Annex C

The financial ecosystem of pharmaceutical R&D

Future scenarios for the financial ecosystem of pharmaceutical R&D

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1 Introduction and methods

1.1 Readers' guide

Annex C describes a work package for this study which developed three future scenarios for the pharmaceutical R&D sector based on insights from prior work, the research team's critical reflection and consultation with the study's Scientific Advisory Committee (SAC). The scenarios aimed to represent a mix of more likely and extreme possibilities for the future. As such, they provided a research tool enabling stakeholder discussion about current issues where actions may be needed to prepare for the future and optimise the future financial ecosystem of pharmaceutical R&D. The scenarios helped stakeholders reflect on ways to maximise opportunities, minimise risks and manage the challenges ahead.

These scenarios were explored in a workshop of international stakeholders from various sectors, as described in more detail in Section 1.2. Stakeholders in the workshop considered each scenario's challenges and opportunities reflecting on important themes and implications for measures diverse societal stakeholders currently need to consider to prepare for the future.

This report is organised in the following sections:

- Section 1.2 describes the methodology used to develop future scenarios, conduct the stakeholder workshop and arrive at results from the workshop
- Section 1.3 identifies limitations and caveats for the reader to bear in mind when interpreting the insights presented in this progress report
- Section 2 describes the future scenarios developed and used in the stakeholder workshop.
- Section 3 summarises key insights from the workshop, organised by theme.

RAND Europe led Annex C and the associated work package.

The overall scope and focus of the research study should be borne in mind when interpreting the findings of this work package. The workshop's scenarios aimed to identify key themes, challenges and potential stakeholder actions to optimise R&D's future financial ecosystem. This included identifying and reflecting on themes related to the wider healthcare and innovation landscape, extending beyond directly implicated factors such as the availability of capital, R&D costs and success rates. This study and work package did not aim to consider specific actions and implementation requirements or attribute specific actions to distinct stakeholders. Instead, the commissioned research was for a predominantly descriptive study characterising pharmaceutical R&D financing, stakeholder motivations and actions, and value creation and transactions. Exploring how broader system-level factors have influenced financial aspects in the past and how they might do so in the future complements the overall study's core focus.

Future research could build on this work package's insights into the current actions that may make the pharmaceutical R&D financing system fitter for the future, as discussed in the following contents. A future research agenda could include analyses of the progress already made in specific

areas where action may be needed to optimise the financial ecosystem of pharmaceutical R&D and identify critical gaps and how these may differ across geographies. Such future research could provide value in supporting the exchange of learning between different stakeholders and geographies about what works in creating supportive health and innovation landscapes, what actions are in the domain of national efforts, and which are dependent on international cooperation and coordination.

1.2 Methodology

Although previous work packages inform this report's findings, this Annex focuses primarily on establishing future scenarios for how the pharmaceutical R&D sector may develop over the next decade and an associated stakeholder workshop to discuss them. The aim was not to predict the future or determine the most likely scenario but to help explore various possible futures and use them to facilitate reflection and critical thinking about the implications of possible futures on the present challenges and risks needing management and opportunities to harness. As with all scenario work, multiple scenarios are possible. The research team selected sufficiently different scenarios – both more likely and more extreme – to stimulate discussion and reflection among stakeholders involved in pharmaceutical R&D.

The methodology for developing future scenarios and details about the stakeholder workshop are described below.

1.2.1 Developing scenarios

The development of future scenarios involved the following stages, each described in further detail later in this section:

- Identifying a longlist of key factors that may influence the pharmaceutical R&D landscape in the next decade based on insights from prior work packages and consultation with this study's SAC
- Conducting an influence analysis to determine the most important and influential factors in the future pharmaceutical R&D system
- Shortlisting the key influencing factors
- Developing projections for how each factor in the future scenarios may develop over the next ten years
- Performing a consistency analysis to evaluate how consistent it would be for combinations of projections for different influencing factors to appear in the same future scenario
- Performing a cluster analysis to identify plausible future scenarios based on consistency analysis, by (i) using the help of specialised software to complete this task and (ii) triangulating software outputs with the research team's qualitative expertise and integrating learning from the SAC's expert views throughout the project
- Developing distinct, clear and easy-to-engage-with narratives for three future scenarios.

RAND Europe undertook this process in close collaboration with the L.E.K Consulting and SiRM project teams, incorporating key advice and feedback from the SAC. Scenario Manager ScMI

software package[1] was used to inform the research team discussions and analysis that led to selecting three scenarios as workshop aids.

Identifying a longlist of influencing factors

Based on insights from this study's previous work packages, the research team identified a list of 25 potential factors[2] influencing the future pharmaceutical R&D ecosystem (

Table 1). Th project's SAC advised on this list's comprehensiveness via email. This exercise resulted in a longlist of potential factors for inclusion in future scenarios and a basis for prioritising key influencing factors.

Table 1. Longlist of influencing factors.

Influencing area	Factors
Availability of capital/funding	1 Overall availability of funding for pharmaceutical R&D
Costs of pharmaceutical R&D	2 Pharmaceutical R&D costs
Scientific and technological developments	3 The scale and pace of scientific and technological advances and how they are incorporated into pharmaceutical R&D 4 Data science and digital innovation advances, and how these are incorporated into pharmaceutical R&D 5 Therapeutic and clinical focus areas within pharmaceutical R&D 6 Major drug failure events once a drug is on the market 7 Success rates in pharmaceutical R&D
Drug pricing /affordability	8 Costs of new and innovative drugs 9 Decisions around drug prices in key global markets 10 New financial models for reimbursement and pricing
Collaboration	11 Pharmaceutical-sector reliance on external sources of early-stage R&D 12 Biotech/SMEs entering later-stage R&D (independently conducting later-stage R&D before being acquired or selling assets to Pharma) 13 Collaborator diversity in pharmaceutical R&D
Nature of investors and investment landscape	14 Public and not-for-profit investors/investment in pharmaceutical R&D 15 Private-sector investment in pharmaceutical R&D 16 The public and-not-for-profit sectors' commercial attitudes around investing 17 Venture-capital (VC) sector consolidation or diversification* 18 New financial models for investing in pharmaceutical R&D 19 Indirect public-sector instruments and incentives*

[1] Scenario Management International AG, Germany, Klingenderstr. 10-14, 33100 Paderborn. Email: info@scmi.de, Web: https://www.scmi.de/en/

[2] Two of these factors were discarded before progressing to the influence analysis stage, which is why only 23 factors were included in the influence analysis exercise.

Geography	20 Global dynamics in pharmaceutical R&D and the rise of emerging markets
Regulation	21 Regulatory innovation 22 Government attitudes to intellectual property
Unforeseeable macro-level events	23 Macro-level events (e.g. conflicts, wars and pandemics) 24 Maintaining and applying learning from Covid-19 pandemic to improve pharmaceutical R&D
Patient and public voice and attitudes	25 Patient attitudes towards and influences on R&D agendas

*Factors were discarded from the long list before progressing to the influence-analysis stage of shortlisting.

Influence analysis

After identifying the longlist of potentially relevant factors for the future pharmaceutical R&D landscape, the research team explored interrelations between different factors to identify mutual influences. We aimed to rank each longlist factor's impact on every other factor and score their impact on one another. For example, we scored how much the availability of future pharmaceutical R&D funding will influence the supply of scientific and technological advances, and vice versa. Every factor pairing was scored from 0–3 to indicate how much a single factor impacts or 'influences' another (where '0' indicates no impact and '3' indicates a strong and direct impact).

It is vital to note that the ranking process entailed a degree of subjectivity inherent in all quantitative approaches to scenario development. Influence analysis is only a tool, with no clear 'right' or 'wrong' ranking. Experts build on assumptions about the future in all scenario-development processes, and the influence matrix aims only to stimulate discussion about the system's interrelationships. Influence analysis helps tease out the most direct and influential relationships from less pivotal ones. Thus, the ranking itself is not the exercises' purpose or output but a tool to facilitate reflective discussion in the research team to identify the most important and closely related variables to consider in scenario narratives.

The research team organised an internal workshop to agree on influence-analysis scores, undertaken on an Excel-based matrix (see Figure 5 in Appendix A).

The outcome of this analysis is displayed in Figure 1, which shows the 'activity' and 'passivity' scores for each factor. A factor's 'activity' score measures the magnitude of its influence on all other factors in the system. The 'passivity' score measures the opposite – the magnitude of all other factors' influence on the single factor of interest. Factors with a high activity score *and* a high passivity score are shown in the top-right of the figure (e.g. investment in pharmaceutical R&D). These factors are strongly interconnected, significantly influencing and influenced *by* other factors. Factors with a high activity score but a relatively low passivity score are shown in the top-left of the graph. These factors are likely to influence other factors but are less likely to be influenced *by* them. Despite a lower passivity score than many other factors in the system, these factors are still very influential and may be important in developing future scenarios. Similarly, factors with a high passivity score but a low activity score (seen in the bottom-right of the graph) are determined by many other factors within the system, justifying their importance in future scenarios. Note that the graph below is based on rankings rather than absolute scores; thus, there will always be items in each quadrant of the graph based on each factor's relative passivity and activity.

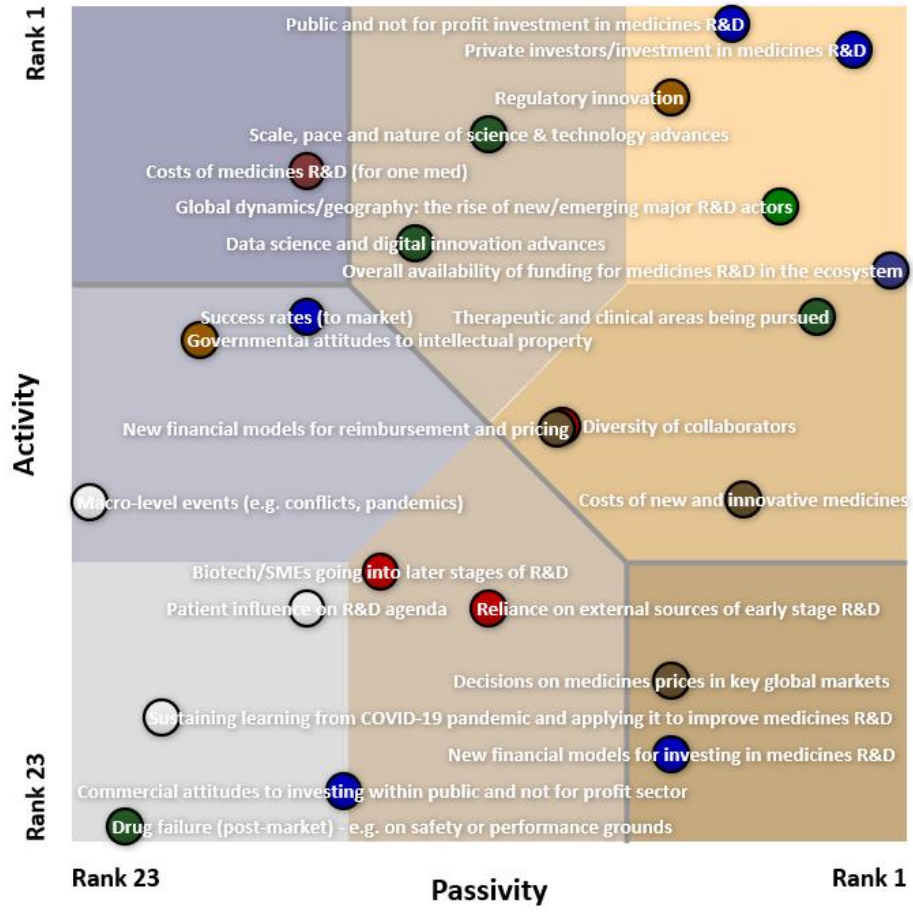

Figure 1. Activity-Passivity graph for the longlist of influencing factors. Note: All 23 factors are ranked in order of highest activity/passivity (1) to lowest activity/passivity (23). Dot colours group factors by influencing area – see Table 1.

Shortlisting factors and creating projections

Developing scenarios requires focusing on a set of key factors to build a narrative around. Given this, the next step was to create a shortlist from the initial longlist, deciding which factors should be central to the scenario narratives. The main aim was to create three sufficiently different scenario narratives for use in the workshop , ensuring a manageable number of factors guided the overarching scenario narrative.

We considered a range of factors in this decision-making process. These included:

- The results of the influence analysis, providing insights into the strength of each factor's relationship with others in the pharmaceutical R&D ecosystem
- The need to consider both highly active and highly passive factors (i.e. those that strongly influence other factors and are strongly influenced by them) and some active factors with lower passivity scores that could nevertheless raise important considerations for stakeholders (e.g. that may strongly influence other factors but not be strongly influenced by other factors)
- The need to ensure a diverse range of topic areas in each scenario that reflect the overall project's aims, e.g. present scenario 'curveballs' that create sufficiently complex and nuanced 'worlds' to encourage creative reflection in the workshop.

These considerations guided the study team to ensure that shortlisted factors met the work package and broader study's needs.

Narrowing down a longlist of factors is essential to develop meaningful future scenarios that stakeholders can easily consider and engage with. However, this process necessarily simplifies the pharmaceutical R&D ecosystem's complexity to identify a manageable number of variables guiding scenario construction. While some scenario aspects are linear (e.g. more funding will likely go into the pharmaceutical R&D system as science and success rates improve), there are also important non-linear relationships where the pharmaceutical R&D system reacts in unexpected ways to specific factors, since it is a complex adaptive system. To help capture this non-linearity manageably, the research team included some 'curveballs' in each scenario alongside the core factors included in the shortlist (see below). For example, one scenario involved pricing discussions in key markets causing global profitability concerns, while another included a major drug failure impacting an entire therapeutic sector's financing. Although it was necessary to simplify some of the pharmaceutical R&D system's complexity in the future scenarios presented to stakeholders, the scenarios were simply a tool that facilitated rich discussions during the workshop. Discussions covered many of the broader influences impacting pharmaceutical R&D's complex financial landscape. Annex B provides a more detailed discussion of the influences, certainties and uncertainties society faces regarding the pharmaceutical R&D's financial ecosystem, discussing insights from in-depth stakeholder interviews and exploring the additional factors involved.

The key factors selected for informing the next stage of scenario development are listed in Table 2. We then created projections for each factor, representing the diverse ways each factor may develop over the next ten years. Projections included likely and more-extreme/less-likely projections that could have significant consequences if they unfolded. Projections for each factor and initial ideas around which factors to consider shortlisting were checked with the SAC to ensure no key factors were omitted.

Table 2. Shortlist of factors and their projections.

Factor	Projections
Overall funding availability for pharmaceutical R&D	• Increases • Remains the same as today • Decreases
Costs of pharmaceutical R&D (trends related to unit costs to develop one medicine)	• Increase • Remain relatively stable, do not increase further • Decrease • Change unevenly (R&D costs increase for some drugs and decrease for others)
Scale, pace and nature of scientific and technological advances	• Accelerate and creates new opportunities • Continue at a rate similar to today (not an accelerating pace) • Stagnate and fail to deliver on initial promises
Therapeutic and clinical areas pursued	• New areas emerge • Some current therapeutic areas become less important, narrowing global portfolios • New areas do not emerge

Public and not-for-profit investment in pharmaceutical R&D	• Increases relative to other funding sources • Remains stable relative to other funding sources • Declines relative to other funding sources
Private-sector investment in pharmaceutical R&D	• Increases relative to other funding sources • Remains stable relative to other funding sources funding • Declines relative to other funding sources
Success rates in pharmaceutical R&D	• Increase • Remain broadly unchanged • Decrease
Global dynamics in pharmaceutical R&D and the rise of emerging markets	• Emerging markets such as China and other countries in the APAC region grow and become more linked to European markets • Emerging markets grow but remain separate from other global markets • Emerging markets do not grow and mature
Regulatory innovation (e.g. supporting smarter trials and better use of R&D data)	• Evolves to facilitate smarter, quicker and cheaper trials • Does not evolve to facilitate smarter, quicker and cheaper trials

Consistency analysis

The next step was to conduct a consistency analysis to evaluate how likely a projection for one factor can co-exist with a specific projection for another factor. We scored each pairwise combination of projections to evaluate how plausible it is that two projections appear in the same future scenario together (see Figure 6 in Appendix for the Excel-based template used for this process). Projections deemed highly consistent were assigned a '5', those deemed highly inconsistent were assigned a '1', those deemed neither consistent nor inconsistent were assigned a '3'. To illustrate, an increase in available funding might be highly consistent with an increased pace of scientific and technological development in pharmaceutical R&D. However, both projections might be less consistent with a future scenario with no new therapeutic and clinical areas pursued.

The project team conducted this scoring in an internal workshop. Again, the scores were not designed as outputs but facilitated discussion about the relationships between different projections.

Cluster analysis and qualitative expertise triangulation

The consistency-analysis data was subjected to cluster analysis to identify plausible and consistent projection bundles (a list of projections with one projection per factor[3]) to select three sufficiently distinct clusters to inform the development of scenario narratives. We used ScMI software to conduct the cluster analysis, which involved grouping alternative projection bundles with similar and overlapping themes. This stage's primary outcome was a final set of three different factor projections outlining three very different futures. We agreed on three scenarios as the optimal number ensuring sufficient variation and detail without compromising workshop manageability. Expertise from the research team (from RAND Europe, LEK and SiRM) and insights

[3] The analysis sometimes indicated that two or more projections were equally valid. In these instances, the research team judged which projection to select.

from Scientific Advisors in previous project phases complemented the cluster analysis approach, incorporating broad and deep qualitative expertise into the final scenarios.

Developing scenario narratives

Finally, we developed titles, narrative descriptions and summaries of each scenario to facilitate engagement by workshop participants. Along with the outputs of the above exercises, we added additional detail and context to create a more vivid picture of the future pharmaceutical R&D environment. We present these scenarios and summarise key themes and influencing factors for each one in Section 2.

1.2.2 Future scenarios workshop

We designed, coordinated and facilitated a workshop for international stakeholders to reflect on future scenarios for the pharmaceutical R&D sector. The workshop aimed to engage workshop participants by inviting them to reflect on possible future scenarios. In particular, participants considered the challenges, risks and opportunities each scenario presents and the implications for possible stakeholder actions to prepare for the future and increase pharmaceutical R&D sector resilience.

Workshop participants spanned a variety of sectors, including pharmaceutical companies, Biotech/SMEs, policymaking representatives, standalone and corporate VCs, not-for-profits, academics, consultants and other innovation experts. Invitees were chosen to represent a diversity of perspectives from different professions, stakeholder groups and geographies. Although internationally focused, the study is also particularly interested in the financial ecosystem of pharmaceutical R&D in Europe. Participants included those who contributed to in-depth stakeholder interviews in earlier project phases. Others were identified based on desk research, recommendations of experts in the pharmaceutical R&D space and RAND Europe's professional networks.

All workshop participants gave informed consent to participate. Representatives from L.E.K. Consulting, SiRM, VWS and the sounding board for the study[4] also joined the workshop as observers. Please see below for a list of participants (Table 3) and observers (Table 4) present in the workshop, along with RAND Europe facilitators and note-takers.

Table 3. Workshop participants.

Name	Organisation	Role	Country
Adrian Towse	Office of Health Economics	Emeritus Director & Senior Research Fellow	United Kingdom
Ameet Sarpatwari	Harvard Medical School	Assistant Professor of Medicine	United States of America
Anonymous	Novartis	Anonymous	International

[4] This is a group of organisational representatives VWS interacts with about various aspects of the study. The research team did not interact with this group aside from their role observing the workshop.

Antonios Rodiadis	DG SANTE	Policy Officer	Europe
Boris Azais	MSD	Director of Public Policy Europe & Canada	International (Belgium based)
Catriona Manville	Association of Medical Research Charities	Director of Policy and Public Affairs	United Kingdom
Chris Molloy[5]	Medicines Discovery Catapult	Chief Executive Officer	United Kingdom
Colin Terry	Deloitte UK	Head of Life Sciences and Healthcare Consulting	United Kingdom
Daniel Chain	TauC3 Biologics Limited	President and Chief Executive Officer	United Kingdom
Florian Schmidt	DG SANTE	Deputy Head of Unit (Pharmaceutical)	Europe
Jeroen Bakker	Novo Holdings	Principal	Denmark
Martin Wenzl	OECD	Health Policy Analyst	International (France based)
Mathieu Uhart	Sanofi	Director Corporate Public Affairs Europe	International (France based)
Neil Bertelsen	Health Technology Assessment International (HTAi)	Steering Committee Member	International (Germany based)
Susan Kohlhaas	Alzheimer's Research UK	Director of Research	United Kingdom
Vijay Karwal	CBC Group/Affamed Therapeutics	Operating Partner/Chief Financial Officer	Hong Kong

Table 4. Workshop observers.

Name	Organisation	Group (Study team, client or sounding board)
Leah Ralph	L.E.K.	Study Team
Simon Middleton	L.E.K.	Study Team
Michiel Slag	SiRM	Study Team
Saskia van der Erf	SiRM	Study Team
Marit Heblij	HollandBIO	Sounding Board
Peter Bertens	Vereniging Innovatieve Geneesmiddelen	Sounding Board

[5] Present for the first half of the workshop.

Wim de Haart	Vereniging Innovatieve Geneesmiddelen	Sounding Board
David Rappange	VWS	Client
Evert Jan van Asselt	VWS	Client
Wiro Stam	VWS	Client

Prior to the workshop, participants received an agenda for the workshop and a document with a detailed description and summary of each scenario to familiarise themselves with the scenario contents (see Chapter 2 of this report).

Workshop conduct

The workshop was conducted on 8 November 2021 using Microsoft Teams and lasted approximately two hours. The workshop covered the following agenda:

- Welcome and introductions (15 minutes)
- Overview of the project and workshop aims (20 minutes)
- Future scenarios: Interactive facilitated discussion to consider the opportunities and risks presented by the future scenarios (50 minutes)
- Break (5 minutes)
- Plenary discussion (25 minutes)
- Next steps and close (5 minutes).

Members of the study team introduced the study and the workshop and gave an overview of the futures scenarios and their development.

The majority of the workshop focused on an interactive discussion about the three future scenarios for how the pharmaceutical R&D landscape may evolve in the next decade. This discussion occurred in three breakout groups and centred on the following questions:

1. What are the key challenges and risks in each scenario, and what are their implications for financing pharmaceutical R&D?
2. What are the key opportunities in terms of potential actions that could be taken now to maximise the opportunities presented by each scenario and manage potential risks?

Following small group discussions, we asked participants to reflect on common themes across the scenarios and key takeaways for making the financial ecosystem fitter for the future as part of a reflective plenary session.

1.2.3 Analysis and reporting

Detailed notes were taken during the workshop, capturing overall reflections on future scenarios, the challenges and risks presented by each scenario and areas of opportunity for potential action now. The study team met to discuss the workshop results, as reported in the following chapter.

1.3 Limitations and caveats

As with all workshops, there is a trade-off between the number of participants and the depth of discussion. To manage this trade-off, RAND Europe invited representatives of diverse stakeholder groups and facilitated in-depth breakout discussions in smaller mixed-stakeholder groups and collective feedback in the plenary session. Although the workshop attracted renowned experts from diverse stakeholder groups, other individuals who did not attend may have had valuable contributions. However, many common themes emerged in the workshops and stakeholder interviews conducted in the previous work package (reported in Annex B) regardless of whether individuals were from public, not-for-profit or industry stakeholder groups. There may be diverse cross-sector implementation requirements to make the financial ecosystem for pharmaceutical R&D fitter for the future, and further research could explore these differences in more detail. However, this was outside the current study's scope and focus. In addition, future research could consider how specific actions needed to optimise the financial ecosystem of pharmaceutical R&D may differ across clinical areas, e.g. between rare diseases and one-time cures on the one hand and chronic conditions (such as hypertensives or oncology-related innovation) on the other.

As with all future-focused methods, the choice of scenarios entails a degree of subjective judgement. The research team sought to use quantitative and qualitative approaches to scenario development, integrate expertise from across the project team, consult the SAC, and use the outputs of previous project phases to inform scenario development. This combination of approaches supports the robustness of the selected scenarios. In addition, and as previously mentioned, scenarios were framed as a tool for enabling reflection and discussion rather than a rigid set of predictions.

Scenario selection also occurs in the context of project and workshop aims. Therefore, it is plausible that researchers might select different scenarios for other projects with different aims, even given the same input variables and projections. For example, if a project had an explicit primary focus on drug affordability, variables such as patient and public advocacy and those related to innovative pricing models might plausibly be selected as more prominent than others. Given the current study's primary focus on the financing of pharmaceutical R&D, variables such as patient and public advocacy and affordability pressures are included in specific scenarios but not the primary variable of focus.

2 Description of future scenarios

Each future scenario used in the workshop is described below and assumes we are in the year 2031. As mentioned above, the scenarios do not predict the future or determine which futures are more likely but encourage reflection and critical thinking about the implications of various possible futures in terms of challenges, risks and areas of opportunity.

2.1 Scenario 1: Golden global age for pharmaceutical R&D

It is 2031, and the pharmaceutical R&D sector is thriving. The past few years have seen significant scientific and technological breakthroughs, increased success rates and a new focus on therapeutic areas that suffered historical underinvestment.

Artificial intelligence (AI), machine learning and other data-driven advancements have improved R&D efficiency, especially in the early stages of drug discovery. Although it took some time for 'big data' to embed into the R&D process, companies have become more comfortable working with greater amounts of diverse types of data by 2031. A healthy supply of highly skilled researchers from diverse disciplines and a flow of innovation between academia/research institutes, biotech/SMEs and pharmaceutical companies have contributed to a vibrant R&D landscape.

Building on prior advances in genetics, genomics, proteomics and bioinformatics, the 2020s saw a more decisive shift towards personalised drugs and a closer coupling between diagnostics and pharmaceutical sectors. R&D success rates have also significantly improved, and prospects unlikely to succeed are identified earlier than in the past. There is also growth in genetic therapies reaching the market. Immunotherapy and oncology breakthroughs have made cancer treatments more effective than before. As cancer has become a more curable and manageable disease, public and private investments have shifted towards new therapeutic areas enabled by scientific and technological developments. Examples include rare diseases, gastroenterology and the microbiome, pulmonology, psychiatry, neurodegeneration and regenerative medicine. Cell and gene therapies are attracting significant investments, as the concerns stifling progress have been overcome.

Advances in science and technology have led to a surge in funding as investors eagerly enter the attractive and lucrative pharmaceutical R&D space.

Government budgets in most developed economies have recovered from the impact of the Covid-19 pandemic through smart fiscal policies and a growing emphasis on health as a determinant of prosperous societies. Many OECD countries and non-members (e.g. China, India) have raised investment in health as a percentage of total government expenditure by 2-4% compared to the early 2020s. Public investment in early discovery research and previously neglected areas and efforts to improve data and clinical-trial infrastructure have paid off, and private-sector investment appetite is high. Not-for-profits have also recovered from the impact of Covid-19 and have managed to raise funds in innovative ways. Many not-for-profits have adopted more commercial

approaches to investing (e.g. taking equity or expecting royalties to support sustainability and provide returns to channel into future investments).

Seeing opportunities in new therapeutic areas, investors are willing to take a chance on an increasingly diverse supply of biotech/SMEs working in new and some established areas. Existing investment funds have grown, and the start-up space is thriving, with a more abundant supply of growth and scale-up capital than in the past. Although the US still leads globally in biotechnology companies, initial public offering (IPO) markets and funding, Europe has also scaled up investments and activity levels and now has a more attractive IPO market. There is a fair bit of competition between different investors for the best investment opportunities, so innovators are in a good position to secure favourable investment terms. A diversity of compounds progressing to later stages of the R&D pathway have also helped boost investor confidence and contributed to attractive valuations in the sector.

As pharmaceutical R&D yields good returns and has become even more attractive compared to other sectors, new types of investors have entered the pharmaceutical space, and new types of collaborations between public and private partners have emerged. Furthermore, new actors from the data and technology space have become involved in the R&D process by creating data-enabled solutions for pharmaceutical R&D. Public and private partnerships are vibrant across many areas, including major challenges like antimicrobial resistance (AMR) and rare diseases, and other fields.

Some innovative financing mechanisms have become more popular over the past decade. Mega-funds have gained momentum for tackling high-cost, high-risk R&D (e.g. for some rare and infectious diseases), and pooling funding for several high-risk projects under a single fund has enabled easier risk-reduction and capital raising. Access to debt financing in addition to equity has become important in enabling access to a larger pool of capital. Innovative R&D and product financing mechanisms have gained scale and traction for some infectious diseases (e.g. TB, AMR) and chronic conditions (e.g. related to neurodegeneration and pulmonology) that needed innovation. Examples include subscription-based models where R&D companies are paid a monthly fee, usually by healthcare authorities, in exchange for securing access to innovations with pre-agreed pricing and volume commitments.

Major shifts in the pharmaceutical R&D landscape have changed the dynamics of global collaboration. Innovators and investors in emerging markets such as China, India and Brazil increasingly collaborate with European and US counterparts.

China and other emerging markets have experienced the same pharmaceutical R&D boom that Europe and the US have enjoyed. Furthermore, regulatory reform in China has increased trust in pharmaceutical R&D quality and its resulting products, increasing investors' ease and collaborations between Europe, the US and the Asia-Pacific (APAC) region. In 2031, it is much more common for biotech/SMEs and pharmaceutical companies to seek approval for products in multiple global regions and receive a mix of funding from global investors. The increased global mobility of labour and global competition for talent and investment has led to pressures on Europe

to maintain competitiveness (including vis a vis increasingly competitive APAC countries), providing further impetus for an improved European R&D funding environment.

Reform in clinical trial regulation has created fertile ground to help decrease R&D costs, but affordability and unequal access to new and innovative treatments remain problematic.

Governments in Europe and the US have adjusted clinical-trial regulation to allow for smarter trial design and reduce the bureaucracy associated with trial design amendments, with adaptive pathways where companies can engage regulators throughout the R&D process to ensure they are on the right path. Trials for personalised drugs with smaller patient populations require fewer patients, and the types of data collected have evolved to include wider societal and economic outcomes. More data can be collected remotely from patients, and there are fewer bureaucratic hurdles without major concerns around safety or efficacy. This process has been a learning curve for all involved in selecting appropriate trial endpoints and therapeutic areas that can benefit from smarter trial design.

Although regulatory reform has decreased clinical trial and approval costs for some indications (e.g. rare diseases, genetic therapies), scientific and technological advancements have had an uneven impact on R&D costs. R&D in some therapeutic areas remains very expensive (e.g. chronic conditions such as cardiology and respiratory). Affordability and access to highly innovative drugs are still a challenge, and concerns about inequitable access are high on the global policy agenda. Drugs offering incremental improvements are somewhat more affordable than in the past. In the US, lobbying by the pharmaceutical industry has prevented any movement towards cost containment, and drug prices remain particularly high. The creation of one-time therapies that save lives or significantly improve quality of life has raised critical questions around affordability and access; governments struggle to enable access while ensuring continued innovation. However, some progress has been made in more flexible and adaptive pricing arrangements (e.g. outcome-based pricing, adaptive pricing and various price-volume agreements).

- Increase in scientific breakthroughs (e.g. AI, machine learning/data; oncology, microbiome, neurodegeneration, regenerative medicine).
- Increased focus on historically under-invested therapeutic areas: Breakthroughs in immunotherapy make cancer easier to treat. Scientific advances also led to a surge in funding in other clinical areas. Cell and gene therapies very attractive to investors.
- Significant increase in R&D success rates, including for personalised medicines.
- Healthy investment landscape:
  - Life sciences are an attractive sector. Public sector investment in health R&D increases as % of GDP post recovery from Covid-19 pandemic; significant growth in VC and biopharma R&D investment; not for profits investing in innovative ways (many expect royalties, equity).
  - Global activity: US a key player but Europe has scaled up R&D investments and activity. China and other emerging markets are thriving, with regulatory reform increasing trust in quality of products, easing investors and innovators.
- Multiple and diverse collaborators globally: Thriving start-up space; public-private partnerships are vibrant; new entrants; collaboration between actors in diverse continents (Europe, US, APAC). Global labour mobility.
- Reform in clinical trial regulation improves efficiency and in some cases decreases costs of R&D. More use of real world data in outcome assessments.
- Innovative financing mechanisms (e.g. mega funds, subscription models, outcome-based payments, adaptive pricing) but impact of scientific advances and regulatory reform on R&D costs and drug prices uneven. Affordability still a significant challenge.

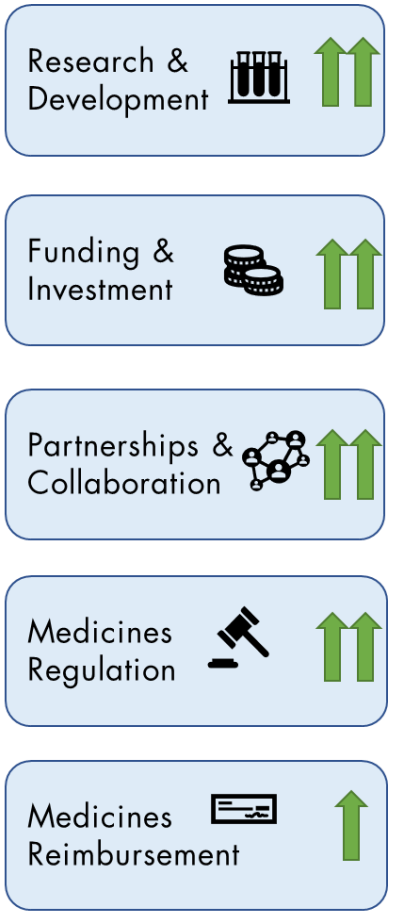

Figure 2. Summary of Scenario 1 (Global golden age for pharmaceutical R&D).

2.2 Scenario 2: Incremental improvements in the pharmaceutical R&D sector

It's 2031, and the pharmaceutical R&D sector has made modest advances since 2021. There has been a steady stream of scientific and technological developments, but few major breakthroughs. R&D success rates and the major therapeutic areas that attract investment have remained relatively stable.

After an initial flurry of excitement around the possibilities that advances in AI, genetics and genomics, and the microbiome would bring to pharmaceutical R&D, scientific and technological advancements levelled off. There continue to be modest scientific and technological developments, although by and large, the pharmaceutical R&D space has not seen major breakthroughs in the past decade. Oncology and immunology still dominate the innovation space, although there is an increased focus on infectious diseases, partly due to the Covid-19 pandemic. Other historically neglected innovation areas, including pulmonology, ophthalmology, psychiatry and many rare diseases, have not significantly progressed in scientific advances and innovation. Exceptions are gastroenterology and the microbiome, which have seen some progress in the past decade.

A small number of innovative biotechnology companies have championed activity in innovative areas such as gene therapies, cell therapies and some rare diseases (e.g. in neurology and haematology) and microbiome-related R&D in gastroenterology. However, investments in these therapeutic areas are still seen as high risk, only pursued by a limited number of companies and investors. Several failures and complexities in gene and cell therapies and new safety-related concerns diminished investor appetite after a period of increased investment in the early 2020s.

AI, machine learning and other data-driven techniques are used to some degree in drug discovery. However, they have not been integrated in a way that has led to major industry transformations in R&D processes, nor have they had a significant impact on success rates, which remain broadly consistent with those of the early 2020s across therapeutic areas. Although the vast amounts of generated data could potentially improve pharmaceutical R&D, the capacity to use these data to their full potential is limited by a lack of infrastructure for quality control, data curation and integration.

Pharmaceutical R&D funding has remained stable, and biomedicine remains an attractive area for investment. However, it faces increasingly competitive investment pressures from areas such as Greentech and Fintech.

Biomedicine remains an attractive investment area but has not surpassed other similarly attractive sectors such as Greentech and Fintech, which continue to present competition for investor interest. Compared to the early 2020s, available pharmaceutical R&D funding has remained relatively stable, with only very modest growth driven mainly by private-sector investors and a small number of therapeutic areas. There is somewhat more growth capital available for biotechnology companies than in the past. However, competition for this funding means it tends to target the most attractive clinical and therapeutic areas.

The mix of public, private and not-for-profit sector investors in pharmaceutical R&D has remained relatively stable relative to the 2020s, with limited new entrants into the pharmaceutical R&D financial ecosystem. Despite an initial period of austerity after the Covid-19 pandemic in the early 2020s, public-sector funding for biomedical research rebounded quickly due to the importance of health on national agendas. However, investment in health as a percentage of GDP has only modestly increased relative to the early 2020s (i.e. by 1–2% in most OECD countries, and slightly more in some emerging markets such as China actively bolstering the biomedical and health sector). Governments continued to fund early biomedical research over the past decade, helping pump-prime additional funding from the private sector. Governments have also supported collaborative R&D efforts, focusing on market-failure areas (including rare diseases and antimicrobial resistance) and technologically novel and uncertain areas (such as the microbiome). The not-for-profit sector saw major post-pandemic declines in resources but gradually recovered. Most not-for-profits still support grant-based funding. However, some – particularly those who struggled most to recover costs or focus on high-risk areas or orphan diseases – have adopted more commercial mindsets regarding royalties or pursuing equity from their investments. However, in 2031, this is still the exception rather than the norm.

With few exceptions, R&D costs have continued to increase for most therapeutic areas, and affordability and access to innovative drugs remain major challenges. While there are several innovative pilots for new pricing arrangements, these have not achieved scale.

Although regulatory agencies have made some gradual adjustments in clinical trial regulation related to bureaucracy in trial protocol amendments, smarter trials are not implemented at scale (with some rare diseases and orphan-drug R&D the exceptions). Clinical trials remain one of the costliest elements of pharmaceutical R&D. Adaptive pathways that allow companies to engage with regulators throughout the R&D process have not materialised in practice at scale, despite efforts to establish them. Overall, costs continued to rise throughout the 2020s, without major scientific or technological breakthroughs or regulatory reform to combat rising costs. R&D success rates have not changed relative to the 2020s.

However, global recognition of the affordability challenge and publicly funded healthcare systems' inability to tolerate rising R&D costs have supported an increasing number of innovative pilots exploring new pricing arrangements for a limited number of clinical areas (including flexible pricing, price-volume agreement, adaptive and outcome-based pricing). How much these pilots will impact pricing negotiations at scale remains to be seen. Some innovative financing models linking R&D funding with price and volume product commitments (e.g. subscription models) have gained slightly more traction than in the early 2020s – especially for areas with challenging market conditions such as antimicrobial resistance and some infectious disease, and for areas like hypertensives where a strong stimulus for innovation was needed. There are moves towards pharmaceutical cost-containment in the US, although this is currently limited to drugs without good pricing benchmarks (e.g. those without existing pharmaceutical standards of care). However, such limited progress leaves the possibility of more substantial future change.

China and some other emerging markets have continued growing their pharmaceutical R&D sector over the past decade, increasing competition with European and US markets.

China and some other emerging markets such as India, Brazil and South-East Asia have experienced moderate growth in the biomedical sector over the past decade. Such markets are closing the gap with Europe and the US. Furthermore, regulation in emerging economies has improved, contributing to higher quality pharmaceutical R&D being taken more seriously in the global ecosystem. Whereas collaboration between the US, Europe and some emerging economies has increased somewhat, geopolitical tensions are still at play between some parts of the world, limiting collaboration. The competitive dynamics that have unfolded led to different innovation blocs and consumer markets emerging. With few exceptions, there has been little movement of innovators or investors between these innovation blocs. However, individual blocs have modestly strengthened their biomedical sectors to serve their own respective markets.

- Modest scientific advances but no major breakthroughs: Oncology and immunology dominate. Somewhat more focus on infectious diseases. Some progress with microbiome R&D but many therapeutic areas underfunded. AI/machine learning/data-driven advances have not yet lived up to their promise (lack of capacity and infrastructure to integrate into practice).
- Relatively small number of companies championing innovation in gene and cell therapies and for some rare diseases but these areas are still seen as high risk. Biotechs driving innovation in these areas. Investors remain cautious (some failures and safety concerns).
- Success rates broadly consistent with the prior decade.
- Medicines R&D attractive to investors but increased competition from other sectors: Modest increase in public and not-for-profit investment vis a vis 2020s. Some increase in private sector funding but in few therapeutic areas. Growth capital only for most lucrative areas. Somewhat higher growth rate for sector in APAC region than in Europe due to government strategies in countries like China to bolster life sciences.
- Collaboration between traditional actors, few new entrants, increased competition between some geographies: Public-private partnerships focus on key areas of market failure and some highly innovative spaces. Increased collaboration between some geographies but increased competition with others (geopolitical factors).
- Clinical trial regulation and HTA assessment undergo modest improvements but not enough to facilitate smarter trials and counter rising R&D costs at scale. Exceptions: some rare diseases.
- Increase in innovative reimbursement pilots to explore new pricing arrangements, but benefits remain to be seen and scaled. Affordability a significant challenge.

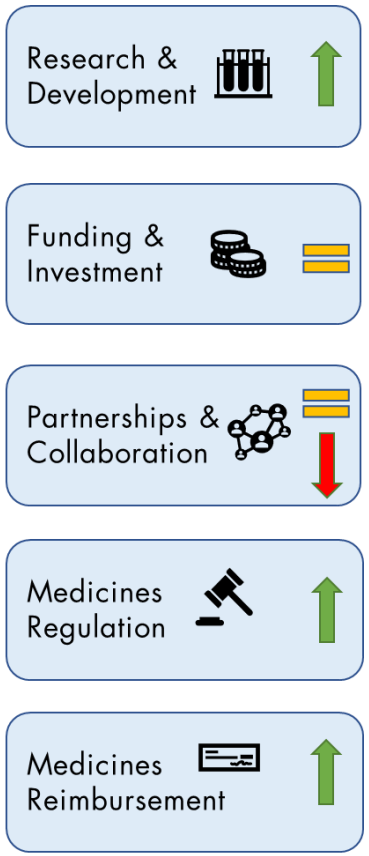

Figure 3. Summary of Scenario 2 (Incremental improvements in the pharmaceutical R&D sector).

2.3 Scenario 3: Pharmaceutical R&D stagnation

It's 2031, and the pharmaceutical R&D sector has stagnated. Scientific and technological developments of the early 21st century have failed to deliver significant progress, and R&D success rates have dropped to the lowest point of the last decade.

The initial promise of data-driven pharmaceutical R&D created more questions than answers. Although AI, machine learning and other data-driven technologies showed early promise, much proved too complex to implement at scale. This can be attributed, in part, to organisational inertia, a lack of industry infrastructure and capabilities, and regulatory and policy challenges that limited opportunities to effectively collect and utilise large amounts of data. Societal movements, a lack of public trust and fear also limited how much 'big data' could be implemented in practice, and the extent industry could use diverse healthcare data.

Without significant scientific and technological developments in most biomedical research fields, and with declining public-sector investment in early R&D (driven by broader macroeconomic pressures and austerity), pharmaceutical R&D failed to advance significantly over the past decade. Government funding was put under significant pressure after the Covid-19 pandemic and has not recovered. Due to limited funding for early discovery research, there are fewer spin-outs from academia in 2031 than in the 2010s and 2020s, further limiting the supply of innovation feeding pharma pipelines. R&D focuses mainly on improving existing drugs or repurposing rather than major breakthroughs.

R&D success rates have reached their lowest rate in the past decade and are lower than in 2021. Globally, there has been a narrowing of R&D portfolios towards fewer therapeutic areas (oncology and immunology still dominate) – partly due to the necessity for both public and private sector actors to stringently prioritise investments. Some highly publicised failures in gene therapy in the early 2020s and increased scepticism towards opportunities related to the microbiome (in part related to the complexity of science and limited advances) led investors and innovators to retreat from these areas; early investors felt let down. Furthermore, historically underinvested areas such as infectious diseases, neurodegeneration and pulmonology remain underfunded and have experienced very little progress. An exception is a small number of rare diseases already well-served since the late 2010s, which have made incremental advancements and modest increases in success rates thanks to patient advocacy and not-for-profit and government investment. Society is facing an increased risk of existing antibiotics becoming ineffective, and unattractive market conditions have led to a reduction in industry involvement in this space.

Funding for pharmaceutical R&D is scarce, and public-sector funding is no longer effective in encouraging further private-sector investment.

The availability of capital for pharmaceutical R&D has dropped to historic lows. Public-sector funding declined throughout the 2020s as purse strings tightened after increased public spending for the Covid-19 pandemic. Despite the need for public-sector investment in early research, austerity and pressures from other sectors have stalled progress. The supply of research talent has

also stagnated. Given that success rates have declined compared to the past, with few exceptions, private-sector funding has declined at an even faster rate than public-sector funding. Not-for-profit funding has also become more limited and narrowly focused. Given substantial resource constraints, some not-for-profits are experimenting with more commercial approaches to their investments (expecting royalties or taking equity). However, relatively low success rates mean these strategies have not boosted their financial positions. Private-sector investors have looked to more commercially attractive areas experiencing a boom, such as Greentech and Fintech.

Today's biotech/SMEs struggle to secure growth and scale-up capital. Given the scarcity of available funding, biotechs are often bought by pharmaceutical companies early, before they have had a chance to fully mature and develop. Failures increasingly happen on commercial and not only scientific grounds, as SMEs run out of capital to mature R&D portfolios. Limited progression of drug candidates through R&D phases has reduced investor confidence and contributed to less attractive valuations and exit opportunities. As a result, patients continue to suffer from a high disease burden in many chronic conditions (e.g. oncology, respiratory, cardiac) and historically under-funded areas (e.g. infectious diseases). Pressures on healthcare services are increasing due to greater demand for care, resulting in higher total healthcare costs.

The R&D collaboration landscape looks similar to 2020 with some consolidation, given few entrants to the pharmaceutical R&D space. Public-private partnerships are limited to areas of key market and scientific uncertainty but struggle from under-investment.

R&D costs have continued rising to the point that pharmaceutical R&D is facing imminent sustainability concerns. Its role as a driver of innovation economies and economic competitiveness is also increasingly under threat.

Pharmaceutical R&D costs continued to rise throughout the 2020s, exacerbated by low success rates, stagnation in science and technology and insufficient investment. Clinical trials have not seen any significant reform. Costs and regulatory demands have continued to balloon to a point where some drugs fail to get through clinical trials and regulatory approval due to insufficient funding. Thus scientific, commercial and regulatory challenges all impact failure rates.

There are serious concerns about developing new drugs for the future, with societal movements and patient advocacy putting pressure on governments to find urgently needed solutions. Advocacy groups warn of infectious disease and chronic condition pandemics, and there is public dissatisfaction with rising inequalities. Without a reinvigorated investment landscape and a decrease in R&D costs, the ecosystem will soon collapse to a point where returns are nearly impossible without sky-high prices that most payers will not be able to afford. This issue is high on the government agendas, who fear that only high-income countries and individuals will have access to even mainstream medications. Affordability is also much higher on US decision-makers' agenda than in the past, with cost-containment reducing differences in pricing between the US and some other markets and supporting affordability. However, it is also causing serious concerns for investors and the healthcare industry about returns, profitability and the ability to take risks and pursue radically innovative R&D. Despite widespread global agreement on the scale of the affordability challenge, there is no consensus on the best way to decrease R&D costs or

reinvigorate the sector. Discussions about novel financing models and risk-sharing practices are still in the early stages.

Stagnation in pharmaceutical R&D is global, as China and other emerging markets have experienced similar innovation challenges and wider economic pressures to Europe and the US.

China and other emerging markets (e.g. India and Brazil) face similar scientific and technological-innovation challenges, funding scarcity and low R&D success rates as other global regions. However, the Chinese regulatory environment has advanced compared to the past (concerning quality control and ability to access and use patient data - although the latter is due to less patient choice in data use than in some other countries). Regulatory developments have helped China and some other APAC countries develop a more competitive edge in a small number of therapeutic areas (e.g. gene therapy and, to a lesser degree, cell therapies and cardiology). However, there are still significant scientific and technological obstacles to breakthroughs. However, emerging economies focus more on generics, repurposing existing drugs and incremental innovation rather than breakthroughs. Compared to the early 2020s, the biomedical sector has seen global stagnation. In 2031, the emerging powerhouses of the early 2020s, such as China, are not major competitive threats or key collaborators for European and US innovators.

- Science and technology have failed to deliver major breakthroughs: AI/machine learning/data-driven advances too complex to implement at scale and raised more questions than answers. Societal movements: fear and lack of trust in big data use.
- Narrowing of R&D portfolios globally: Failures in some areas (e.g. gene therapy) and lack of success and scientific complexity in others (e.g. microbiome, neurodegeneration) lead investors who were optimistic to retreat. Focus on small number of commercially attractive areas (e.g. oncology) and areas with high public advocacy (e.g. some rare diseases). Most innovation focuses on incremental improvements or drug repurposing.
- Success rates have generally declined: They are at their lowest point of the past decade.
- Challenging investment landscape: Slow recovery post Covid-19. Pressures on government budgets lead to reduced investment which limits supply of innovation from academia/ SMEs to pharma. Not for profit resources constrained. Availability of capital from private sector drops to historic low. Limited supply of research talent as a result of funding challenges.
- Collaboration landscape looks similar to 2020 with some consolidation (not many new entrants and narrowing of therapeutic areas). Limited public-private partnerships
- Emerging markets (e.g. China, India, Brazil) face similar scientific and technological challenges and economic pressures as European and US markets. China more competitive than in the past but in a small number of therapeutic areas. Quality control and regulation a challenge in some emerging markets. Global collaboration dynamics similar to a decade ago.
- Little reform in clinical trial design, regulation and HTA: no significant reduction in R&D costs nor efficiency gains. Serious concerns about sustainability of sector. Affordability and access key concerns. Move towards cost containment in the US closing pricing gap, but also causing concerns about returns, profitability and ability to invest in radically innovative areas.

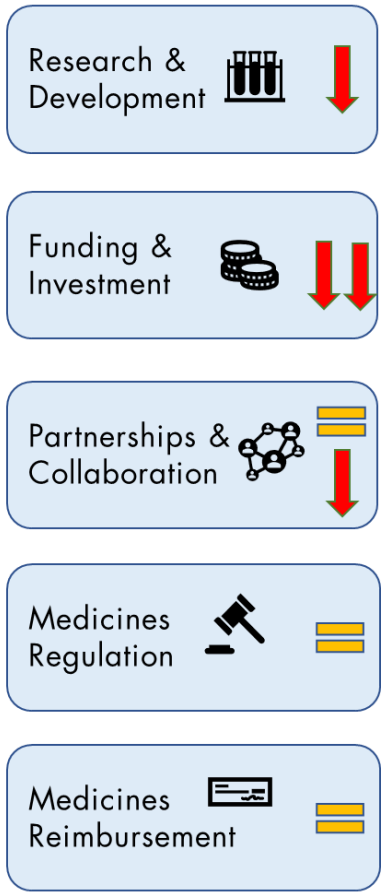

Figure 4. Summary of Scenario 3 (pharmaceutical R&D stagnation).

3 Key learning points from the stakeholder workshop

The scenarios presented in the previous chapter were used as a vehicle to facilitate exploration of the main challenges, risks and opportunities presented by plausible futures and encourage stakeholders to reflect on the critical issues that may require present action to prepare for the future – regardless of how it unfolds. Given the workshop's time pressures, scenarios were individually discussed in breakout groups, with each group discussing a different scenario to ensure all scenarios were covered collectively. The core themes for consideration to prepare for the future were common across all scenarios. Given that the key influencing factors are consistent across scenarios, this is expected. However, the projections are different, encouraging workshop participants to consider theme-based actions that could enable preparedness across different futures. Therefore, this chapter is organised by theme, highlighting scenario-specific insights where relevant.

The core themes that emerged during the workshop and from participant reflections relate to the challenges society faces and their implications for potential opportunities for action to optimise pharmaceutical R&D's financial ecosystem. These themes relate to the following areas:

- Scientific and technological advances
- The role of data and digital innovation in pharmaceutical R&D
- Pharmaceutical R&D financing
- Global collaboration and competition.

Several cross-cutting themes relating to each of the core themes above were also discussed during the workshop:

- Pricing, affordability and reimbursement
- Regulation.

It is important to flag that the areas of opportunity for potential action to improve the financial ecosystem for pharmaceutical R&D would need to include many stakeholders in the public, private and not-for-profit sectors. Although policymaking and political choices can influence pharmaceutical R&D's financial ecosystem, how this system evolves and its ability to establish informed and implementable policies requires the collective efforts of many stakeholders.

Finally, it must be noted that the themes below reflect broad areas for consideration rather than prescriptive actions. Additional evidence would be required to determine specific actions addressing issues in the financial ecosystem pharmaceutical R&D, explore implementation requirements in different contexts and evaluate learning from past interventions. This is outside the scope of the current study.

3.1 Scientific and technological advances

3.1.1 Challenges

The pace and nature of scientific advances will influence the supply of medical innovation and the private sector's willingness to invest in higher-risk therapeutic areas.

Several key challenges relating to scientific and technological advances emerged from the workshop discussions. Stakeholders noted that the pace and nature of scientific and technological advances would influence the challenges and risks that need to be addressed. Both a slow and fast pace of scientific and technological advancement could present future challenges and risks.

Slow-paced advancement in scientific and technological innovation (such as in Scenario 3 and within specific therapeutic areas in Scenario 2) would likely decrease investor appetite for pharmaceutical R&D and impede radical innovation. For example, slow progress could lead to an insufficient innovation supply in the pharmaceutical space, influencing investor appetite for higher-risk and radical innovation. Without breakthroughs in science and technology, pharmaceutical R&D would likely focus more on lower-risk clinical innovation, leading to drugs that only offer incremental improvements in care. Such medicines would influence the private sector's position in pricing negotiations, as they would lead to modest gains in value compared to existing standards of care.

However, rapid major scientific advances (such as in Scenario 1 and within specific therapeutic areas in Scenario 2) would also raise challenges, most notably regarding societal ability to pay for innovative treatments and industry's ability to absorb and integrate novel science and technology into R&D processes. Scientific and technological advancement may outpace society's ability to absorb innovation. For example, health systems may lack the capabilities to deliver innovative new treatments if the skills or facilities are lacking in healthcare delivery settings. Industry may also lack the skills to fully integrate novel technologies (e.g. AI) into R&D processes in ways that improve efficiency. If R&D leads to major breakthroughs such as one-time genetic cures or other highly innovative drugs, there will likely be significant challenges to healthcare systems' ability to pay for such treatments, exacerbating the risk of inequitable drug access.

3.1.2 Opportunities to address the challenges

Stakeholders identified a series of important considerations and potential action areas that could help mitigate risks and challenges related to scientific and technological progress. These span themes such as public-sector investment, skills and capability building, translational research capacity, the R&D workforce's labour mobility and connectedness, and advances and innovations pricing models.

These include:

- **Ensuring appropriate levels of public sector investment in basic science and research infrastructure – a pre-requisite for downstream innovation and leveraging private-sector investment**. Public-sector funding is important for ensuring sufficient scientific and technological advancement levels to feed later-stage pharmaceutical R&D and innovation

pipelines and mobilise downstream investment by private-sector funders such as venture capital, corporate investors, pension funds and other institutional investors. The absolute financial amounts of public and not-for-profit sector investment versus private-sector investment do not reflect the relative importance of different investment sources. This is because public and not-for-profit investment to ensure a supply of science is often a necessary pre-requisite for more downstream private-sector investment and because different R&D phases are associated with different costs. It is important to consider health and biomedical R&D specifically when considering public-spending levels rather than the broader health-expenditure category that encompasses other non-R&D expenses.

- **Ensuring that the private sector invests in R&D not only in the most profitable areas, but also in diverse areas addressing unmet societal need – including those which may not command the largest profits**. This requires appropriate push-and-pull incentives to align societal needs with industry's commercial structures. It also requires innovative risk-sharing agreements between industry and public-sector investors and payers. There may be scope to learn from the innovation experiences in response to the Covid-19 pandemic and areas with market viability challenges (such as antimicrobial resistance) to inform sustainable and scalable business models for pharmaceutical R&D in areas of unmet societal need.
- **Building healthcare systems' skills and capabilities to absorb the innovation supply and support the implementation of novel drugs in healthcare pathways (and the de-implementation of incumbent practices)**. This requires an information-and-communication infrastructure and strategy to raise awareness about the medical innovations available and how they compare to existing standards of care in cost-effectiveness. It also requires training healthcare professionals as prescribers and deliverers of care to implement new drugs regimes effectively and developing conducive healthcare-delivery pathways for innovations.
- **Building translational research and innovation capacity by supporting a mobile labour market for pharmaceutical R&D and a well-connected, skilled workforce**. Educating and training the pharmaceutical R&D labour force to apply new scientific developments in the R&D process involves nurturing porous interfaces between academia, industry and the healthcare service (which houses clinical entrepreneurs) to support appropriate labour mobility. Encouraging the back-and-forth movement of talent can help foster transferable skills. Partnerships and collaborations can help foster mobility between these sectors, as can a better understanding of the cultural barriers that may present career-related challenges to people moving between sectors, e.g. academia and industry. Fostering labour mobility is likely to require industry and public-sector actions. Future research could examine the relative degree of labour mobility in different geographical and cultural contexts and its impact on investment attractiveness and functioning of the pharmaceutical R&D system. It could also explore the mechanisms that might support appropriate mobility in the pharmaceutical R&D labour markets (e.g. exchange programmes between industry and academia, secondments and shared posts).
- **Managing societal ability to afford innovative drugs and keep up with scientific and technological development**. Payers will need to balance affordability concerns with rewarding innovation and encouraging investment across diverse therapeutic areas. As one example of more innovative pricing approaches, value-based pricing models may be useful in

future pricing debates. However, there is a need for greater stakeholder dialogue and decisions on applying them to breakthrough treatments in practice (i.e. what constitutes value, how it will be measured, how incremental gains in value influence pricing decisions). Conversations about innovative and flexible pricing models and risk-sharing arrangements between innovators and payers will need to tackle pricing and affordability, one of the most challenging issues facing the future of the pharmaceutical R&D ecosystem that ultimately impacts R&D financing as well. Affordability discussions will need to acknowledge that unique considerations may apply to innovations representing one-time cures versus more longer-term treatments and those for chronic conditions.

3.2 The role of data and digital innovation in pharmaceutical R&D

3.2.1 Challenges

R&D systems' ability to leverage data and digital technology advances will influence the pace and nature of pharmaceutical R&D, but there are several challenges to integrate them into R&D practice.

Many scientific and technological advances will depend on companies' ability to effectively collect and use high-quality data in the R&D process and their access to data (both proprietary and from the wider healthcare system). The current pharmaceutical R&D sector is not fully prepared to integrate increasing amounts of data and digital advances into R&D processes at scale, although some companies are making investments towards that end. Challenges relate to data access issues, data infrastructure, the skills and capabilities to use data and harness digital innovation in the pharmaceutical R&D process, and a limited capacity to effectively collect, analyse or share high-quality data. Such challenges separate the rapid progress in Scenario 1 – partly enabled by the capacity to use data and digital innovations – from the relatively slow progress of Scenario 2 and the challenges harnessing new developments' potential in Scenario 3.

Greater use of data from electronic health records, for example, could play a key role in designing innovative and potentially more efficient clinical trials and inform post-market value assessments. However, data-access challenges are significant, both technological (e.g. related to the existence of platforms that can link diverse data sets, data quality) and social (e.g. diverse public attitudes and trust in data sharing and how industry uses data). Public trust in data and data-driven technologies and debate about data security and privacy are also persistent challenges in some geographies and cultures. How much this will escalate or decrease in the future remains to be seen.

There are also challenges in the current data infrastructure, including data-quality standards, interoperability, efficient data flows and data-sharing in healthcare innovation systems. There are also skills challenges, highlighting the need to bolster data-science capabilities and the capacity to collect, process and analyse vast amounts of patient data. These skills are in limited supply.

Although improved integration of data and digital advances in pharmaceutical R&D may contribute to smarter and more efficient R&D, a greater focus on integrating data and digital advances into the R&D process can also introduce additional demands on companies to build the capacity and

infrastructure for more significant amounts of data in the future. This would necessitate additional near-term investment. Such investment may be difficult to secure if the expected investment returns are longer-term or heavily dependent on developments in the external landscape (e.g. how data access will be regulated).

3.2.2 Opportunities to tackle these challenges

Stakeholders highlighted potential areas of action that society needs to consider to prepare for the greater integration of data and digital approaches to pharmaceutical R&D. These include improving the data infrastructure, mobilising public support, advancing regulatory and legal frameworks, building skills and capability for data collection, interpretation and use, understanding levers that could enable greater data sharing between innovating companies, and understanding the capacities and capabilities needed in the healthcare system for more diverse data types to feasibly inform drug-pricing discussions.

More specifically, workshop participants discussed the following themes:

- **Industry and public-sector investments in improving data infrastructure** (e.g. standards, interoperability and data-linkage architecture to support effective data flows). This will likely require engagement from the public and private sectors. Industry needs to invest in internal infrastructure to ensure high-quality data curation and safe and secure use with appropriate safeguards. Similarly, the public sector also needs to invest in high-quality data collection in safe and secure ways. Stakeholders noted that improving data systems and data infrastructure will be vital in supporting innovation and ensuring that R&D and health systems can incorporate the insights from large amounts of data and data-driven technologies.
- **Tackling public hesitancy to share data and address concerns about data security and privacy.** This could be achieved through dialogue and engagement about the potential benefits of greater data sharing for medical innovation and societal needs and transparency about risks and safeguards. While conceding their necessity in debates about regulation, some workshop participants felt data security and privacy concerns should be balanced with data's benefits to innovation. The public should be engaged in discussions around data, which can help foster public trust. Patient groups may be able to define the circumstances they are willing to share data in and health data use for innovation and post-market research. Industry would need to develop appropriate levels of transparency in what data is used for and how and the safeguards in place.
- **Advancing regulatory and legal frameworks for pharmaceutical R&D data use** to support safe and secure data use. Though particularly important, this is a challenging ask for the EU given the culturally and politically diverse EU landscape and different public attitudes and policy responses to industry's data use and re-use. The need for solutions that transcend any one country's borders adds to the challenge. Decisions and arrangements related to financial aspects of data access (who will pay, for what, in what ways) also raise difficulties.
- **Strengthening skills and capabilities for data collection, curation and use.** This includes bolstering data science capacities in the pharmaceutical R&D workforce in industry, the public sector and the healthcare workforce.

- **Examining what is needed to increase future data sharing between companies involved in pharmaceutical R&D.** Depending on data availability the capacity to utilise it in R&D processes effectively, data-sharing may increase between companies in the future, contributing to more efficient R&D processes and reducing unnecessary duplication of effort. There is a need for further discussion about what types of incentives, capabilities, policies and infrastructure could support increased data-sharing (e.g. how to share data while protecting commercial sensitivities). Increased data sharing between companies may be more likely in areas where returns are especially difficult to secure and future scenarios with lower innovation levels.
- **Considering how increased data use and more diverse data types can inform innovative pricing approaches.** The ability to use data in decision-making about value depends on the right kinds of data being available to measure relevant patient outcomes and the ability to share, use and interpret such data. This may include building capacities and capabilities for HTA agencies, regulators and payers to engage with more diverse types of outcomes data and the wider healthcare system's capacity to collect such data (including amongst healthcare providers and organisations conducting traditional and real-world phase IV trials).

3.3 Financing the pharmaceutical R&D sector: creating sustainable landscapes

3.3.1 Challenges

The pharmaceutical R&D sector's ability to attract investment from the private sector will depend on diverse factors. Critical factors identified during the workshop include the relative attractiveness of other sectors of the economy, the supply of scientific and technological advances, the nurture of the R&D workforce, success rates and societal ability to pay for innovative drugs. Current investment challenges largely relate to resource constraints in the public and not-for-profit sectors, partly due to the impact of the Covid-19 pandemic.

The pharmaceutical R&D sector's ability to attract funding will partly depend on its attractiveness to investors compared to other sectors of economic activity (e.g. cleantech, fintech), partially determined by broader economic factors (as demonstrated in the scenarios). The pharmaceutical R&D sector's attractiveness to investors will partly depend on the supply of science and innovation and investors' ability to secure good returns on investments (for example, in Scenario 1). A lack of investment would pose significant risks for society and likely result in fewer products reaching the market and, ultimately, fewer advancements to benefit patients (for example, in Scenario 3 and in many therapeutic areas in Scenario 2).

Some stakeholders felt that insufficient clarity about healthcare-innovation priorities could also present challenges ensuring investment in underfunded areas of unmet societal need. High-risk therapeutic and clinical areas with potentially significant benefits for society (or for at least some underserved segments of society) may struggle to secure investment if other areas are seen as more attractive and lower risk in potential success rates and returns. Private-sector R&D investment will move towards what is profitable, which the public sector can impact by influencing supply, demand and reimbursement. This potential misalignment between investment areas and

unmet needs applied to all scenarios, even those with greater investment in pharmaceutical R&D and a relatively attractive market.

Innovations in pharmaceutical R&D will only improve health if somebody pays for them, and investment will only occur if investors are confident in the willingness to pay for innovation. There may be future challenges in ensuring a balance between affordability, access and rewarding innovation. Existing challenges related to societal ability to pay for drugs, especially for highly innovative treatments and one-time cures, exist are likely to present one of the trickiest challenges to address. Unequal access to drugs and innovative treatments within and across countries may also need tackling, depending on healthcare systems and payers. Affordability issues and unequal treatment access risk reputational damage to the pharmaceutical R&D industry and may enhance public pressure regarding affordability concerns. Pressures around affordability can interact in non-linear ways, such as in Scenario 3 where discussions around affordable pricing in the US caused debates around profitability and the sector's viability.

3.3.2 Opportunities to address challenges

Stakeholders noted opportunities for action related to the pharmaceutical R&D sector's longer-term financing and competitiveness. They highlighted themes related to the importance of public and not-for-profit investment for ensuring a sustainable pipeline of research talent and scientific and technological advances, tackling affordability challenges through innovative payment and risk-sharing arrangements, research prioritisation, and ensuring clear signalling in the healthcare system about areas of demand and what will be paid for.

Stakeholders reiterated the importance of the following themes:

- **Sustaining required public-sector and not-for-profit investment levels in basic and applied science to ensure a sufficient supply of research talent and a healthy supply of science and technology for downstream innovation to build on.** This is also key for tackling potential workforce sustainability issues. The sustainability of the pharmaceutical R&D workforce merits attention, especially given public and not-for-profit sector resource constraints in diverse clinical areas' diverse R&D funding and their impacts on the future supply of talent. This is particularly true given the prioritisation of Covid-19 research and the general impact of the pandemic on available funds for other types of R&D.
- **Supporting innovative healthcare systems and tackling affordability challenges, including ensuring demand for innovation in the healthcare system.** This matters as the demand for innovation (i.e. creating a viable market) influences the willingness of private-sector investors to channel resources into R&D. The public sector can support the demand side of innovation by creating feasible pathways within healthcare services to adopt and uptake new or improved classes of treatment. Industry would need to engage in ways to support affordable access and workforce training on the safe and effective use of novel drugs in wider healthcare pathways.
- **Implementing innovative and flexible risk-sharing and payment models through collective efforts of public sector decision-makers, payers and industry actors**. Returns on investment will always be critical considerations for private-sector innovators. However, there are limits

on societal ability to pay that need to be considered in negotiations and discussions about new financial incentives and reimbursement models. Value-based pricing models could be applied to local economic situations and priorities in context-sensitive ways. Any considerations around value-based pricing models should include discussions around determining value for highly innovative drugs and one-time cures. Post-market value assessments could also inform reimbursement negotiations. Such assessments require collecting patient-outcome data and potentially other types of administrative data (e.g. impact on healthcare-service utilisation) from the healthcare system. Coordination between payers, the public sector and the healthcare sector would be needed to help ensure that the right data is accessible to support value-based pricing models. Subscription models were also identified as a potentially underexplored vehicle for incentivising and rewarding/reimbursing innovation. Using subscription models, health authorities help de-risk R&D through upfront payments to support R&D in exchange for guaranteed volumes and prices of potentially successful products.

- **Reflecting on how to prioritise R&D to address unmet needs most effectively**. When prioritising pharmaceutical R&D financing, it is critical not to lose sight of the end goal and identify clear areas of unmet need and demand. Pharmaceutical R&D is a tool that helps towards healthier populations. Research prioritisation needs to balance diverse therapeutic areas and patient populations, and highly innovative R&D versus repurposing and more incremental innovation. These considerations should ensure a balance between investing in unlikely areas with high payoffs and more certain areas with modest gains in societal value. Using data more effectively can also assist with prioritisation, although healthcare systems will need support in collecting useful data for prioritisation. Prioritisation exercises should include consultations across stakeholders to engage patients and the public.
- **Clear signalling from payers about areas of demand and what will be paid for and how**. Clear communication about what will be paid for and how value will be determined will be important in boosting investor confidence in pharmaceutical R&D and incentivising innovators. Private-sector stakeholders noted that, from their perspective, policymakers and payers need to clearly communicate priorities, budgeting (including timeframes covered by budgets) and procurement arrangements.

3.4 Global collaboration and competition

3.4.1 Challenges

While changes in the global landscape present opportunities for new collaborations between established actors in pharmaceutical R&D (e.g. in Europe and the US) and emerging economies (e.g. China), they also raise challenges. These include potentially increased competition for investment and research talent between different geographies and uncertainty related to how innovative pharmaceutical markets may influence companies' locations and global pricing dynamics.

The competitiveness of the life sciences sector in different parts of the world and collaboration dynamics can influence where investment into pharmaceutical R&D goes and how it flows.

Collaboration between different types of stakeholders (e.g. biotech/SMEs, large pharma, diagnostics companies, academic collaborators) also influences the flow of funds into pharmaceutical R&D and value transactions.

Workshop participants discussed several key challenges related to global collaboration and competition. Global dynamics in pharmaceutical R&D are evolving and are likely to continue doing so. Workshop participants focused their discussion primarily on collaboration and competition dynamics between Europe, the US and emerging markets such as China. Some of the latter have prioritised building their pharmaceutical R&D sector's competitiveness and may continue investing in advancing the regulatory landscape governing pharmaceutical R&D, as described in Scenario 1. There has also been some progress in these markets on establishing attractive ways for companies to obtain reimbursement while reducing inequalities in access and controlling profits. Europe may face opportunities in these emerging markets as a potential collaborator and supplier of skills and capabilities in pharmaceutical R&D, but also as a competitor for investment (such as in Scenario 2) and as a potentially attractive and sizeable new market for innovators. Geopolitical dynamics and policies related to cooperation are likely to influence how the landscape evolves.

At present, decisions on pricing made in key global markets (e.g. the US) significantly impact global innovation landscapes and investment behaviours. If the composition, configuration or pricing strategies of key global markets change, this could potentially impact global pricing behaviours, although how remains to be seen.

While there is a good supply of science and free movement of innovation communities in Europe, there may be challenges in the future related to access to capital compared to the US or emerging markets such as China. For example, workshop participants flagged challenges related to the state of the IPO market in Europe that could potentially detract investors and make it more challenging to attract and retain companies and talent in Europe.

Europe's fragmented regulation in aspects such as the classification of new drugs and technologies and different requirements governing data and cost-effectiveness thresholds for reimbursement can decrease the region's attractiveness for pharmaceutical R&D investors compared to regions with more harmonised regulations. The diversity of regulations within Europe can make it cumbersome for innovators to navigate the fragmented landscape.

3.4.2 Opportunities to address challenges

Workshop participants flagged opportunities for Europe to secure its longer-term competitiveness vis a vis changing global landscapes for pharmaceutical R&D by building learning healthcare innovation ecosystems, tackling the long-standing challenge of regulatory fragmentation in some areas, and reflecting on interventions that can strengthen the attractiveness of the European IPO markets.

More specifically, this includes themes such as:

- **Ensuring learning in healthcare innovation systems**:

  - **Learning from what is working in other geographies**: There is an opportunity to learn across geographies about supporting innovation in pharmaceutical R&D, including looking at how emerging economies support innovation.
  - **Learning from innovation experiences in response to Covid-19 and learning how to support rapid and efficient innovation in times of crisis**: For example, how to sustain practices that enabled faster innovation in response to Covid-19. The pandemic challenged the health and innovation system, with lessons to be learned from global responses to Covid-19 in terms of rapid innovation, flexible and accelerated ways of conducting remote trials at scale, reduced bureaucracy related to regulatory processes and substantial public-private sector collaboration. The critical role of governments and the public sector in creating conducive clinical-trial infrastructure, mobilising and orchestrating investments and encouraging data-sharing and collaboration between different companies and between the public and private sectors was highlighted through Covid-19, particularly in geographies such as the US. What industry, public-sector, government and regulatory actions will be taken to sustain the efficient innovation enabled in response to Covid-19 remains to be seen, as does the appropriate safeguards that should be in place. Lessons about the potential benefits and united consequences of unfolding innovation in response to the pandemic are still being learned. Further research will be needed to fully understand the implications of Covid-19 on pharmaceutical R&D financing.
  - **Learning about how innovation happens in different spaces** (academia, industry, healthcare services) to sustain and further reinforce a connected European healthcare innovation landscape and prevent organisational siloes and inertia.
- **Tackling fragmented regulation and policies in some areas across Europe**: European countries can work together to reduce fragmentation and improve regulatory cooperation. This requires dialogue and prioritising areas where regulatory harmonisation may be most feasible in practice. Dealing with fragmented decision-making across different member states (e.g. regarding reimbursement, regulation of new technologies, intellectual property policies, approvals for drug repurposing, rules related to data use and re-use by industry) matters for the attractiveness of Europe to investors. However, it is politically and operationally challenging to address – though not impossible, as exemplified by the European Medicines Agency's (EMA's) work on other regulatory fronts. European policymakers may also need to tackle challenges related to differing regulations between the US Food and Drug Administration (FDA) and EMA concerning where trials need to be conducted geographically, as this can have a significant impact on R&D costs.
- **Bridging siloes between research policy, industrial policy and healthcare policy**: Some workshop participants emphasised the importance of ensuring that policy affecting pharmaceutical R&D is informed by research-policy, industrial-policy, and health-policy priorities. Closer interaction between these policy domains is needed to ensure a competitive sector that attracts funding and an innovation supply to improve health and prioritise areas of need in alignment with commercial realities. Less siloed policymaking is important for aligning supply with demand.

- **Continuing to support and sustain international cooperation, building on existing efforts and further expanding on them**: International cooperation will be vital for maintaining Europe's competitiveness in pharmaceutical R&D given changing global dynamics.
- **Strengthen economic incentives and opportunities**: Considerations for Europe may include supporting capital markets, enabling a more globally competitive IPO market and furthering the dialogue about the provision of tax incentives for innovation to attract investors and innovators to the region and retain them long term.

3.5 Concluding thoughts

Workshop participants' engagement with the future scenarios highlighted that the financial ecosystem of pharmaceutical R&D functions as a complex and interrelated system. Decisions and developments about financing connect inextricably with other parts of the system, including the availability of capital, R&D phases and clinical areas that will attract funding, science and technology supply, pricing and affordability, regulation, and policy governing collaboration and competition.

The diversity of actors in this broader ecosystem highlights the need for joined-up approaches to policymaking to support sustainable financial ecosystems for pharmaceutical R&D. A considerable range of actors have a stake in pharmaceutical R&D: Researchers in the public sector; innovators in biotechs, SMEs and the pharma industry, government and not-for-profit investors, venture capitalists (standalone and corporate), other industry and institutional investors such as pension funds and debt-finance providers, regulators, payers, and the healthcare systems and patients that adopt and use innovations. Furthermore, the pharmaceutical R&D space is influenced by different policy spheres: research, innovation, industrial strategy and healthcare policies. Therefore, the collaboration between decision-makers in these policymaking spheres is critical for ensuring coordinated approaches supporting a sustainable financial ecosystem for pharmaceutical R&D.

Many of the opportunities and areas for consideration highlighted in the workshop are not novel in themselves. Stakeholders have been seeking to address some of them for a considerable time already. For example, decision-makers across the European Union have been working on health-data and data-access infrastructure. The importance of public-sector investment in fuelling biomedical R&D is also widely recognised and prominent in both national and international R&D strategies, with Horizon 2020 being one example. Similarly, the need for innovative payment models for highly innovative drugs is not new, although not yet implemented at scale. The challenges fragmented-regulation challenges across the European Union (e.g. in classifications of some new technologies and health-technology assessments) present to innovators and investors are also well known, influencing clinical-trial designs, clinical-evidence requirements and associated R&D costs. However, existing recognition of the themes discussed above makes them no less important to highlight, given their challenges and impact on pharmaceutical R&D's financial ecosystem. In addition, a future research agenda may benefit from 'deeper dives' into individual themes. This will help assess progress in addressing challenges, making the most of future opportunities in different geographical contexts, identifying areas that require coordinated international action that extends beyond national borders, and considering detailed implementation and success criteria.

Some of the opportunities for potential action identified through the future-scenarios workshop may be, in relative terms, less prominent in current debates than the data, public-sector investment, innovative-payment models and fragmented-regulation themes discussed above. For example, many discussions related to innovation uptake focus primarily on affordability; however, uptake also depends on broader factors such as incentives, accountabilities, available skills for implementing new care pathways and de-implementing incumbent practices, and public buy-in. The workshop also flagged the potential merits of closer collaboration between research, industrial and healthcare policies, currently seen in pockets but not at scale in many parts of the world. Similarly, there is potential scope for more established markets learning from successful innovation experiences in pharmaceutical R&D work in some emerging economies that have rapidly improved their pharmaceutical R&D sector's competitiveness (or parts of it) in recent times. Moreover, despite considerable discourse about the importance of learning from the Covid-19 crisis, a deeper understanding of how applying and adapting some of the ways innovation happened in response to Covid-19 in the future might influence the financial ecosystem for pharmaceutical R&D in other areas is needed. There are also knowledge gaps about how sustainable the pace and nature of innovation in response to Covid-19 will be.

Although the multiple factors influencing pharmaceutical R&D were already clear, our work has highlighted their intimate links with pharmaceutical R&D *financing* – including through investor appetite and confidence, the product progression through the R&D pathway, and R&D costs. Our findings emphasise that multiple forces shape pharmaceutical R&D financing within a complex system.

Finally, the opportunities in areas where action may be needed are multiple and interrelated and often not straightforward to address. Inevitably, decision-makers will need to prioritise actions that may be taken and consider their feasibility. Such prioritisation will likely require identifying shorter-term actions that can make a difference (i.e. identifying 'low-hanging fruits') and longer-term interventions that may require more complex and fundamental changes in the pharmaceutical R&D system. Identifying which actions may be tractable is outside the scope of this study; however, some efforts may be more tractable to shorter-term actions than others, which will be critical for policymakers and other stakeholders to consider. Future studies could explore the areas of opportunity our research has identified and support prioritisation and implementation efforts.

Any potential prioritisation will partly be influenced by how the challenges and opportunities ahead are framed. This requires reflecting on whether and how much the key challenges to optimising pharmaceutical R&D's financial ecosystem are related to innovation's supply end, demand end, or both.

More specifically, given that pharmaceutical R&D financing and the supply of innovation are so closely related to the ability to ensure demand and adoption, decision-makers face three options for framing the challenge ahead and prioritising potential stakeholder actions:

- One is to ask: 'If we tackle challenges related to ensuring affordability and ensuring viable markets first (e.g. tackling the demand side through clear demand signalling, innovative payment models, innovative and flexible risk-sharing agreements between the public and private sectors, and innovating in procurement models), what else would we need to do on

the supply end (e.g. nurturing collaboration, tackling regulation and ensuring a supply of R&D capital) to optimise the financial ecosystem of pharmaceutical R&D?' Such a framing prioritises the 'securing demand, adoption and affordability' challenge.

- The alternative framing asks: 'What do we need to do on the supply-side to make the demand-side challenges easier to tackle?' Such a framing assumes addressing matters such as the availability of capital for R&D, public and not-for-profit sector investment in early R&D and infrastructure and other interventions to de-risk R&D, innovating in regulation, and nurturing needed collaborations can impact R&D costs in a way that minimises the affordability and demand-side challenge. It may also assume significant spill-over benefits related to prioritising supply-side interventions (e.g. employment and tax-revenue benefits from vibrant pharmaceutical R&D ecosystems). However, further research is needed on how much a reduction in R&D costs would impact pricing decisions and affordability in the absence of government pricing regulation.
- The third framing approaches both ends of the challenge simultaneously, asking: 'What are the key demand-side interventions that can help support affordability and secure demand, and what supply-side interventions need supporting in parallel to ensure a sustainable supply of pharmaceutical R&D and optimise R&D costs?'

Ultimately, the framing that could guide stakeholder action and policymaking in Europe will depend on how decision-makers prioritise the resources, time and investments at their disposal to channel into building sustainable and resilient financial ecosystems for pharmaceutical R&D and future sector competitiveness.

Appendix A: Tools for scenario development

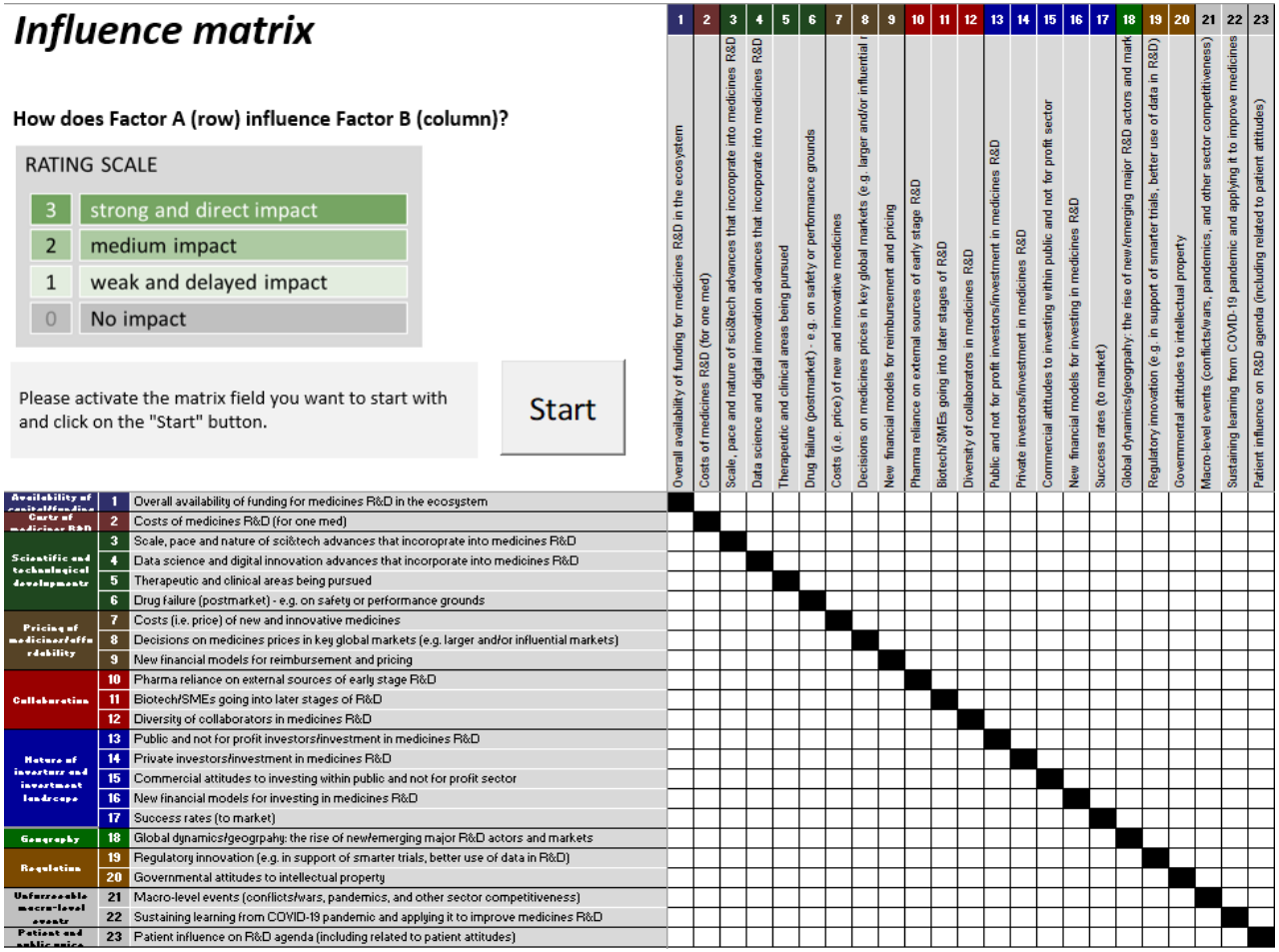

Figure 5. Influence matrix.

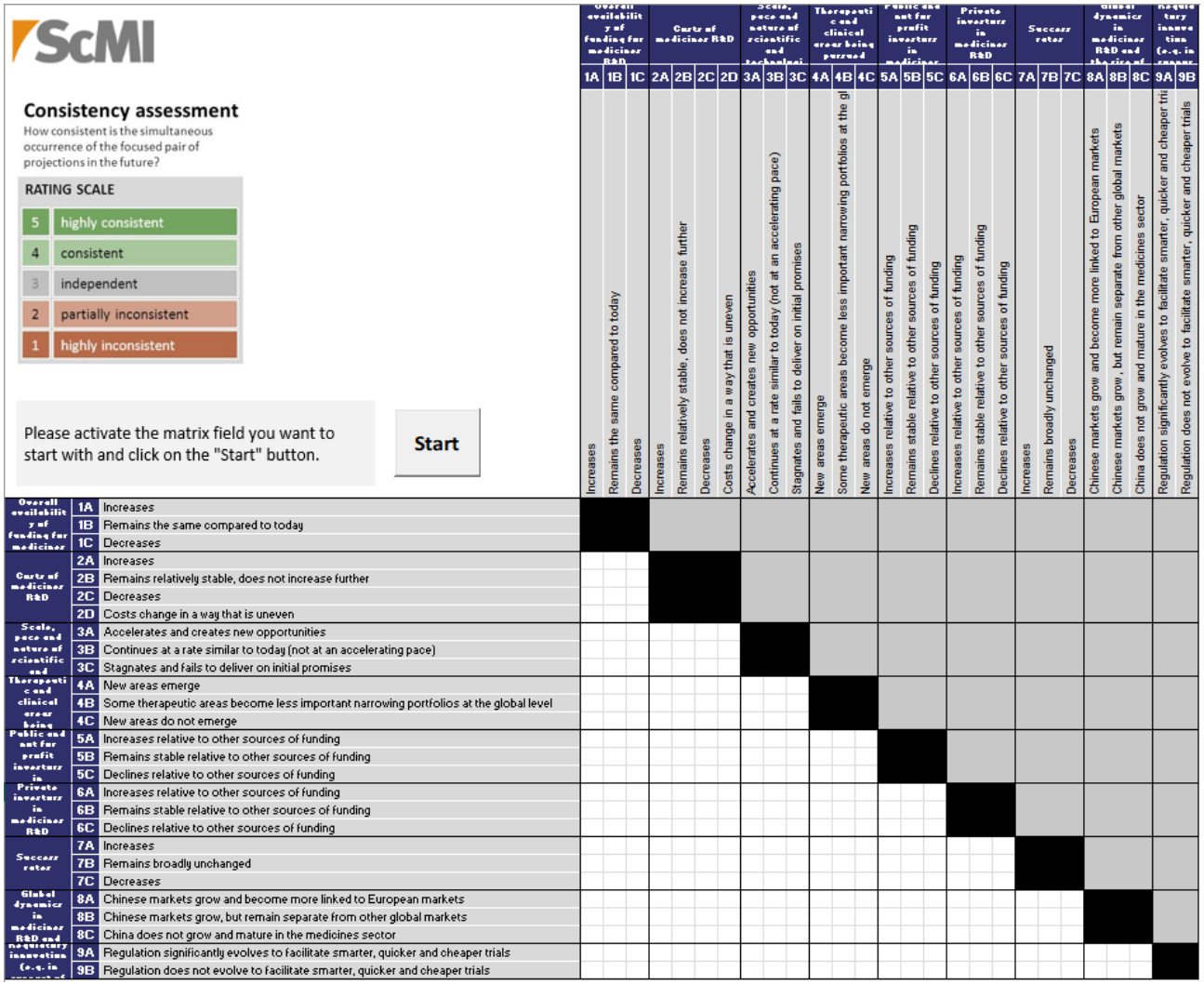

Figure 6. Consistency matrix.