Cancer is a complex, heterogeneous disease, driven by multiple molecular pathways. There are hundreds of known oncogenes, which arise in myriad combinations, making every case of cancer a rare disease. As a result, traditional, high cost, tertiary centre clinical trials are reaching the limits of their power, even with their recent adaptive and stratified innovations. Here we explore how to repurpose the whole cancer care system, using stratified outcome registries, to create a system-wide continuous learning loop. The learning starts by capturing and aggregating molecular markers, treatments, and outcomes from every individual. This data will provide invaluable insights into the comparative effectiveness of approved therapies and dosing schedules for patients with a given phenotype. For patients being treated experimentally with off-label drugs and cocktails, it will yield early signals on promising new therapies, which can then be efficiently validated in adaptive and stratified trials. Exceptional responders and non-responders at every stage can be studied in depth to advance our understanding of cancer biology and treatments. The patient throughput, and so research power, of such a system is orders of magnitude more than that of traditional trials, and the learning rate orders of magnitude faster. Because the bulk of this data is harvested from routine clinical practice, the cash investments required are modest. However, this model will require profound changes in behaviors across the system to encourage collaboration and align incentives. A trusted global data consolidator is needed to develop and run the underlying information infrastructure, and share its benefits fairly across all stakeholders. We explore how to structure the incentives to offer compelling benefits for all participants and outline the important role that national healthcare systems can play in its establishment.
Introduction

We are beginning to understand the molecular mechanisms underlying cancer. Many new therapies are in development using this knowledge – cancer drugs are 20% of phase III trials. Where we have matched the right drug and patients, treatment has been transformed as in CML thanks to Gleevec. Repeating this success is proving hard. Many possible mutations can occur. They appear in many combinations. The disease in a single patient is often heterogeneous – different cancer cells have different mutations, and their progeny continue to mutate. Cancer, it turns out, is a highly complex and adaptive set of rare genetic diseases.

An analysis of Lawrence et al 2014 illustrates how complex the challenge is. Of the hundreds of driver genes discovered, only 13 are mutated in more than 5% of patients across cancer. Most are mutated at frequencies around or lower than 1% of patients. Unique mutation pairs – useful for combination therapy - are even rarer, as we have explored previously2 [Marty Nature Reviews]. This doesn’t even consider that genes can be mutated in many possible places, and that the clinical utility of each of these allelic variations needs to be understood. We will also have to understand the impact of regulatory mutations and immune competence, for which we are only just beginning to develop the tools to study at scale, let alone understand their clinical impact.

Conventional clinical trial designs, developed at a time when nobody understood the molecular complexity and diversity of cancer, have reached a point of diminishing returns. First, they rely on an assumption that phenotypically similar patients have the same underlying disease, which we know is false in the vast majority of adult cancer3,4. Second, the crude population-based statistics they produce provide little guidance about which therapy is most effective in a given patient. A traditional trial provides little insight, and even a stratified trial only gives insight for a few factors. Third, many valuable drugs have almost certainly been abandoned not because they didn’t work but because the trial design was incapable of identifying the right subpopulation of patients who could benefit. The converse is also true: such trials expose large numbers of patients to drugs from which they do not benefit5 [ref. IOM]. Another challenge to the conventional approach is economic. There are too many rational combinations of targets, drugs, dosages, and patient profiles to explore through the rigid, slow, and expensive trials scripted by the US FDA and European regulators. Costs for late stage oncology trials are now greater than $75K per patient, and the total cost of single indication late stage trials runs in the hundreds of million (some would argue billions)6.

Outside the major tumours and most common mutations there simply is too small a market for pharma to justify the commercial randomised trial investment. Unless we find new ways of working, we will fail to develop licensed therapies for patients with less common cancers, even if they have drug-able mutations. Inevitably, this asymmetry has led to extensive off-label use of targeted therapy in systems such as the US where payers will support it, especially in advanced patients. Sadly, information from such experimentation is seldom captured for the greater good.

Pan-cancer non-silent mutation frequency (%)

Figure 1: Open reading frame mutation rate over 21 cancers (from appendices of Lawrence et al, Nature 2014). Only 141 genes with mutation rates >1% shown.

> 5% rate
- 13 genes

2% to 1% rate
- 78 genes
(not shown: another 120 genes with mutation rates <1%)

Lawrence et al. overall false positive risk (Q) estimate:

- Q<1%
- Q<10%
- Q>10%

Lawrence et al. Nature 2014 - mutation rate is straight average over 21 cancers
The limitations of traditional trials in cancer have spurred several innovative approaches, notably adaptive trials, basket trials and umbrella trials. But while these designs improve efficiency and are better for patients, they don’t solve the most fundamental problem: With thousands of subtypes of cancer and tens of thousands of drug combinations to test, there simply are not enough patients to go around. As a result, we must regard each patient as an opportunity to learn as much as possible about cancer biology and therapies.

In contrast to trials and ad hoc experimentation, the emerging science of precision oncology applies omic technologies and systems biology to understand cancer within individuals, by inferring the molecular networks and processes driving each tumour, and intensively monitoring their response to therapy. In this approach, every drug is a probe, simultaneously treating the patient and providing an opportunity to test and improve our molecular understanding of the disease it targets and treatments. Such “N of 1” studies do not eliminate the definitive role for prospective, randomized controlled trials (RCTs) in establishing efficacy. They simply serve as recognition that given enough omic data, many research and clinical questions can be answered with a small number of the right patients. The results of these N of 1 experiments can then be used to guide patients to the right trials for them, and conversely to de-risk trials by recruiting the right patients. However, we again hit the problem of cost. Although -omic costs have fallen faster than Moore’s law, full -omics is still beyond the cost of routine clinical care. To defeat cancer we need a strategy that is robust to these complex issues and deploys our scarce resources to unlock the potential of precision medicine and make it cost effective on a population-wide scale. We must leverage existing clinical practice and its natural variation, with broad enough molecular profiling and low cost IT solutions to capture clinical data and outcomes for all patients. This is a huge organisational task given the structure and misaligned incentives in the care system. In this paper, we lay out how this can be achieved with current technology and new ways of working to align everyone’s incentives better with the patient.

The proposal: closed learning loops built off observational, stratified data

One solution is to make the entire health system a living research machine, using biomarker stratified observational data, captured as economically as possible to allow broad access. Using generic NGS panels and off-the-shelf registry solutions we believe such a system can be delivered for about $500-$1000 per patient, 50x to 100x lower than conventional trials. That is affordable within routine care, as demonstrated by previous point-of-care trials, registry trials, and ASCO’s CancerLinQ prototype.

Here is how it works:

1) Patient biopsy specimens are run through a modern, low cost molecular diagnostic panel to identify potential, clinically-actionable mutations (say 50-100 targets by NGS). Only markers with proven clinical utility (orange) and trial recruitment opportunities are reported to most clinicians. The rest are for research use, until clinical utility is established. Patients are consented at biopsy so that their clinical records and specimens can be used for research.

2) Treatment then occurs, as each patient and clinician sees fit (and can get reimbursed for).
3) The treatment chosen and simplified standardised outcome metrics such as progression, major complications and survival are reported electronically to an anonymised central registry.

4) By mining that data, we can discover two important “signals” - strong positive responders (hypothesis for best practice therapy) and cohorts of patients who are not responding (confounders).

5) These cohorts can be referred to clinical trials and “N-of-1” studies as appropriate (red arrow off of the main loop in Figure 2), the results of which would be added to the biomarker panel (1) and database (3) to continuously improve treatment decisions. Note that although there may be few cases in a given cohort, the data obtained from these in-depth studies will be quite rich in molecular and case detail, setting up opportunities to validate promising hypotheses either on the research side in trials, or observationally in the main loop.

This proposal works on the premise that for the medium term only 50 to 100 genes are likely to have clinical utility or be predictive (see table 1). We know we will discover yet more driver genes - Lawrence et al estimate the total at 500+1, but for now we won’t generally know what to do clinically with that information. This is a question of resource prioritisation. We argue that it is a better to deep sequence those genes with emerging clinical utility on hundreds of thousands of patients, at presentation and relapse and in a clinically actionable timeframe, than it is to run a few thousand tumour-normal pairs with clinical interpretation that often takes months today. Over time, as costs fall and our knowledge of other driver genes expands, we would adapt and expand the biomarker panels, incorporating new “omic technologies as they reach clinical maturity and cost effectiveness.

By always exploring more than we can reliably report to clinicians, we can future-proof the system in a cost-effective way.

Shrager and Tenenbaum (2014) proposed a subtly different model, termed Global Cumulative Treatment Analysis (GCTA), in which advanced patients were randomized at the point of care (as VA STUDY) to standard or experimental treatments. In the GCTA model, research is tightly integrated with clinical care and there is the opportunity to coordinate treatment decisions across the system to efficiently explore the space of biomarkers and novel treatment combinations. However, the GCTA approach is more costly and hence less applicable to a broad population. A hybrid approach in which the observational data on a broad population is used to select “interesting” patients for in depth study under a GCTA protocol, might be optimal.

Our proposed system has some unique properties that make it beneficial to all stakeholders.

Firstly, and most importantly, it will immediately increase care options for patients by facilitating access to stratified trials and special access programmes, just as France’s national molecular diagnostics programme has done.

Secondly, it can improve the performance of care systems by identifying variations in outcomes, costs and other value metrics. This competitive benchmarking could adjust for the “riskiness” of the patients each hospital and clinician sees, given their mutation burden, stage and grade.

Thirdly, it creates a closed learning loop that allows continuous diagnostic improvement. New biomarkers and algorithms can be prospectively validated at marginal cost in the research activity (5 in figure 2), and incrementally launched (by updating the biomarker panel or its reporting (1 in figure 2)) as soon as there is sufficient supporting evidence.

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**Table 1: Estimates for the number of genes that are clinically actionable now and in the future, based on Lawrence et al 2014.**

<table>
<thead>
<tr>
<th></th>
<th>Broad TARGET A1</th>
<th>Broad TARGET A2</th>
<th>lower clinical significance</th>
<th>Total</th>
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<tr>
<td>Highly conserved &amp; &gt;1% mutation rate</td>
<td>6</td>
<td>8</td>
<td>10</td>
<td>24</td>
</tr>
<tr>
<td>Less conserved &amp; &gt;2% mutation rate</td>
<td>3</td>
<td>11</td>
<td>33</td>
<td>47</td>
</tr>
<tr>
<td>Less conserved &amp; mutation rates between 1 and 2%</td>
<td>5</td>
<td>13</td>
<td>52</td>
<td>70</td>
</tr>
<tr>
<td>Total</td>
<td>14</td>
<td>32</td>
<td>95</td>
<td>141</td>
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Table 1: Estimates for the number of genes that are clinically actionable now and in the future, from ref 1. Obvious break-points are around 50 (Broad TARGET database levels A1 and A2 and mutated in >1% patients, dark orange), around 100 (extended into highly conserved or higher frequency mutations of unknown significance, pale orange) and around 150 (all ORFs mutated in >1% patients). MutSigFN scores at p<1% used as a proxy for mutation conservation.
Fourthly, it can drive faster and more effective cancer drug development. The real world observational data gives unprecedented insight into patient populations and the effectiveness of current therapies, which can be used for label expansion, reimbursement, adaptive licensing, early access schemes, and other proprietary purposes. The system also provides a unique recruitment point for biomarkered patients into clinical trials and deep-omic studies. Using N-of-1 and small-N studies for discovery and initial validation, then graduating to small-scale, highly targeted, open-label trials for registration, has the potential to slash the time and cost of drug development.

Finally, it can be powered to understand the complexity of cancer as its stratification is affordable enough for routine clinical use over whole populations. We can explore this with the following thought experiment. To get a clinical “signal” that establishes clinical utility we need perhaps 250 patients a year with a biomarker. Table 2 shows the host populations required in 5 cancers, from common to rare, to find those 250 patients. For comparison, good cancer registries exist in Ontario (population = 14M – green) and England (population = 52M – lilac). Tumour genomes over the incident patients in a country like the UK would cost billions today.

Building the right ecosystem
The closed loop learning described above will flourish only if the following are true:

- We can get reliable pathology, mutation and clinical history data on each patient and their tumour.
- We can classify cancer treatments into a universal taxonomy.
- We have global standards for, and routinely collect, quality outcome data on every patient.
- We have some way of sharing the information that is ethically compliant.

Anyone who knows healthcare will know that these are challenging requirements. The siloed and often competing nature of healthcare systems makes collaboration hard. This is especially true in for-profit care systems like the US, where a fragmented provider system is competing for patients. As a result, the US is at risk of building a series of “walled gardens” that do not serve patients interests as they are too small. Roche –Foundation One – FlatIron Health20,21 or Optum labs2 are examples of emerging walled gardens that are exactly these stratified observational learning loops. As captive systems, they will only ever be powered to study the most common mutations in the most common cancers.

Instead, we need to design an “open garden” that will allow competing interests to collaborate and create novel research and service models that can transform cancer care. This will be easier to achieve in the national health systems in Europe, notably France and the UK. As an illustration, France already has standardised molecular diagnostics over its patients, thanks to its national laboratory service INCa19. The UK has already created a taxonomy of cancer treatments to power the systemic anti-cancer therapy dataset23, captured via its national cancer registries and with one year survival now reported into local NHS management dashboards.

However, even these systems have yet to tackle the ethical and political issues that building the full closed loop system entails. The molecular panel could pick up heritable risk factors. Consents and data handling norms are generally narrow in their institutional permissions. Anonymised data is not untraceable data. The European public feel strongly that their data should generally be private. Yet patients who have this system explained to them are generally comfortable as long as they believe this system will be used for their benefit.

At the heart of any solution to these ethical issues will be fairness and trust, as seen both by patients and potentially competing private sector collaborators. As a result, the “open garden” needs the active involvement of patient-led not-for-profits and a social enterprise model to create that trusted neutral party. There are two moral leaderships tasks it must achieve— to create and maintain patient trust, and to drive effective cooperation across the care and research ecosystem. A possible model for that future ecosystem is shown in figure 3.

The first innovation is a set of broadly agreed standards for what data to collect, how to provide quality assurance and finally how to manage the data over time (A). There need not be one standard (although that is preferable), as long as key parts of the data are interoperable and global data syndication is possible. Some efforts are underway already in this area, for instance, standard setting for the exchange of genomic data sets (e.g. GSC24, GA4GH25), minimum outcome standards (e.g. ICHOM26) and pathology lab accreditation (e.g. CAP27).

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<table>
<thead>
<tr>
<th>Incidence Rank</th>
<th>Site</th>
<th>Incidence (per m)</th>
<th>Mortality</th>
<th>X=30%</th>
<th>X=10%</th>
<th>X=5%</th>
<th>X=1%</th>
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<td>3</td>
<td>Lung</td>
<td>530</td>
<td>83%</td>
<td>1.6</td>
<td>4.7</td>
<td>9.4</td>
<td>47</td>
</tr>
<tr>
<td>8</td>
<td>Pancreas</td>
<td>111</td>
<td>94%</td>
<td>7.5</td>
<td>23</td>
<td>45</td>
<td>226</td>
</tr>
<tr>
<td>14</td>
<td>Kidney</td>
<td>82</td>
<td>46%</td>
<td>10</td>
<td>31</td>
<td>61</td>
<td>306</td>
</tr>
<tr>
<td>17</td>
<td>Ovary</td>
<td>62</td>
<td>62%</td>
<td>13</td>
<td>40</td>
<td>81</td>
<td>405</td>
</tr>
<tr>
<td>25</td>
<td>Brain</td>
<td>38</td>
<td>81%</td>
<td>22</td>
<td>66</td>
<td>131</td>
<td>657</td>
</tr>
</tbody>
</table>

Table 2: Minimum populations required to understand the clinical effect of cancer mutations. Millions of population for 250 incident cancer patients a year with biomarker that occurs in X% of patients.
Data, analytical tools & consulting

Potentially for profit  Social enterprise or not-for-profit

However, there are three big gaps. The first is the standardisation of consent processes at biopsy so that patient samples and their anonymised outcomes can be routinely syndicated for research. The second is a common, hierarchical taxonomy of regimens and treatment protocols so that we can globally map similar treatments, administered under different names in different institutions and countries, into common families. Finally, this requires governance, data security, and access norms that encourage data sharing and are acceptable to most patients and most systems. In particular, governance will need to recognize the acute sensitivities of many socialised healthcare systems (which are natural locations for this development) to the for-profit monetisation of patient data.

Models for these standard setting bodies exist in many industries besides healthcare. Most are not-for-profit, expert society driven and often funded through membership or accreditation fees (as shown). We anticipate similar models here, but working collaboratively across fields. Treatment and outcome data can only be routinely collected by care delivery organisations, and survival data from the national death registries (B). They need encouragement to do this systematically. A number of counties have made strong progress on establishing such outcome data, notably the Nordics, UK and Italy where national healthcare systems make this easier. Controlling payers in the US, for instance United Health or Kaiser Permanente, also have good outcome data. It helps them improve their cancer services.

The challenge with such registries is to get compliance from the frontline clinicians. Data collection must be easy and relevant for them to “make the pain worth the gain”. We believe that there will be real, quantifiable benefits in patient management, practice improvement and trial drug access.

Firstly, patient management. If a patient has a mutation that might be actionable by an off-label drug not in the guidelines, their clinician has one option – read the primary literature. That is hard for busy clinicians.

In this system a number of other paths are open. Analysis can show how other, similar patients have been treated and how they responded. It can identify accessible local academic clinicians for consults who have managed similar patients. And it can capture and share relevant tumour advisory board deliberations, which can provide insights by top physicians into the latest treatment options for the sickest patients.

Secondly, clinicians are eager to improve their practice and are naturally competitive. This system allows them to interrogate their performance relative to peers and identify areas where they can improve. The experience in Sweden is that clinicians see significant benefits in this applied continuous education using registries. As an example, incontinence occurs in 50% of German prostate cancer patients 6 months post-surgery. In Hamburg, it is only 1 in 20. If German clinicians had this data routinely, that gap would be closed by frontline-led variation-in-care management.38

Thirdly, involvement in this system will generally expand a physician’s access to drugs. As an example, France’s national testing programme led by INCa has transformed the ability of patients outside of academic centres to participate in trials. It has also transformed the attractiveness of France as a cancer trial destination.39

We then come to the most important innovation in the ecosystem – a data syndication engine run as a social enterprise (C).

We believe it is essential that the data be broadly accessible, because one cannot know in advance through what combination of data and expertise the relevant discoveries will come. The biggest challenge to such collaborations is self-interest. Those that believe they have valuable data won’t share it for the greater good, be it academics chasing citations or for-profit entities chasing patents. However, the data we are describing have value that is proportional to their scale. As a result, sharing data makes it more valuable, and structured appropriately can create the right incentives to collaboration.
What is needed to unlock this data ecosystem is a trusted third party that is willing to share the benefits of pooled data generously with other participants. A formal social enterprise, or charity owned company, is likely the right model for the syndication engine. This would allow the vehicle to make a profit (and so be sustainable), but also clearly demonstrate that those profits would be reinvested back into cancer research for the benefit of patients.

Revenue would come initially from data access fees. We envision this would run on a “premium” model. Those needing relatively simple summary data, like patients looking for good local providers or physicians seeking data to support treatment decisions, would be charged nothing. Those needing patient level access into the health economics and molecular biology, such as pharma, would be charged a market rate. IMS uses a similar model for prescription information with free summaries and expensive detail. Alternatively, a classic syndication model would provide free data access to those who contribute, while others pay to access.

The revenues would be used to build and maintain the syndicated datasets, along with an ecosystem of third-party oncology data providers, apps and services. Profits will be reinvested into cancer care, partially through a profit share with providers and partially through the promotion of non-commercial clinical research, such as generic repurposing and the development of molecular markers.

We envision the data catalysing a vast new ecosystem of apps and services, from information portals for patients to high end specialist pharma R&D consulting, which will unlock the value in the data for the benefit of all. (D).

Like the communities surrounding iPhone and Android, the ecosystem would be seeded with some basic apps and services, and then opened to the world through standardised APIs and developer toolkits, accompanied by active community building efforts. The starter apps might support rapid learning by helping patients and their physicians identify appropriate treatments and trials for their tumour’s subtype, report and record outcomes, and discuss treatment strategies with peers and scientists. Additional apps might help clinical researchers analyse the outcomes and update molecular subtype classifications and treatment recommendations accordingly.

The open nature of the platform should encourage widespread development of innovative new apps that use the data to accelerate cancer research and improve patient outcomes. Some examples:

Patients and caregivers need services that help them navigate treatment alternatives and make informed decisions. Examples of such services today are Doctor Foster in the UK which helps patients find good hospitals and Patients-like Me that provides peer-to-peer communities in rare diseases. Patients need to know that they are in good hands – these tools provide that reassurance.

Providers and clinicians need treatment planning and decision support services, connected to care quality improvement. Core to this are benchmarking information, coupled with real world treatment best-practice identification. Risk-normalised hospital to hospital 1 year survival and complication benchmarking would be a key component of this, along with peer-to-peer audit and service improvement consulting.

Payers urgently need data-based tools that support rational reimbursement decisions for precision oncology. Targeted therapies are increasingly being tried off-label in different cancers than the ones for which they were approved, provided the right molecular markers are present. Payers are understandably reluctant to provide reimbursement for such treatments without prior evidence of efficacy. Instead of evaluating petitions on an individual basis, might payers approve reimbursement contingent on capturing all of the relevant data, and thereby provide a rational foundation for future decisions? This could start with basic risk-shares with pharma on precision medicines, such as occur in Italy.

A related challenge is discovering which patients won’t benefit from an approved therapy. It has been estimated that for every person that the ten highest-grossing drugs in the United States help, between 3 and 24 others derive no benefit yet suffer the side-effects and costs. Today the best payers prevent access to angiogenesis drugs unless the patient is both positive for their targets (such as EGFR) and negative for known therapy confounders (such as KRAS). This both controls costs and saves patients side-effects for no benefit. With no natural commercial allies, confounder research is under-supported today.

Payers can also exploit this system to optimise entire care pathways across treatment modalities. Surgery, traditional chemotherapy, targeted- and immunotherapies, and radiotherapy interact in complex ways that are generally not well understood. Oncologists frequently disagree on even the most basic decisions, like whether chemotherapy should precede or follow radiotherapy (or be administered concurrently) when both are indicated?

Even small improvements in care (either in outcomes, or cost) over large populations are highly valuable. Pathway optimization can vary for different sub-populations. Geriatric patients, for example, are underrepresented in commercial trials, have different mutation burdens from younger patients and can progress slower. They are fully represented in this system, allowing payers to better optimise their geriatric formularies and help use “watch and wait” strategies more appropriately.

An alternative example would be radiotherapy service development, where the WHO has a target of 50% of patients to receive therapy. Many European systems are under this target and are investing to catch-up. Yet 20-30% of cancer is radiotherapy insensitive. If we could identify those patients, minimal new service investment would be needed (and we would reduce patient harm from radiation side effects). There is emerging evidence that molecular diagnostics could do this.

Pharma’s needs span therapy development and uptake. Stratified observational data can help improve the effectiveness of their investments in 4 broad ways:
• Signal discovery: The observational data from off-label use and extended access programs can be used to discover new indications for a drug. The database can then be used to rapidly recruit active patient cohorts for cheap and fast stratified phase Ib studies, even in uncommon cancers.
• First indication choice: the observational data has the right information to provide “molecular market intelligence” – patient numbers, current care and outcomes by mutation and ICD code. This is critical to making the right price-volume-risk trade-offs in drug development.
• Signal validation: Large N late stage trials can be recruited at scale, and potentially asynchronously.
• Health economics: The system provides the ideal data to support health economics analyses – real world outcomes and activity changes within the health care system.

As a result, we believe the proposed system offers compelling benefit for all participants. For patients, it accelerates access to better medicines, and helps them navigate to better providers. For providers and physicians, it helps them access and use innovation (both pills and beyond) faster and more effectively. For payers, it allows their money to be directed more effectively to treatments that deliver in the real world. For Pharma and biotech, it can both cut the cost and time it takes to bring a precision drug to market. The only losers are the suppliers of ineffective treatments and care.

How could we get there?
This powerful alignment of incentives provides real hope that we can, with patience, make this vision a reality. A detailed roadmap is beyond the scope of this paper, but, broadly speaking, there are two paths.

The first is through a coalition of not-for-profits and socialised healthcare systems. As an example, if France had outcome systems as good as the English cancer registries, England had national testing as good as the French INCa system, we would be 100M population or so into our global target. The Veterans Administration in the US is also a natural partner given its integrated model, as are the Canadian provincial systems.

The main challenge to this path is getting broad political buy-in and especially overcoming objections from the European political left about charging for patient data access. A truly open, non-profit data and services network, backed by a global army of millions of patients, and run by charities such as Cancer Research UK, the American Cancer Society or Cancer Commons, would neutralize those objections.

The second path is through a pre-competitive consortium, funded by all the players that have significant financial resources and could benefit, most notably pharmas, payers, and national health services. While it would be challenging to establish such a consortium, especially as a for-profit, there are successful precedents, for example Sematech, established by leading US semiconductor manufacturers to regain global competitiveness and Viiv Healthcare in HIV, created by the #2 and #3 players in the face of Gilead’s success in combination therapy. The market structure in oncology is favourable for a similar coalition of companies playing catch-up, given the dominance of Novartis and Roche, perhaps again driven by the need for combination therapies.

The best of both worlds would be a public-private partnership that combined both paths, and so had both results orientated management behaviours and a social mission. That would be the ideal start to perhaps the grandest scientific endeavour of our time – the Global Cancer Treatment Alliance.