A DOSE OF INNOVATION

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BAILLIE GIFFORD

RISK FACTORS

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DOSE OF INNOVATION

We are at the dawn of a golden age of medicine. We will soon have the ability to treat and cure diseases that have long been untreatable and incurable.

Our industry is unique. We save, extend, and enhance lives by alleviating the scourge of disease. Our mission is to change the course of each individual's life for the better. To achieve this, we acknowledge that we have a moral obligation to develop the best medicines and ensure that every person who may benefit has access to them.

OPEN LETTER BY 215 BIOPHARMA CEOS AND INDUSTRY LEADERS, 8 JANUARY 2020

We believe that we are in the midst of a rapid acceleration in the pace of scientific discoveries. As this has occurred, the growth in transformative treatments has been accompanied by ever-increasing prices. This has heightened the tension that has always existed in society between the health systems' profits and patients' moral right to access treatments affordably. This is not surprising as the matters at stake are of health, life and death. For a case in point, consider that in developed economies around half of patients with chronic diseases do not take their medicine as prescribed due to cost, leading to complications, premature death and higher costs for healthcare systems as diseases progress.

WHERE THE TENSIONS LIE

The relationship between drug prices and access is not one-to-one, but rather an outcome of a complex interplay of incentives for many players in the healthcare ecosystem. The tensions are highest in the US where biopharma companies, insurers, regulators, pharmacies, hospitals, governments and pharmacy benefit managers are just some of the players who determine the economics of a drug. Many of these actors' incentives are misaligned with the interests of patients and contribute to inflationary pressures in the system. In addition, drugs are highly regulated, and regulation raises costs and stifles competition.

The simmering tension between profits and access has been exacerbated by a handful of eyewatering examples of companies that have attempted to profit unwarrantedly at the expense of public health. The most obvious example is Turing Pharmaceuticals. Its chief executive Martin Shkreli was labelled "the most despised man in America" when he announced that he was going to increase the price of Daraprim, a generic drug without competition used to treat parasitic infections, from $13.50 to $750. Shkreli tried to justify the move by saying that the company gives away half of Daraprim bottles for a dollar or less and would provide the drugs for free to patients who cannot afford it. He even promised that a portion of profits would go toward vital research into a rare, but potentially fatal, parasitic infection. Rather than winning public opinion over, it led to the US think tank the Lown Institute setting up the 'Shkreli Awards', an award presented annually for profiteering and dysfunction in the US health system.

But it's not just the headline-catching price increases that give cause for concern, smaller recurrent pricing increases compound over time. Take insulin. It was discovered almost 100 years ago and sold to the University of Toronto for $1 as the inventors felt it would be unethical to profit from a discovery that would save lives. Since then, the list price of Eli Lilly's Humalog insulin has risen from $21 per vial in 1996 to $250 in 2019.

The world's best-selling drug is Humira (circa $20bn sales) and is another case in point. It is used to treat various conditions from arthritis to ulcerative colitis. In 2016, when the core patent expired in the US, its maker, AbbVie applied for dozens of follow-up patents to deter competition in the US. So now, while there are at least six approved generic drugs ready to go, the earliest date they can be released in the US is 2023. In the meantime, US patients have, on average, endured a 12 per cent per annum price rise since 2006.

If we as a society are unwilling to pay for those medicines today, they won't get invented.

JOHN MARAGANORE, ALNYLAM CEO

As a result, many policymakers and observers call for heavier regulation surrounding pricing of treatments. The challenge is to balance policies designed to protect patients by limiting excessive pricing with rewarding innovation of transformative medicines.

INNOVATION-DRIVEN DEFLATION

There is no one obvious answer that balances paying a fair price for innovation with improving access to treatment, while at the same time ensuring the sustainability of the healthcare system. Yet, as the pace of change and innovation in healthcare continues to accelerate, there are reasons to believe that we are on a path to striking a better balance over time.

Here are some of the ways in which we anticipate this happening.

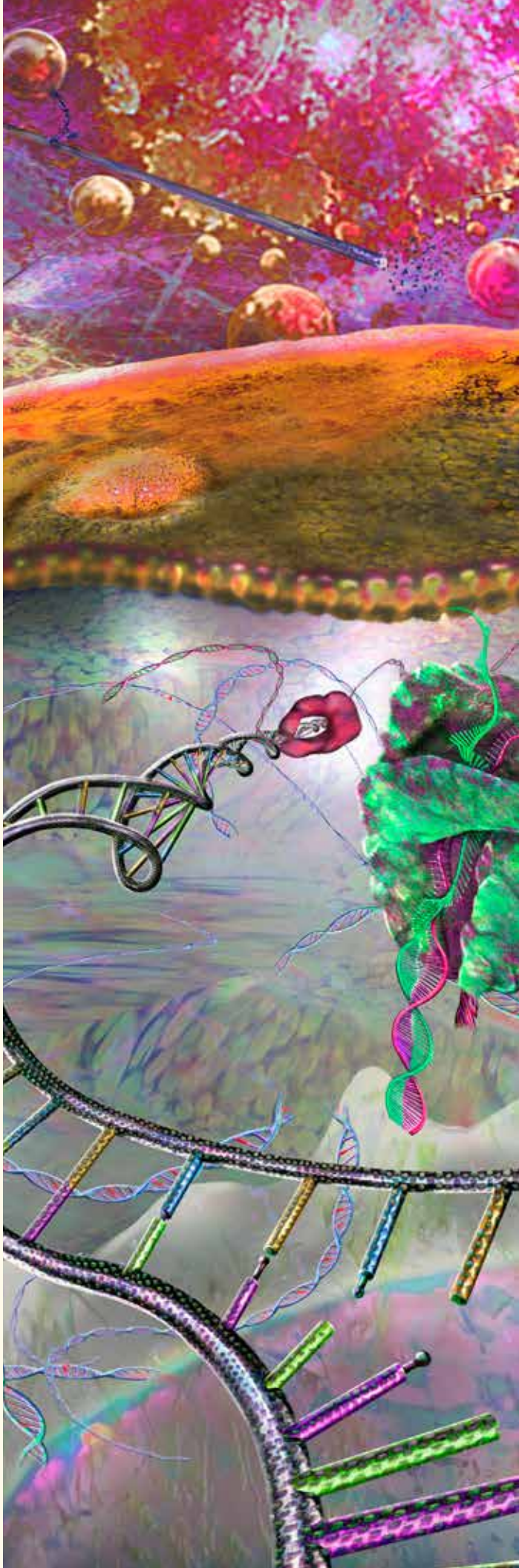
INNOVATION IN DRUG DISCOVERY

Drug discovery is becoming faster, more predictable, repeatable – and therefore, cheaper.

Biology is becoming a data science problem – this started with gene sequencing at scale and is further accelerating as new techniques and tools to study biology in ever greater detail are developed. Together these are helping to increase the success rate for drug discovery. One of the most underemphasised results of this biotech data revolution is the dramatically accelerating understanding of biology of patient subgroups. This is enabling companies to rationally design drugs for patients that are most likely to benefit from them.

Currently, nine out of ten drugs fail in clinical trials and biopharma companies need to recoup the losses for these nine from the one that succeeds. As drug discovery becomes more predictable, the cost burden of failure should decrease. The more drugs a company believes it can bring to the market, the less likely it is to feel pressured to maximise the returns it generates from a single drug.

This can be seen with Alnylam, whose drug platforms have enjoyed a 60 per cent track record of success, against the industry average of 10 per cent. It takes its role in pricing responsibly seriously and has initiated a 'Patient Access Philosophy Report' in order to increase transparency and hold itself accountable to patients.



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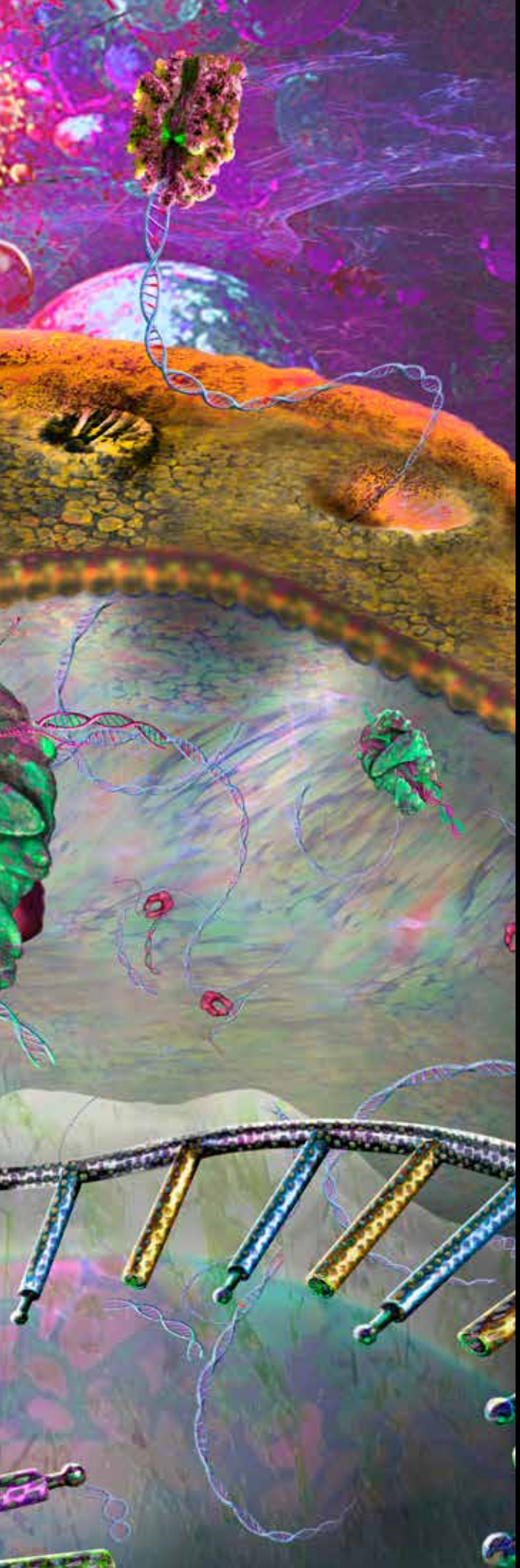

COLLABORATING WITH PATIENTS TO INCREASE ACCESS

Alnylam has recently published its second patient access philosophy report. In the introduction, it states:

At our best, biotechnology companies reinvent the way science and medicine treat disease. Alnylam remains relentless in ensuring that patients who need our innovation have access to it. The reason is simple. Patients should never have to wait for hope.

Some of that hope comes from the patient-facing programmes that Alnylam has developed, which allow it both to provide support and services to patients, and to learn from them. It believes its efforts to do so create a virtuous circle within the innovation ecosystem. So, for example, by seeking input from the patient community, Alnylam was able to announce agreements-in-principle for a new value-based pricing framework for its recently approved therapy, OXLUMO, and to improve access to it: “Patient insights have also been instrumental in helping us develop more effective clinical and real-world endpoints to streamline access to new RNAi therapeutics.”

INNOVATION IN TREATMENT APPROACH AND PAYMENT MODELS

Access to drugs and affordability are about much more than drug prices. Most of the costs of healthcare today are associated with the consequences of care that are not transformative. As diseases progress, they lead to complications and become more difficult and expensive to treat. Chronic conditions account for as much as 90 per cent of healthcare costs.

The improvements in our understanding of biology are enabling earlier diagnosis and the treatment of disease causes, rather than symptoms of late stage disease. Not only is this better for patients, it can also save costs for the system. Sensors, diagnostic tools built from smartphone components and machine learning are enabling continuous monitoring and personalised dosing of drugs to which a patient is responsive. Innovative treatments that can cure, slow down or prevent diseases from progressing can end up being cheaper for healthcare systems than long-term chronic care, despite prices that initially seem high.

However, transformative treatments pose a challenge for healthcare systems. This is because, while the benefit of a treatment can last a lifetime, the costs are frontloaded. Demand for such treatments can overwhelm payers, whose business models revolve around annual budgets. This can make it tricky for patients to access transformative drugs. For instance, Gilead's drug Sovaldi – a cure for hepatitis C and a real breakthrough – was originally deemed "cost effective, but not affordable" meaning many patients struggled to access it. This challenge calls for innovation in pricing and reimbursement models.

When bluebird bio developed its first gene therapy, it realised that its biggest advantage – only one treatment is needed – could prove a stumbling block for patients accessing the treatment. To improve affordability, it has shaped its pricing approach to adapt to payers' needs and spread costs over time.

After an initial upfront payment (20% of maximum), bluebird will receive annual milestone payments based on how well the treatment works for the patient, stopping after five years. It is far too early to declare its approach successful. However, initiatives to introduce risk – and value-sharing arrangements between the government, payers and companies are likely to prove important for enabling transformative therapies to reach patients at scale.

COMPETITIVE INNOVATION


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Decades of scientific and technological progress are leading to disease biology being addressed successfully in a variety of ways. This is increasing the number of biopharma companies who may succeed with different approaches targeting the same underlying cause. Over time, we expect this to feed through into more competition and lower drug prices.

China may play an important role as it has a very rapidly developing and increasingly competitive biotech industry. It is notable that the head of the Food and Drug Administration's (FDA) Oncology Centre of Excellence Richard Pazdur personally urged Chinese companies to bring their cancer drugs to the US market: "it could potentially be a great thing for everyone because we haven't seen the major western pharmaceutical companies moving on price." He noted that six competing PD-1 oncology drugs have been approved in the US and "there are no differences in price."

INNOVATION IN THE SUPPLY CHAIN

The challenge surrounding any discussion of drug prices is the complexity of healthcare systems and skewed incentives of its different actors. The inflationary pressures stemming from the drug supply ecosystem are more acute in the US than in countries with a single payer system. New business models are starting to emerge that aim to simplify the supply chain, improve price transparency and pool purchasing power to lower drug prices.

For example, GoodRx enables users of its app to compare drug prices between different pharmacies in the US and it also negotiates discounts on behalf of its members. EQRx plans to sell lower-priced drugs at scale to a large number of payers around the world by following fast in the footsteps of innovative drugs, while avoiding key patents. Meanwhile, the rise of telemedicine could lead to lower drug prices as dominant players, such as Ping An Good Doctor in China or Teladoc and Amazon in the US remove middlemen from the supply chain and buy in bulk.

OUR ROLE AS INVESTORS IN INNOVATION

We aim to invest in companies that transform outcomes for patients while putting healthcare systems on a more sustainable path. One way in which we do this is to identify companies that can lower the overall cost of drug discovery. Companies such as Alnylam can make drug discovery more repeatable, predictable and scalable and can reinvest the proceeds of success at a high return and so compound their returns over long time periods. When assessing the business models of biotech companies, one of the most important considerations for us is the scalability of a company's approach. If a company can innovate in a scalable manner to design many drugs then it does not rely on pricing of a single drug to grow its revenues. We expect the companies that we invest in to price responsibly and encourage them to lead towards a sustainable pricing environment.

As investors, the long-term capital we provide is important to the companies we support. Without it, companies are at the mercy of quarterly reporting cycles, which encourages higher than necessary price setting and price increases, and the urge to fight biosimilars or extend the exclusivity of patents at all costs. In contrast, our long-term, patient capital frames the companies' ambitions and allows them to manage risk by investing in teams, technology and science. This increases their chances of success and builds resilience to setbacks. Crucially, it also enables companies to be more ambitious, increasing the potential success and, with it, the chances of becoming one of those rare and valuable companies that can generate extraordinary, outlier returns – for society and for investors.

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Marina is an investment manager in the Health Innovation strategy. She joined Baillie Gifford in 2008 as a portfolio analyst. She worked in a number of global teams before joining Long Term Global Growth, where she focused on analysing companies with the potential for sustained rapid growth. It was here that Marina developed an interest in healthcare, intrigued by the accelerating pace of progress in the field. She joined the Health Innovation team in January 2018 as a Portfolio Manager, to fully focus her attention on exploring the potential consequences of such progress and how Baillie Gifford can help. Marina graduated from the London School of Economics and the Higher School of Economics in Russia with BSc degrees in Banking and Finance and in Economics, having studied on these programmes simultaneously.

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