2030 life sciences and health in the digital age Part 2

As part of its mission to help members anticipate and prepare for changes in the pharmaceutical industry, The Pistoia Alliance has developed a research paper which sets out to consider what the life science, biopharma R&D and healthcare ecosystem might look like in 2030, in particular how the increasing adoption and sophistication of technology will affect companies and patients alike. This article is the second part of a two-part series based on that paper. Written in retrospect from the world as it is in 2030, it looks at how healthcare has changed in the intervening decade.

By Dr Steve Arlington and John Wise

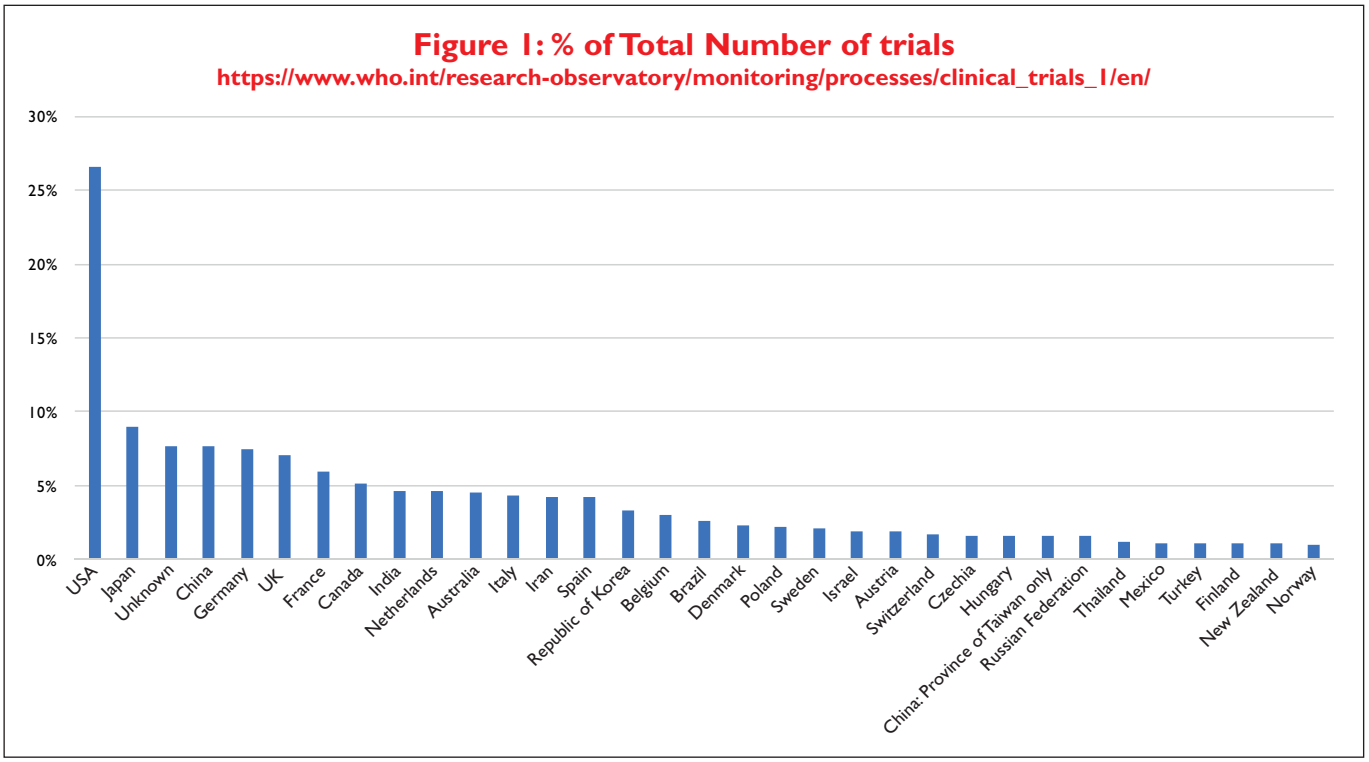
The intention of this 2030 report is to stimulate debate as to what the future may hold. There are many scenarios one could legitimately put forward and challenge. We have chosen one such set of scenarios. It is not to say it will be correct. However, in presenting these scenarios it is hoped that one can identify signals that identify the likely drivers of change over the next decade.

The first article covered the socio-economic and political evolutions that have happened, the subsequent effects on population health and the innovative technologies which have had the greatest impact. This article builds on those assessments and looks at the patient-centric innovations we can expect to see in the next decade, as well as some of the expected changes in regulation, and how life science, biopharma and healthcare organisations can work together to tackle the growing skills crisis.

Patient-centric innovations

Outside of the technological advances we explored in the previous article, the last decade has seen several important scientific advances which have significantly improved patient care:

Real World Data (RWD): RWD, or 'data relating to patient health status and/or the delivery of health care routinely collected from a variety of sources', has been transformative for the pharma industry's approach to clinical trials with external control arms, disease models and natural histories, site selection, patient recruitment, etc[1]. The better quality and wider availability and accessibility of RWD – due to the increasing deployment of the FAIR data principles[2] – has enabled more precise *in silico* clinical trials to increase the efficiency and effectiveness of clinical development programmes to meet unmet medical needs[3,4].



RWD is being used extensively to inform Health Technology Assessment (HTA) and the value of therapies. Projects such as the MIT Leaps project[5] are using AI and Machine Learning (ML) to enable patients to receive timely access to the most appropriate therapeutics for their needs, while providing key stakeholders with the Real World Evidence (RWE) they need to improve their decisions related to the development, access and use of therapeutics for the target disease.

Precision medicine: The promise of genomics-based, precision or personalised/stratified/autologous medicine came to fruition enhanced by the increasing scientific understanding and targeting of combination therapies[6]. The fundamental work of organisations such as UK Biobank[7], Genomics England[8] and the All of Us Research Program[9] from the NIH provided much-needed insight into the correlation between phenotype and genotype. The age of patient empowerment arrived in the mid-2020s with a handful of start-up companies leading the way through secure, patient-friendly applications; these apps allowed patients to choose whether or not to participate in research and share elements of their medical records with participants in the healthcare ecosystem.

The improved data security offered by companies decreased the cost of end-user sequencing by moving some of the cost to the researchers who accessed the data, and then compensated the end-users when researchers accessed their data. By the early 2020s it was possible to get one's genome sequenced and to retain ownership and control of the data. This could be achieved via web-based, blockchain-based, third-party providers such as Nebula Genomics[10] and Shivom[11]. The breakthroughs in medical devices, monitoring and diagnostics (including companion diagnostics) have also continued rapidly to expand and show considerable promise, although often their deployment has been based on the ability to pay[12].

Patient registries: Patient registries have been a long-term facilitator of patient-centric research. Now in 2030, In this era of 'very big real world data', they have been harmonised to align with commonly-agreed standards so that patient registries could effectively be mined to promote research – helping organisations to find the right patients in the right places with the right inclusion criteria, and the right principal investigators for clinical trials.

One of the major challenges in drug development has been an historic under-representation of patients recruited into clinical trials from regions other than the USA and Europe. For example, in 2019 as a percentage of world-wide

population share, there were more people in the US and Europe recruited into clinical trials and provided with access to new medicines than in APAC[13] or Africa. 15% of the worldwide population lived in Africa yet recruited only 2-3% of the worldwide patients into clinical trials. 57% of the worldwide population lived in APAC yet they, too, were significantly under-represented in clinical trials. **Figure 1** reveals that the US, with about 5% of the world's population, was carrying out more than 25% of the world's clinical trials. However, China and India, accounting for approximately 35% of the world's population, collectively performed only about 12% of the world's clinical trials.

However today, through improved patient registries in those regions of the world, and with the deployment of digitally-enabled clinical trials, substantially more patients as a percentage of their population are able to participate and gain access to innovative medicines.

The challenges of clinical trial enrolment, a long-standing problem for drug developers, have been to a large extent overcome by the deployment of digital technologies. These technologies have empowered physicians, and indeed patients themselves, to find relevant clinical trials based on disease, age, gender, location and biomarkers.

Stem cell and gene-based therapies: By the mid-2020s, stem cell[14] research and cell therapy such as CAR-T, genetics and gene therapies including CRISPR-Cas9, etc were all providing breakthroughs in numerous disease areas, but implementation was not being fully realised. These new therapeutic modalities had created a new market for the products and services needed to support tissue engineering therapies, such as the culture of tissues for therapeutic purposes, the management of stem cell banks, or the highly regulated and precise delivery of cell-based therapies directly to patients.

Discovery research in pharma had for many disease areas moved to 3D tissue models[15]. Today, there is a substantially reduced need for animal models in drug R&D and the move has both increased the precision of efficacy and toxicity prediction and improved the ethics of drug testing. Such developments have dramatically reduced the drug attrition rates typical in the industry and reduced time to market. Additionally, the use of new diagnostic imaging techniques has further reduced attrition rates in later-stage clinical trials. Together these two factors alone have reduced the overall costs and time required to obtain regulatory approval.

Oncology: Tumours are now treated with well-established, mainstream, chronic therapies including immunotherapy[16] and most cancers are being identified and treated earlier, not least due to progress in Liquid NGS[17]. Research initiatives, such as ASCO's Center for Research & Analytics (CENTRA)[18], has provided the infrastructure to analyse the RWD and deliver deep insights into the etiology, diagnosis, treatment and prognosis of cancers. However, the ongoing cost pressures of therapeutics remains an issue and new pricing models are being experimented with. Proteolysis-targeting chimeric molecules (PROTACs)[19], protein-slaying drugs, look destined to become the next wave of blockbusters.

Genomics: Genetics has moved centre-stage in recent years and personalised medicine is available across the globe. The markets for cell and gene therapy[20] are immense. CAR-T[21] and stem cell therapy[22] have matured and become available for treating serious disease. Gene therapy and gene editing are now seen as being able to cure rare, monogenic diseases such as severe combined immunodeficiency due to adenosine deaminase deficiency (ADA-SCID)[23], or the one-time gene therapy to restore functional vision in children and adult patients with biallelic mutations of the RPE65 (retinal pigment epithelial 65kDa protein) gene[24]. The vastly-improved knowledge in the field of genomics coupled with phenomics allowed the understanding, tackling and the cure of some polygenic diseases to be contemplated. Cure as a primary endpoint for some new therapies was possible. However, it came at a cost (**Table 1**).

The business model for such curative therapies had been difficult to implement. As *Bloomberg Opinion* noted: 'Wall Street Wants the Best Patents, Not the Best Drugs'[25].

Table 1: Figures relate to the late 2010s

DISEASE	DRUG	TREATMENT COST $
Hepatitis C	Solvadi	84,000
ADA-SCID ('boy in the bubble syndrome')	Strimvelis	665,000
Inherited retinal disease	Luxturna	850,000
Beta thalassaemia	Zynteglo	1,800,000
Infant spinal muscular atrophy	Zolgensma	2,125,000

Table 2: Impact of new technologies in R&D value chain

Discovery	AI/ML/NLP (including text mining), RWD, data validation and cleaning tools, Quantum Computing
Development	New development, eg virtual trials, AI/ML, Digital/Wearables, Blockchain, RWD
Medical Practice	AI/ML, Digital/Wearables, digitally-enhanced patient engagement, automatically produced PROs, intelligent home, RWD
Clinical Outcomes	Digital/Wearables, Blockchain, RWD
Regulatory Policy and Compliance	Predicting regulatory policy evolution and streamlining compliance to regulatory change, RWD
Business Development and Licensing	Augmenting search, evaluation and licensing with AI/ML, RWD

These breakthrough treatments have been criticised for being unaffordable – just as the cost of antibody-based cancer treatments in the 1990s were declared out of reach for most. However, experiments with new healthcare systems, including outcomes-based, annuity-based reimbursements[26,27], aims to reward the biopharmaceutical industry for these new breakthrough drugs.

Some companies have been prepared to accept reimbursement in installments over three to five years or to provide discounts if a patient did not see specific benefits from the therapy. Where it became possible to measure pay for performance, many payers forced industry to accept pay for performance pricing paradigms. Furthermore, companies were increasingly requesting tests to identify such genetic diseases to be added to mandatory newborn testing programmes[28] in an attempt to develop these markets and, by doing so, improve health delivery and reduce per capita costs.

Microbiome: The human microbiome has an estimated 100 trillion microbes, the bulk of which live in the gut. Advances in genome sequencing technologies and metagenomic analysis have greatly increased our understanding of the microbiome[29]. This had led to a whole new field of medicine with as much potential as genomics held 25 years ago. However, implementation was slower than anticipated due to the sheer complexity of the mechanisms of action[30]. The microbiome had been implicated in different disease areas. For example, enterotype I and enterotype III bacteria were strongly associated with dementia[31]. By the early 2020s researchers were pursuing the potential of the microbiome and had moved beyond gut-related inflammation such as Crohn's disease and colitis, to central nervous system and cardiovascular diseases. A greater understanding emerged in the early 2020s on how to balance the gut microbiome and test the effects on multiple disease phenotypes. However, researchers struggled to make headway due to the plethora of data sets published on microbiome experiments as enabled by the genomics era, until universal data and tools emerged on the molecular interactions between microbiome and host physiology.

Diagnostic pill: The paucity of knowledge about gut microbiota higher up the GI tract was resolved by researchers at Tufts University developing a 'Diagnostic Pill' which could be swallowed and recorded bacterial samples while passing through the gut[32,33]. Such 'lab on a pill' devices revolutionised understanding of the spatial diversity of the gut microbiome and its response to medical conditions and treatments.

Today we are able to witness the benefits of joined-up healthcare embracing the food industry. This had become a reality with health, welfare and social services combining in most economies to provide wellness and prevention programmes for the population based on their individual needs. This change to focus on the public health agenda of disease prevention[34] had dramatically reduced the number of lifestyle-related illnesses, including cancer. The reduction in obesity in the general population had seen the incidence of some cancers being reduced and while no specific causal link had been elucidated, obesity was seen as an important risk factor and the population had responded positively.

Skin microbiome: Skin micro-organisms have been discovered to have important roles in educating the cutaneous immune system. Some skin diseases had been associated with an altered microbial state of the skin. Reversion of this dysbiosis had helped prevent and/or treat the disease[35]. Indeed, some studies had indicated that bacteria in the skin microbiome could inhibit skin cancers[36].

Skills for 'R&D Technology'

Over the past decade, the relevant skills needed by the biopharmaceutical industry have evolved constantly due to the impact of new and emerging technologies (**Table 2**).

Table 3: 2018 Gallup poll of 25 US business sectors asking Americans to give their overall view of each. Of the 25 industries, pharmaceuticals achieved a score of -23 (second from the bottom)[43]

RATING		TOTAL POSITIVE %	NEUTRAL %	TOTAL NEGATIVE %	NET POSITIVE %
1	Computer industry	60	28	10	50
2	Restaurant industry	58	31	10	48
3	Farming and agriculture	56	24	18	38
4	Grocery industry	53	27	18	35
5	Travel industry	50	35	13	37
6	Retail industry	48	31	20	28
7	Automobile industry	47	33	19	28
8	Accounting	39	46	12	27
9	Real estate industry	46	32	21	25
10	Publishing industry	43	34	20	23
11	Airline industry	43	31	24	19
12	Internet industry	45	26	27	18
13	Telephone industry	41	34	25	16
14	Electric and gas utilities	42	28	29	13
15	Banking	42	28	29	13
16	Sports industry	42	27	30	12
17	Movie industry	40	28	29	11
18	Television and radio industry	40	26	32	8
19	Education	44	17	38	6
20	Advertising and public relations industry	35	31	32	3
21	The legal field	34	30	34	0
22	Oil and gas industry	31	23	44	-13
23	Healthcare industry	34	18	48	-14
24	Pharmaceutical industry	30	16	53	-23
25	The federal government	26	19	53	-27

Table 4: Skills required for Pharma R&D Data Science[44]
A strong educational background. 88% of data scientists have a Master's degree and 46% have PhDs

TYPICAL DATA SCIENTIST TASKS	BUSINESS SKILLS	TECHNICAL SKILLS REQUIRED IN THE YEAR 2020
Collecting large amounts of structured and unstructured data and transforming it into a usable analytics-ready format	Domain Knowledge such as molecular biology, medicinal chemistry, clinical R&D, regulatory affairs, epidemiology, pharmaco-economics	R Programming (43% of data scientists use R)
Solving business problems using data-driven techniques	Intellectual curiosity, creative problem-solving and strategic thinking	Medical statistics/pharmaceutical statistics[45]
Staying on top of analytical techniques such as machine learning, deep learning and text analytics, including benchmarking of methods	Relevant business acumen and awareness of industry trends	Procedural and compiler coding Database query languages: SQL SPARQL Data modelling in relational and RDF form
Communicating and collaborating with both IT and the business	Communication skills to different levels of audience	Familiarity with cloud-based environments (AWS, Google, Microsoft)
Looking for order and patterns in data, as well as spotting trends that generate value	Relationship-building, teamwork and conflict resolution	Data visualisation techniques
Validating models and analyses	Understanding of legal, regulatory and ethical issues	Machine Learning and AI
		Text mining and related ontology use in semantic based text mining

In the early 2020s, many organisations suffered delays in their R&D programmes due to a shortage of relevant skills. Today, the executive leadership of the biopharmaceutical industry has widely recognised the importance of the technology-biology interface to innovation. R&D IT – or R&D Technology as it has increasingly become known – is now seen as a strategic discipline and, importantly, different from the traditional IT that supports line of business activities.

Management has largely accepted that the rate of change of the technology-science continuum is so rapid that extra effort has to be expended to keep the workforce's skills up-to-date. As such, increased investment in training, development and education kept up-skilling personnel, allowing new technologies to be brought in without causing unnecessary redundancies in the workforce. Such training curricula were provided in large part by external organisations such as universities, eg Oxford University's MSc in 'Nanotechnology for Medicine and Health Care'[37], or Harvard's 'CRISPR: Gene-editing Applications'[38], or the Pistoia Alliance's globally-recognised educational programmes, including its member-driven 'Technology Observatory', which keeps members up-to-date on emerging trends in life science and healthcare.

In 2017, PhRMA commissioned a report addressing efforts to attract and grow the biopharmaceutical industry[39] and the availability of STEM skills. In 2018, the ABPI had produced a report entitled 'Bridging the skills gap in the biopharmaceutical industry'[40].

Digital experts needed to be encouraged to join the biopharma industry and biopharma needed to compete against other industry sectors, such as the well-funded FinTech, as every company was fishing in the same limited talent pool. One of the key hurdles to overcome in recruiting talented young people was the negative perception held by society of the biopharma industry, caused by many serious and on-going issues to do with transparency (for example Humphrey Rang's review of Ben Goldacre's book *Bad Pharma: how drug companies mislead doctors and harm patients*[41]), and problems of pricing[42].

As highlighted in the PwC Pharma 2005, 2010 and 2020 reports, the perception that society had of the pharmaceutical industry continued to be very poor (see **Table 3**). Even today, the industry has still failed to grasp this fundamental problem

and society has not been convinced. As the industry attempts to become more patient-centric, so this fundamental trust issue needs to be addressed. In part this will be driven by the delivery of 'cures' for some hitherto untreatable and distressing conditions, using gene editing and cell therapy, which is stimulating more positive thinking in society and appreciation of the impressive biomedical capabilities of the industry.

Another hurdle has been the comparatively conservative, slow-moving nature of biopharma compared to the dynamic and agile nature of digital technology innovation and development. 21st century Agile development methodologies did not sit well with the constraints of 20th century regulations controlling the deployment of computer-based technologies in the regulated domains of the biopharma industry.

Today, the industry is more confident in its recruitment of data scientists. Although the tools with which data science is executed continue to develop, the requirement for biopharma/life science/healthcare domain knowledge, along with the data analytical and statistical skills, was now accepted as the *sine qua non* for carrying out the required tasks.

During the late 2010s, there had been much discussion in the pharmaceutical industry about the urgent requirement to recruit data scientists, driven by the need to deploy data analytics on rapidly increasing volumes of RWD. Finding such staff with the requisite skills was problematic – they needed both the technical skills of data analytics along with domain knowledge of the pharmaceutical industry. **Table 4** captures some of the skills required in and around 2020; such a view needed to be kept up-to-date as the decade evolved to 2030. In particular, the ongoing need to ensure that staff were sufficiently resourced needed not to be overlooked. This included enabling attendance at conferences and similar events so that data scientists could communicate with the wider community and keep abreast of developments. Furthermore, career expectations needed to be managed carefully and understanding specific employee motivations for pursuing data science were key factors in staff retention[46].

Regulation

In the years leading to 2030, regulatory agencies have been striving to adopt processes, such as adaptive licensing[47], that would allow them to get good drugs into the market while continuing their important vigilance to ensure bad drugs did not get approved.

For example, in the US it had been predicted that by 2025 the FDA would be approving 10 to 20 cell and gene therapy products a year. This statistic was based on an assessment of the pipeline and the clinical success rates of these products and as such the FDA expanded its workforce including additional Marketing Authorisation Applications reviewers.

During the late 2010s, major regulatory agencies (eg CFDA, FDA, EMA, PDMA) delivered strategy reports embracing the need to support and expedite the development and marketing approval process for many new treatments. For example, the EMA Regulatory Science to 2025 Strategic Reflection[48] identified the need for five key objectives:

- Catalysing the integration of science and technology in medicines development.
- Driving collaborative evidence generation, improving the scientific quality of evaluations.
- Advancing patient-centred access to medicines in partnership with healthcare systems.
- Addressing emerging health threats and availability/therapeutic challenges.
- Enabling and leveraging research and innovation in regulatory science.

Furthermore, the FDA produced several guidelines to help drive clarity in the processes of the deployment of regenerative medicine[49] and cellular and gene therapy[50] including the longer-term follow-up of gene therapy patients.

The Chinese FDA also implemented considerable change in its regulatory environment designed to reform the administration of clinical trials, accelerate the evaluation and approval process and the promotion of drugs innovation and the development of generic drugs[51].

The Japanese Pharmaceuticals and Medical Devices Agency (PMDA) had similarly been working on its efficiency to ensure new drugs got to market safely and effectively and in a timely manner. Indeed, by the mid-2010s the average number of days between an NDA filing and approval of a standard drug in Japan was 306 days, compared to 322 days in the US (FDA) and 366 days in the UK (MHRA).

Nonetheless, despite all these efforts, the rate of change of drug discovery and development and the impact of new, precision-medicine research modalities have continued to stretch the resources of the regulatory agencies.

Health Technology Assessment (HTA)

For many years, HTAs had been used to help assess the value (and indeed affordability) of therapies.

The pharmaceutical industry regarded the HTA assessment as the 'forth hurdle'; the first three hurdles being the need to demonstrate to the regulatory agencies that a therapy was safe, effective and could be manufactured with consistent quality. Overcoming the fourth hurdle was essential to obtain reimbursement from many payers in many regions. NICE[52] (the National Institute for Health and Care Excellence), the HTA in England and Wales provides a useful exemplar of the role of an HTA.

However, now in 2030, global RWD standards[53] are in place that allow outcomes measurement to be useful and the many disparate Health Technology Assessment Agencies, including NICE, are aligned into a global consortium (similar in concept to EUnetHTA[54] but with global reach) which provides support and advice to the life science and medical device industries. The development of such HTA methodologies has been instrumental in the migration of the reimbursement paradigm from 'payment per pill' to 'outcomes-based payment'.

Pre-competitive collaboration

Another key development in the last decade has been that all major biopharmaceutical and life science businesses have been closely aligned and collaborating openly in pre-competitive programmes that delivered cross-industry results[55]. The multi-company, multi-year Open Targets[56] initiative, launched in 2014, provided one example of many of these pre-competitive collaborations that have transformed the efficiency of biopharma R&D. As KPMG wrote in its 2018 report *Reinvent innovation and become an R&D frontrunner by 2030*[57]

"…by 2030, we anticipate R&D funding to be facilitated through cost and resource sharing practices among multiple healthcare stakeholders as a way to lower R&D costs. Equity partnerships between CROs and industry players will ease the R&D financial burden and drive innovation and cost effectiveness. In addition, crowdfunding for financing drug R&D will accelerate drug development and distribute the financial risk among various stakeholders, and perhaps even the wider public.

"To remain successful in the market while developing an innovative and sustainable R&D capability, fundamental change is now a necessity and companies need to adapt to these new market dynamics."

The multiple regulatory agencies agreed to try to move beyond the ICH[58] model of harmonisation and move towards establishing a global regulatory body. The WHO had taken a leading role in these negotiations as indicated in its report *Towards Access 2030*[59].

Conclusion

In this two-part series, we have tried to imagine the future of the health ecosystem in the year 2030. This research has involved 75 subject matter experts drawn from 65 different organisations, and what has emerged is a life sciences and healthcare industry with tremendous opportunities for development and for contribution to world health and the public good.

We do not expect all of the predictions to be accurate, in fact we are certain time will show that some are not. Having said this, we are confident that many of the signals we have noticed will deliver the expected changes. Socio-political changes are certainly moving in the direction of healthcare being seen as a human right; macroeconomic analyses say that overall healthcare costs as a percentage of GDP cannot continue to rise as they have been, and the mechanisms we have to pay for healthcare require a radical rethink. Our agenda must shift from treatment of disease to prevention and cure, and with that the reward systems we have to promote these solutions must adapt to encompass the new agenda.

However, it is also evident that such opportunities will only be realised if, and only if, the industry embraces the substantial and continually developing technical and scientific advances we are seeing in the life sciences. New research modalities such as cell and gene therapy, the new wave of digital technologies supporting biomarkers, diagnostics, therapeutics and health devices, and the profound developments in capability of AI/ML/NLP and robotics will deliver exciting progress. Moreover, the analysis of the large volumes of data that will be generated by this digital revolution – when powered by the next generation of high-performance computing, including quantum computing, and undertaken in collaboration with all stakeholders in the ecosystem – will make a profound contribution to the understanding of disease, the delivery of new therapies and the palliation of the human condition.

In many instances these advances will be found at the intersection of technologies, and the intersection of technologies and science. These dramatic developments in scientific-technological progress will continue to create stress for social and political institutions. We cannot sweep under the carpet the legitimate concerns society has regarding the security of our personal health data, nor can we overlook

the lack of trust that already exists with many players in the healthcare ecosystem and with some of the newer technology businesses.

However, the large multinational companies, with their awareness of world-wide challenges, along with their understanding of the opportunities that collaboration across industries and geographies create, will become increasingly effective in helping to calm these concerns. As such, the Pistoia Alliance, along with many other organisations, should reconfigure to ensure that they reflect and promote these developments and, by so doing, increase the chances of success. DDW

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