 2000), and only half as many breast cancer patients as would be required to fill active clinical trials diagnosed each year.

Traditionally, recruitment has been limited by the geography of investigator sites, which deprioritises patients and limits the generalisability of results. By going directly to patients and identifying investigators close to them, researchers may be able to improve enrolment and retention as patients may have to travel less to reach the investigator site. In future, the patient experience will become an increasingly key differentiator within the competitive trial landscape, exerting even more influence on recruitment and retention.

Methods of making trials more appealing to patients include a hybrid design, whereby patients can provide data from home (e.g., via wearable devices) as well as in the clinic, and arranging transportation for patients when clinic visits are required (e.g. for scans). In addition, access to a clear, single point of contact for patients before, during and after the trial would facilitate positive relationships between patients and sponsors, ease the addressing of any concerns or questions and reduce the overall mental burden of trial participation, potentially reducing dropout rates.

It is logical that if pharma companies were to make consistent, collaborative efforts to integrate patient preferences into their study designs, more successful recruiting (e.g., through greater trial appeal, positive brand recognition and word of mouth among patient networks) and keeping patients enrolled throughout would be much more likely than if these efforts were not made. In the longer term, integrating patient insights can benefit drug developers beyond recruitment and retention, as the chances of providing regulatory and reimbursement decision makers with compelling patient-relevant evidence are significantly higher. Moreover, drugs developed using patient-centric trials have been shown to not only have a 19 percentage point increase in phase II and III likelihood of launch compared to drugs developed in standard trials, but to also be more likely to be adopted by payers.

Patient engagement is key to staying competitive

Finally, the most long-term benefit to pharma of patient insights in oncology R&D is the future of the drug company. The pharmaceutical landscape is changing, and companies will do well to work with, rather than against, this evolution.

In the flourishing patient economy, where patients are increasingly empowered and equipped to collaborate with industry, deepening and expanding upon patient engagement will be essential for drug developers to be considered relevant and trustworthy in an industry increasingly demanding of value demonstration and transparency.

Companies that do not advance in this direction may be left behind in years to come. Indeed, drug developers competing in an increasingly crowded oncology space will need to make the most out of technological innovation and meet evolving relationship and value expectations if they hope to remain competitive. Patient engagement may be new to some, but expertise in this field is taking strong roots. Undeniably, the evidence is there to support patient centricity as a standardised business essential across all subsectors of pharma.

The ROI

To revolutionise pharma as a whole, the return on investment/engagement cannot be communicated solely within R&D. Importantly, the ROI/E is not only identifiable across, for example, commercial and market access subsectors, but also clearly measurable. Hence, financial rewards await companies if they have the foresight to persist with the long-term investment, as patient centricity ultimately results in better products and outcomes. For commercial teams, it may be intriguing to see that money spent on patient engagement could produce more than a 500-fold return in investment via the consequent reduction of protocol amendments and improvements to trial recruitment and retention. Furthermore, 86% of pharma executives were shown in a 2015 survey to agree with the statement "a focus on patient centricity is the best route to future profitability". Looking at market access, patient support programs have been shown to improve adherence by 29% and cut disease-related and all-cause medical costs by 35%.

Moving forward

That's all very well, but how does one navigate the complexities of engaging patients directly? Patient engagement frameworks (yes, even covering compliance), toolkits, case studies, guides and recommendations are arising and evolving all the time, and Prime Global Medical Communications will soon be launching PEP Talks as a best practice training resource and safe space where pharma can rapidly get up to speed with the how and why of patient engagement.

Thus, dismissive avoidance of patient engagement – e.g., "It's not compliant/legal for us to talk to patients directly" (note: it's promoting to patients which is not allowed), "It's better for HCPs to do any patient work", or "We don't know where to start" – no longer holds the power it once did. It's time for a pharmaceutical culture shift, whereby company-wide infrastructure is established across the industry to anchor the patient at the heart of all business strategy. After all, drug developers will be left behind if they neglect to jump on board.

The bottom line: patient engagement in oncology R&D, although implemented to a small degree, remains a vastly untapped resource and opportunity to secure a triple win for pharma, patients and society.

About the author

Olivia Kersey is a patient engagement strategist (with a particular interest in health and trial literacy) contributing to Patient360 Insights programmes within the Prime Patient Center of Excellence at Prime Global. Patient360 is a service that delivers long-standing patient insights and engagement strategies focusing on the ABC – access to medicine, behavioural change, and care support. This service highlights how to overcome obstacles to creating a standard of patient engagement care and implementing this standard into medical guidelines. Patient360 also helps to bridge the patient-pharma relationship and support business sustainability.

PRIME PATIENT: triple win engagement services

03
Objectives

Amplify the patient voice in healthcare

Ensure patient insights are activated

Deliver a 'return on engagement' for all

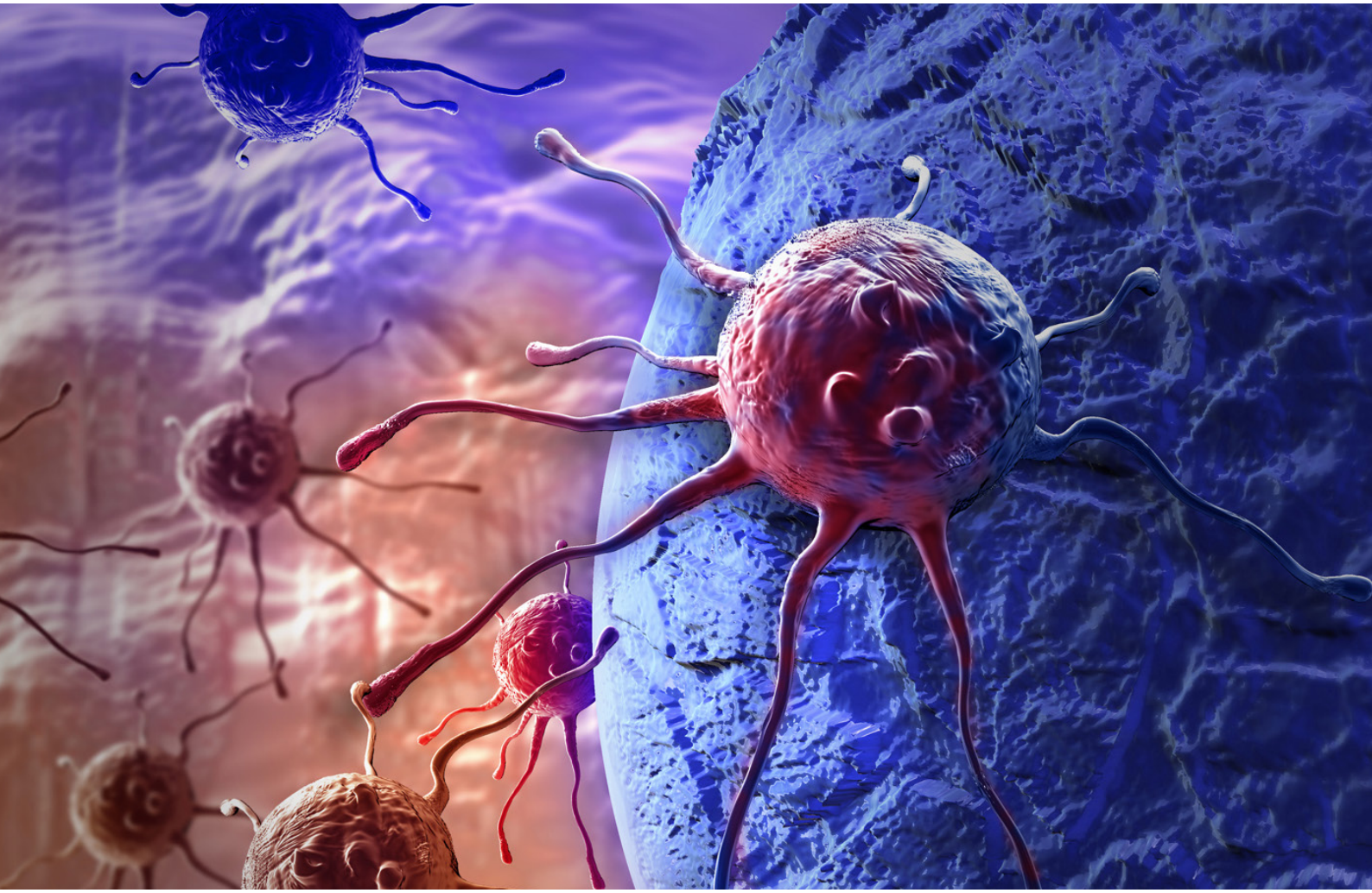
02
Approaches

Support end-to-end engagement from PFDD to enduring patient programs

Normalise patient engagement strategy and services as business essentials in a patient-directed organisation

01
Outcome

So that our clients achieve 'Triple-win thinking': better outcomes for patients, for pharma, for society



AMPERSAND

How digital pathways are changing healthcare

As demonstrated throughout COVID, digital health is no longer experimental. Digital technologies are proving their value by allowing for better care, improved adherence and a more connected ecosystem between doctors, patients and pharma. Ampersand Health has been working in the space since 2015 and has seen it evolve from a niche approach with limited acceptance to widespread acceptance and deployment across disease areas in a matter of years. We sat down to talk to the founders about their journey and the future of healthcare.

We are at the beginning of a "new era" in healthcare, driven by digital technologies that are bringing patients and physicians closer together, taking pressure off healthcare systems and making self-care more accessible than ever.

That's according to Dr Gareth Parkes – a full-time gastroenterologist who co-founded Ampersand Health, which develops digital therapeutics for inflammatory bowel disease (IBD) and other immune mediated inflammatory diseases (IMIDs).

"We're already seeing mental health interventions paving the way in this, because approaches like CBT and Acceptance and Commitment Therapy lend themselves so well to digital," he says. "There's an enormous market for similar approaches in other disease areas.

"In an ideal world, we'd like every patient to have their own pain specialist, psychologist, dietitian, etc., but the reality is that the healthcare systems like the UK's NHS cannot provide that.

"Where I see the digital revolution having the biggest impact is in democratising healthcare and allowing almost anyone to have access to these services at scale, and at a much lower cost."

"There have always been activated and engaged patients who take care of themselves well," adds Nader Alaghband, co-founder and CEO of Ampersand. "But, by lowering barriers to better self-care, digital therapeutics are allowing even more people to look after their own wellbeing, with resultant improvements in quality of life and mental health."

"It's important to remember, though, that clinicians are still an absolutely essential part of any digitally enabled model of care, because they provide guidance, accountability, and a crucial safety net."

Alaghband says that while 'digital health' as a term can be used in a broad variety of ways, in general he would define these tools as being "fundamentally evidence-based and looking to move the needle for patients in a variety of different ways to do with clinical outcomes, quality of life, mental health, etc."

This can include everything from tools that help physicians remotely monitor patients, apps that facilitate self-care and help patients monitor their own disease, or even digital tech that has a pharmaceutical-like effect on people's health.

"One of the benefits of digital compared to traditional treatments is its ability to provide clinicians with a useful stream of objective data about the patient," he adds.

"Combining those sources – such as patient reported outcomes, medication adherence, digital biomarkers – with traditional clinical tools like blood tests allows us to collect unique, real-world datasets that clinicians and researchers can benefit from in a variety of different ways."

“Improvements in the quality and flow of data between primary care, secondary care and the patient leads to an infinitely better overall level of communication,” says Parkes, “which in turn leads to more engaged and educated patients.

“We know that patients who understand their medications and their disease – e.g. how long a medication might take to be effective or what non-adherence might lead to – are more activated, have higher levels of medicine adherence, and are more likely to do better in the long term.

“One big NHS buzzword at the moment is patient-initiated follow-up (PIFU), and you need tools to enable that by allowing patients to report how they are doing efficiently and substantively. That way we can see who needs to be seen urgently, and who can actually stay out of the hospital for the time being.”

Alaghband notes that allowing clinicians to remotely monitor patients in this way also gives doctors data that helps identify the patients that should be on advanced treatment.

“Likewise, advanced treatments come with pretty significant audit and data collection requirements. Doctors will often have to collect patient reported outcome measures (PROMs) at specific intervals in order to keep a patient on a particular course of treatment, so automating data collection makes life easier for physicians and helps reduce barriers to prescribing.”

Bu Hayee, co-founder and joint chief medical officer at Ampersand and clinical lead at NHSX – the healthcare system’s digital transformation unit – says digital therapeutics are “unquestionably” going to be a huge part of the way the NHS develops its services over the next few years.

“We need to focus on how we’re going to implement digital as a standard way of working within the NHS. We’re not talking about replacing the existing healthcare model – but it’s more efficient, it’s better for patients, and it’s more auditable, traceable, and secure.”

Hayee notes that while not every patient will want or be able to use digital therapeutics, widespread adoption in health services will result in benefits for everyone.

“It will free up staff time, result in fewer outpatient appointments, improve disease control and reduce unplanned visits to emergency departments. It’s going to enable us to deliver more efficient, effective and responsive care for everyone, regardless of whether or not they are actually using digital tools.”

Digital therapeutics in practice

Ampersand's own tech seeks to bring all these benefits to a disease area physicians and patients often find particularly difficult to manage – immune-mediated inflammatory conditions including inflammatory bowel disease.

"Inflammatory conditions like Crohn's or rheumatoid arthritis are characterised by periods of relapse and remission that are difficult to predict – but the way that care gets delivered in a traditional model is very linear and episodic," says Alaghband. "You get a diagnosis, you get put on a treatment pathway, and then every three months for the rest of your life, whether you're in relapse or remission, you're supposed to show up at the hospital – often without purpose or benefit.

"Gareth and Bu realised that if clinicians had better access to patient data between appointments, they'd be able to see who was well and who was unwell, and they could then focus their scarce clinical resources on the unwell."

"There was previously very little support for patients in between appointments," Parkes says. "In the past we've offered things like telephone helplines or email addresses, but we were looking for something to try and help support patients throughout the year, or even throughout the whole of their lives."

After searching, Parkes and Hayee discovered that there weren't any existing tools that fit their needs – so they decided to develop a solution themselves.

The result was My IBD Care, an app that provides information and courses to help patients manage their disease, allows them to log information about their appointments and medicines, and facilitates communication with doctors, among other functions.

"Patients can answer questionnaires to provide PROMs, and the app links up with a clinical platform that the care team uses to understand what's going on," Parkes explains.

Ampersand has also added CBT and acceptance therapy functions to the platform, focused on the psychosocial aspects of the disease – such as stress – as well as physical symptoms like pain and fatigue.

The company has also expanded the platform into similar inflammatory conditions in rheumatology, dermatology and oncology.

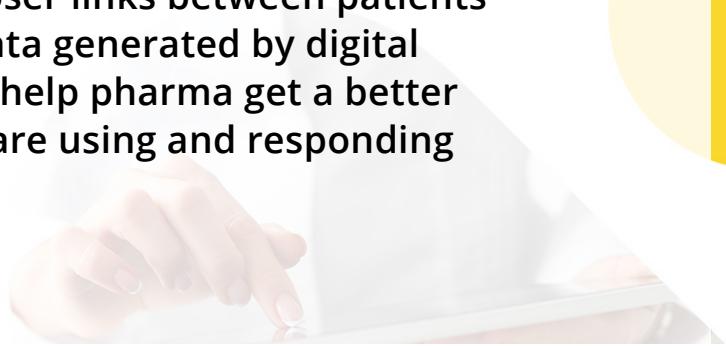
Parkes says that most of the app's functions were built based on patient insights.

"We have a really active patient group that advises us, and we actually started this project by asking patients on Facebook what they wanted from their treatment. That included everything from being able to log their symptoms and communicate better with physicians to things we haven't implemented yet, like more support managing flares and diet."

"We've tried to make My IBD Care as easy and as logical as possible for patients and HCPs to use," adds Hayee. "We wanted to ensure everything was only a couple of clicks away, and that there was as much automation as possible. We almost want people to forget about the operational side of things, and just be able to seamlessly interact with it – just as you would with your phone."

Linking pharma & healthcare

Beyond facilitating closer links between patients and physicians, the data generated by digital therapeutics can also help pharma get a better view of how patients are using and responding to treatments.



"With patients able to provide insights into their medications on a weekly, or even daily basis, we can collect unique, real-world data that would have previously been impossible to gather," Parkes says.

And by joining up pharma and healthcare, these tools can create an ecosystem where the two sectors are working together to put the patient at the centre of care, he says.

Ampersand itself has worked with a number of pharma companies on a variety of projects – relating to PROM collection, automating audit requirements and clinical trials – and Parkes says a key advantage of such an approach for the industry is being able to utilise established, trusted apps.

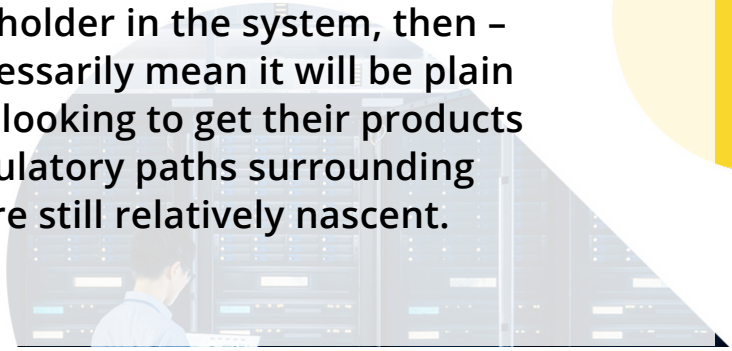
"This means companies aren't having to develop something entirely by themselves, and we can create tools that will allow collecting data, especially for a novel product coming to market, in really exciting ways."

Alaghband notes that digital therapeutics like My IBD Care can easily provide these services without deviating from their core business.

"We can stick to our main objective – to help doctors and patients improve care – but also find areas where those goals align with pharma's objectives – such as improving adherence to medicine."

Regulation barriers

The benefits of digital tools are becoming clear to almost every stakeholder in the system, then – but that does not necessarily mean it will be plain sailing for companies looking to get their products on the NHS, since regulatory paths surrounding digital therapeutics are still relatively nascent.



Ampersand's platform is CE marked,regulated by the MHRA and is NHS-compliant by design, and Hayee says that gaining regulatory approval is essential in order for health systems to trust a digital therapeutic.

But he acknowledges that gaining regulatory and other approvals can be extremely difficult, particularly when many digital health companies are relatively small and don't have the market access resources of big pharma.

"The process can be incredibly laborious, time-consuming, and painful," he says. "Every single hospital has a different process and a different set of forms to fill in."

"It's almost the equivalent of having a mini-MHRA at every hospital," Parkes adds. "Why it isn't centralised, I don't understand.

"Things are improving though, and MHRA, NICE, NHSX and other organisations are all on a rapid learning curve.

"It wasn't that long ago that we were basically standing by the door waiting for them to develop these pathways. They were probably not quite sure where to put digital therapeutics, and so they erred on the side of caution, but I think that will ease in the next few years."

NHSX, for example, has recently launched its Digital Technology Assessment Criteria (DTAC), which aims to begin harmonising national approvals of digital tools.

"At the very least, DTAC will reassure an individual hospital IT team on the ground that a form of diligence has been undertaken for a product," Hayee says.

Beyond this, though, the team at Ampersand believe the NHS is generally quite keen to adopt digital tools as much as possible.

"The Long Term Plan has already set out that digital health needs to be a key pillar of the NHS in the future – largely from a cost savings point of view," says Parkes.

"Across the board, people want patients to have a much greater understanding of their own disease and better ways to manage it, because we know that leads to better outcomes."

"This transformation can't come soon enough – and it's great to see that the general atmosphere in the NHS around data and digital is so positive," says Hayee. "I'm excited and reassured by the direction of travel – and the huge benefits on the horizon for pharma, healthcare and patients."

About the interviewees

Dr. Gareth Parkes is a consultant gastroenterologist at Barts Health NHS Trust. Gareth has been involved in research in a number of areas including Crohn's Disease, the effects of smoking on inflammatory bowel disease and the use of probiotics and prebiotics. In 2018, he co-founded Ampersand Health and developed My IBD Care. Gareth has sat on the British Society of Gastroenterology IBD committee, co-authored the current UK guidelines and has a number of publications in the field of IBS and IBD.

Dr Bu Hayee is a consultant gastroenterologist at King's College Hospital and has been chief of service since 2015. He is clinical lead for gastroenterology, training lead for endoscopy, and co-director of the King's Institute of Therapeutic Endoscopy. He combines his two main interests (IBD and Endoscopy) in clinical service and research. He has projects investigating graft versus host disease of the gut, cystic fibrosis, chromoendoscopy for colitis surveillance, and has an active interest in novel treatments for IBD.

Nader Alaghband is co-founder and CEO of Ampersand Health. Nader read philosophy and biology at university and has spent his career working at the intersection of impact and technology. Prior to Ampersand, Nader founded a startup that worked with the NHS and pharmaceutical companies to implement digital strategies, platforms and pathways that supported tens of millions of patients and tens of thousands of clinicians globally. Nader has a deep interest in helping improve quality of life and quality of care for people with long term inflammatory conditions.

About Ampersand Health

AMPERSAND

Ampersand Health is pioneering the development of behavioural, and data-science based digital therapies for people with immune-mediated diseases like Crohn's, Colitis, Arthritis and Psoriasis. Ampersand Health is recognised in the Digital Health Global 100, and has won the HSJ Award, the NHS Ideas Lab, the NHS Hackfest and competitive grants from government and industry. The company was selected for the 2018/19 PWC Scale Health programme and the NHS's 2019/20 Digital Health London accelerator. Ampersand Health was also one of 18 digital innovations identified to support vulnerable people during the COVID-19 outbreak as part of the TechForce19 challenge.

Digital health developments: a new investment era for start-ups

Healthware Labs' Kristin Milburn explores how digital health start-ups can harness the huge potential for the sector in a post-COVID world and the paths they need to take to grow their business.

Digital health has come a long way in the past decade – and Kristin Milburn says that the sector could now be about to enter its most exciting period yet.

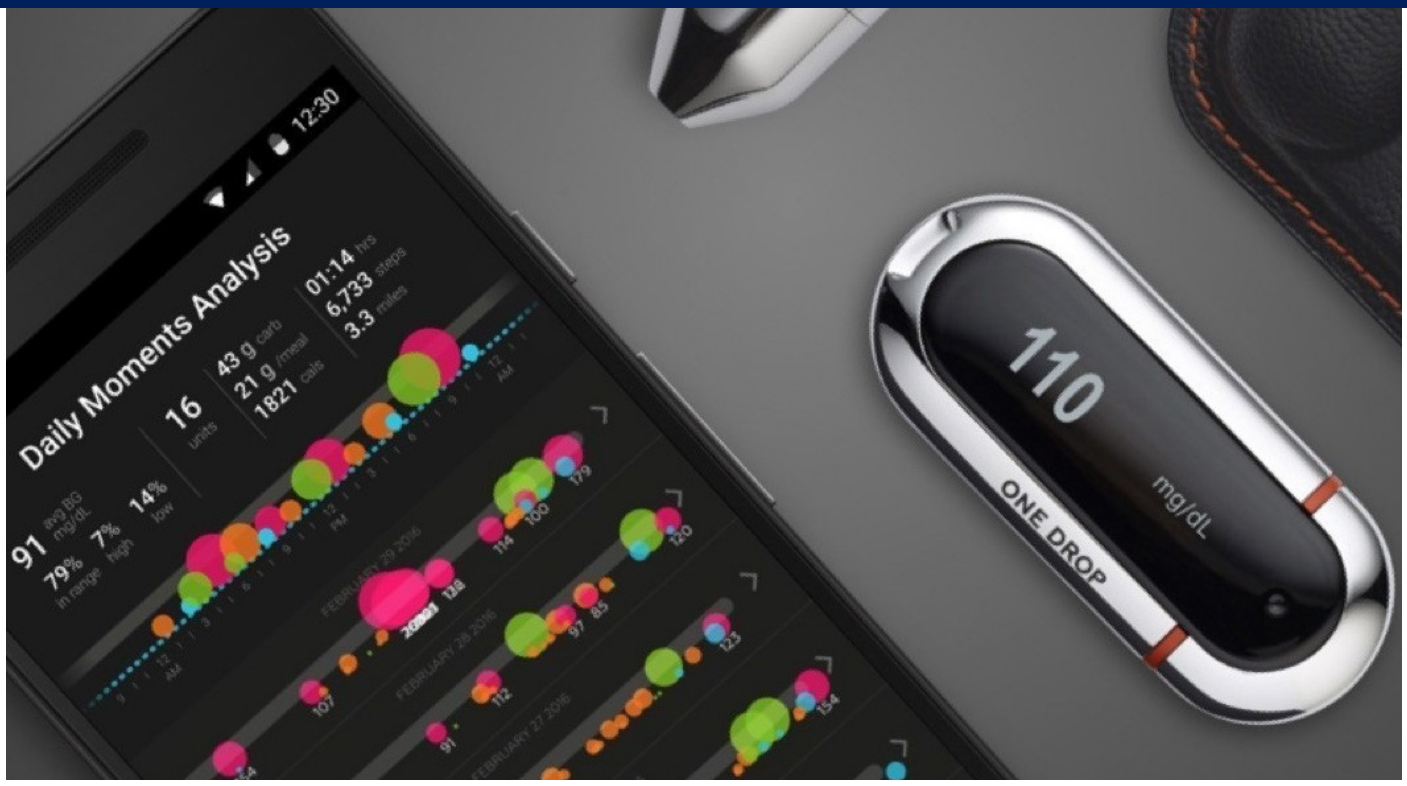
Through her role as managing director of innovation consultancy Healthware Labs, Milburn has seen first-hand how digital health has evolved. In particular she points to a move beyond tools that surround or support medications – such as adherence solutions – or those that take proven analogue programmes, such as CBT or physical therapy solutions, and digitise them for wider availability.

"Now we're starting to see more solutions that have novel modes of action with no analogue equivalent," she says. "The next frontier is really around digital solutions that cause drug-like changes in the body; so far, these are typically seen in CNS – the video game Akili for ADHD being one example."

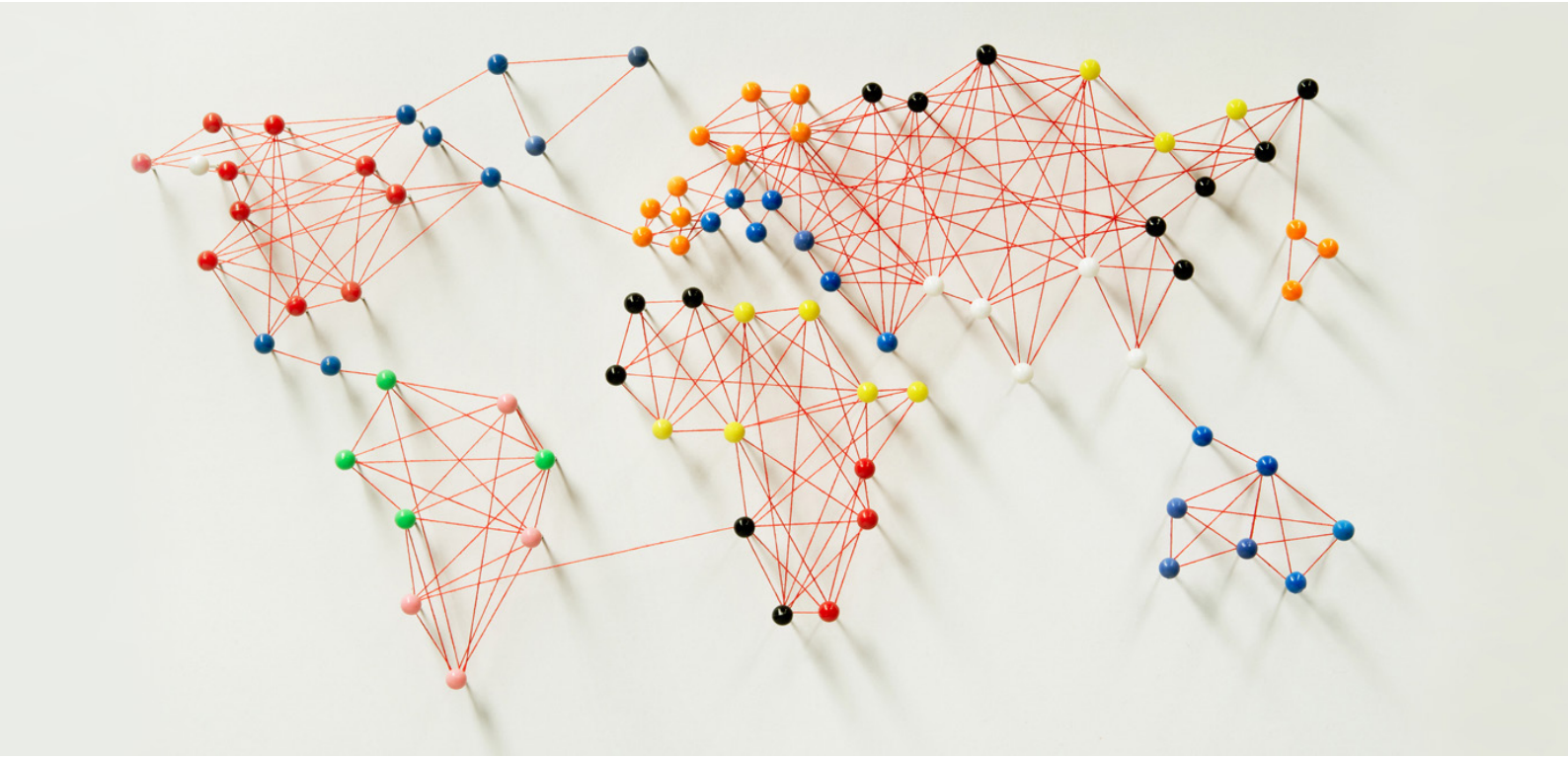
Although the digital health sector began by mostly targeting highly prevalent conditions like diabetes, cardiovascular disease and respiratory conditions, Milburn says it is now expanding to more specialist disease areas like oncology, gastroenterology, or dermatology, as well as rare diseases.

“Sometimes we find that clients don’t think they can learn anything from digital tools in disease areas they aren’t working in – but what’s happening in one area will eventually start happening in another,” she says.

“A lot of these platforms, such as One Drop for diabetes, were originally built for one disease area but ended up expanding into other conditions. Once you show that your app or your solution can have traction and user engagement, you can apply those same learnings to other disease areas. Of course it’s always going to need to be customised to suit the needs of a specific user-base, but the baseline, core functions of how you create a usable service can remain fairly consistent.



"Generally, the pharma industry lacks the experience to build those kinds of consumer-focused solutions – so that's where specialist digital companies can help."



User-centric digital start-ups

The sector's maturation also means that robust evidence is becoming more important than ever for companies who want their digital solutions to be widely used.

"Payers, doctors and patients aren't going to take your product seriously unless you have studies to support its value," says Milburn. "In the world of healthcare that would typically involve conducting an RCT. However, some digital start-ups – such as One Drop – proved their value by providing a valuable service to their customers, and then showing real-world evidence of impact."

Meanwhile, COVID has acted as an accelerant for digital adoption, and in a post-pandemic world the sector is likely to see even more rapid growth.

Milburn says this is evidenced by the increasing numbers of M&A deals in the sector that are creating end-to-end service companies – such as the merger of Teladoc and Livongo.

"I don't think either of those companies were necessarily thinking about combining forces before COVID, but the pandemic demonstrated that these kinds of solutions can be more powerful when working together.

"The merger is a combination of an episodic care platform with a chronic care management platform – which shows that as the space matures there's a need for more platforms versus point solutions, as companies start to consider the entire patient journey."

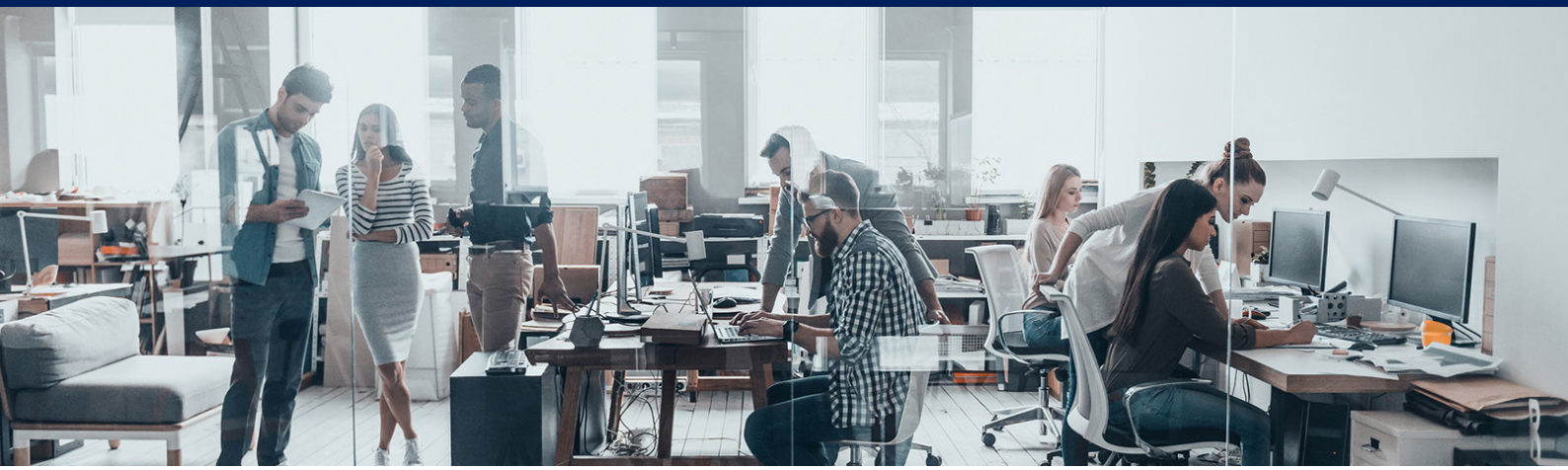
She adds: "I think we're going to see similar mergers happening in the future – there's been talk about Omada joining with Amwell, another big telemedicine provider, for example. Meanwhile, the number of healthcare-specific SPACs [special purpose acquisition companies] happening also shows that start-ups are stronger when bonding together.

"All the signals are pointing towards more consolidation in the market overall, and newer companies really need to keep that in mind."

As such, Milburn says that start-ups need to be building their companies with the knowledge that they could likely be a part of a larger platform down the road.

"It's still smart for start-ups to think about solving a specific challenge, but eventually they should also consider merging with adjacent solutions to create end-to-end services for patients – whether that's integrating into another platform or partnering with another start-up that has a complimentary service.

"This requires knowing what the patient journey looks like and knowing specifically where your solution fits.



"Oftentimes start-ups have just got their heads down, trying to get traction with their own solution. That is of course important, but from a strategic standpoint, they also need to have a vision for what their next step might be and where they can fit in the overall scheme of things."

Milburn says that if a company is truly building a solution from a user perspective, they need to consider how they can support patients at every stage of their journey – not just how they can get the solution into patients' hands.

"In other words, a solution needs to be user-centric, not healthcare system-centric."

Digital start-up investment rises

On top of this, Milburn says that the high levels of investment flowing into digital health suggest the sector will be buoyant for years to come.

"We're seeing more and more late funding rounds. Weight management app Noom, for example, just got $540 million in a series F round, and they're probably going to IPO soon.

"That's a lot of money for an investment round, which really goes to show that there's a huge need for the service that they're providing. It also highlights the importance of being able to demonstrate evidence of impact in a difficult area like behaviour change."

Milburn believes the environment for start-ups over the next few years will continue to be positive, assuming the financial recovery post-COVID continues.

"The pandemic has highlighted more inequities, more challenges, and more gaps in healthcare. It has also made people overall less resistant to adopting technology. That creates more opportunities for digital health solutions to step in and fill those gaps.

"Now that we're starting to move past the pandemic and resume some semblance of 'normal life' – and given the vast amount of money flowing into the digital health space – this is probably the best time ever to launch a digital health start-up."

Startups to watch

Milburn runs through a few of the most exciting start-ups Healthware has worked with:

YourCoach – "This platform helps health coaches to run their business. It reaffirms the need for a human element as part of any kind of behaviour change."

Savor Health – "A nutrition bot designed to help support patients with cancer. There aren't enough nutritionists, and certainly not enough oncology nutritionists, and what you eat during your treatment can have a huge impact."

Health Tunes – "This app combines music tracks with binaural beats to help alleviate stress, anxiety and pain. A unique solution in a sea of mental health apps with a built-in mode of action people actually enjoy – listening to music."

Patch AI – "This ePRO for clinical trials is currently gaining a lot of traction in oncology trials."

Hi.Health – "This company recently launched their digital health expense account service in the EU. It makes it easier to submit expenses for reimbursement – allowing for immediate reimbursement of costs – which I believe could be a real game changer."

About the interviewee

A twenty+ year veteran of consulting and digital marketing, Kristin Milburn's experience has had a consistent focus on healthcare, technology and the intersection of the two. She is a strategic and innovative thinker, who has held leadership roles in strategy/planning and client engagement at various digital firms with numerous Fortune 100 pharmaceutical and technology clients. After launching her own digital shop and rising through the ranks on the agency side, Kristin jumped to the client side and joined the Digital Medicines team at Novartis for several years. Looking to gain experience on the start-up side, she then joined the digital mental health start-up called Headspace, helping integrate meditation and mindfulness into healthcare. Kristin is now the managing director of Healthware Labs, the digital health innovation consultancy of Healthware Group.

About Healthware Group

Healthware Labs is the digital health innovation division of Healthware Group.

Healthware Group is a global consultancy and digital health organisation that has been driving the transformation of health for almost 25 years by offering a unique set of services and expertise in strategic consulting, communication, technology, and innovation to companies striving to improve patient outcomes and transform business results in the life sciences, medical device, and health insurance industries.

Founded in Italy in 1997 by CEO and digital health pioneer Roberto Ascione, Healthware Group encompasses several vertical brands, including flagship full-service marketing and communications agency Healthware International, media consultancy Healthware Engage, innovation consultancy Healthware Labs, and virtual events specialist SWM.

Healthware Group is also the co-host of the global leading digital health conference Frontiers Health and operates Healthware Ventures, the corporate investment arm that supports digital health startups with a focus on digital therapeutics and telehealth.

Together with its joint venture partner, Intouch Group, Healthware has a combined team of over 1,300 communicators, connectors, and builders of future health and 15 offices in Europe, the US, and Asia.

For more information, please visit healthwaregroup.com and follow us on LinkedIn and Twitter.

Enabling healthcare's digital future

Debiopharm Innovation Fund's Tanja Dowe on investing in digital health start-ups and supporting them on their rollercoaster rides to improve patient outcomes

The weight of expectation hangs heavy over the digital health sector. Even before COVID-19 struck, shattering established societal and healthcare norms, much was expected from start-ups that could combine health and tech.

Now, with the pandemic's acute phase beginning to recede, the rapid gains digital health start-ups were making pre-COVID have become ever more important as new and better ways are sought to improve patient outcomes in a hugely changed environment.

Someone with a keen eye for health, tech and investment trends is Tanja Dowe. A biochemical and microbiology engineer by training, she's headed up the Debiopharm Innovation Fund since 2016, prior to which she spent 15 years as a strategy and transaction consultant in the life sciences.

"There's no such thing as a perfect business, but you can develop any company"

Although a start-up's long-term vision will always come from the entrepreneurs behind it, the challenges that founders face can come thick and fast as they navigate both financing options and operating risk.

Investment focus:
Digital Health

Fund type:
Evergreen

Company stage:
Early commercial stage, large pilots / early sales

Investment round:
Entry at Series A, follow to subsequent rounds

Typical initial investment:
€3-5m

Current investments (digital health portfolio):
Novadiscovery, Nucleai, Carevive, Voluntis, Oncomfort, BC Platforms, and Kaiku Health (exited 2020)

Past investments (diagnostics/ therapeutics portfolio):
Immunexpress, GenePOC, Biocartis, Agendia, Spinomix, Diagnoplex, OSE Immunotherapeutics, Neovacs, Eclosion

Track record of success:
Portfolio companies have achieved 10 FDA clearances, 13 CE marks, 2 IPOs and 5 trade exits

Core areas of expertise:
Combination of tech and health, market access in healthcare, drug development value chain

Therapeutic focus:
Digital health in oncology and infectious diseases

"You can't waiver and you can't be unsure," Tanja explains, "but things happen, and we all sometimes get lost in the everyday struggles."

Nevertheless, there are always ways to bolster a company's position if you can assess what makes them special and where they need more work.

"Over the years, working with such a variety of companies in med tech, pharma, diagnostics and digital health, what I learned was to quickly understand how to strengthen a company's strengths and mitigate the risks it might face. There's no such thing as an absolutely perfect business, but you can really develop any company," she says.

Supporting start-ups with strategic guidance and long-term financial investment is at the core of the fund Tanja oversees – whether these emerging companies want to bring a completely new type of digital health product to market or convince traditional corporations to integrate smart data innovation into their operations.

A digital health fund

The fund that Tanja leads is part of the independent Swiss biopharmaceutical company Debiopharm, which was established in 1979 to develop innovative therapies that target high unmet medical needs in oncology and bacterial infections. Its business model is to identify high-potential compounds for in-licensing, clinically demonstrate their safety and efficacy and then select large pharmaceutical commercialisation partners to maximise patient access globally.

The Debiopharm Innovation Fund has been operating since 2008, but with an initial focus on diagnostics, driven by the company's desire to better understand personalised medicines and the companion diagnostics they rely on.

"In the early days the fund helped Debiopharm take a closer look at how patients are diagnosed before they are treated, because we can become better drug developers when we better understand that, and we also wanted to develop companion biomarkers for our drugs," Tanja says. "But when I joined the fund, the goal given to me was to build a digital health portfolio."

"As much as we talk about big data in healthcare, it doesn't exist today"

Considering why Debiopharm's investment aims pivoted to digital health in the mid-2010s, Tanja says: "We are facing a huge disruption in the whole healthcare industry, both in terms of how patients are treated and how treatments are developed. The pharmaceutical industry has access to an amazing pool of technology, and at the same time we have a market pull from increasingly digital native population and push from soaring healthcare costs."

Today Debiopharm has two main areas in which it invests: the digital transformation of pharmaceutical development and bringing better outcomes to patients through digital tools.

On the digital transformation side its investment portfolio features companies like Nova Discovery, a French in silico clinical trial company using AI and mechanistic modelling to predict the clinical benefits of new drugs in virtual clinical trials before human trials begin, and Swiss high performance genomics and clinical big data management platform firm BC Platforms. Another portfolio company is the Tel Aviv-based Nucleai, which is working to transform precision medicine through the application of AI-pathology and digital biomarkers, while the Miami-headquartered firm Carevive helps providers and pharma look at real-world patient experience in oncology enabling best treatment choices and new therapies.

These companies are working to make data smart. "As much as we like to talk about big data in healthcare, it doesn't exist today because it's really fragmented. These companies are changing that by aggregating data from different sources and analysing it," Tanja says.

In terms of the patient journey, the Debiopharm Investment Fund's interests include the French digital therapeutics firm Voluntis, a leader in the field of digital therapeutics, and Oncomfort from Belgium, whose digital sedation is being applied to pain and anxiety management. The Fund has also invested in, and now exited from, Finnish Kaiku Health, which provides personal digital interventions for cancer patients to help improve their outcomes and quality of life.

"We invest in these types of companies to learn from them, to see the newest technologies and be early adopters so that we are able to ride on the front line of this technology wave," Tanja says. "This is what will make us better drug developers going forward."

The digital transformation of drug development

As companies like Nova Discovery and BC Platforms work to apply digital technology to pharma's traditional drug development processes, one of the challenges that start-ups face in the sector is what Tanja terms pharma's 'pilot-itis' affliction, whereby pilot after pilot is run but collaboration is slow to progress beyond that stage. One way to counteract that is to keep your eyes on the long-term goals.

She says: "The biggest way that we help start-ups is to bring long-term perspective and financing. As a partner we have to support the CEO and the management team to keep their eyes on the long-term goal. Without having a long-term view to financing companies, it's hard because the roller coaster ride with start-up companies is not easy. You can't waiver and you can't be unsure. You have to be able to take that risk and then support the company."

By successfully supporting its portfolio companies in this way Debiopharm's strategy saw it go from zero to eight investments in digital health in its first four years, working with companies that combine tech and health, improve patient centricity in healthcare or tackle the drug development value chain. Pharma's rocketing R&D costs are very much on Tanja's mind as she helps guide digital health start-ups.

"We can't develop drugs in a sustainable way for patients when our development costs are skyrocketing. It's just not good enough and it's not possible in the long term. Every other technology area in this world becomes cheaper as the time goes on, but the complexity of pharma and biology sees life science technologies just get more and more expensive. There's something wrong there and we think there's a lot we can do to improve this, for example, with data and AI."

Improving future patient care

There is plenty of room to improve patient care too. In an era when digital health advances mean that pharmaceutical regulators are assessing – and approving – medical software, and digital tech is being passed for reimbursement by healthcare technology assessment bodies, it is clear that ideas about moving beyond-the-pill have reached to a new level.

As the industry journeys beyond its traditional treatment paradigms and ideas about 'the drug', there will be further new ways for patients to be treated in the future, Tanja says.

"At the moment, we give patients a pill and then there's an outcome. But there are other ways that we can improve those outcomes, either by selecting the patient better or assisting the clinician making a decision on a particular patient's profile to determine which treatment will cure them or give them the best outcomes. That type of things we can do already – for example, patient monitoring is bringing incredible results."

One technology type that is changing what is possible in treating patients is the use of 'digital companions' or digital therapeutics. Application of sensor technologies or mobile apps in oncology to track how patients are doing and adjusting their treatments accordingly can extend overall survival by several months, not to talk about the possible improvements in quality of life.

The most advanced of digital therapeutics companies have gone public or received Series D financing in the hundreds of millions of dollars as their data-driven insights are clinically validated, but there are many more who have yet to finalise their strategic roadmaps for this rapidly growing sector.

Helping digital health entrepreneurs achieve their ambitions

Digital health is often overflowing with promise, but what are the key success factors for new start-ups? For Tanja, as she looks back on Debiopharm Investment Fund's years of experience in the area, these come down to a handful of factors.

"Team, of course; every industry says the team is the most important thing and it really is, because it's such a long term commitment. Then you have to have conviction and a great vision – you must believe in what you're doing."

Alongside this need to hold onto their beliefs, start-up founders need market understanding, in terms of where the market is today and where it will be tomorrow.

Tanja advises: "Start-ups benefit from understanding that they are not just bringing a new technology to an existing market, but that the market is also changing. If they are able to anticipate some of that structural change in healthcare, and provide solutions for that future, then they will certainly be in a stronger position.

"When we look at a start-up company, although there are all these 'low-hanging fruits' for digitalisation of, for example, hospital workflow processes that are still very important, we try to look one step beyond and go for more disruptive innovations."

Although, as with any life science and technology investment fund, there will be a desire to bring financial returns, the key question for the Debiopharm Investment Fund is whether the start-ups it chooses to fund will enable the future of health and pharmaceutical development in a way that will be sustainable.

"I believe that the best commercial successes are those that bring long-term solutions, that bring sustainable solutions. Not something that works for a little while but doesn't really take into consideration that it will only help those in wealthy countries in the top 10% of the world," Tanja says.

As, more and more, the true potential of digital health is revealed, it brings with it a responsibility for the healthcare of the next generation, wherever they live and whatever their circumstances. Healthcare has its fair share of big, difficult problems and with digital technology many of them should be able to be solved.

The meeting of technological solutions and pharmaceutical know-how

The current climate in digital health can best be described as a race. The speed at which a technology start-up typically works means that these firms are continually pushing regulators for new guidance and systems. To their credit, the authorities have been accelerating their usual timeline. Amid this rapid regulatory and technological development, digital health start-ups can find they have gaps in their market understanding that an experienced pharma partner could help them fill.

Tanja says: "As a pharma company, we can give our portfolio companies a lot of insight into what challenges pharma is facing, especially with the continuous change in healthcare stakeholders. If a start-up's customers are pharma companies, then we can really help them understand where a customer's pain-points will be. They may even test drive or co-create their solutions with our pharma developers – we're a friendly partner, helping to develop solutions that will sit even better with customer needs."

That assistance encompasses regulatory insight, market access guidance and health economics knowledge, as well as understanding the huge shifts foreseen in the health payer sector. As Tanja notes: "Their role is probably under even a bigger disruption than the pharma industry role – everyone has a changing role."

For her fund, which typically invests at a Series A stage, as start-ups bring their product to a proof-of-concept stage, what's then also becoming increasingly important is how to turn those great ideas and the certain amount of traction they have into a good business. Today that requires clinical validation, but for those outside the pharma sector, designing clinical studies to deliver the proof needed for a product's main claim is often really challenging. Debiopharm can give guidance for their portfolio companies also in this area.

With so many moving targets for digital start-ups, there has never been a better time for assistance from an investment partner that can marry traditional pharma know-how with an innovation mindset.

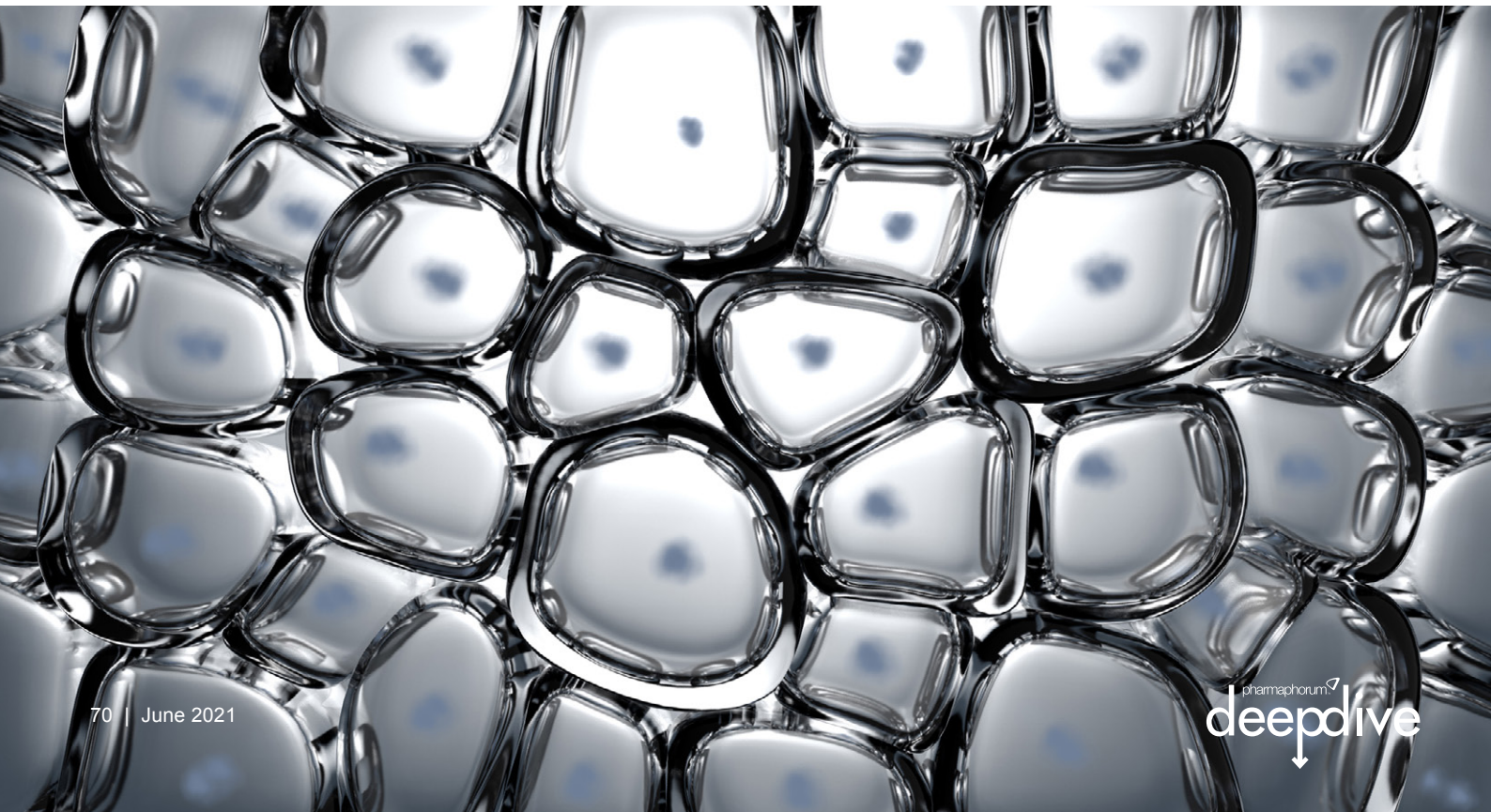
About the interviewee

Tanja Dowe is the CEO of Debiopharm Innovation Fund, the strategic investment arm of the Swiss pharmaceutical company Debiopharm. Former entrepreneur and strategy and transaction consultant, she invests in startups with disruptive technologies that transform the pharmaceutical industry.

About Debiopharm Innovation Fund

Debiopharm™
WE DEVELOP FOR PATIENTS

As Debiopharm's strategic corporate fund, the Debiopharm Innovation Fund invests in digital health, smart data, and innovative tech start-ups. Find out more about seeking digital health start-up funding.



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Why pharma shouldn't forget about sites in a post-COVID world

The pandemic forced massive changes to oncology sites to ensure patient safety and research continuity – but we must recalibrate and work with sites to understand the value proposition of the technologies and methodologies adopted, says Syneos Health's Angela Hirst.

Formerly an oncology nurse and now director of Sites and Patient Services at Syneos Health's Oncology Catalyst Site Network Program, Hirst saw first-hand the challenges sites faced when COVID hit, and the many innovative ways in which they adapted.

She says the US network sites reacted as most sites globally did, with anxiety and concern for their patients at the onset of COVID.

"The US healthcare system is complicated and is unlike state provided healthcare models in other countries. During the initial stages of the pandemic, patient onsite visits dropped due to trial cancellations and disruptions, leaving a financially devastating impact on many clinical research sites.

"Through our close relationships with our sites, it very quickly became clear that a significant concern, apart from the continuity of their patient's care and treatment pathways, was financial stability. Annual surveys conducted by the Society for Clinical Research sites show that circa 60% of sites have three months or less cash flow."

Syneos Health deployed an initiative to work together with pharma and sites to request any hold back payments to support financial stability.

“Approximately $15 million in back payments was released to sites. Today, SYNH continues to work with sites to target prompt site payments.”

Meanwhile, Hirst says the EU saw the hospital administrators adapt and flex their model by redeploying research teams in support of clinical areas to manage the surge of COVID-19 admissions. The impact of this was a sudden reduction in activity for the research units and their patients.

“Fortunately, we are witnessing a return to some normality,” says Hirst. “However, we must be conscious that patient footfall to sites continues to be reduced due to COVID-19 protocols and site staff resources.

“Restarting clinical trials placed on hold is complicated – 2020 was unprecedented, and we all still have much to learn in regard to starting scenario planning.”

In both regions, sites showed a great deal of innovation and agility to ensure the safety of their patients and staff.

Regulators were also agile and flexible, issuing timely guidance on IMP direct to patient, remote monitoring and telemedicine. Sites found alternative methods outside the traditional clinical trial visit to deliver study medication either by courier or coordinators, visiting patients at home, all whilst being socially distanced and with PPE techniques. In other cases, new technologies were introduced; sites adapted and implemented technology to ensure participants could continue to take part in clinical trials.

“As the world returns to some form of normal, we need to take this opportunity to learn what worked well and what we can improve upon,” Hirst says.

Decentralised sites

Although the increase in decentralising clinical trials has been essential to continue research over the pandemic, Hirst says these new processes have introduced an element of burden for sites to effectively support the increase in the number of systems required for all studies.

"Technology adoption in the industry has traditionally been quite gradual – for example IVRS introduced in the late 1980s took almost 20 years to reach 67% adoption. But the pandemic has accelerated everything – over the last 15 months almost 40% of sites began using eConsent, eSource and remote monitoring, which has resulted in significant challenges in terms of operational adjustment and system integration.

"A new approach to clinical research must always be to improve patient's involvement, recruitment and timely completion of clinical trials by decentralising aspects of clinical trials, but we need to work together with sites to drive a patient centric approach in support of both the site and patient experience.

If the pharmaceutical industry is to continue progressing with drug development, and more importantly in a decentralised way in these post COVID times, a true understanding of how a research site conducts patient care alongside research activities is required, says Hirst.

"If we are decentralising elements of a clinical trial that would otherwise have taken place on-site, we need to first look independently at each stage of the trial and identify which elements could be replaced by virtual or home solutions, where applicable.

"Oncology decentralisation may be a little more complicated than other indications, for example."

As a result of these fast paced innovative times, Syneos Health has launched a Decentralised Clinical Trial Site Advocacy Group, working with and listening to sites. "This will inform Syneos Health of our current and future DCT strategy to alleviate both site and patient burden," Hirst says.

She adds that points to consider in the future will be:

- Will decentralisation of these elements significantly reduce the burden on sites and patients, and therefore improve recruitment and retention?
- Will reducing site visits accelerate timelines by allowing us to gather data faster, but be to the detriment of the patient experience, thus reducing retention?
- Will changes to processes reduce workload for clinical trial sites, resulting in time and cost efficiencies, or will it increase and cause site staff to become demotivated?

About the interviewee

Angela is currently a director, Site and Patients Services at Syneos Health, with senior oversight for the company's Catalyst sites, Oncology in the EU and USA. During her time at Syneos Health, Angela has grown and developed the Oncology Network in the EU, whilst continuing to maintain carefully selected sites within the US. She finished her nursing career in 2005 as the lead breast cancer research nurse at the Royal Preston Hospital. Upon leaving the NHS, Angela was a site lead within IQVIA's Access to Patients programme.

About Syneos Health

Syneos Health is the only fully integrated biopharmaceutical solutions organisation. The company, including a contract research organisation (CRO) and contract commercial organisation (CCO), is purpose-built to accelerate customer performance to address modern market realities. Created through the merger of two industry-leading companies – INC Research and inVentiv Health – it brings together approximately 26,000 clinical and commercial minds to help its biopharmaceutical customers shorten the distance from lab to life. Learn more at syneoshealth.com.

Surprise pandemic lessons for pharma

Ask people in most western nations to think back to 2019 and consider what they would have said then about the potential impact of a pandemic on their everyday lives and my guess is that the vast majority of us would have had little insight into what would happen.

Residents of Southeast Asia who had experienced the SARS outbreak in 2002-04 would likely have had a much better understanding, but even they could not have imagined just how disorganised the response would be in many other parts the world. The unpredictability of the progress of the pandemic continues to affect our business and personal lives in many different ways. It also continues to surprise us.

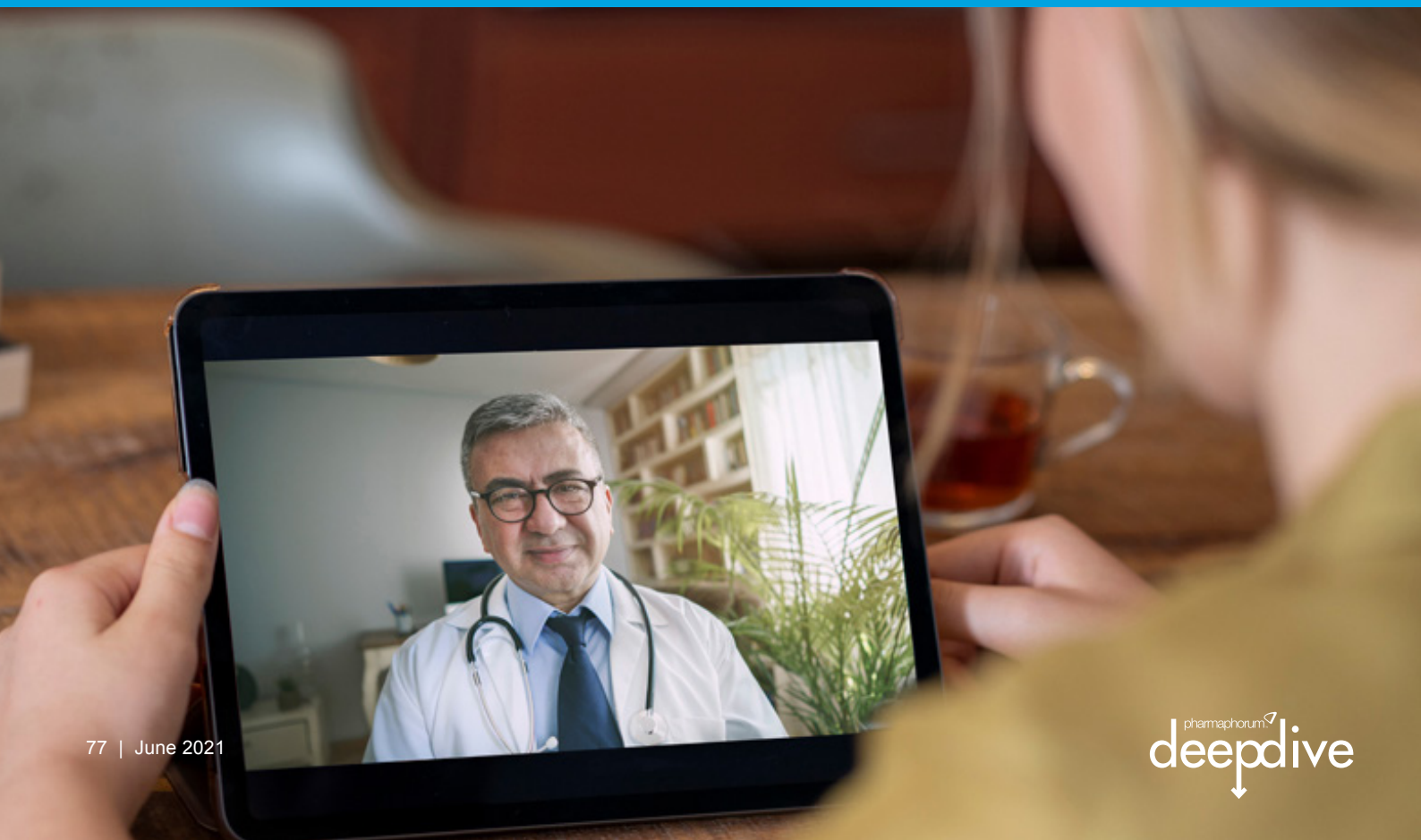
Over the last year I have written regularly about what our team at IQVIA sees in the developing picture of commercial activities in the life sciences industry across the world. Throughout this journey there have been a number of surprising developments that I think have important implications and opportunities for our industry in the years ahead.

The vaccines' success

I recall conversations with colleagues last March, in the early days of the pandemic, about our expectations of when effective vaccines might be available. Past experience led most of us to place an optimistic scenario at 12 months, but more realistically 18 months. How wrong we were.

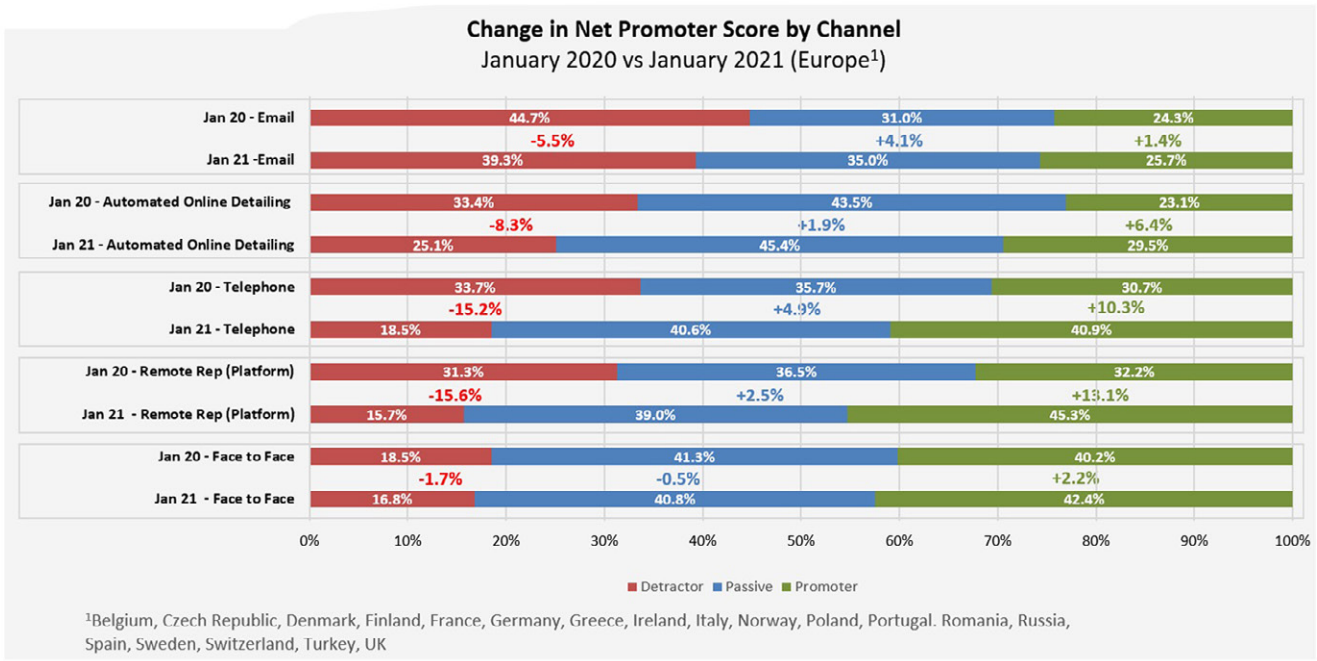
It is testament to the talented people in our industry and the partners and governments they work alongside that we have a host of effective vaccines already providing millions with a high degree of protection against the virus. Few would have thought it possible to reduce what can be a decade long process of development down to as little as nine months, nor would many of us have predicted the level of positive collaboration between industry and governments to get these vaccines to patients quickly.

Across all our activities, this now presents a once in a generation opportunity for industry to re-position itself in the minds of patients, government, regulators and healthcare providers (HCP). We have shown ourselves to be partners in the solution to the biggest challenges in human health, something we have a duty to emphasise and amplify across everything we do. And we should be confident in representing our value to these same stakeholders.



So, does absence make the heart grow fonder?

For many of our HCP customers this value would appear to be something they have developed a better understanding of when it has been disrupted. The chart below comes from our ChannelDynamics survey for Europe, illustrating the change in attitudes of HCPs towards the different channels of communication used by companies for promotional activities over the period from January 2020 to January 2021. This shows a positive shift in perceptions of all channels irrespective of whether the total activity via the channel has risen during the pandemic (as for telephone and remote e-detailing) or reduced (face-to-face). At the same time every country in the survey saw an overall reduction in total promotional volumes during this period. This suggests HCPs developed a better understanding of the value of promotional activity as it reduced and where there was an increase in experience of any one channel, particularly remote engagement, they found this beneficial.

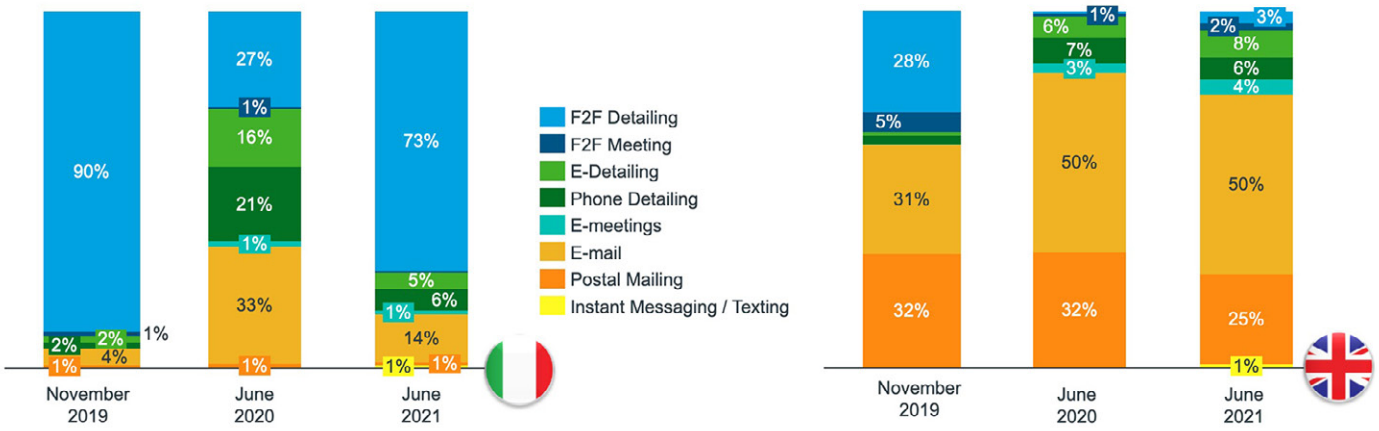


Indeed, results from a research survey we conducted with HCPs across four European countries supported this more positive view, with one UK Specialty Physician telling us: "I've got a lot more out of my interactions with the industry in the past six months than I've had before. Virtual interaction has been much more beneficial."

It may come as a surprise to many, but others focused more on how they missed the personal interactions that come with face to face meetings. As a German Physician told us: "I would very much like personal contact to be maintained... it's simply at a different level for me. It establishes a trusting relationship."

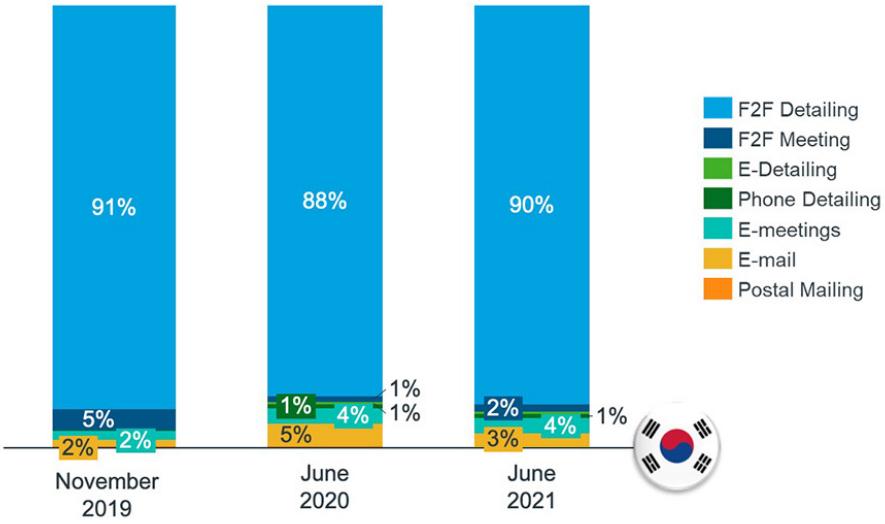
The ongoing value of face to face interaction

Much has been written in the last year about how the shift to remote and on-line engagement throughout the pandemic is going to replace a lot of face-to-face engagement in the future. However, qualitative and quantitative data confirms that HCPs still highly value face-to-face interactions. In Italy, for example, face-to-face engagement continues to rise and return towards pre-pandemic levels compared to other channels. This suggests it will continue to be the most important channel post pandemic. Contrast this with the UK, where face-to-face volumes have not recovered even as lockdown restrictions have begun to ease. Even here, both the net promoter scores and feedback from our survey suggest that HCPs still view face-to-face activity positively and value the interaction with industry. Companies operating in the UK will need to think carefully about where face to face interactions can return and add most value and concentrate efforts on a true multi-channel engagement strategy.



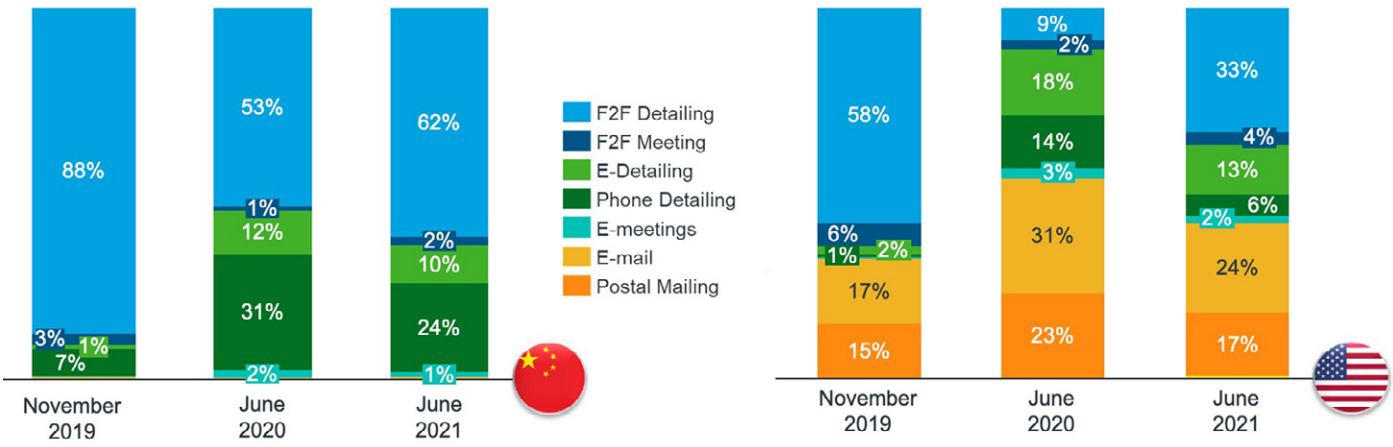
Is the ‘new normal’ the ‘old normal’?

The UK is indeed a good example of where the future promotional channel mix is likely to look very different post pandemic. Italy on the other hand is likely to have a situation that looks quite similar to what came before, but with virtual and remote interactions playing a more significant part in a more mixed model. However, it might come as a surprise to many who made bold predictions about changing engagement models that in some countries the future may look very similar to the past. Let’s take Korea for example, where data suggests talk of a ‘new normal’ may well be redundant.



Data suggests Korea is somewhat of an outlier and most countries will likely end up in a place where face-to-face volumes are not what they were and other remote channels in particular become more prevalent to fill the gap. The fact that HCPs globally have had to adopt these channels more significantly as part of their everyday clinical practice (the speed and degree of acceptance of which has been a surprise in itself) will be a key factor in maintaining increased volumes. When it comes to decisions about where to spend promotional resources the main question for companies is going to be 'when will the channel mix stabilise and what will it look like?' Here we can draw on the experience from two large markets.

China is somewhat further on in its journey through the pandemic and whilst it has a very different system and pre-pandemic experience to countries like the US it may provide a useful benchmark to the speed and stabilisation of channel activity. In the US we have seen a gradual return of face to face activity over the last six months or so and this continues. At the same time remote engagements are falling as a percentage of the total but maintaining a level well above where they were pre-pandemic. So where will these levels stabilise?



In China face-to-face has been the predominant channel in the past and had recovered around 70% of its pre-pandemic level before the end of 2020. Latest data shows activity levels coming into June 2021 almost identical to where they were in November '20, suggesting this may indeed be the 'new normal'. If the US were to follow a similar pattern then we might expect face to face to stabilise at around 40% of total promotional volume sometime in the next three to four months.

Big changes to field forces?

Life Sciences companies across the globe will have already invested much time and effort considering the implications of the pandemic for their future business and how to respond. Our Consulting teams at IQVIA have experienced this first-hand, working with customers on challenges that span the product lifecycle. Surprisingly we have yet to see this translate into companies making very significant or large-scale changes to their sales forces. Here, our insight is more anecdotal than quantitative, but if we look at the feedback from our contract sales teams across the globe a pattern does seem to emerge of a cautious approach from our customers.

Speaking with a top ten pharma leadership team recently we had the same feedback, with their focus more on making small changes now whilst still debating if and when they should introduce fundamental changes to their commercial model. When I first wrote about the impact of the pandemic almost a year ago I indicated that we had observed customers taking a 'wait and see' approach and a reluctance to make major changes to sales team sizes in light of the ongoing uncertainty. My sense is that this continues, albeit with companies having a lot more data, insight and experience on which to draw for their decision-making process when they eventually get to it.

More surprises to come?

Looking ahead, the experience of the last 18 months may also provide an insight into a few additional surprises that might come along:

- **Field force sizes may not decline as predicted**, partly driven by HCP interaction preferences, partly due to an improved understanding of the value they add and a reluctance from companies to reduce investment for fear of the competitive impact.
- **Total promotional volumes could well increase** as HCPs take up more remote interactions as well as maintaining some face to face contact.
- Alongside this, **average call durations may increase**, linked to the increased use of remote engagements. Conducting these at more convenient times for HCPs helps extend time spent on promotional and non-promotional contacts.
- We see **real innovation in HCP engagement being driven by emerging BioPharma** and companies with little or no prior commercialisation experience who are not tied to pre-pandemic models of commercial engagement.
- **Collaborations with healthcare organisations and governments** may flourish across the globe as they seek additional help from life sciences companies as trusted partners, creating a more favourable commercial environment.

Uncertainty linked to the pandemic will be with us for some time and making bold decisions against this backdrop will not be easy. However, thinking will eventually have to turn to positive action and those maintaining a 'wait and see' approach will eventually find it counter-productive. Indeed, companies can take positive action despite this uncertainty – as leadership theorist Peter Drucker is credited with saying "You cannot predict the future, but you can create it".

About the author

John Procter is VP offering development, IQVIA's Contract Sales & Medical Solutions Global Business Unit (CSMS GBU). John leads global strategy and service development for IQVIA's CSMS, covering patient services, medical affairs and contract sales. His expert knowledge in health solutions comes from 30 years in the healthcare industry. He joined Quintiles in October 2010 to run the Patient Services, Medical Affairs and Market Access business in the UK and then moved on to work in global service development and then head of Europe for these businesses. He took up his new role in the GBU global team in January 2018. Prior to joining Quintiles John spent eleven years at Pfizer.

About IQVIA

IQVIA is a leading global provider of advanced analytics, technology solutions and clinical research services to the life sciences industry. Powered by the IQVIA CORE™, IQVIA delivers unique and actionable insights at the intersection of large-scale analytics, transformative technology and extensive domain expertise, as well as execution capabilities. Formed through the merger of IMS Health and Quintiles, IQVIA has approximately 68,000 employees worldwide.

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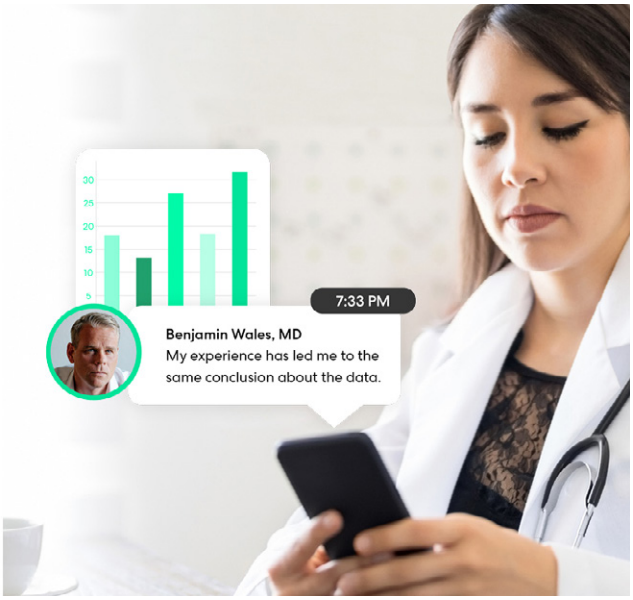
How hybrid virtual engagement is accelerating oncology communication

COVID has revolutionised the way pharma engages with healthcare stakeholders – but to be truly successful, digital engagement needs to move away from an overreliance on real-time meetings, say experts from Within3.

By making virtual meetings a necessity, COVID has forced pharma to adopt a more flexible, digitally-driven approach to stakeholder interaction – but in many ways the industry is still on the back foot when it comes to making the most of its engagement strategies.



"Pharma has been one of the last industries to move into digital," says Natalie DiMambro, vice president of Learning and Development at Within3. "Before COVID, these companies were still mostly doing meetings in-person, just because they'd been doing it that way for decades."

This is despite in-person meetings having many obvious drawbacks.

"Bringing a global group together is a massive undertaking – not only from a logistics point of view, but from a time point of view, a compliance point of view and a carbon footprint point of view," says Sarah Diffen, senior director, client relationships lead at Within3. "Because of that, companies are under a lot of pressure to get a return on investment from these meetings."

Video conferencing has addressed some of these challenges during COVID, but DiMambro points out that many of the same challenges will exist in a Zoom or Teams meeting as in a live in-person meeting.

> "You still have to schedule everybody, you still have to control the environment and manage the discussion in a way that's productive towards your goals. There are still many human aspects to consider."

Luckily, things are starting to change, and companies are turning to more asynchronous and hybrid engagement approaches in order to allow for more flexibility and lower costs.

Asynchronous engagement involves participants interacting over the course of several days or weeks, usually on virtual platforms where they can provide insights in their own time.

These platforms can also allow participants to view and comment on documents, watch video resources, and use different rooms for different topics, among other functions.

DiMambro says that Within3, for example, has made sure to set up its platform "almost like a university course" where users can see the tasks they have to complete when they log in.

> "Giving people a finite set of tasks to complete, a clear deadline and clear instructions can encourage them to provide insights much more quickly."

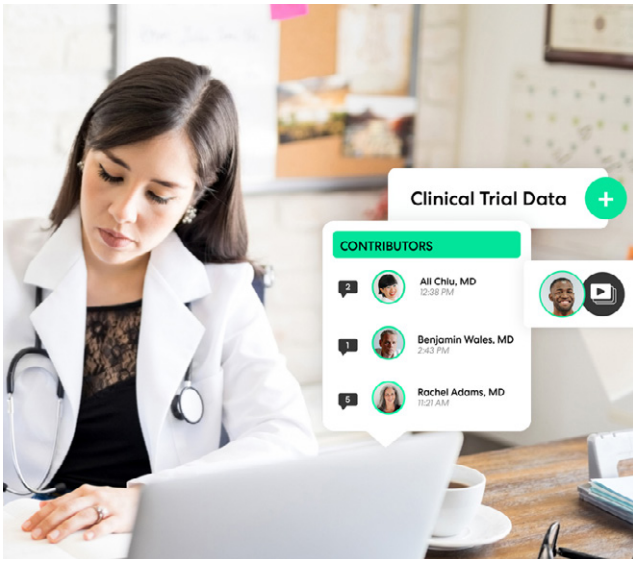
Hybrid approaches, meanwhile, use a combination of real time engagement (such as live video calls) and asynchronous engagement.

DiMambro says that these strategies generally represent a more "thoughtful" approach to engagement.

"That means thinking about the goals of the engagement and fitting the medium to those goals. Maybe a certain project would work best as a three-month initiative where participants interact online once a month; maybe another would lend itself to regular Zoom calls with online interaction supplementing that."

She adds: "When I was planning in-person live meetings in my previous roles, I was always constrained. I was only allowed a certain number of people, it had to be at an airport hotel, it had to be on a certain day, I had to deal with late-notice cancellations, etc.

"It was extremely stressful and my focus was never on the actual content of the meeting. It was always on all of these other aspects. Now, with asynchronous engagement, the focus has shifted back to the science itself, which is much more rewarding for everyone."



The appeal from the advisors' point of view is that these meetings can now be more respectful of their time.

"Many of these advisors are busy with patients, papers, or other speaking commitments," says DiMambro. "An ad board might be low down on their list of priorities. Now they can be in a hospital when they participate in an ad board, and after 15 minutes they can return to their patients.

"Because of this, the advisors are always the first to adopt this approach – and clients then start to realise they are getting more feedback from more people."

"These people want to share their opinion," adds Dr Mike Abbadessa, PharmD, executive director, Medical Affairs at Within3. "They are experts in their field and they're happy to engage, so you need to give them as many options as possible for doing so. Some will still want to engage face-to-face, of course, but the key is to be agile and have a flexible approach to engagement."

Engagement accelerates cancer research

Being more agile and flexible can be particularly useful in areas like oncology, where the number of sub-specialities for specific cancers means there is often a limited number of HCPs a company can engage with, most of whom are particularly busy with patients.

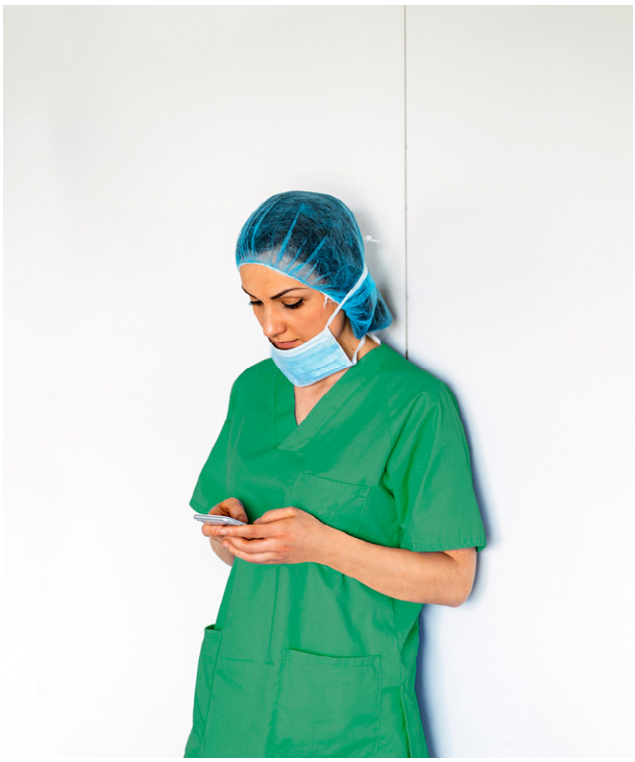
"Because of that, your chances of getting them to come a long way in person are smaller," says Abbadessa. "But with asynchronous engagement you can much more easily engage the right people at the right points in a drug's lifecycle."

This includes gathering KOLs from a wider range of countries.

"Especially in rarer cancers, oncologists' experience is usually limited to what they see in their own regions," says DiMambro.

"Now companies can more easily run sessions with people from all across the globe – with the virtual platform able to translate their words at the click of a button. Clients are thinking differently because they're meeting people they usually would never have talked to.

"That, to me, is the future."



Abbadessa adds that it's also easier to bring in more allied oncology healthcare professionals like practice managers, nurses, and care coordinators, as well as patient advocates, and therefore get a more complete picture of what each group is thinking.

“It means you’re transparent across the whole oncology care team,” he says. “You’re holding everyone accountable with their roles, and you’re giving everyone equal time to get into the conversation. They can be more uninhibited online and in asynchronous situations, whereas in-person some people might be intimidated by speakers at a higher level to them.”

Within3 have found that, in general, asynchronous engagement encourages people who might not normally speak up to be more vocal.

“Previously people might have only invited speakers who were more talkative, which would input bias into the responses,” says Diffen.

“But in asynchronous engagement, it’s often the case that every single expert will answer every single question. The total word count of responses increases too. That’s something you wouldn’t necessarily see at a face-to-face meeting.”

Diffen adds that the overall quality of debate improves when people are able to edit themselves before and during discussions on virtual platforms and add in more citations and references (See side box).

“We’ve found that insights and engagement are so much deeper when you give people the time to think about the subject.

“I’ve organised ad boards in the past where we presented physicians with complicated data and expected them to process it in ten minutes. We were only getting their first impressions.”

One of the knock-on benefits from all these methods is the increased speed at which insights can be gathered – which in turn will accelerate treatment advances in areas like oncology.

“Previously, getting all the right people in the same room at the same time would take months of organisation,” says Diffen. “Now, taking compliance into account, we can begin engagement within a couple of weeks.

Asynchronous in action

Showing how asynchronous engagement can improve insights, Diffen highlights an example of a medical affairs team that wanted to engage a group of hematology and oncology specialists on various topics around a rare type of cancer.

The team held a three-part session, beginning with a one hour kickoff webcast to review key data and set expectations for the next part of the meeting. The team then launched a two week over-time session. Approximately half of the questions were open during the first week of the session, with the remaining questions released in the second week.

For some questions, resources such as PDFs were available in a secure viewer, so participants could review and consider before responding. After the conclusion of the two-week over-time session, a closing webcast provided the opportunity for participants to review areas of consensus and probe for more details.

Session moderators were highly engaged throughout the over-time session, and 100% of the contracted participants contributed to the discussion. The team met its stated objectives for the session.

"The combination of real-time with overtime is often really successful. The platform can capture all the feedback and insight in one place, allowing people to immediately view and act on it – whereas historically it would have taken days, if not weeks, to write up a report, making it difficult for advisors to cast their mind back to what happened.

"Now, we can be much more agile."

Because of this, DiMambro says it's important for platforms like Within3's to be built with pharma complianceand security considerations in mind.

"With those security features built in, clients don't have to worry about compliance and can go straight into focusing on the engagement."

A more engaged future

As virtual, asynchronous engagement becomes increasingly vital for pharma's engagement strategies, the benefits are spreading into other corners of the industry.

Abbadessa notes, for example, that MSL and medical affairs field teams interacting with HCPs can now more easily connect with their headquarters.

"Traditionally MSLs would connect KOLs with company medical directors at scientific congresses, but now they can do it online asynchronously, and more easily fit it around everyone's schedules," he says.

"They can also still take daily debriefs from congresses and connect them with headquarters, keeping them up to date with what's actually happening at the event.

"COVID-19 has shown the industry the importance of staying connected even when the world is shut down, and platforms like this are really moving the needle on that."

Abbadessa says that the potential of using data and technology to improve industry communication in this way is what drew him to the tech sector in the first place.

"When I was in hospital pharmacy the UPS guy had more technology than we did, and it drove me crazy. Now we can use these platforms to make things better for teams and, ultimately, for patients."

While the wider industry can still sometimes be slow to adopt new tech, DiMambro says pharma is already seeing the benefits of these new approaches to engagement.

"When I'm working with clients who want to do a live ad board, I always ask them what their expectations actually are, and if there's really anything they can only accomplish in-person.

"Tech can empower everyone in this space to make decisions based on what's best for the goal versus just falling back on traditional approaches.

"People are going to become more discerning with their travel, so let's make it count and make sure we've done the work online ahead of time. That way, when you end up in-person the meeting is about consensus or what wasn't accomplished online. That's a much better use of everyone's time."

Diffen adds that while face-to-face is unlikely to vanish completely once COVID restrictions are fully lifted, the variety of tools now available means that pharma can find the right engagement strategy for the right situation rather than taking the blanket approach it used in the past.

"People are humans; they like that in-person interaction. But people are also realising that we can achieve so much more virtually.

"We will likely all become more selective in what we do face-to-face and what we do online. Ultimately, the dominant model will be a combination of face-to-face, virtual real-time, and overtime discussion on platforms like Within3, where stakeholders can continue the conversation."

To learn more and request a demo, visit www.within3.com

About the authors

Natalie DiMambro is vice president of Learning and Development at Within3. In this role, she develops and facilitates virtual live and on demand training programmes for Within3 team members. She also supports clients with strategic guidance and training to maximise effectiveness with the Within3 technology solutions offered.

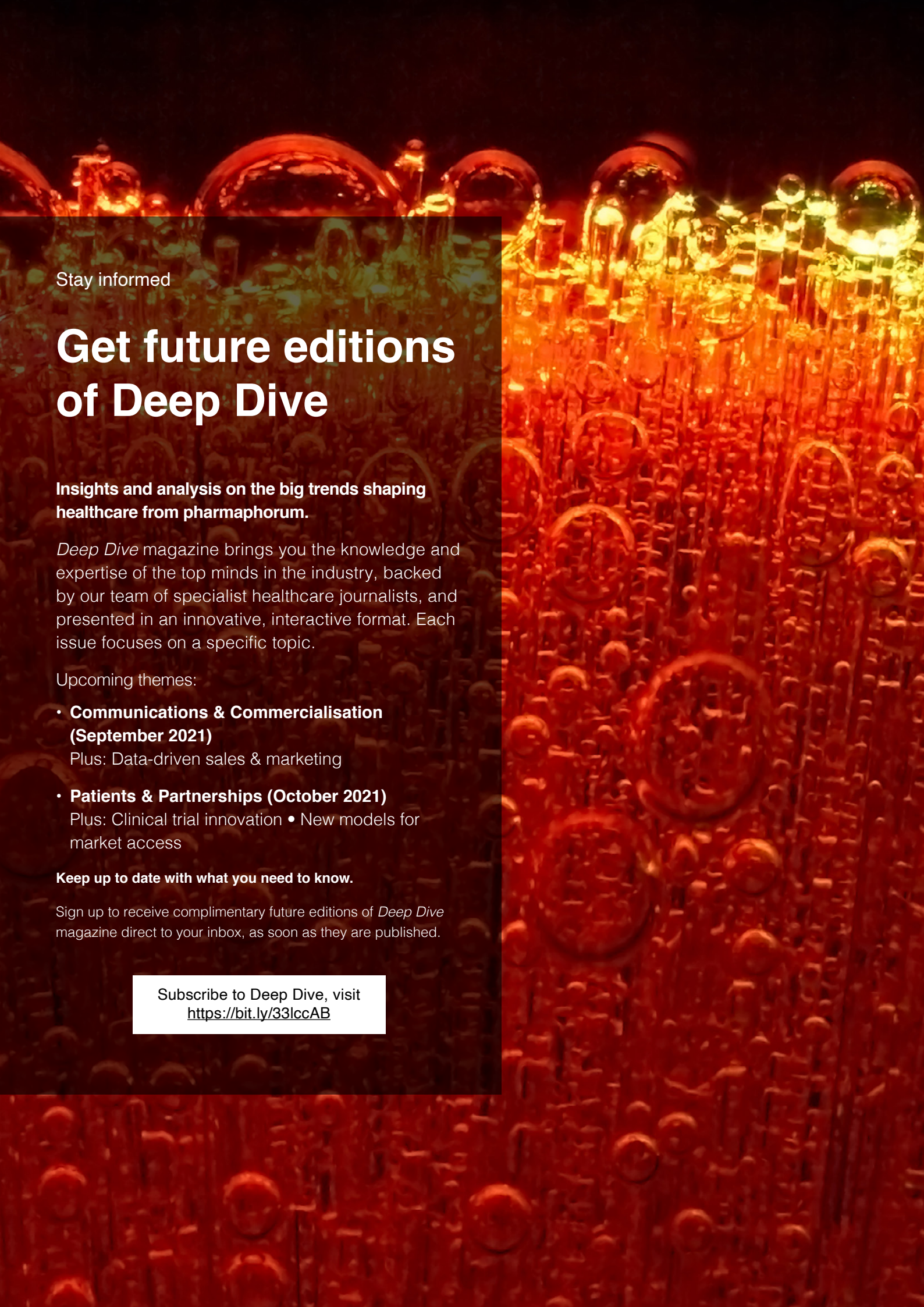
Sarah Diffen is senior director, client relationship lead at Within3. Sarah originally trained as a pharmacist but moved across into the pharma industry and then into medical communications, where she spent many years as the strategic and operational lead to clients across a wide variety of medical education programmes.

Mike Abbadessa is the executive director of medical affairs for rMarkBio. Mike has been a leader in healthcare and the pharma industry over the past 20 years. He began his career in acute care hospitals, as pharmacist, director and chief operating officer. He transitioned to pharma as an MSL, director of field teams, and then senior director of innovation/ analytics for medical affairs at Takeda. After his career in pharma and before joining rMark, Mike expanded his knowledge of field medical's success factors as a consultant for Tardis (Amplity) and various pharma companies.

About Within3

Within3

Within3 invented a better way for life sciences companies to have conversations with the people who matter most – from doctors to patients to payers, and more. Our virtual engagement platform gives stakeholders the freedom to communicate anytime, anywhere, on any device. With tools for meaningful discussions and a dedicated client success team on every project, most Within3 projects achieve 100% stakeholder participation.



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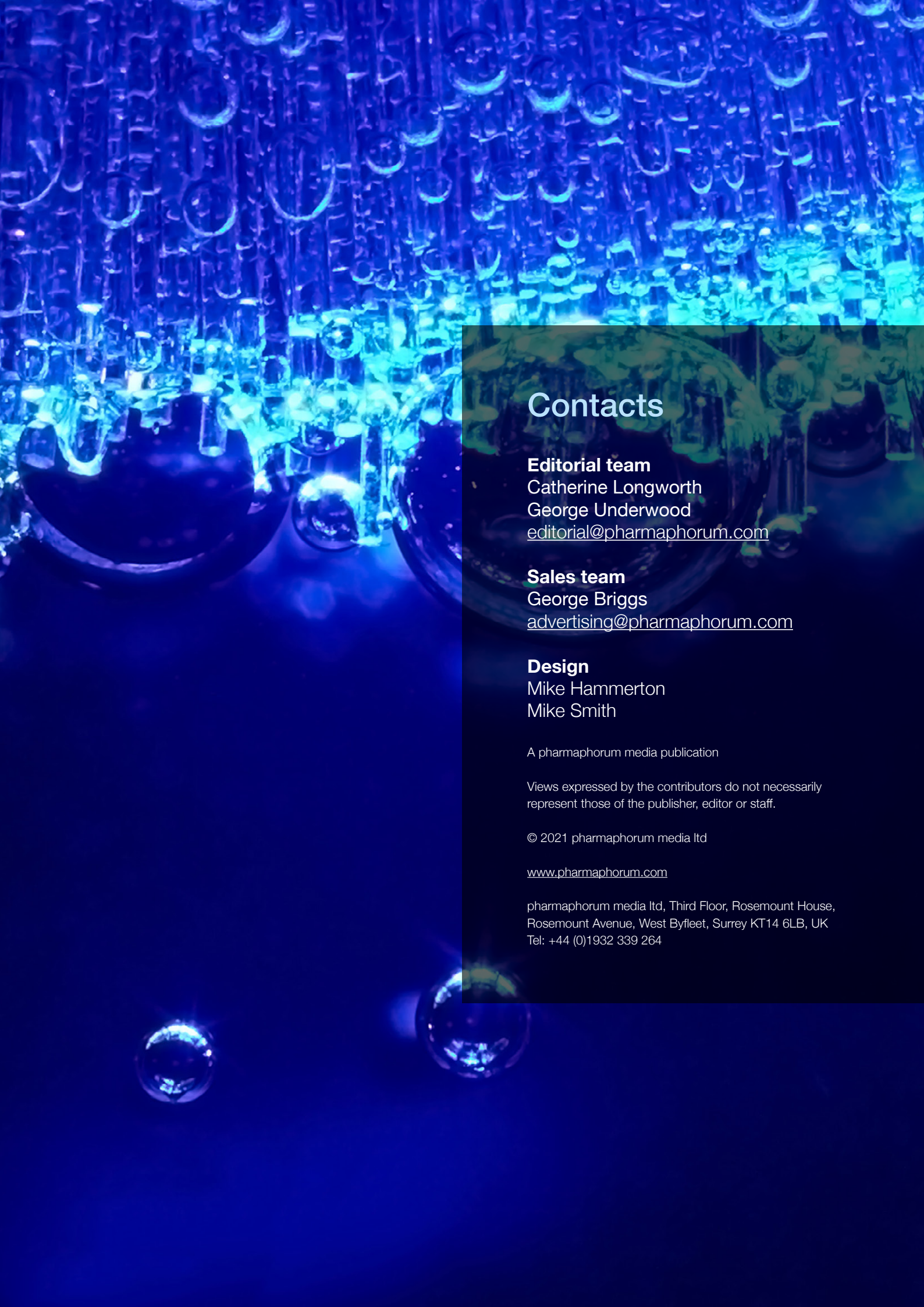

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