CHAPTER 2

The "Entrepreneurial State" and the Leveraging of Life in the Field of Regenerative Medicine

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Introduction: The Entrepreneurial State and Translational Medicine

Innovation has become the linchpin of industrial policy in advanced economies. It is seen as an important generator of economic growth; a mechanism for enhancing national strength through job and wealth creation. This imperative to innovate is particularly prominent in the biomedical and healthcare sectors. Biomedical innovation is being

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championed as both a source of novel treatments to address unmet clinical need and a new source of economic growth. In particular, advances in biology, such as stem cell biology, tissue engineering, gene-editing and synthetic biology, are being lauded for their potential to generate both health and wealth.

In many countries the State is seen as having an important role in facilitating biomedical innovation. However, rather than sponsoring specific innovation projects or commercial endeavours (that is, "picking winners"), state involvement today entails a more general, facilitative approach towards innovation. The economist Marianna Mazzucato (2015) has suggested that this is indicative of what she describes as the *Entrepreneurial State*, one that supports wealth-generating innovation by funding knowledge-production in labs and universities, mobilising the resources that allow knowledge and innovations to diffuse broadly, and developing strategies for technological advances in priority areas (2015, 39–40). Mazzucato calls for a reconceptualization of the roles of the State and the private sector in innovation: far from being a bureaucratic drag on innovation, she argues, the State has a track record of investing in key, innovation-underpinning research, particularly at the high-risk early stages before the private sector is willing to invest. The failure to recognize the State's entrepreneurial activities facilitates current inequitable practices whereby risk is socialized but rewards are privatized.

In the biomedical and healthcare sectors, this Entrepreneurial State activity is reflected in the Translational Medicine (TM) policy agendas of the US, Canada, Europe and the UK. TM policy aims to tackle a perceived set of challenges or barriers to the translation of basic science research into clinical therapies at the bedside (Mittra and Milne 2013). Promising new developments in biology (e.g. stem cell biology, tissue engineering, synthetic biology) are seen to have additional "translational" demands precisely because of their scientific, technical, regulatory and clinical complexities, which are far removed from traditional pharmaceutical drug innovation that has predominated in the healthcare ecosystem. TM policy has been designed to overcome the so-called "broken middle" or "valley of death" in drug development, which refers to the gap between basic science and initial invention, and downstream commercialisation and clinical utility (Mittra 2016). Various Government-supported initiatives have been launched, including: interdisciplinary research programmes that aim to foster collaborations between clinicians, researchers, and industry; the formation of research infrastructures to facilitate the gathering and exchange of data; mechanisms for securing

intellectual property rights; and adjustments to governing systems such as regulatory frameworks. Hence, driven by promissory visions of health and wealth, the TM policy agenda has become an organising principle for reconfiguring the biomedical research landscape and healthcare sectors. New alliances are being forged, new collectives are emerging, and existing ones are continually being adapted. These changes characterize what has been called the "new health bioeconomy" (Mittra 2016).

In this chapter, we critically explore the reconfiguring of the biomedical research landscape and the healthcare sector in relation to the emerging field of regenerative medicine (RM) within the United Kingdom. RM—a field that is emerging from new developments in biology—has generated high expectations about its future "health and wealth" potential, and many governments have incorporated the field within their industrial policies. It thus represents a rich case study for examining the "Entrepreneurial State" and its role in shaping an emerging health bioeconomy. We examine some of the major, state-supported supply-side measures that are being implemented within the field of RM. New organizational forms are taking shape and existing infrastructures are being adapted within a collective initiative to establish a RM industry for "health and wealth". We illustrate that this entails: the establishment of "business-focused" innovation accelerator agencies; the promotion of interdisciplinarity; the reconfiguring of governance mechanisms, and the repurposing of the healthcare system as an innovation asset. Building on recent social science studies of value practices in the life sciences and medicine (e.g. Dussauge et al. 2015), we examine the values that are invoked within this collective initiative. In so doing, we argue that the power of the Entrepreneurial State in reconfiguring the bioeconomy derives from its capacity to appeal to diverse values, and consequently, mobilise and orientate actors into a common political project aimed at creating both health and wealth. We also highlight some of the tensions and countervailing processes at play in this process.

Methods

This chapter draws on both primary and secondary data collected as part of the UK ESRC-funded "REGenableMED" project, which is exploring the social dynamics of innovation in RM. Data include over 80 interviews with a range of stakeholders and practitioners in the field of RM, including stem cell scientists, clinicians, regulators, consultants, public

officials, and representatives of commercial organizations, patient associations, and charities, many of whom are directly involved in the initiatives that form the focus of this chapter. Secondary data include publicly available government reports into RM, public agency meeting minutes, clinical trials databases, and company reports.

Our conceptual framework draws on recent work on value-practices in the life sciences (Dussauge et al. 2015) to explore the values that are appealed to and enacted within specific initiatives aimed at facilitating RM. Historically, the distinction has been made between value as it is understood economically (reflected in, for instance, the price of goods), and value(s) as they are understood sociologically (that is, shared standards or assumptions about what is important). However, we wish to avoid making an a priori distinction between economic value and other types or regimes of value, and instead focus on how actors articulate, both implicitly and explicitly, what they count as desirable or worth caring for or "knowing". As Dussauge et al. rightly note (2015, 10), a multiplicity of values may be enacted—both implicitly and explicitly—within a common project; these values may align or may be in constant tension or flux. This problematizes any attempt to strictly delineate the economic and the social components of value. In our analysis, we demonstrate that certain values relating to commercialization and global competitiveness feature heavily in many government-supported initiatives, but also that other values are invoked alongside these, reflecting the diverse communities of expertise and different practices that are being mobilised.

Regenerative Medicine and the Leveraging of Life

RM represents a heterogeneous collection of emerging technologies, techniques and practices. What counts as RM has varied somewhat over the last decade (Webster 2013), but usually it is defined as that which "replaces or regenerates human cells, tissues and organs, to restore or establish normal function" (Mason and Dunnill 2007, 4). In general terms it refers to the use of tissues, cells (embryonic stem cells, induced pluripotent stem cells, and adult stem cells) or genes to treat or manage illness and disease, and for this reason it is considered to be distinct from more conventional drug or device-based therapies. Advocates proclaim that the regenerative capacity of cells, tissues and genes means that the field has the potential to produce curative treatments for a range of conditions for which there is currently unmet clinical need, including

cancers as well as cardiovascular, neurological, and autoimmune diseases. In addition to the promissory expectations about its clinical value, RM has become the focus of considerable optimism about its economic potential. Policymakers and industrialists, in particular, believe that RM may precipitate the creation of a new wealth-generating industry. In several countries, RM has become entwined with state initiatives aimed at generating a high-wealth, knowledge-based economy. Japan, for example, is aiming to take advantage of its strengths in stem cell science and has positioned RM as one of the pillars of its economic growth strategy (Ogawa 2015). Canada and several US states—particularly California—have made similar moves, and in the UK, RM has been named as one of the "Eight Great Technologies", which will propel the UK to future growth (Willetts 2013).

Currently, there are hundreds of clinical trials worldwide for RM therapies, mostly at clinical phases I and II. Although a few RM products have received regulatory approval in some jurisdictions, none have been widely and routinely adopted within healthcare systems. The field, then, is still in its infancy. Indeed, the complexity of cell, tissue and gene-based therapies presents a range of scientific, technical, regulatory and reimbursement challenges for investigators and manufacturers working within the field, which raises concerns that the translation of promising scientific developments into useful health- and wealth-generating RM therapies will be laboriously slow (Gardner et al. 2015). Producing RM therapies is often labour-intensive, and as yet there is little in the way of automated manufacturing platforms or established standards (Tait and Banda 2016) that would enable cost-effective scale-up of production and successful delivery to the clinic. The cost of maintaining appropriately licensed manufacturing facilities is high, and investigators are having to develop new assays for quality, safety and potency in order to meet regulatory requirements. Many promising RM therapies are likely to be, at least initially, high-cost, and this may create challenges for securing reimbursement, particularly for novel therapies for which there is little associated data on their cost-effectiveness and long-term clinical benefits (Malik 2014, 2016). RM therapies may also require specific skill-sets and supporting infrastructure that may be difficult to integrate with workflows in existing clinical settings (RMEG 2014).

It is in response to these challenges that several governments have launched strategic initiatives to facilitate the translation of RM therapies. These generally entail the establishment of innovation "accelerator"

agencies (such as the Canadian-government-supported Centre for the Commercialization of Regenerative Medicine and the Californian Institute for Regenerative Medicine), funding initiatives to support research and to assess and adapt existing governance structures, notably regulatory frameworks and health technology assessment methodologies. In the UK, which serves as useful exemplar for this type of activity, the Government established the Cell and Gene Therapy Catapult innovation agency, funded the formation of an interdisciplinary collaboration—the UK Regenerative Medicine Platform—to tackle particular scientific and technical challenges, and launched a review of current governance structures, with the aim of assessing and potentially introducing "accelerated access" to innovative clinical treatments. Additionally, the National Health Service (NHS) is being encouraged to become a "more innovative" adopter of these new technologies, and a variety of activities have been instigated in an attempt to bring this about. Each of these can be seen as mobilising particular communities of expertise: groups of experts with skill-sets and professional backgrounds deemed to be "innovation-facilitative".

More broadly, these developments reflect a supply-side, neo-liberal strategy, as opposed to the demand-side Keynesian approach, that underpins the development of new products to the market—in effect the socialization of economic costs and risk. In this context, the State essentially intervenes in funding the early stage development of expensive new therapies (when the risk of failure is high), and then must purchase these very expensive therapies, if they make it to the clinic. State intervention, therefore, is aimed at facilitating the development of privately-owned products. In effect, public investment is converted to private profit.

In the remainder of this chapter we examine these four key state-sponsored activities. We describe the rationales that have been used to justify them and their socio-technical networks. In particular, we consider how the Entrepreneurial State is implicated in the emergence of the "new health bioeconomy", and discuss the invoking of values that relate to profitability, innovativeness, cost-effectiveness, public good, and patient-centredness, which serve to legitimate this process and drive the commercial and policy value of RM. However, such legitimacy depends on the interplay of different actors whose localised practices of valuation work in different ways to prepare RM products for the market.

The Commercialisation Imperative: The Cell and Gene Therapy Catapult

Over the last 5 years consecutive inquiries have sought to comprehensively assess the UK's capacity to support a RM industry, and this has driven the launch of particular innovation initiatives (RMEG 2014; HoL 2013; MRC 2012; BIS 2011). Generally, these inquiries emphasize the UK's significant potential to become a "world leader" in RM due to its world-class universities and hospitals, and its ability to attract and retain highly-skilled scientists and engineers. Realising this potential, the reports argue, requires a coherent, government-supported strategy to align existing infrastructures and create new collaborations to solve key scientific and technical challenges.

The inquiries reaffirm the importance of biomedical innovation in generating health and wealth, and they tend to advocate a particular *mode of innovation* that explicitly entails *commercialization*. That is, through the development of products and securing of intellectual property, it is expected that publicly funded research will eventually attract sufficient private investment, ideally from large multinational companies, to take the product to market. This commercialization imperative is most obviously reflected in the establishment of the Cell and Gene Therapy Catapult (CGTC).

The Cell and Gene Therapy Catapult was established in 2012 by a grant from the Technology Strategy Board (now Innovate UK), a public agency that reports to the Department for Business, Innovation and Skills (now part of the new Department for Business, Energy and Industrial Strategy). It is based in London, currently has approximately 100 staff, and its stated purpose is to: "Lead the UK cell therapy industry to create health and wealth from the UK's outstanding science foundation" (CGTC 2015). It is expected that long-term funding will be maintained by continued public investment, competitively-won contracts with businesses, and through its collaboration in both private and publicly-funded research projects. As with equivalent agencies in Canada (CCRM) and California (CIRM), the CGTC is an autonomous body with its own decision-making capacity. Its board of directors and management and advisory teams include extensive experience in industry, reflecting a strong emphasis on commercialization. The members of the management team, for example, have professional backgrounds in the life sciences industries, and the advisory group includes representatives

from large companies including Johnson & Johnson, GlaxoSmithKline, AstraZeneca and GE Healthcare. In effect, a particular orientation to innovation (i.e., commercialization) has been institutionalized within the management structure of CGTC (Gardner and Webster 2017).

The commercialization priority is also reflected in the operations of the CGTC. The catapult functions like a consultancy. It provides assistance to manufacturers, clinicians and scientists on a range of innovation challenges: IP and legal assistance, detailed technical assistance on manufacturing processes, assistance with clinical trial design and adherence to regulatory frameworks, and assistance with reimbursement and commissioning challenges. CGTC staff also regularly visit UK universities in order to identify promising new developments, and facilitate collaborations between academic investigators, industry and regulators. Currently it is involved in over 40 RM projects. Its role involves the assessment of IP potential, delineating the "value proposition" of prospective RM products, how they can be developed and their potential markets. Through these activities, the CGTC coordinates what might otherwise be diverse research and clinical interests within RM into particular innovation pathways where commercialization is a main objective.

According to our interviewees, the commercial expertise of the CGTC provides it with considerable authoritative weight, and having CGTC involvement in their projects lends credibility that can lead to further investment from other funders, including other public funders. Here the CGTC is generative of important reputational value in addition to providing technical and organizational assistance. As one interviewee (a CEO of a small RM company) stated:

> The Catapult were important to us… they gave [our company] a vote of confidence by putting their support behind us… So that was a huge boost for us and a tick in the credibility box. It enabled us to get the [public agency] grant at that time.

The CGTC appears to have been endowed by stakeholders with the authority and legitimacy to judge and improve the commercial viability of RM projects, enabling it to "de-risk" these projects for other investors, an important role for the Entrepreneurial State in fostering new markets. It is worth noting in the above example that the reputational value of the CGTC led to further public funding to facilitate commercialization

(Gardner and Webster 2017). This is indicative of a context that equates public interest with innovation, and innovation with commercialization.

The ultimate realization of market value within RM requires socio-technical systems for producing, circulating, and exchanging RM products as commodities. The CGTC is enabling of these systems by providing assistance to manufacturers on logistics for cell and tissue transportation and, more significantly, with the construction of the large cell and gene therapy manufacturing centre (in Stevenage), at an initial cost of £55 million. This facility is intended to provide the capacity required to produce the quantity of RM products needed for phase III trials and commercial market supply. Companies will be able to rent space within the facility, take advantage of CGTC expertise, and therefore reduce their own costs by not having to build their own research infrastructure.

We also see other values, beyond the envisaged realisation of commercial value, reflected in official CGTC accounts of their activities, particularly in their annual reports. *Clinical value*, for example, is reflected in the CGTC rationale for supporting specific projects, which makes reference to considerable clinical need in particular disease areas (CGTC 2014). These reports also reflect what might be called *pathfinding value*, that is, a value that derives from creating new pathways to the clinic that can subsequently be used by other actors (CGTC 2014). In the life sciences, unlike many other technological fields, there is no advantage in being the first to build a route to market, given the high costs and risk of failure, so the CGTC is seen as having an important role in this context. We also observe what could be called *global competitiveness value*, which is most obviously illustrated by the official vision of the CGTC: "For the UK to be a global leader in the development, delivery and commercialisation of cell and gene therapies" (CGTC 2016). These qualities—satisfying clinical need, pathfinding, and global competitiveness—are framed within official accounts as being *valuable* in themselves and therefore provide legitimacy and motivation for CGTC activities.

The CGTC is an example of a community of expertise that has been mobilised to facilitate RM, and has, according to our respondents, been relatively successful so far. It positions itself with reference to a broad range of values, but it is the value of commercialization that is prominent in its interactions within the field of RM. We see priority given to this in its structure, its consulting-like work with stakeholders, and in its establishment of a new manufacturing centre. It represents an important

means by which the State is attempting to facilitate RM with the creation of a publicly funded but autonomous agency with its own industry-oriented and commercially responsive decision-making capacity.

The Promotion of Interdisciplinarity

Interdisciplinarity broadly refers to mechanisms of knowledge production that traverse conventional disciplinary boundaries, and which have often been established to tackle specific scientific, technical or societal problems (Gibbons 1994). It has been championed as an important facilitator of R&D and as a crucial driver of innovation for at least the past two decades, particularly within biomedicine as part of the broader TM policy agenda. According to Barry et al. (2008), its emergence reflects a perception that the problems encountered in innovation are too complex to be managed within one disciplinary framework, alongside the view that science and innovation need to be accountable to the public. This perception is particularly apparent in the European Commission's Responsible Research and Innovation framework, which proclaims that accountability is best achieved if science and innovation are directed towards user or societal need, which is more likely to be seen if multiple perspectives, including potential end-users, are actively informing R&D and innovation processes (Von Schomberg 2013).

Interdisciplinarity can broadly be seen, then, as an attempt to incorporate a wider range of values into innovation activities. It has gained further traction in regard to the "innovation challenges" that characterise RM—expanding and directing the growth of cell lines, creating cost-effective manufacturing processes, navigating regulatory and reimbursement hurdles, etc. These are all complex problems that have been deemed to be in need of interdisciplinary problem-solving (MRC 2012). Specific government-supported initiatives have been launched to encourage and support interdisciplinarity within the emerging field, and as a result, interdisciplinarity (and new communities of expertise) has become institutionalized. It is, as Mittra (2016) notes, becoming increasingly consolidated in "bricks & mortar" infrastructural forms (indeed within the CGTC itself).

Academic networks are also being redrawn in accordance within this emphasis on interdisciplinarity. One example is the establishment of the UK Regenerative Medicine Platform (UKRMP) which, like the CGTC, was launched in response to the government inquiries into RM. The

UKRMP was established in 2013 by several of the UK research councils with £25 million in funding. The official, stated aim of the platform is to address "key translational challenges in regenerative medicine" via:

> …five interdisciplinary and complementary research Hubs that collectively provide a national resource through the generation of new tools, protocols, and resources that can be utilised by other UK research groups in both academia and industry… [The UKRMP is] a cornerstone of the broader and integrated UK research strategy…which is seeking to support high quality UK research activity and translational activity that will help deliver the great promise of regenerative medicine to benefit both patients and future economic growth. (UKRMP 2012)

Here we see that the official rationale for establishing UKRMP makes reference to several values: *clinical value* and of course, *the value of commercialization itself*—also reflected in statements such as "help[ing] to de-risk future commercial investment" (UKRMP 2015, 4). It represents a community of expertise, then, which is oriented towards a particular, commercialization mode of innovation.

Other values are also articulated. These include the value of safety, and also epistemic/scientific value, manifested in practices aimed at creating shared infrastructures and standards that transcend disciplinary boundaries. This is exemplified in the following rationale of a leading scientist within the platform:

> Safety is obviously paramount, and 'safety' is about good science. It will come from the science… 'Safety' requires a holistic approach – bringing together pharmacology, pathology, physiology… (Interview field notes)

These values are reflected in the structure of the platform, which consists of five hubs, each being a multi-institutional, interdisciplinary collaboration involving academic scientists from various disciplinary backgrounds. Two of the hubs focus on clinically-oriented biological problems; two are exploring technical challenges "further" along the translational pathway; and one is focused on identifying safety challenges and methodologies to assess risk. This last hub brings together a particularly diverse array of specialisms (stem cell biology, biostatistics, nanochemistry, multimodal imaging, and clinician disciplines such as nephrology and hepatology), and it reflects an emphasis within the UKRMP on what can be called *clinical safety* value.

The UKRMP, we suggest, is an exemplar of the new life sciences academic networks within advanced economies. These are networks of expertise that are increasingly interdisciplinary, appear to reflect a range of values, and are emerging from often government-supported translational medicine initiatives aimed at facilitating a wealth-generating industry. A similar example in the US is the National Institutes of Health (NIH) Road Map Initiatives launched in 2004 with the aim of "fostering collaboration" for "high-risk/high reward research" (NIH 2011). Such initiatives are disrupting conventional disciplinary boundaries and conventional institutional and professional norms (Mittra 2016). The rise of the "clinician-scientist", perceived as being particularly capable of moving between conventional disciplinary spaces and the clinic, is an example of this (Wilson-Kovacs and Hauskeller 2012).

Reconfiguring Governance Mechanisms: Accelerating Access to Regenerative Medicines

For much of the second half of the twentieth century, promising therapeutic medical technologies were regulated under either pharmaceutical or medical-device frameworks. Both emerged as politically-supported governance mechanisms in response to much-publicized medical scandals: the thalidomide scandal in respect to pharmaceuticals, and a spate of defective cardiac pacemakers in respect to medical devices. Regulatory agencies such as the US's Food and Drug Administration (FDA) and the European Medicines Agency (EMA) were thus mandated to protect citizens, and the resulting regulatory frameworks, which have been subject to ongoing incremental adjustment, impose complex requirements on manufacturers to demonstrate the safety and efficacy of their products before they can be placed on the market. The consequence of these requirements is that bringing promising therapeutic technologies to the market is a costly process that takes considerable time. In response to pressure from industry and patient groups, regulatory provisions have been launched by both the FDA and the EMA to provide expedited access to promising therapies in certain circumstances. These include the "orphan drug" legislation and "fast-track" drug approval processes, which provide incentives for manufacturers to innovate in areas of considerable unmet clinical need (Milne and Tait 2009). With the adoption of such measures, the role of regulators is recast not only as protectors of citizen well-being, but also as facilitators

of innovation. The potential conflict between these two positions has not been acknowledged.

Developments within RM have tested the limits of conventional regimes. In both the US and Europe, it has been decided that RM technologies are sufficiently incommensurable with conventional frameworks to warrant new frameworks that both protect patients and facilitate innovation (Omidvar et al. 2014). Hence, after considerable debate and consultation, EMA established the Advanced Therapies Medicinal Products (ATMP) framework, and the FDA has established its Cellular and Gene Therapy Products framework, both of which have been tailored to mitigate the particular safety and quality-related risks presented by cell and gene-based medicines, while also providing what is intended to be an innovation-facilitative degree of stability and harmony to the emerging field. Currently, however, few RM therapies have been approved within these frameworks (eight ATMPs have received market authorisation by the EMA). This has fuelled calls to explore additional measures to accelerate translational medicine (RMEG 2014). A more permissive regulatory regime, it is argued, will encourage the investment required to tackle technical and scientific challenges related to the complex biology of the field (HoL 2013).

The "reimbursement hurdle" has also been identified as a problematic governance mechanism (RMEG 2014; HoL 2013). Of those ATMP products that have received market approval, none have been widely adopted, as manufacturers have struggled to secure commissioning arrangements from payers. In most jurisdictions, commissioning decision-making is guided by a formal Health Technology Assessment of the candidate therapy, in which cost-effectiveness and clinical benefit are determined. In the UK, one influential report (RMEG 2014) suggested that such mechanisms could unfairly disadvantage novel regenerative medicine therapies due to their potentially high upfront costs and lack of longer term data.

Hence, there has been a concerted, government-supported movement in several countries towards additional mechanisms that would "accelerate access" to RM therapies. The most radical of these is Japan's RM legislation that allows "conditional marketing authorization". In effect, it enables a product to be placed on the market after completion of phase II clinical trials once safety has been demonstrated and efficacy has been predicted. The product is then subject to close post-market surveillance to monitor safety and obtain efficacy data, and the manufacturer must

then reapply for "full" marketing authorization within 7 years (Sipp 2015). During this time, patients pay a significant proportion of the costs (Nature Editorial 2015). Similarly, the EMA is piloting an adaptive pathways approach that is intended to allow for "early and progressive patient access to a medicine" (EMA 2016) in the case of new medicines for which there is unmet clinical need and which are intended to treat chronically debilitating or life-threatening conditions. This would represent a significant change compared to already in-place "fast-track" provisions (Mittra 2016).

Similarly, the UK government has launched the Accelerated Access Review with the intention to "speed up access to innovative drugs, devices and diagnostics for NHS patients" (GOV.UK 2016). It has been tasked with examining three areas of reform: existing regulation and the potential for quicker methods of assessing safety and efficacy; reimbursement and possible adaptation of health economic systems to better accommodate recent technology advances; and clinical adoption and better ways to support and drive innovation within the NHS (DoH 2015). The initiative has an external advisory group whose composition reflects an apparent commitment to industry-orientated innovation, but also a commitment to including a wider range of values and perspectives. It includes representatives from industry and from patient-advocacy and charity groups, senior academic clinicians, and regulatory experts.

The review group's interim report (Accelerated Access 2015) is based on a number of propositions. The first is that "patients should be given a stronger voice at every stage of the innovation pathway" (2015, 11). This can be achieved by "directing innovation towards the outcomes that matter most to patients" and taking into account the "patient appetite for risk". As a next step, the review will thus "explore the scope for identifying and codifying patient-led outcome measures" (2015, 12). Here we see a clear attempt to align an early marketing of products with patient-centred values defined primarily in terms of their preparedness for risk, which assumes that patients are less risk-averse than the regulatory system has previously been on their behalf. Other values are invoked in the remaining propositions. Proposition two is "getting ahead of the curve", and includes a set of potential measures aimed at ensuring that the UK remains on the leading edge of innovation and remains a "go to" place for industry (2015, 13). Here we have the invoking of *global competitiveness value*, and *commercialization value*. Proposition three, "Supporting all Innovators", invokes "innovation" as a value in its own

right that requires constant support, via, for example, creating a more flexible and streamlined health technology appraisal process. Proposition four, "galvanising the NHS", suggests ways in which the NHS can be improved to better support innovators and provide more space for patient-involvement. (This will be more broadly discussed in the following section.)

The accelerated access review, then, represents a significant government-mandated initiative to adjust governance mechanisms to make them more facilitative of innovation. As Mazzucato has noted in regard to earlier orphan drug "fast-track" regulatory provisions, such initiatives are an important means by which the Entrepreneurial State can attempt to "de-risk" innovation and support the formation of new markets in biomedicine (Mazzucato 2015, 81). What we see within this UK initiative is that a range of values are invoked to justify this "de-risking" activity, several of which—such as commercialization value and global competitiveness value—are actively championed in relation to other TM initiatives such as the CGTC.

Reframing the Healthcare System as an Innovation Asset

Healthcare providers such as hospitals have always played a key role in innovation. However, over the last decade TM initiatives have been launched in an attempt to enhance and make more visible the hospital's role in innovation. In 2006 in the UK, for example, the National Institute for Health Research (NIHR), a government body, was launched to coordinate research across the NHS. The NIHR describes itself as "improving the health and wealth of the nation through research". A major NIHR project was the establishment of 11 Biomedical Research Centres (BRCs) across the UK. Each represents a partnership between leading NHS research hospitals and universities, and they receive substantial levels of funding to create and consolidate innovation-facilitating dynamics, such as interdisciplinary collaboration. The BRCs are intended to "drive innovation", "translate advances in biomedical research into benefits for patients" and "provide a key component of the NHS contribution to our nation's international competitiveness" (NIHR 2016). There is, then, a clear articulation of values: *innovation as a value* in its own right; *clinical value;* and *global competitiveness value*.

Despite such initiatives, there is an ongoing discourse in UK policy circles in which the hospital, and the wider healthcare system, is

represented as being a hindrance to innovation. For example, recent government-supported reports into the UK's readiness for RM (RMEG 2014; HoL 2013; BIS 2011) have stated that existing hospital workflows present a significant hurdle to the uptake of clinical developments in RM, which require new skill sets and supporting infrastructures. There is, then, ongoing pressure to make the NHS more conducive to, and supportive of, innovation.

This is exemplified by the fourth proposition of the Accelerated Access Review, "galvanising the NHS". The review notes that the NHS is widely perceived to be too slow in adopting new technologies and is resistant to change. In light of this, various initiatives have been proposed, such as: providing clear incentives to induce innovation leadership among particular NHS organisations; an earmarked fund or specialized supplementary funding to facilitate the implementation of promising technologies; and making use of clinical leaders by encouraging them to act as "champions of change" (Accelerated Access 2015, 20–21).

These proposed changes would align with current NHS strategic objectives. In 2011, a specific innovation strategy for the NHS was published, titled *Innovation*: *Health and Wealth* (2011). One outcome of this was the formation of the Government-supported regional Academic Health Science Networks in an attempt to create better linkages between the NHS, academia and the private sector, and ensure that healthcare delivery is better aligned with clinical research (NHSE 2016a). Making the NHS more supportive of innovation has also been identified as a priority in NHS England's *5 Year Forward View*, which outlines the official strategic trajectory of NHS England (NHS 2014). This led to the establishment of seven NHS England "test-bed" sites, which are being used to test new clinical delivery models based on novel combinations of interconnected technologies (NHSE 2016b).

The NHS, then, is being reimagined in official discourse as an important source of innovation generating "health and wealth", as well as being a provider of universal healthcare. Consequently, various government-supported initiatives have been launched to reconfigure elements of the healthcare system, particularly hospitals, in ways that are perceived to be more facilitative of innovation. New research infrastructures are being established, interdisciplinary collaborations are being actively encouraged and strengthened, new expectations are being placed on health professionals, and new roles, such as the "research champion", are being created. Within this activity is a clear articulation of clinical value,

the value of innovation, and of course, global competitiveness value. In effect, the NHS, as with healthcare providers in other countries, is being *instrumentalized as an innovation system*.

Discussion and Conclusions

Government-supported TM endeavours are instrumentalizing biomedical R&D and the healthcare sector in the name of "health and wealth". The formation of accelerator agencies such as the CGTC, the institutionalization of interdisciplinarity, the adjustment of governance frameworks, and the repositioning of healthcare providers as innovators, constitute a significant reconfiguring of the biomedical landscape. Mittra (2016) has described this as the new health bioeconomy, in which novel therapies emerge from new innovation pathways involving heterogeneous actors and interests. Who these actors are and how they are aligned will foster forms of clinical innovation that might reflect traditional distinctions of public vs private (health) goods, but increasingly are seen to reflect a hybridised relation favouring a wealth-generative bioeconomy.

The Entrepreneurial State is actively championing and enacting a particular mode of biomedical innovation that entails commercialization. This is reflected in the establishment of commercialization-oriented accelerator agencies such as the CGTC that draw on considerable expertise from industry and commercial enterprise. There is, as illustrated above, a clear prioritisation of commercialization value in these translational medicine endeavours, and this is closely tied to the value of global-competitiveness—actively invoked in all the initiatives explored above. In effect, this Entrepreneurial State involvement in driving the new health bioeconomy is a form of nation-building driven by promissory visions of health and wealth: state resources are being redirected into innovation-facilitating activities in order to create future wealth-generating markets. However, it remains open to doubt that the capital generated by such activity is in some way bounded within a UK-specific bioeconomy, given the mobility of capital (and its returns) in a global economy. It is likely that an RM industry would entail a variety of markets, characterised by different technological platforms, business models and regulatory pathways. However, in broad terms, the envisaged RM markets will align with what Aspers (2007) refers to as fixed-role, standard-based markets: buyers are expected to be national health services and health insurers, while sellers are expected to be large pharma companies with

the resources necessary to obtain marketing authorisation, and which have swallowed up smaller, specialist companies that drove the initial development of the project. The status of the RM therapies themselves (especially their status as "safe" and "clinically effective") will derive from their adherence to standards entrenched in regulatory provisions.

This envisaged market raises some important issues relating to the State's role in attempting to serve as a broker between public and private good. In effect, large companies stand to profit significantly from products whose original development was, to a considerable extent, funded with public resources. National health systems such as the NHS will be expected to buy what are likely to be high-cost products whose development they had been repurposed to facilitate. There is, then, a socialization of risk and a privatization of rewards. Mazzucato notes that such a situation exacerbates inequality, and that current taxation would fail to sufficiently compensate the state for its investment. She suggests several measures for addressing this injustice: the establishment of a national innovation fund in which royalties from state-supported technological breakthroughs could be paid; the State could grant income-contingent loans and equity; and the establishment of state development banks. Currently, none of these options have been mooted in the UK for RM.

The pursuit of "health and wealth" in RM involves the delegation of innovation-facilitating, "de-risking" work to particular communities of expertise, and a range of actors are therefore involved in the creation of new innovation pathways. Mittra suggests that this complex ecology of the new health bioeconomy provides openings for the enactment of a multiplicity of values that, in the past, may have been excluded from innovation processes, values that may inform and shape innovation processes. To what extent such values will actually be enacted as the RM field unfolds is uncertain, but our assessment of the current situation is that this delegation to communities certainly involves the invoking and articulation of various values, in addition to those relating to commercialization and global competitiveness. These include, of course, values relating to safety, innovation as a value in its own right, and also patient-centeredness as a value. We suggest that the power and influence of the translational medicine agenda derives from its capacity to appeal to, and ultimately legitimate, such diverse interests, and consequently mobilise a range of actors (industry, scientists, clinicians and patients) into a common project aimed at generating "health and wealth".

Indeed, the example of RM provides valuable insights into the mechanisms by which an essentially neo-liberal, market-creating (and sustaining) political project gains a sense of legitimacy among various groups. In light of this, it is necessary for social scientists to examine which groups are being excluded from the rewards of such a project, and whose aims and interests are elided as governments engage in nation-building via the deployment of supply-side policy. It is worth noting that in England, this translational medicine agenda is being deployed at a time when public funding is being withdrawn from social services, and when health providers are grossly underfunded. (Again, it is important for social scientists to be attentive to the ways in which hospital managers and clinicians respond to the innovation imperative in such a climate.) As the field unfolds, it is also necessary to be attentive to how particular values are enacted in specific settings. "Patient-centredness" and the emphasis on "patient empowerment", for example, can be mobilised as a means of disciplining patients into particular neo-liberal technological projects (Gardner 2016). More generally, if the societal goal is to maximize health and well-being of citizens, it is necessary to ask whether public funds might be more usefully deployed elsewhere, rather than towards the instrumentalization of biomedical R&D and the health sector in the name of commercialization. Finally, it is important to note that the four state strategies described above, toward which significant public funds have been directed, do not guarantee "wealth", for success in the market-place requires customers prepared to buy the products, either through reimbursement (via insurance or public-sector procurement) or through private sale. Underpinning by the neo-liberal state only goes so far.

It should also be noted that the government-supported activities outlined above have encountered some resistance from particular groups, which themselves reflect various, potentially conflicting values. Clinical groups, for example, have shown some resistance to the commercialization mode of innovation that is embodied in the CGTC. More generally, it can be questioned whether such a mode is likely to render public health gains that could be secured through less commercial routes. Relatedly, another government-funded institution, the UK Stem Cell Bank, has received criticism that its policy of only providing non-exclusive licences for the use of deposited stem cell lines—a policy which is intended to support open science (and which thus enacts scientific value)—will discourage commercial investment in the field. Furthermore, despite the optimistic discourse on

interdisciplinarity, interdisciplinary organizational forms have been difficult to operationalize. A recent study has noted, for example, that interdisciplinary grant proposals are much less likely to receive funding (Bromham et al. 2016). Proposed governance changes to accelerate access to innovative medicines have also received criticism. A group of scientists, for example, have voiced concern about the assumptions underlying the EMA's Adaptive Pathways pilot project, particularly the apparent assumption that existing frameworks stifle innovation and are "bad for all parties" (Epha 2016). Similarly, a recent *Nature* editorial suggests that such initiatives will create a plethora of safe but clinically ineffective therapies (Editorial 2016). There are, then, tensions and countervailing processes at work within the emerging new health bioeconomy. Its emergence may be driven by powerful government-supported initiatives aimed at generating health and wealth, but it will inevitably entail a set of entangled and contested processes in which a multiplicity of conflicting values will be enacted so that assembling and leveraging such values in order to drive the translational process in RM is, and will remain, a challenge for the Entrepreneurial State.

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