Four scenarios for the future of medicines and social policy in 2030

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The future of medicines is likely determined by an array of scientific, socioeconomic, policy, medical need, and geopolitical factors, with many uncertainties ahead. Here, we report from a scenario project, analyzing various trends, crucial and complex developments in the medicines' space. From a range of 'critical uncertainties' we derived two scenario drivers: global convergence, ranging from very high (trust and solidarity), to very low (fragmented ecosystems); and disease orientation, ranging from public health first to interceptive medicine. This resulted in four contrasting portraits of the future of medicines and social policy: deprioritizing the high-end; sustainable flow; transformative healing; and global divide. All those involved in drug discovery and development can use these for strengthening preparedness for the crucial challenges ahead.

Keywords: Future medicines; Scenario analysis; Social policy; Global health; Future trends

Introduction

The history of drug discovery and development shows that science-based medicines did not enter the clinic earlier than during the mid-1950s of the previous century.[1] Before this, health threats, especially communicable diseases, were lacking vaccines or antibiotics, not to mention antivirals or monoclonal antibodies.[2] Thus, in a timespan of one or two generations, tremendous progress in biomedical innovation has been realized, from effective products for hypertension, diabetes, or rheumatoid arthritis to chimeric antigen receptor (CAR) T cell products and mRNA vaccines. However, it is not all good news. We see governments and healthcare systems struggling with rising pharmaceutical costs and drug shortages.[3–5] The global annual spending on oncology drugs was ~US$150 billion in 2020, a troublesome economic burden for any health system.[4] There is increased pressure from policy-makers, social activists, and also financial investors, on the private sector to rethink its business model. Moreover, the global divide in access to essential medicines is an escalating concern.[6]

Many foresee coronavirus disease 2019 (COVID-19) as a catalyst for change.[7] COVID-19 amplifies the very best and the very worst of nations and health systems in combatting a global health crisis. On the positive side, we see enormous resources for research being mobilized and scientists working round-the-clock shifts in labs, both in the private and public sector.[8] We see also increased international collaboration on regulatory reviews and setting vaccine standards.[9] On the negative side, we see nationalism, fragmentation, and lack of solidarity for

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ensuring timely and equal access to vaccines across the globe.[10] In May 2021, the WHO estimated that, at that moment, four out of five COVID-19 vaccines went to high- and upper middle-income countries, leaving low-income countries largely deprived from necessary immunization.[11] The ongoing debate on vaccine patent waivers and their potential impact on vaccine manufacturing shows a troubled combination of divergent arguments, including fairness and morality to back such waivers and minimizing adverse effects on future pandemic preparedness. In addition, there are also doubts whether transferring of intellectual property (IP) rights as a single factor could make any difference for global vaccine production.[12]

Changes to the ecosystem of how medicines are discovered, developed, and used in clinical practice have always been a mixture of top-down and bottom-up transitions, and more incremental advances through adaptive flows of events. Interactions between science, technology readiness, and societal demands (e.g., medical needs, bioethics, and equal access) have been driving various social outcomes, often wanted and appreciated, sometimes seen as negative and opposed. The highly variable impact across the globe of, for instance, regenerative medicine on new therapies has been illustrative for the ambiguities associated with such interactions.[13,14]

The medicines space across the globe is inherently connected to myriad ambitions and policies, whether we talk about the Pharmaceutical Strategy for Europe or the European Union (EU) New Green Alliance or advancing global health by WHO.[15–17] There is no such thing as medicines development and pharmaceutical science in splendid isolation.

Previous scenario work on the future of medicines and pharmaceutical science revealed many critical trends and uncertainties in science, health systems, economics and society at large.[18,19] Analysts from academia, nongovernmental organizations (NGOs), policy-makers, and the business environment have sketched and expressed arrays of plausible scenarios for the future of medicines based on thoughtful analyses of predetermined elements (e.g., demography, scientific advances in cell biology, or data science) and critical uncertainties (e.g., trust in science and equity in access to medicines). In particular, analyses of critical uncertainties have been used in scenario planning for selecting drivers of the highest importance and the greatest uncertainty as axes creating a 2D space to plot different contrasting scenario stories. Typical examples of such scenario drivers include 'societal trust in technology', 'culture of academic science', 'level of public control', 'power of institutions', or 'more or less market economy'.

In January 2020, various pivotal trends and challenges for the future of domains such as precision medicine, pharmacovigilance, and clinical pharmacology at large, were coined.[20] In addition, reflections on the future of real-world data (RWD), innovative trial design, and preclinical research were shared. However, whether and how these scientific advances will have an impact on the future of medicines, thinking in the context of such scenario drivers, remains difficult to say. Nevertheless, scenarios could help here to gain a better understanding and insight.

Scenario building

In this review, we report from a scenario project in which we analyzed in a systematic and analytical way various trends, and crucial and complex developments in medicines space. We worked around these by thinking from the lab to the patient in a scientific and global context, rooted in current challenges and societal ambiguities. Scenarios in the sense we have applied them in this project do not intend to 'predict' the future.[18,19] Their real value lies far beyond that. Scenario analyses act as 'thinking devices' to guide stakeholders' policy and strategy ambitions and to communicate with a broader academic, health sector, and public audience. As such, they are also time capsules that signify what is seen as important at a certain moment in time.[21]

Given COVID-19 restrictions, scenario inputs were collected through 'Digital tables' in autumn 2020 with 37 international experts, thought leaders, and boundary spanners from the public and private sector, academia, NGOs, philanthropy, and different time zones, with a North–South balance in (see Appendix A in the supplemental information online for a more detailed description of the methods applied).

Based on the observations, dialog, and reflections during the 'Digital Tables', we engaged in an analytical process of selecting those trends and drivers with relatively high certainty, called 'predetermined elements', and those with a high level of doubt on impact or direction, called 'critical uncertainties' (Boxes 1 and 2). 'Predetermined elements' are considered relevant, and as relatively stable and predictable for the backbone of the scenario space and are part of all the scenarios described herein.

From the range of 'critical uncertainties' we derived, through iterative weighing and selecting, two scenario drivers: (i) global convergence, ranging from very high (supranational collaboration, trust in institutions, and solidarity), to very low (frag-

Box 1 Predetermined elements

- Science and technology will continue to deliver; more on precision and transformative medicine; blurring boundaries between pharma, AI, and MedTech.
- Growing concern about the global divide in access to, and affordability of, (new) medicines; pharma business models under critical scrutiny.
- Future medicines are more complex, need more monitoring and guidance for use; critical role of clinical practice after approval.
- International and interdisciplinary collaborations will advance pharmaceutical science; more interconnectivity and open science.
- Geopolitical tensions, nationalism, failed states, and climate change impact science direction and progress.
- Role of, and trust in, science are at stake; fake news, science skepticism, and political capture of science are threatening credibility.

Box 2 Critical uncertainties

- Future direction of clinical evidence building remains uncertain; what kind of methods will be acceptable, will RWD and real-world evidence (RWE) add to randomized clinical trial?
- Ambiguity about role of regulators: facilitators of innovation or gatekeepers? Variation in support of HTA for expedited regulatory pathways.
- Broken incentive system for drug development and usage; many alternatives are suggested, few have been shown to work, what is next?
- Will prioritization of cancer and other high-end medicines remain or will we see a broader spectrum of diseases (e.g., pandemics or antimicrobial resistance)?
- Power of international institutions and global collaboration are at stake; what will be the risk of fragmentation and lack of leadership?
- Science policies are moving in various directions; top-down versus bottom-up, role of philanthropy and public–private, more open science?

mented ecosystem, nationalism, and geopolitical tensions); and (ii) disease orientation, ranging from public health first (population focus, communicable diseases, lifestyle, and prevention) to interceptive medicine (cancer focus remains, rare diseases, and early disease interception). These scenario drivers served as axes creating a 2D matrix to plot four contrasting portraits of the future (Fig. 1).

Four alternative futures for medicines and social policy

Scenario 1: Deprioritizing the high-end

The deprioritizing the high-end scenario is positioned in the lower-left quadrant of the scenario space, reflecting a dramatic and, for many years, unexpected shift in disease orientation away from high-end oncology and medicines for rare diseases in a fragmented science and global pharma ecosystem. This is a scenario of disease reorientation, of broken expectations, and of promises of high-end technological solutions.

Frustration in terms of all the resources that went into high-end medicines with mixed outcomes collide with major economic and social concerns. For decades, scientific advances in cell biology, genomics, and biochemistry had major impacts in oncology and some impact in rare diseases. Since the end of World War II, the American Cancer Society has funded 49 investigators who went on to win a Nobel Prize.[22] The Nobel Prize for Chemistry 2020, awarded to Charpentier and Doudna for their ground-breaking work on CRISPR/Cas9, was a sign of opening new avenues for innovative cancer therapies.[23] Over many years, the spirit of 'this research will pay off in cancer' has been an influential factor in almost all areas of the life sciences. From research funding, building infrastructure, and conducting trials, oncology has paved the road to many advances in novel drug targets and signaling pathways, product delivery and targeting, monoclonal antibody platforms, COVID-19 vaccines, nanoscience, biomarkers, and personalized medicine. The pipelines of biosimilars and next-generation biotherapeutics have been catalyzed by expired patents of some major blockbuster biologicals in oncology.

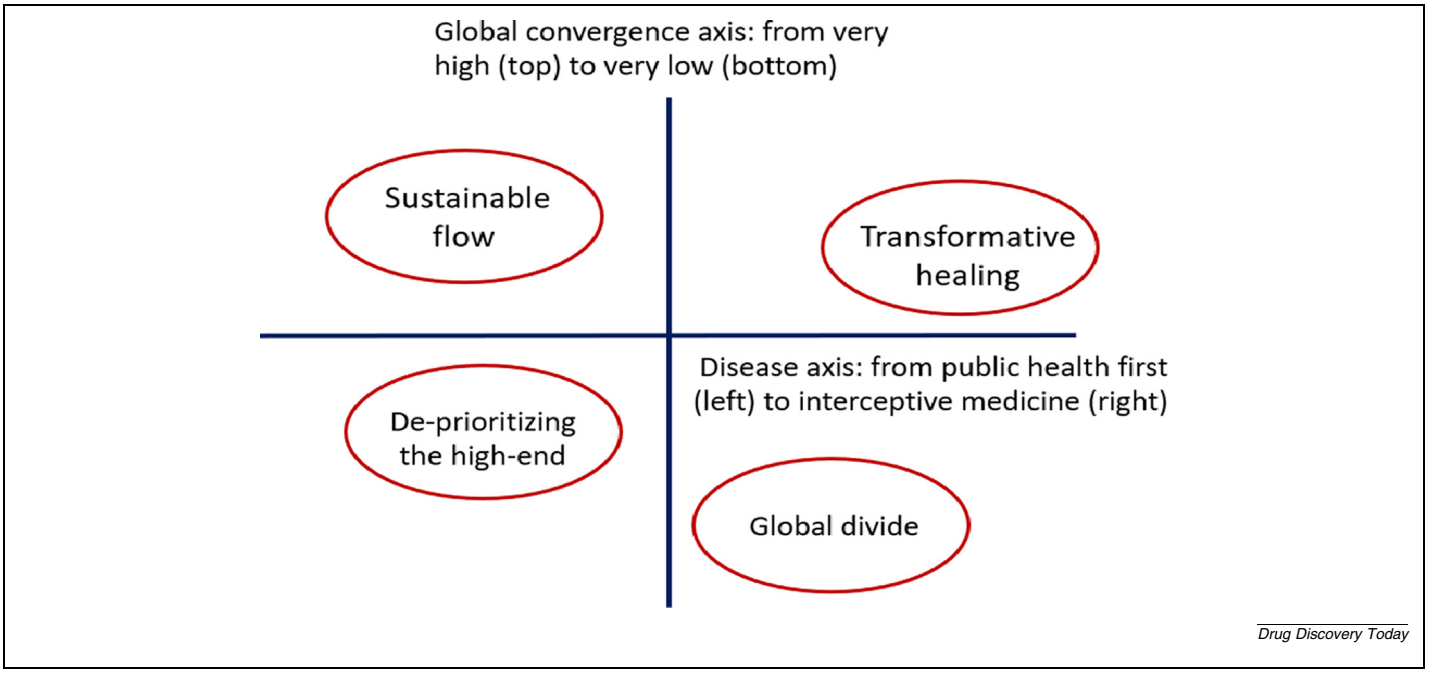

FIGURE 1
Four scenarios for the future of medicines and social policy in 2030.

From 2010 to 2020, the proportion of oncology products entering the global market increased from 30% to over 50% of total new drug launches, particularly for rare, hematological types of cancer. In 2020, of all products in late-stage pipeline development, more than 30% were anticancer drugs.[24] To compare, for cardiovascular or vaccine products, these proportions were less than 5%.

In this scenario, a tipping point in the dominant position of oncology and other high-end products is reached. Several triggers contribute. First, what oncology products really mean in terms of clinical and societal benefit is heavily debated, and contested. The temperature of the debate goes up and down, but in the end, criticism appears to prevail. Progression-free survival gain of 4 months between treated and nontreated, a response rate of 65%, but no survival benefit, single-arm studies with challenges to interpret the results, agnostic indications with all the inherent discussions about robustness of evidence and clinical meaning: all of these stir feelings of uncertainty and skepticism around oncology. Medicines for rare diseases, pharma's high-end favorite for about two decades, receive similar critical exposure. Also in the business arena, the flow of capital takes another route away from oncology and high-end products (too risky, too complex, and too many competitors for an acceptable return of investment).

Patients and physicians struggle, the medical needs in cancer have not disappeared, but there is an increased common desire for more quality of life instead of more years of survival or some improvement on a biomarker or surrogate endpoint. Although this is obviously not everywhere; some patient advocates still march for enabling everything that is possible.

What really moves this scenario are rising healthcare costs with increased spending on high-end medicines, reaching unsustainable levels for many countries, including affluent ones. Payers and Health Technology Assessment (HTA) bodies push very hard for the defunding of the high-end. They hold regulators responsible for being too flexible on approving oncology products with relatively modest, incremental, and uncertain benefits. They themselves are blamed for using clinical arguments as an excuse for budget concerns. However, their influence becomes stronger when industry leaders also admit that the underlying business model of oncology and rare diseases [i.e., high prices for low-volume products, often acquired from small- and mid-sized enterprises (SMEs) for huge amounts of money] is out. This upward spiral comes to an end.

In 2030, we observe a shift in pharmaceutical and biomedical sciences away from dissecting deep complex molecular mechanisms. It becomes increasingly difficult to collect sufficient funding to run labs and conduct clinical trials. Competition for research funding is devastating. Science is less seen as part of the solution. Lifestyle interventions and disease prevention peak on policy agendas. The pharma ecosystem is becoming fragmented. Practice research and repurposing, getting more out of existing and off-patent pharmaceutical products, appear to blossom, not as priority choice, but as a last resort option to push innovation.

Scenario 2: Sustainable flow

The sustainable flow scenario is one of a new social contract, a clear reset after the public sector being in command in many places during the COVID-19 pandemic. There is a convincing push to rethink the existing global pharma ecosystem. This is not a scenario of skyscraper pharmaceutical innovation; instead, it is about prioritizing social policy in innovation, including transparency, digital ethics, and open science models.

Investing massive resources in the few contrasts with the health needs of the many, backed by business models that do not appear to be helpful in shifting investments to priority medicines and public health needs. Although this is not a new observation, it is a wakeup call that resonates more loudly at a time when ensuring equal access to pharma innovations (e.g., COVID-19 vaccines or medicines for rare diseases) and restoring trust in global institutions are embraced at many levels. In addition, the learnings from the commons (i.e., something central to life but not owned or controlled by one person, company or state) give impetus to major changes in the way that medicines are developed and marketed. Originally applied in areas such as climate change and biodiversity, such thoughts give inspiration to translate these to change and renewed policies and strategies in the life sciences and pharma business space. Flow of capital is increasingly driven by sustainability, fairness, and social justice.

This scenario is positioned in the upper-left quadrant of the scenario space, reflecting a shift in disease orientation and convergence of science and the global pharma ecosystem. The access debate highlights divisions at the high-end with innovative therapies only accessible and affordable for the lucky few, which is less accepted. There is increasing focus on structural inequalities and the economic and social context of the divide. Societies in many regions of the world want innovations to be better aligned with societal demands. Greater weight is placed on developing the infrastructure, skills, and capabilities needed for scientific advances in medicines translating to public health benefits. Scientific excellence is not enough. Research agendas and funding are navigated to do more for the greater good.

Pharmaceutical science in this scenario is based on increased knowledge sharing, open science, and partnerships with citizen science. We observe a push for smart innovation (i.e., public–private alliances), widespread technology transfer, and social entrepreneurship. In terms of capacity building, we see an influx of the humanities, social science, and knowledge sharing in a field that traditionally was hosted by (bio)chemistry, pharmaceutics, and biology. Connectors are in the hot seat. Life-time scientists become exceptions, science and society integrate. However, academics struggle with these new responsibilities. Prioritizing societal impact of research is not without failures (i.e., acting on new reward systems incentivizes also prioritizing short-term hypes in science).

Marching for universal healthcare when it comes to access to essential medicines is high on many health policy agendas. Ensuring the availability and affordability of medicines at the global level is in a rather progressive roll-out. Calling for alternative economic models to counter high prices and monopolies goes hand in hand with a rethink of patents and IP. Not that they disappear, but alternative forms of private and public IP sharing are gaining momentum. In this scenario, we see a smart mix of for-profit and community players in drug development and investments, especially with a larger role for end-users. Responsible licensing, new stick-and-carrot models with more balanced levels of fairness, are key. Academic institutions are much better orga-

nized than in the past; they become stronger players in the ecosystem and there is more interconnectivity. The role of empowered patients, healthcare workers, and researchers from low-and middle-income countries (LMICs) changes rapidly (i.e., becoming more engaged and more demanding).

Regulators also collaborate by referencing, convergence, and sharing data. There is far-reaching harmonization and strong support for LMICs to strengthen their own regulatory systems, nationally or in the region. We see a greater role for global institutions, such as WHO, the International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use (ICH), or the Global Alliance for Vaccines and Immunizations (GAVI). Philanthropy peaks on ethical leadership and maximum societal impact.

However, this not all good news for delivering new innovations. Healthcare practice is increasingly politicized and technology aversity is widespread. Law makers, governments, NGOs, and civil society interact, interfere, and push agendas. Although there are many attempts to march for win-wins, this scenario is poor on, for instance, finding solutions for mental health or building successfully pandemic preparedness for the future.

Scenario 3: Transformative healing

Transformative healing is the scenario of harvesting major scientific breakthroughs in cell biology, medicinal chemistry, and nano- or data science. There is widespread optimism about the role of science and entrepreneurship for bringing health benefits to society. This is a scenario of high hopes and promises of cure, although, in many aspects, with challenges for ensuring equity, digital ethics, or other social values.

This scenario is positioned in the upper-right quadrant of the scenario space, reflecting a high-end disease orientation and a coordinated science and global pharma ecosystem. The successes of pharma leveraging effective and safe pandemic vaccines to the world so swiftly, brings new confidence to the private sector. mRNA platforms, glycobiology, exosomes and follow-up technologies, artificial intelligence (AI) and big data, all are well funded. Philanthropic funding is skyrocketing. Desiloing and blurring lines between sciences and technologies are important features of the bioscience landscape. The role of academic entrepreneurship, SMEs in generating IP, and acquisition opportunities for big pharma is unprecedented. China leads the new 'Silk Road' for pharmaceutical research. The USA and Europe follow at a distance.

The combination of pharmaceutical science, bioinformatics, and MedTech has become a game changer. There is ample interest in advanced therapies (e.g., gene and cell therapies) making curative, long-term treatments a reality. Early disease interruption strategies are becoming successful while targeting the origins of distortions of biological systems in a very early and pre-symptomatic phase. Machine learning, real-world evidence (RWE) for evidence generation, 3D printing, wearables, logistic chain technologies, all appear to have immense opportunities. In addition, technology giants, such as Google and Amazon, have stepped in. They link and integrate through advanced AI networks the various medical needs to high-end diagnostic and therapeutic platforms.

The nature of medicines has changed dramatically. More curative, transformative strategies enter the system. We see more platform technologies, not everybody gets the same therapy, and medicines are becoming less forgiving of the usage context (i.e., in 2030, about four out of five approved medicines have prescribing limitations, specific directions, and conditions for use). They are not easily fit for use in community settings, more limited to secondary and highly specialized centres. This is a trend to stay, with major implications for healthcare practice. The underlying business model remains attractive for the private sector. Technological innovation is also seen in less affluent regions, such as drones delivering medicines in rural Africa or speedy mobile labs in Brazil.

The clinical trial industry has become extremely lean and efficient. Better study designs, better clinical data sets, and a buy-in of regulators and HTA bodies to adaptive and flexible approaches for unmet medical needs, are the main drivers. Omics and robust approaches for *in vitro*/*in vivo* correlation are used to decrease trial times and data complexities. Alignment with clinical practice (e.g., physicians and pharmacists) has been very developed in enabling translational science. Big companies keep buying promising projects and IP from SMEs. This market is very competitive (i.e., more buyers than sellers), leading to huge acquisition costs and high prices to recoup investments, but the financial ecosystem remains resilient. Flow of capital is still sustainable. The rewards for innovation remain high and attractive. However, healthcare costs are on the rise, solidarity is at stake, and political opposition to counter is weak.

Trust in science is a major driver of this scenario. Push for entrepreneurship and value creation is back again at university campuses. Knowledge sharing and open science are seen as old school ambitions. Collecting IP instrumental to foster innovation and economic return is celebrated and contributes to academic successes.

International medicines regulation is at a crossroads. Global regulators are contributing to this transformative wave with various expedited frameworks enabling efficient trials, rolling reviews, and conditional pathways. Regulatory science is pivotal to underpin these balancing acts. We see more international collaboration, convergence, and reliance. Impact of European Medicines Agency (EMA) or US Food and Drug Administration (FDA) decisions on regulatory processes in neighboring regions in South America, Asia, or Africa is there to stay. HTA agencies are less on the solidarity track and more on enabling diversity of choice options. International competition and a greater role for patients as end-users are key drivers for innovation. With bed-side manufacturing, advanced biomarker strategies, and high-tech dispensing, medical practice is in transition.

Scenario 4: Global divide

Global divide is a scenario of a serious geopolitical clash and chaos in the aftermath of the COVID-19 pandemic. This is a 'dark' scenario from a global perspective (e.g., decline of the institutions, innovation gaps, and persistent mistrust between nations and regions). However, some regions, particularly in Asia and South America, are doing very well.

The messy global manufacturing and distribution of COVID-19 vaccines, failed virus containment policies, and increased nationalism all contribute to make this scenario happen. It is positioned in the lower-right quadrant of the scenario space,

reflecting a fragmented science and global pharma ecosystem. Disease orientation has become a mixed basket of existing priorities and national preferences, a defunding of global health needs. Bilateral alliances between nations tailor pharmaceutical needs and priorities toward their own political agendas, whereas taking care of the great global good is far away.

There are major changes in the geopolitical situation with significant power shifts, such as the rise of Africa and some regions in South America (e.g., Brazil), and the boosting of China and other regions in Asia (e.g., Japan and Singapore). The USA tries to reshape its leadership internationally and UK restores bonds with old friends, such as Canada and Australia. We see the EU struggling with post-Brexit decisions, fighting internally on how to position between the USA, Russia and China. Moreover, the EU is heavily engaged in a delicate balancing act between economic and industrial policies and the long political wish list on climate change, data ethics (battling the power of tech giants and AI), solidarity, social justice, and human rights. Global institutions, such as the WHO, World Bank, and Organisation for Economic Co-operation and Development (OECD), fail to bridge and lead. The global commons appear to be forgotten.

As a result of increased global fragmentation, the international pharma chain is under great pressure. Seamless production, logistics, and trade between countries and regions are hampered by the lack of coherent regulation, bureaucratic and political complexities, unilateral decisions, and clientelism. This spiral catalyzes a broken global pharmaceutical market. Drug shortages, lack of trust, and delays in almost everything, from research, conducting clinical trials, regulation, and production to market access, dominate the ecosystem. On top of industrialized production, there is more on individualized bed-side preparation of high-end products, local production, and pharmacy compounding as alternatives for drug shortages or high-priced medicines. Not to forget the 'Do-It-Yourself' movement in which interested parties (e.g., patients and some NGOs) create their own enabling context of drug development and production.

This situation raises many regulatory, economic, and professional questions. Regulators respond to national, often political and ad hoc, pressure. We see less harmonization in decision making and regulatory systems. Groups such as the ICH and the International Coalition of Medicines Regulatory Authorities (ICMRA) struggle to survive and WHO is unable to compensate. There are more differences between countries and regions when new products are allowed to enter the market. What was seen during the 1980s (i.e., drug lags) is back again.

Increased disintegration in science, from priority setting to conduct and outreach, is reaching momentum. However, from a contents and metrics perspective, the situation for the pharmaceutical sciences in this scenario is not as bad. We see peaks in molecular biology (e.g., RNAi or antisense nucleotides) and glycan science; identification of new drug targets progresses quickly. Combinations of pharmaceutical science, bioinformatics, and MedTech is blossoming, particularly in China and the broader Asian region. Capital flow follows. In addition, tech giants, such as Google or Amazon, are ready to step in. Knowledge sharing, open science, and collaboration are over the hill and dreams of the past. 'Forget ethics and social justice, innovate . . .' is a slogan that resonates widely.[25] Sovereignty and top-down national policies drive research agendas and funding. The increased role of philanthropy fits well with this fragmented landscape. What once started as humanitarian and altruistic is taking a bigger power stake in research agenda setting and driving the interests of donors. Philanthropy drives certain high-end clinical domains for the few willing and able to pay, while overall public health investments are lagging behind.

In 2030, we observe an increasingly scattered pharma landscape, with some regions doing very well in biopharmaceutical research, but many others lagging far behind. The existing global health divide is more pertinent than ever before. Pharmaceutical research is fragmented when it comes to priority setting, collaboration, and funding. Failed solutions for climate change, biodiversity, and sustainable energy contribute to the global misery.

Discussion

The four scenarios depicted above are narratives of plausible, contrasting futures of medicines and social policy. The scenarios are no predictions, no dreams, and no warnings.[21] All four of these futures could happen. They are intended to confront key players in the field with alternative portraits of the world ahead. The scenarios are built on several realistic assumptions, collected insights, and analyses from Digital Tables with international experts and thought leaders. However, there are large differences between all four scenarios, not on all aspects, but on critical ones (Table 1).

TABLE 1

The four scenarios in key words.

Pivotal theme	Scenario			
	Deprioritizing the high-end	**Sustainable flow**	**Transformative healing**	**Global divide**
Science and technology	Decline, broken promises and dreams	Openness, citizen science, desiloing	Competitive, high-end focus, rise, promise	Highly fragmented, forget ethics, innovate
Incentive structures for innovation	Frustration, pharma ecosystem fragmented	Pull focus, IP sharing, ethical philanthropy	Push focus, IP driven, rich capital flow	Scattered landscape, China as global lead
Access and affordability	Stringent regulation, limited access	Regulatory rethink, equity high priority	Regulatory flexibility, high willingness to pay	Uncoordinated regulatory space, unequal access
Addressing global health needs	Priority for primary care, basics	Universal health care, global dialogue	Not a priority, except for willing payers	Decline of institutions, huge health divide
Healthcare practice	Repurposing, practice innovation	Public health, community drive	Innovative, tech heaven, highly specialized	Fragmented, highs and lows, Do-It-Yourself

Essentially, scenarios are qualitative stories. However, the direction, tone, and story line of the narratives allow for quantitative modeling and underpinning. In Figs. 2 and 3, the 2020–2030 weighted estimates derived from the substance of the four scenarios (real data 2010–2019, standardized for 2020 = 100) of two indicators on clinical development for all therapeutic categories and early-stage pipeline for oncology are presented. The estimates of overall clinical development of new medicines doubles in the transformative healing-scenario, whereas, for the deprioritizing the high-end scenario, new entrants in clinical development slow down with about 20%. Only in the sustainable flow-scenario is no change seen. For the early-stage oncology pipeline, the 2030 picture will be different for all four scenarios. Whereas between 2010 and 2019 this indicator increased from 40 to 100 (standardized), the curves flatten or decline in all four scenarios between 2020 and 2030, most dramatically in the deprioritizing the high-end scenario.

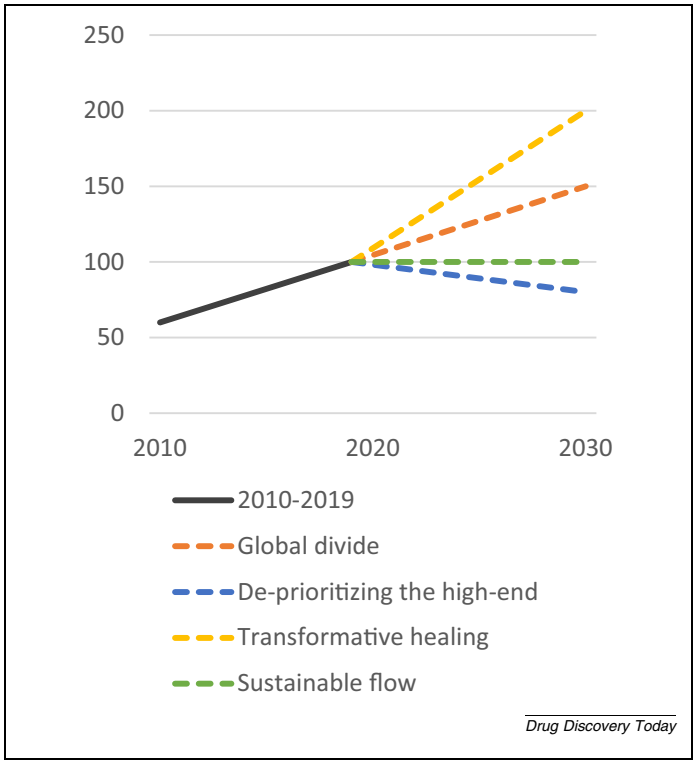

FIGURE 2
New entrants in clinical development (Phase II) in all therapeutic categories.

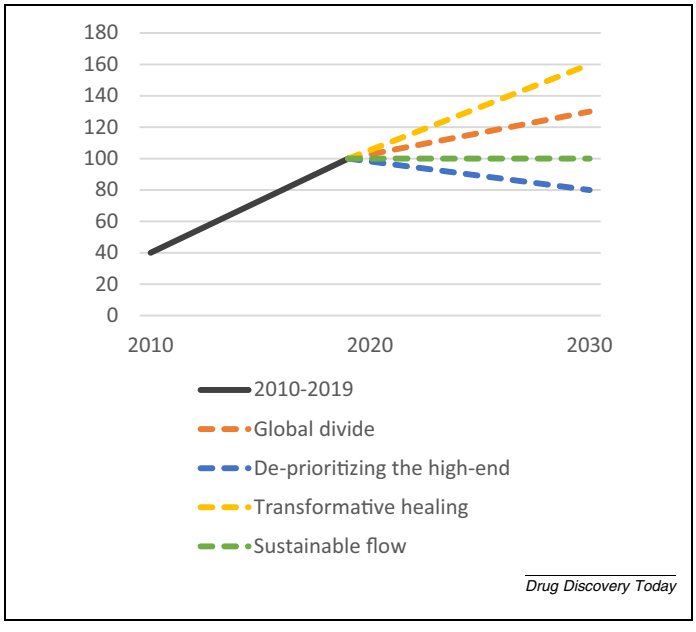

FIGURE 3
Early-stage oncology pipeline, including discovery, preclinical, and Phase I.

In Fig. 4, we present medical patent filing data to translate plausible impact on medical innovation potential for the four scenarios in major geographical regions across the globe. In all four scenarios, Europe's share in the global medical innovation potential decreases to below 20%; in 2010, this was still 30%. The USA remains close to China in innovation potential (i.e., 25–35%) in all scenarios except in the global divide scenario. In the latter, China is by far the patent champion, with about a 50% share in global innovation potential, leaving the USA and Europe far behind.

A key aspect regarding medicines and social policy has always been the intriguing, and often troubled role of industry, and the private sector in general, in an environment full of public expectations, demands, and social concerns. There is probably no sector in society, depending of course in which part of the world you live, where the confrontation between public and private is so loaded with public outcry to control, regulate, or incentivize. History shows for good reasons. There is ample frustration about drug prices, about lack of equity in access, but also about research priorities leading to therapeutic gaps (e.g., antimicrobial resistance and neglected diseases). Whether public interventions have always delivered and whether they are proportionate and effective remains controversial. Interestingly, COVID-19 also here inspires for lengthy recipe books for 'doing things differently'. In all four scenarios, the balancing act between public and private sector is highly visible, particularly when contrasting the transformative healing scenario (i.e., private sector in the lead) and the sustainable flow scenario (i.e., public sector push).

All four scenarios portray science practice, research priorities, and trust in science in a sketchy manner. Trust in science is high in the sustainable flow and transformative healing scenarios. However, science culture and practice are very different between the two (e.g., open, vocational, and collaborative in the sustainable flow scenario, whereas entrepreneurial and competitive in the transformative healing scenario). Trust in science is broken in the deprioritizing the high-end scenario, whereas, in the global divide scenario, science is fragmented globally, with China dominantly in the lead. These contrasts work out differently when looking at progress in the clinical development of new medicines. Here, transformative healing and global divide continue to rise, whereas a drop in progress is seen in the other two scenarios (Fig. 2). The four scenarios do not differ very much on the science contents, given that these are a predetermined element (e.g., more on cell biology and data science, blurring borderlines between pharma and MedTech).

The role of regulators and their requirements for evidence building for making decisions on quality, safety, and efficacy

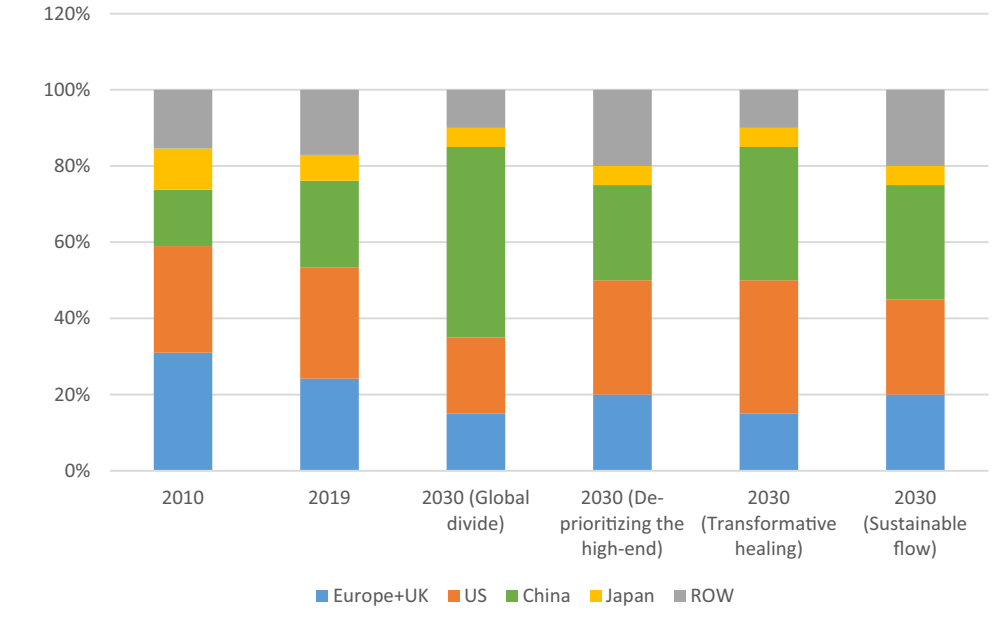

FIGURE 4
Patent filing by country (World Intellectual Property Organization stratified for medical innovation).

vary across the four scenarios. Particularly in the space of clinical evidence building, we see heavy debates on study design and endpoints, data, and measurements.[26,27] Most regulatory systems as we know them today were established 50–60 years ago. Since their inception, there has been a heated debate on how much and what kind of evidence is needed and how much uncertainty is acceptable. Several scholars in the field of regulatory science have underscored the shift over the past decades to less rigorous methods of evaluating clinical benefit, with inherent challenges for drug labeling and HTA, fuelling pertinent questions on future directions.[28,29] Given that medicines regulation has many international dimensions, the level of global coherence is key.[30–32] As a consequence, the sustainable flow and transformative healing scenarios both peak on this axis (Fig. 1). In both scenarios, global coherence of regulatory requirements and procedures are important features. By contrast, we see the opposite in the deprioritizing the high-end and global divide scenarios. Thinking through the four scenarios presented here could help to strengthen the field and fuel strategic thinking ahead.[33]

When looking at the four scenarios, stakeholder or personal preferences can color appreciation of the chance or likelihood that the world will be as sketched in the four individual narratives. The transformative healing scenario might be seen as a blessing by industry, whereas the same could be true for NGOs or patient activists when looking at the sustainable flow scenario. The global divide scenario is possibly terrifying for many in the Western world, particularly in Europe, whereas the deprioritizing the high-end scenario might be the most unlikely or illusory one. Who wants to deprioritize innovation in cancer? Ask people in your local high street.

Readers are invited to stir their imagination, to think loudly. Readers might find one or two scenarios more preferable or more likely to happen than the others. Some readers might find bits and pieces they like in all four scenarios and prefer to sketch their own most preferred or likely scenario.

Readers are most welcome to play around with the four narratives, moving their position in the 2D scenario space, amplifying or downgrading certain scenario features. However, at the end, the four narratives aim to stimulate thinking, reflecting, and asking the right follow-up questions given that the world in 10–15 years might look like that depicted here. What does that mean for me as prescriber, me as clinical scientist, me as regulator, me as policy maker and even me as a patient or citizen? Who will win, who will lose? These are tough questions that are not easy to answer, but are significant and useful for being prepared for an uncertain future. Scenarios are intellectual devices for being confronted and for bolstering future preparedness. COVID-19 has showed us in an alarming way that the world was not very well equipped to think ahead, despite numerous warnings in the past that serious emerging infectious diseases were never far away and that trust is needed to overcome the challenges ahead.[34] Pandemic preparedness appeared to be always more in minds or plans rather than in reality.

The scenario analysis presented here results from various choices on methodology, invites of experts for the Digital Tables, time horizon, and the authors' own positions and roles. We selected for an academic, multiangle approach, but cannot exclude that our own presumptions and biases have affected the outcome of the analysis. The same is true for the selection of the participants of the Digital Tables. Most were global thought leaders with relatively high-level positions in the ecosystem. Thus, we might have missed relevant odd or outsider perspectives. Along similar lines, we selected our Digital Table participants for their strategic and overseeing competences which might also have been done at the expense of diversity, equity, and inclusion (DEI).

Concluding remarks

The future of medicines and social policy will affect us all, as pharmaceutical scientists, healthcare professionals, clinical pharmacologists, policy makers, patients, or citizens. There are many uncertainties ahead, some more pertinent than others. We present four plausible scenarios for that future as an invitation to use these for strengthening preparedness for the critical challenges that are there and those that will come.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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Appendix A. Supplementary material

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