Article

A New Vision for Europe's Bioeconomy in a Post-COVID World

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INTRODUCTION: THE POST-COVID LANDSCAPE FOR THE EU BIOECONOMY

In response to the COVID-19 global pandemic, the European Commission (EC) provided inclusive leadership, working as a team including EU member (national) officials, biopharmaceutical industry, NGOs, academic researchers and frontline health care personnel – acting with unprecedented collaboration and cohesion. The emergence in early 2020 of the greatest public health threat in a century required new approaches and new collaborations. While the United States failed to provide leadership in 2020, the EU did not disappoint.

While the burdens of COVID-19 were felt within national borders, the Commission's efforts to enhance transparency and cooperation proved critical in terms of assimilation and equitable distribution of healthcare solutions across Europe, e.g., including Personal Protection Equipment (PPE), diagnostic tests, repurposed as well as ongoing evaluation and commercialization of novel therapeutic interventions and vaccines:

> *The devastating impact of COVID-19 in a social, economic and human sense has underlined the critical importance of collaboration as a first principle for success for Europe's biopharmaceutical industry and more broadly for the discovery, development, commercialization, and enhancement of equitable access to novel diagnostics, therapeutics, vaccines to respond to global health threats as well as to respond to the EU's unmet health threats and human needs.*[1]

Through this collaborative effort, time-consuming regulatory processes were streamlined without sacrifice of public safety in the best interests of patients. COVID-19 not only showed what could be done, but what should be done to safeguard the health of Europeans.

Recent launch of a number of novel COVID-19 vaccines give hope for a healthier 2021, even while Europe and the world struggles to contain ongoing COVID-19 infections. Looking ahead to a post-COVID world, the EU's Pharmaceutical Strategy for Europe[2] released November 25, 2020 offers a new vision for vibrant and sustainable growth of the EU biopharmaceutical and appears to have learnt some lessons from managing the COVID – 19 crisis.

EVALUATING THE EU BIOPHARMACEUTICAL STRATEGY

This is the first-ever European comprehensive strategy for the pharmaceutical sector, based on explicit recognition that "the pharmaceutical industry is of key importance for the EU's economy."[3] Biopharmaceuticals remain of central

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1 Recommendations, EU Health Coalition, October 2020, https://www.euhealthcoalition.eu/

2 "A Pharmaceutical Strategy for Europe," published online 25 November 2020, and noting that implementation will notably include proposals for legislation by or before 2022. https://ec.europa.eu/health/human-use/strategy_en

3 A Pharmaceutical Strategy for Europe: Questions and Answers, 25 November 2020 https://ec.europa.eu/

importance for the European bioeconomy,[4] responsible for the lion's share of value creation through research and development of healthcare products that generate social and economic benefit.[5] In a supporting memorandum provided along with the EU Pharmaceutical Strategy, the European Commission notes:

> *In 2019 it invested more than €37 billion in Research and Development (R&D), it is responsible for 800.000 direct jobs and almost 110 billion € in trade surplus. At the same time the EU is the second largest market in the world for pharmaceuticals. The EU's total pharmaceutical spending was around €190 billion in 2018. The overall pharmaceutical sales is even greater when including the medicines used in hospitals.*[6]

For its part, the European Federation of Pharmaceutical Industries and Associations (EFPIA) estimates that Europe's biopharmaceutical sector is valued at nearly €230,000 million, more than doubling the value of the pharmaceutical sector as compared to 2010.[7]

In the context of the COVID-19 pandemic, the critical importance of the innovative biopharmaceutical industry became obvious to the 'man on the street' as country after country went into (repeated) lock-down, without recourse to vaccines or safe and effective therapies. Given the absence of American leadership in 2020, the EU's coordination and encouragement of industry collaboration proved critical. Companies ranging from Fortune-100 to start-up answered the call.

Nearly 20 innovative biopharmaceutical pharma companies focused their R&D capabilities on developing a vaccine to stop the epidemic, with even more companies worked to commercialize faster, better diagnostic tools for COVID-19 detection and effective COVID therapeutics. These companies raced to develop the "magic bullet" of a vaccine or a therapeutic – benefiting from decades of past work and without diminution of good clinical practices (GCP). Development of the Hepatitis B vaccine, for example, took 12 years before full commercial development following decades of primary and translational research.[8] Commercialization of the HPV vaccine took 16 years.[9] Certainly COVID-19 innovators stood on the shoulders of giants; nonetheless, we have seen extraordinary acceleration in development of healthcare solutions brought about by collaborations going beyond biopharma R&D to supply chain solutions, enhancing access to therapies. It is interesting to note that the first vaccine approved by the FDA was the result of a partnership between Pfizer and a small German R&D company BioNTech .

As the world faced a new wave of COVID-19 infections in mid-2020, several companies announced key vaccine development milestones, enabling potential availability of one or more COVID vaccines by year's end. Experts cautioned that even if that was to happen, the vaccine might only be 50% to 70% effective, however by the end of 2020 two vaccines demonstrating 94% to 95% effectiveness (almost unprecedented efficacy) – the vaccine from the Pfizer-BioNTech collaboration and another from Moderna –were authorized for emergency use in the US and UK; approval of AstraZeneca's vaccine developed in collaboration with Oxford University followed days later in early January 2021, with indications that an additional vaccine from Johnson & Johnson could be available as early as February 2021. Other vaccines have been announced by regulatory officials in India, China, and Russia . At the same time, many research collaborations are underway for novel therapeutics to treat COVID-19, including repurposing of approved medications that appear helpful to treat COVID symptoms.[10] Even with approval of several COVID vaccines, ongoing R&D is critical to find better

commission/presscorner/detail/en/qanda_20_2174

4 A decade of EU funded GMO research (2001 – 2010)" European Commission Directorate General for Research and Innovation, Biotechnologies, Agriculture, Food (2010) EUR 24473 (En), 2010, p. 9. (Noting that the bioeconomy: "refers to economic activities relating to the invention, development, production and use of biological products and processes" such as "industrial and pharmaceutical biotechnologies, and includes significant know-how on the health-related aspects of the Bio-Economy.")

5 This is due in part to the policies resulting in exodus of agricultural biotechnology from the EU. See discussion below: Limitations on Advanced Agricultural Technologies in the EU, pp. 69-71.

6 A Pharmaceutical Strategy for Europe: Questions and Answers, 25 November 2020 https://ec.europa.eu/commission/presscorner/detail/en/qanda_20_2174

7 EFPIA Report: The Pharmaceutical Industry in Figures Key Data 2020, p. 5, available online at https://www.efpia.eu/media/554521/efpia_pharmafigures_2020_web.pdf

8 See, e.g., Beasley RP. Development of Hepatitis B Vaccine. *JAMA*. 2009;302(3):322–324. doi:10.1001/jama.2009.1024 https://jamanetwork.com/journals/jama/fullarticle/184248

9 Inglis S, Shaw A, Koenig S. Chapter 11: HPV vaccines: commercial research & development. Vaccine. 2006 Aug 31;24 Suppl 3:S3/99-105. doi: 10.1016/j.vaccine.2006.05.119. Epub 2006 Jun 23. PMID: 16950023. https://pubmed.ncbi.nlm.nih.gov/16950023/ (paywall)

10 For example, dexamethasone, a steroid developed in the late 1950's appears very effective against COVID-19. See **Michelle Roberts** "Coronavirus: Dexamethasone proves first life-saving drug," BBC News online 16 June 2020 https://www.bbc.com/news/health-53061281

therapies and cures for COVID variants, not to mention other urgent healthcare priorities. However size and large R&D budgets do not guarantee success in the search for a COVID vaccine, as three of the largest vaccine companies have struggled to develop a vaccine.

Pillars of the EU Pharmaceutical Strategy

It may be interesting to speculate what would have been included in the EU's Pharmaceutical Strategy if it had been published in January 2020, before the realization that Europe – and the world at large – faced an unprecedented global epidemic from COVID-19.

There are four main pillars to the European Pharmaceutical Strategy:

- Ensuring access *to affordable medicines* for patients and addressing unmet medical needs (e.g. in the areas of antimicrobial resistance, cancer, rare diseases)
- Supporting *competitiveness, innovation sustainability of the EU's pharmaceutical industry* and the development of high quality, safe, effective and greener medicines.
- Enhancing *crisis preparedness and response mechanisms,* diversified and secure supply chains, address medicines shortages
- Ensuring a *strong EU voice in the world* by promoting a high-level quality, efficacy and safety standards.[11]

The accompanying EC Communication provides more a more detailed overview on these pillars, as follows:

> *The Pharmaceutical Strategy for Europe builds on these foundations. It will foster patient access to innovative and affordable medicines. It will support the competitiveness and innovative capacity of the EU's pharmaceutical industry. It will develop the EU open strategic autonomy and ensure robust supply chains so that Europe can provide for its needs, including in times of crisis. And it will ensure a strong EU voice on the global stage. The strategy has four work strands which flow from these objectives. Each strand contains flagship initiatives and flanking measures to ensure the objectives deliver tangible results. Taken together, they will ensure Europe's pharmaceutical policy evolves in line with the green and digital transitions, demographic change and remains relevant given the realities of today and the ambitions of tomorrow, as part of a stronger Health Union.*
>
> *The strategy will also help to deliver other Union objectives. By boosting innovation to address unmet needs, including vaccination against treatable infections that cause cancer, as well as medicines for paediatric and rare cancers, it directly contributes to 'Europe's Beating Cancer Plan'. Together, the Pharmaceutical Strategy and the Cancer Plan will ensure that patients across Europe can access high-quality treatment and new therapies when they need them and ensure the availability and affordability of essential medicines for cancer patients across the EU. The strategy's actions to address access to medicines will also help to meeting EU-level commitments under the UN's sustainable development goals.*
>
> *The strategy is also complementary to the European Green Deal and more particular the Zero Pollution ambition for a toxic-free environment, notably through the impact of pharmaceutical substances on the environment. The pharmaceutical strategy paves a way for the industry to contribute to EU's climate neutrality, with a focus on reducing greenhouse emissions along the value chain. It also contributes to the action plan to implement the European Pillar of Social Rights, the strategic frameworks on achieving a Union of Equality, the upcoming Green Paper on Ageing, the strategy on Shaping Europe's digital future, the European strategy for data, the work on the creation of a European health data space, the European One Health Action Plan against antimicrobial resistance and the new industrial strategy for Europe.*
>
> *Finally, the strategy is of key relevance for non-EU countries as well, in particular in the Western Balkans and the EU's neighbourhood, as candidate countries, potential candidates and DCFTA countries have an obligation to align to the EU acquis of the pharmaceutical legislation.*[12]

The EC announcement of the Pharmaceutical Strategy for Europe and accompanying supporting materials reaffirm the importance of incorporating the

11 A Pharmaceutical Strategy for Europe, 25 November 2020 https://ec.europa.eu/health/human-use/strategy_en

12 Communication from the Commission to the European Parliament, the Council, The European Econoimc and Social Committee and the Committee of the Regions, Pharmaceutical Strategy for Europe Brussels, 25.11.2020 COM (2020) 761 final, https://eur-lex.europa.eu/legal-content/EN/TXT/HTML/?uri=CELEX:52020DC0761&from=EN

lessons of COVID-19. just as the proof of the pudding is in the eating, time will tell whether this is indeed the case. In the meantime, it is helpful to highlight what has been learned from the global COVID-10 pandemic and the European experience.

What are the lessons of COVID-19?

- *For Healthcare 'just in time' is too late*

In times of crisis, it is essential that all required resources needed by first responders and patients alike, e.g., Personal Protection Equipment (PPE) supplies, should readily available. The first lesson of COVID-19 is that EC and EU member states need to prioritize healthcare as an investment in public health and not as a cash cow for savings that come at the cost of European patients. Crisis does not come with the lead-time to get essential supplies; next time we must be ready.

- *Transparency, collaboration and meaningful incentives spur meaningful R&D*

For example, over just a few months in 2020, the EU's Innovative Medicines Initiative (IMI) fast-track proposal process attracted 144 proposals, of which fully 120 met IMI requirements. Given the high number of quality applications, IMI increased available funding from €45 to €72 million and selected 8 project for funding.[13] Looking forward, spurring R&D for unmet needs is vital. In particular it is crucial that R&D to address anti-microbial resistance (AMR) will clear action plans. and accountability so that the needed R&D will be done. We also need to see greater transparency over evaluation of the value of innovation to ensure equity of access.

- *Science based, time-sensitive regulation is critical for European Leadership*

Whether we are talking about COVID-19 vaccines and therapies, AMR or new drugs for rare diseases, the patient is waiting. It should not require a global pandemic to ensure that safe and effective new medicines and vaccines are brought to market as quickly as possible. At the same time, regulatory processes should be apolitical and not developed in reaction to pressure-groups without a basis in science. What would the results have been in 2020 if EU policies had undermined vaccine R&D in Europe as they have with regard to GMOs?

- *Integration of EU-wide and national supply chains is essential*

European patients need to be able to rely on supply chain management for healthcare products and associated services, without respect to EU member state boundaries. COVID-19 has shown us how important it is to coordinate supply chain processes both within EU Members boundaries and across the EU.

- Monitoring and Tracking is key to success

We count what matters. Just as the EU success during COVID-19 has stemmed from unprecedented communication and collaboration among stakeholders, the process also relied heavily on monitoring and tracking. The COVID lesson here is the need to work with stakeholders to develop key metrics for monitoring, including annual reports to track progress and possible online or in-person events.

THE WAY FORWARD:

While comprehensive reform of policies adversely affecting the European Bioeconomy may not be in the offing, the EU Biopharmaceutical Strategy offers an important opportunity to reinvent European biopharmaceutical development in a post-COVID, post-Brexit world. Rather than focus on specific elements of the European Strategy, the authors offer the following suggestions for EU policymakers:

- Establish an enabling environment for inclusive consultation

It is essential to take the pulse of key stakeholders – including industry, VCs, civil society, academia, relevant EC Directorates in Brussels and EU member state governments, before framing out an issue and identifying a sustainable policy direction. Soliciting views, investing time to for meaningful consultations with stakeholders and listening carefully to their concerns ensures that relevant issues are aired prior to reaching the decision-making stage. As an additional benefit, the consultation process generally builds trust across the table and strengthens the working relationship between policymakers and stakeholders. The process of gaining agreement may, by necessity, include a great deal of repetitive discussion, e.g., where nothing has been said until everyone has said it.[14] This also accords with the recommendation of

13 IMI announces COVID projects, boosts funding pot to EUR 72 million, 5 December 2020 https://www.imi.europa.eu/news-events/press-releases/imi-announces-covid-projects-boosts-funding-pot-eur-72-million

14 This is a paraphrase of the dictum: "Everything has been said but not everyone has said it yet," attributed to Congressional Representative Morris Udall at the 1968 Democratic National Convention.

the EU Health Coalition,[15] recommendation for establishment of a "multi-stakeholder Forum for Better Access to Health Innovation, covering all aspects of innovation, from disease prevention, therapies, technologies, and supply chains, to improvements in care pathways and healthcare services," and involving all stakeholders – from Member States and regional authorities to patients and civil society, from healthcare professionals to industry."[16]

- Gather Empirical Data

EU biotechnology policy writ large, and the new pharmaceutical strategy, should be based on reality and the actual experiences of stakeholders either at the local, regional or EU Member State level, including the actual experiences of Academic researchers, Industry, Funders, and related non-government stakeholders. There should be a concerted effort to recognize and understand the ground realities by which businesses operate and how investment decisions are actually made, so that appropriate incentives are balanced against necessary regulatory restrictions for the benefit of all stakeholders.

EU policy should similarly look beyond the immediate impact of a policy, e.g., price controls, to gain a better understanding of the broader impact to ensure that adopted policies support job creation, research productivity and sustainable long-term growth. This includes greater transparency around the process of evaluation and pricing, with appropriate reward for innovation based on its value to patients, health systems and society based on agreed principles.

- Adopt Transparent, Science-based Regulatory Processes

EU biotechnology policy should strive for transparency, predictability, consistency, durability and non-discriminatory regulation across areas of technology – including agricultural biotechnology where Europe has essentially lost a generation of industrial development due to the expansive interpretation of the Precautionary Principle – and should also revisit problematic intellectual property policies (e.g., Patent Disclosure, curtailment of Supplemental Patent Certificate terms) that have had a documented chilling effect on products development.

- Identify and Implement Best Practices for Technology Clusters

EU biotechnology policy broadly speaking should reflect best practices in highly innovative, successful biotechnology clusters both within EU Member States and around the globe, taking into account the increasing importance and impact of technology clusters for R&D productivity. The relative success of the UK in attracting investment and growing its bio-cluster may provide insights, as well of course as leading biotech clusters in the United States and Israel.

CONCLUSION

The hard-won lessons of 2020 on the critical value of collaboration and cooperation between stakeholders at all levels hold enormous potential for the successful implementation of the EU pharmaceutical strategy.[17] Drawing on the lessons of COVID-19 collaboration and dialogue to identify the right incentives, EU can revitalize innovative biotechnology in the 21st century, but the EU must recognize the lessons learnt from the COVID19 crisis.

Two questions remain: Does the European Commission's vision for biopharma has focused on the lessons learned from the Covid-19 epidemic? Will the Commission implement the European Pharmaceutical Strategy in a post-COVID world with a focus on collaboration and transparency? How will things be different than before?

ANNEXES:

Status of Europe's Biopharmaceutical Research Enterprise in 2020

Impact of Brexit on the European Bioeconomy

Limitations on Advanced Agricultural Technologies in the EU

15 The EU Health Coalition is currently composed of 33 organizations including patient organizations, EU research-oriented medical societies, healthcare providers, industry organizations as well as regional and local health authorities.

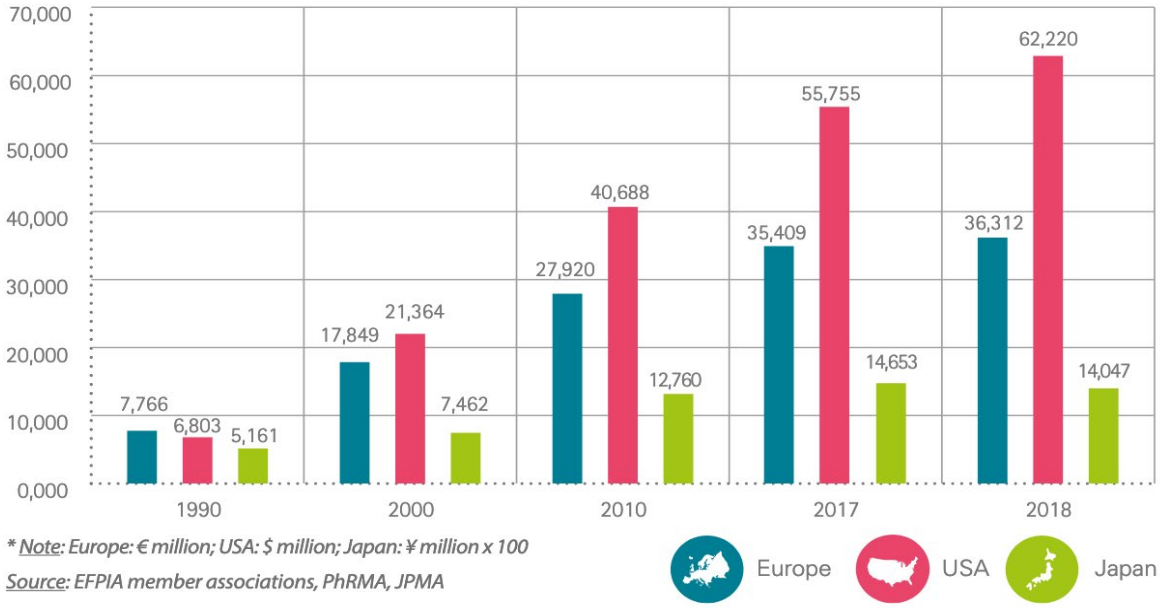
16 "A Shared Vision for the Future of Health in Europe: Lessons Learnt from the COVID-19 Pandemic," EU Health Coalition, October 2020. p. 4, https://www.euhealthcoalition.eu/wp-content/uploads/2020/10/FINAL-lessons-learnt-from-the-COVID-19-pandemic.pdf

17 "A Shared Vision for the Future of Health in Europe: Lessons Learnt from the COVID-19 Pandemic," EU Health Coalition, October 2020. ("The COVID-19 pandemic has also shown us the importance of cooperation between sectors and actors in ensuring our healthcare systems work to their optimum ability in preventing premature deaths.") https://www.euhealthcoalition.eu/wp-content/uploads/2020/10/FINAL-lessons-learnt-from-the-COVID-19-pandemic.pdf

STATUS OF EUROPE'S BIOPHARMACEUTICAL RESEARCH ENTERPRISE IN 2020

Contrasting the fruitful collaboration during the 2020 COVID-19 pandemic with sustained losses of the last three decades demonstrate the lack of sufficient recognition by policy makers in as to the value of inclusive policy development and implementation, including industry as a key stakeholder. Despite year-on-year growth, Europe has been in decline as a commercial R&D destination for a generation. EU biopharmaceutical R&D has long been losing ground to the US, China and India. In 2018, U.S. pharmaceutical R&D spending exceeded $62 billion; dwarfing that of the EU at €36 billion.

PHARMACEUTICAL R&D EXPENDITURE IN EUROPE, USA AND JAPAN (MILLION OF NATIONAL CURRENCY UNITS*), 1990–2018



Note: Europe: € million; USA: $ million; Japan: ¥ million x 100

Source: EFPIA member associations, PhRMA, JPMA

The European Commission has long recognized the need for intervention to enhance European biopharmaceutical productivity,[18] however was in the past unable to identify the right approach to stem erosion of European R&D competitiveness and retake its historically leading role.

The high caliber of European academic research centers is unquestionable: "Europe has world-class research institutions, medical centers, and hospitals that provide a strong basis for sourcing and developing scientific and clinical innovations. The region is home to 16 of the world's top 50 universities for life sciences and publishes roughly the same number of articles in top ten journals as the United States does and three times as many as China."[19]

EU academic research institutions continue to attract ambitious scientists from around the globe: Finland,

18 Nathalie Moll, The EFPIA View (blog), March 1, 2020 https://www.efpia.eu/news-events/the-efpia-view/blog-articles/would-the-last-pharmaceutical-investor-in-europe-please-turn-the-lights-out/ ("In its 1994 Communication on the *Outlines of an Industrial Policy for the Pharmaceutical Sector in the European Community,* the European Commission stated that the pharmaceutical "*industry is a substantial asset for growth and employment in the European Union*" and that "*there are signs that the competitiveness of the Community industry is yielding in comparison with its main competitors.*")

19 Franck Le Deu and Jorge Santos da Silva,"Biotech in Europe: A strong foundation for growth and innovation," McKinsey & Company (August 2019), available online at https://www.mckinsey.com/industries/pharmaceuticals-and-medical-products/our-insights/biotech-in-europe-a-strong-foundation-for-growth-and-innovation.

Sweden, Germany and Switzerland, which are among the world's top science spenders, attract thousands of foreign researchers each year.[20] Fixed-term research positions and training opportunities for non-EU scientists and students are available at universities and research institutes across Europe. European and national funding agencies and academic exchange services, scientific societies and private foundations offer a wide range of support for early-career scientists from around the world. Moreover, visiting scientists generally "find that conditions for science — including funding, training opportunities and access to research facilities and lab reagents — are much better than in their native area."[21]

However, the continuing attraction of Europe for academic researchers has not translated into broader biotechnology success in terms of commercialization of new products and services, and Europe risks becoming the world's research hub while innovative products and processes and the jobs and growth that go with their development, will be found elsewhere."[22] Nathalie Moll, EFPIA Director General, sums up the situation with hard truths: "The sobering reality is that Europe has lost its place as the world's leading driver of medical innovation. Today, 47% of global new treatments are of US origin compared to just 25% emanating from Europe (2014-2018). It represents a complete reversal of the situation just 25 years ago."[23]

Both investment and the number new biotech start-ups are flagging.

> *Further down the innovation chain, European companies were responsible for originating 13 percent of the new drugs produced by biotechs and approved by the US Food and Drug Administration in 2017 and 2018, while US biotechs were responsible for 78 percent. However, Europe's share of new drugs could grow if its biotechs are able to attract more investment; they currently receive only 20 percent of the funding their US counterparts do.*[24]

Despite the political expansion of the EU and a continuing commitment by the European Commission to public funding for high-quality academic research, half of all European biotechnology companies are concentrated in France, Germany and the United Kingdom (UK), and start-up activity in France and Germany has been falling for several years.[25] As a follow-on, the pace of start-up activity in the EU also is adversely affected by the lower growth in R&D spending, given that most new biotech companies are staffed by alumni of global biopharmaceutical companies. The relative decline of European biopharma thus becomes a vicious cycle where the greater success of new companies in Boston, San Diego and San Francisco becomes a siren call to bio-entrepreneurs in Europe. R&D location and incentives, sources of funding and the impact of (and the unintended consequences of) government policies have all contributed to the decline in "D" in Europe. Moreover, the UK biopharmaceutical sector has been an outsize contributor to European biopharmaceutical sector and so the impact of Brexit specifically in this area may be profound.

20 Quirin Schiermeier, "Europe is a top destination for many researchers," 21 May 2019, available online at https://www.nature.com/articles/d41586-019-01570-3

21 Quirin Schiermeier, "Europe is a top destination for many researchers", 21 May 2019, p. 590, available online at https://www.nature.com/articles/d41586-019-01570-3

22 Ernst & Young EuropaBio Biotechnology in Europe Report (2014)

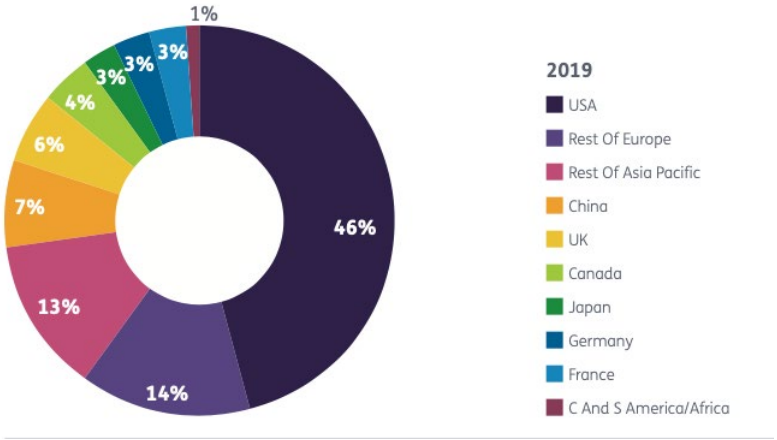
23 Ibid.

24 Franck Le Deu and Jorge Santos da Silva,"Biotech in Europe: A strong foundation for growth and innovation," *McKinsey & Company (August 2019), available online at* https://www.mckinsey.com/industries/pharmaceuticals-and-medical-products/our-insights/biotech-in-europe-a-strong-foundation-for-growth-and-innovation.

25 Franck Le Deu and Jorge Santos da Silva,"Biotech in Europe: A strong foundation for growth and innovation," *McKinsey & Company (August 2019), available online at* https://www.mckinsey.com/industries/pharmaceuticals-and-medical-products/our-insights/biotech-in-europe-a-strong-foundation-for-growth-and-innovation.

IMPACT OF BREXIT ON THE EUROPEAN BIOECONOMY

The UK has been a bright spot for the European biopharmaceuticals sector. This pie chart from 2020 EFPIA report demonstrates that UK R&D equals the total R&D of Germany and France combined, and is nearly a quarter of total EU R&D, in addition to showing the falling share of biopharmaceutical R&D being carried out in Europe broadly.[26]



Within the European Union, the UK represents the single largest biotechnology cluster, and accounting for more than a third of all EU biotechnology companies: "In fact, the United Kingdom has not only played a disproportionate part in multiple technologies and disease areas but also been home to 35 percent of all biotech start-ups in Europe since 2012."[27]

Beyond start-up activity, British biotechnology companies also attracted the lion's share of venture capital and other funding: "According to data from information provider Informa provided to the UK BioIndustry Association, the country's biotech sector attracted ~$870 million in risk capital last year, including $590 million in series B round financings — a record-breaking amount. In 2019, UK biotech attracted nearly three times as much venture capital as the sectors in France or Germany."[28] Among EU members, the United Kingdom has gone its own way in terms of domestic support for biotech, and is the consistent leader in terms of fundraising, "In Europe, the UK has maintained its pre-eminent position – accounting for just over a quarter of total VC funding in 2019."[29] At a time when start-up activity in Germany and France has been decelerating, Brexit will be a great loss to the European bioeconomy.

Loss of the UK biotechnology sector represents a goliath blow to the EU's bioeconomy. In this context, Brexit offers an important opportunity to re-invent and rebuild the European bioeconomy on a solid, sustainable foundation. At the same time the UK understands the importance of continuing scientific connectivity within Europe and has opted to continue to participate in the ongoing EU Horizon 2020 research collaboration program and is likely to contribute financially to participate on an associate basis in 2021 and beyond.[30]

26 Ibid

27 Ibid. (also noting in contrast that "biotech start-up activity in France, Germany, and Sweden has decelerated over the past few years.") See also Mark Terry, "Ranking the Top 10 Biotech Clusters in Europe, Biospace", October 30, 2019, https://www.biospace.com/article/ranking-the-top-10-biotech-clusters-in-europe/ ([T]he UK ranks at the very top in public funding, with 7,981 Horizon 2020 grants and 2,153 biopharma companies according to Bioscience and Health Technology Statistics 2018, which was published in May 2019. It ranks second in biopharma jobs, with about 121,000, and fourth in patents, with 276 granted and 549 applications in 2018."

28 Making the best of Brexit. *Nat Biotechnol* **38,** 249 (2020) https://doi.org/10.1038/s41587-020-0463-x

29 Global and Growing: UK biotech financing in 2019, UK BioIndustry Association (January 2020) https://www.bioindustry.org/uploads/assets/uploaded/cc26cb0f-3097-43f4-9b5a6d0008941b2d.pdf (Presumably 2019 investments have 'baked-in' remaining uncertainties relating to the details of Brexit and serve to underscore VC and other funders preferences for the UK biocluster.)

30 Quirin Schiermeir, "Horizon 2020 by the numbers: how €60 billion was divided up among Europe's scientists," Nature 22 December 2020 https://www.nature.com/articles/d41586-020-03598-2
("UK politicians have repeatedly stated their intention to join Horizon Europe as an 'associated country', which would enable researchers based in the United Kingdom to participate in the same way as those in the EU. There are currently 16 non-EU associated countries, which pay a mandatory contribution to the bloc's research programme in exchange for access to grants.")

LIMITATIONS ON ADVANCED AGRICULTURAL TECHNOLOGIES IN THE EU

Until the 1990's, the U.S. and Europe pursued similar approaches to advanced agricultural technologies, however harmonization of European regulatory processes in the 1990's led to critical differences in evaluation and approval of bio-enhanced or genetically engineered (GE) agricultural products, also known as genetically modified organisms (GMOs). European Union members with more strongly held views against adoption of agro-biotechnology technologies held sway. In the process, science advisors and sectoral experts lost control of the debate, which was driven by highly politicized, emotional populism that proved impossible to address on a rational basis:

> *Genomic studies of the last decade have demonstrated that a genome is not a static entity but a dynamic structure continuously refining its gene pool. So, for a scientist in genetics, the act of splicing to generate a transgenic organism is a modest step when compared to the genomic changes induced by all the 'crosses' and breeding events used in agriculture and husbandry. The molecular biology tools simply add a new precision, speed and reach to this indispensable process of species domestication. So it was a surprise for many scientists to discover that pub – lic opinion did not 'buy into' this line of thought. Some European interest groups even opposed the idea of GM crops with a religious zeal. The Precautionary Principle – which some interpret as saying that, if a course of action carries even a remote chance of irreparable damage, then one should not pursue it, no matter how great the benefits may be – gave Europeans a firm philosophical basis for saying no to GMOs. Political leaders and public servants in the Member States and the EU institutions were ill-prepared for this emotional uproar.*[31]

In sum, EU policy relating to advanced agricultural products and processes ignored all of the science, rigorous regulatory processes implemented by these same policy makers, and global empirical data on the safety of genetically engineering.

Over time the European Commission implemented labeling standards for bio-enhanced products that further demonized agrobiotechnology, where "the real benefits of the technology to agriculture and the environment were lost because consumer values were ignored. And when public acceptance and trust collapsed, serious support for the products evaporated."[32] Not surprisingly, innovative agricultural companies transitioned R&D activities to more receptive venues. While the EU has continued to support academic research,[33] there has been no meaningful progress towards a science-based regulatory process for agrobiotechnology products.

There has been markedly little progress in demystification of genetic modification to address important societal challenges sustainable development in the context of climate change and population growth.

> *Meeting the challenge to 'prove that GM crops are safe!' is not so easy. It looks like a scientific issue, but it isn't. Science can certify the existence of danger, but not its absence. Moreover scientists will continue to question any negative results that surface, and there will certainly be reward and recognition for the person who finds proof of harm. Expert contention that a 100 % GM variety approved for commercialisation is neither more*

31 Marc Van Montagu, Chairman, Institute of Plant Biotechnology for Developing Countries (IPBO) . Ghent University, Belgium "A decade of EU funded GMO research (2001 – 2010)" European Commission Directorate General for Research and Innovation, Biotechnoloies, Agriculture, Food (2010) EUR 24473 (En), 2010, p. 9.*http://www.ipbo.UGent.be http://www.psb.Ugent.be http://www.efb-central.org http://www.pubresreg.org , p. 21 – 22*

32 "Hearts and Minds," Nature Biotechnology, February 2007.

33 "Still, the results and even the existence of GMO biosafety research are often ignored in the public debate on the biosafety of GMOs. As a consequence, the already established strong basis for a science-based discussion on GMO biosafety is not fully explored in Europe or worldwide. In line with the complex public debate on the use of genetic engineering in agriculture and food production, the European Commission has been funding projects supporting science-based political decisions and improving the communication on 'green genetic engineering'." Prof. Dr. Joachim SCHIEMANN, Julius Kühn Institute (JKI) Federal Research Centre for Cultivated Plants, Head of the Institute for Biosafety of Genetically Modified Plants , "A decade of EU funded GMO research (2001 – 2010)" European Commission Directorate General for Research and Innovation, Biotechnologies, Agriculture, Food (2010) EUR 24473 (En), 2010, p 209

nor less of a health or environmental problem than its parent crop will not answer the question.[34]

Sadly, reliance on the Precautionary Principle as a policy making tool for advanced agricultural policies has proven to be a blind alley: "after 25 years of field trials without evidence of harm, fears continue to trigger the Precautionary Principle. But Europeans need to abandon this knowingly one-sided stance and strike a balance between the advantages and disadvantages of the technology on the basis of scientifically sound risk assessment analysis." While facing an intractable political environment, the European Union's own independent research concludes that GMO technologies provide no greater risks to health or the environment than conventional agricultural methods.[35]

Case Study: Stagnation of Italian Advanced Agricultural Technologies

Going back a quarter of a century, Italy led Europe in in agricultural biotechnology with over 250 experimental projects at a national level ranging including olive oil and fruit varieties. Italy's innovative agricultural sector has long since fell prey to internal EU politics over GM agriculture. In 2001, the Italian Ministry of Agriculture banned all agricultural biotechnology research trials. Despite subsequent EU decrees from Brussels that have been less negative over time, Italy has never reversed course; the curtailment of public research funding for agrobiotechnology, hamstringing competitiveness and reducing productivity of Italian companies.

In the absence of domestically produced GM products, like other EU Members, Italy became dependent on imported GM corn and soy. Far from being a GMO-free state, it is now recognized that GE agricultural products are widespread and essential inputs for "Made in Italy" exports, including pasta, regional cheeses, Prosciutto and others.

In 2014 Italian farmers and scientists appealed to Senator for Life and highly respected scientist Elena Cattaneo to weigh in on the issue in favor of science and advancing technology for Italy's struggling agricultural sector. Cattaneo responded positively, calling on Italy to adopt a science-based position favoring GE agriculture:

GE crops are not more risky than non-GE or organic ones. Moreover, the scientific community has clearly expressed the usefulness and safety of GE crops, calling for further research and testing of these products in field trials in Italy. Therefore, the so-called 'precautionary principle' should be abandoned and Member States should allow the cultivation of approved GE crops.[36]

This exchange had little apparent impact. While the EU approved limited cultivation of select GE crops based on scientific consensus, an Italian Inter-ministerial Decree officially banned planting of GE crops in January of 2015. Italy then pressed for a new exception to EU regulations to enable opt-out for non-science reasons. The EU acceded, publishing the Amended Directive in March 2015 (Directive (EU) 2015/412).

Italy's commitment to address 21st century food challenges explicitly includes agricultural biotechnology methods. In February of 2016, the Ministry of Agriculture initiated a three-year €21 Million Sustainable Biotech program for next-generation technologies,[37] seeking benefits of agricultural biotechnology with new GE techniques – and without the old GMO baggage. As Italy's Council for Agricultural Research and Agricultural Economic Analysis (CREA) asserts, this research focuses

34 Marc Van Montagu, Chairman, Institute of Plant Biotechnology for Developing Countries (IPBO) . Ghent University, Belgium "A decade of EU funded GMO research (2001 – 2010)" EC Directorate General for Research and Innovation, *Biotechnoloies, Agriculture, Food (2010) EUR 24473 (En), 2010, p. 9.http://www.ipbo.UGent.be http://www.psb.Ugent.be http://www.efb-central.org http://www.pubresreg.org , p. 21 – 22*

35 Forward, "A decade of EU funded GMO research (2001 – 2010)" EC Directorate General for Research and Innovation, Biotechnologies, Agriculture, Food (2010) EUR 24473 (En), 2010, p. 10. "The main conclusion to be drawn from the efforts of more than 130 research projects, covering a period of more than 25 years of research, and involving more than 500 independent research groups, is that biotechnology, and in particular GMOs, are not *per se* more risky than e.g. conventional plant breeding technologies." https://ec.europa.eu/research/biosociety/pdf/a_decade_of_eu-funded_gmo_research.pdf

36 Ibid, translation curtesy of the USDA Foreign Agricultural Service, p. 18.

37 Omella Bettini, "Italian Agricultural Research System Overview," USDA Foreign Agricultural Service Report, May 8, 2017, noting that: The research focuses on genome editing and cisgenesis. Minister Martina noted, 'These techniques are much different from transgenesis (insertion of a gene from a different gene pool) and will allow Italy to produce crops resistant to climate change and diseases.'" https://apps.fas.usda.gov/newgainapi/api/report/downloadreportbyfilename?filename=Italian%20Agricultural%20Research%20System%20Overview_Rome_Italy_5-24-2017.pdf

on molecular techniques and field plan phenotyping that are "far away from the GMO method."[38] CREA may be right, or Italy may be pouring new wine into old bottles.[39]

Continued political opposition at the local and regional level further complicate prospects for GM agriculture in Italy. Lacking advanced agricultural technologies, Italy has not only lost out on potential avenues for industrial biotechnology – it is unable to meet domestic demand for polenta, becoming a net importer of corn for this staple of Italian cuisine. Italy's loss is Spain's gain – as in other states where farmers are allowed to choose, Spanish farmers are choosing GM corn and now account for 90% of all EU BT corn production.

38 Ibid.

39 The jury is still out on the impact of Italy's research program which was extended in 2018 with an additional €6 million commitment over three years. Omella Bettini, "Italian Agricultural Research System Overview," USDA Foreign Agricultural Service Report, September 12, 2018, https://apps.fas.usda.gov/newgainapi/api/report/downloadreportbyfilename?filename=Agricultural%20Biotechnology%20Annual_Rome_Italy_10-18-2018.pdf