

# AstraZeneca R&D: Turning science into medicine

September 2022



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## Led by science. Driven by patients

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# Our R&D culture

We are driven by science, united by science, and every day, we push the boundaries of science to deliver life-changing medicines.

We have a unique R&D culture where people with curious minds are inspired to think creatively. Free from fear of failure, free to ask the right questions, make bold decisions, and dig deep into the biology of complex diseases.

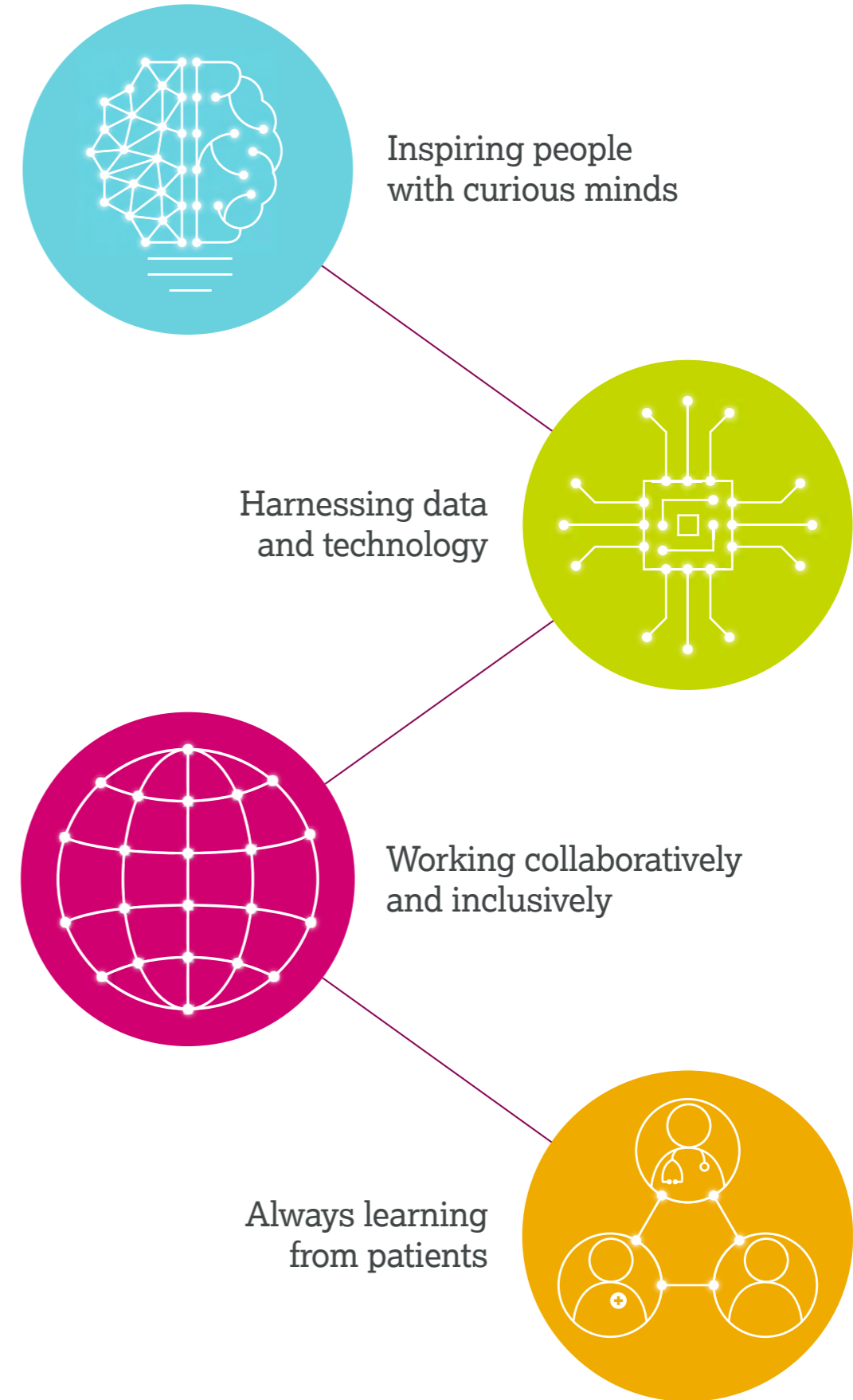
At the same time, we are harnessing data and technology to fast-forward the pace of our science. Helping us achieve the next wave of breakthroughs and do things that have never been done before.

It is a culture where people are able to work collaboratively and inclusively together. In an environment where all doors are open, talent and diversity are celebrated, and every voice is heard.

We are always learning from people who live with the diseases our medicines treat. So we can understand their needs and make sure that great science born in the lab can make a real difference to their lives.

It's by creating and sustaining this culture that we are able to help unlock the power of what science can do. This is AstraZeneca R&D. This is what we are made of.

✓ Medical Chemist in our labs in Macclesfield, UK





Three organisations. One aim

## Our therapy areas – Oncology

At AstraZeneca Oncology R&D, we are pushing the boundaries of science to change the practice of medicine and transform the lives of patients living with cancer, with the aim of eliminating cancer as a cause of death. We have one of the broadest and deepest oncology pipelines in the industry, based on six scientific platforms: Immuno-Oncology, DNA Damage Response, Antibody Drug Conjugates, Tumour Drivers and Resistance Mechanisms, Cell Therapies, and Epigenetics.

Our approach to eliminating cancer is to identify and treat patients earlier in the progress of their disease when there is potential for cure, and to improve the treatment of relapsed or refractory patients by addressing emerging resistant populations, particularly in later stages of disease. With a focus on monotherapy and combinations, biomarker-driven innovative clinical trials and digital technologies, we are confident that cures for cancer are within our grasp.



**Antibody-drug conjugates (ADCs)**  
A cancer-killing drug is attached to the monoclonal antibody through a stable connection (the linker), creating the ADC. The ADC binds to specific proteins on the surface of cancer cells, and it is then internalised into the cell. Once inside the cancer cell, the cytotoxic drug is released, destroying the cancer cell.



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## Our therapy areas – Cardiovascular, Renal and Metabolism

Our ambition is to stop, reverse, and cure these diseases by delivering innovative, life-changing medicines and solutions for patients. To do this, we need to unravel the underlying causes of these diseases by identifying novel targets linked to disease biology to create the next generation of therapeutics.

We have built knowledge and invested in key technologies to develop both our pipeline and our level of scientific expertise. We couple this with a patient-centric approach aimed at better understanding the interplay and potential causal relationship between these diseases, which often present in the same patient. Our approach is opening up unprecedented opportunities for novel treatment paradigms to help more patients and strengthen our pipeline with further differentiated medicines.

### Cardiovascular, renal and metabolic diseases

CVRM diseases such as heart failure, cardiovascular disease, diabetes and chronic kidney disease share common and distinct mechanisms. AstraZeneca is researching the interplay and potential causal relationship between these diseases with the aim of improving outcomes in patients with one specific diagnosis before co-morbidities emerge.



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## Our therapy areas – Respiratory and Immunology

Our ambition is to transform Respiratory and Immunology care for patients, moving beyond symptom control to disease modification, remission and one day cure. We push the boundaries of science to tackle tough and complex, unsolved problems by targeting the underlying biology and disease drivers to create innovative new therapies with effective new drug modalities and combinations.

Through our in-depth knowledge of these underlying disease drivers and identification of biomarkers and gene profiles, we are applying a precision medicine approach from the start of drug discovery, working to match patients with treatments that are most likely to benefit from.

Our approach is to target patients earlier in the progression of their disease to prevent and reverse damage and we are applying state of the art tools and technologies to accelerate the way we identify novel targets to develop next generation therapeutics. Our patient centric approach to clinical trials means we are incorporating digital health solutions and transformative study endpoints to enable better outcomes for patients by demonstrating disease modification as well as symptom reduction.

### Respiratory and immunology diseases

When lungs are stressed by allergens, pathogens or irritants, epithelial cells produce cytokines that trigger multiple downstream inflammatory pathways in the lungs. AstraZeneca is researching multiple drivers of respiratory and immunology disease areas with the aim of designing disease modifying medicines that prevent, reverse or even cure these diseases.



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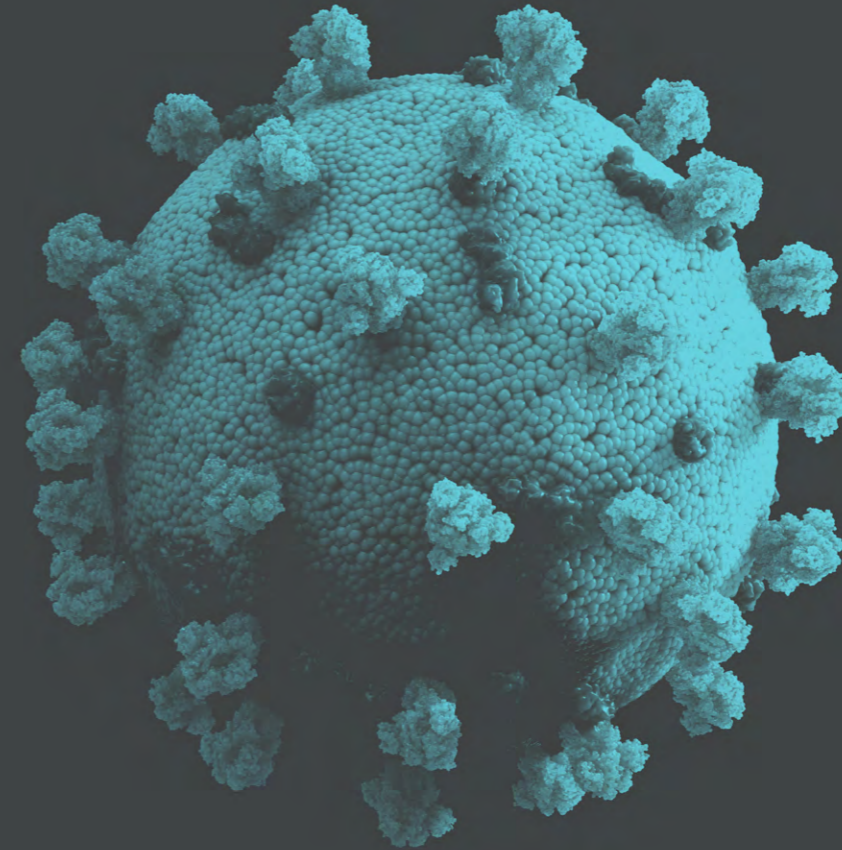
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# Our therapy areas – Vaccines and Immune Therapies

As one of AstraZeneca's newest therapy areas and a future growth driver, our ambition is to develop and deliver transformative vaccines and antibodies to provide long-lasting immunity to millions of people, where the burden of disease is greatest.

To achieve this, we are optimising the potential of both vaccines and antibodies. We are engineering next generation vaccines combining self-amplifying RNA with novel antigen design, with the potential to generate potent and long-lasting immune responses. At the same time, we are pioneering novel approaches to develop highly targeted, long-acting antibodies, using our proprietary half-life extension technology. This complementary approach, with vaccines providing protection for those able to mount their own immune response, and antibody therapies for those who cannot, will ensure no patient is left behind.

With an initial focus on some of the most common and debilitating respiratory diseases, we have a portfolio of medicines that includes vaccines for COVID-19 and influenza, long-acting antibodies for COVID-19 and respiratory syncytial virus (RSV), and a pipeline of next generation therapeutics and scientific platforms.





## Our therapy areas – Rare Disease

Alexion, AstraZeneca's Rare Disease group, pursues opportunities to transform the lives of people affected by rare diseases and devastating conditions. We are building on our pioneering leadership in discovering and developing therapies that target the complement system, a foundational part of the body's immune system, by driving innovative research and development across new disease targets and modalities.

Combined with disciplined business development activities, we are expanding our pipeline into new rare disease indications where there remains great unmet need. By understanding patients' unique needs, we can research and develop innovative medicines, support access and advocate for the rare disease community.



### Unlocking the potential of the complement system

The dysregulation of the complement system, an essential part of the immune system, is a key driver of many devastating diseases. Targeting and inhibiting the complement system before it can trigger tissue damage or destruction can help restore balance. We are committed to continue unlocking the potential of the complement system, to discover new life-changing therapies for even more patients.



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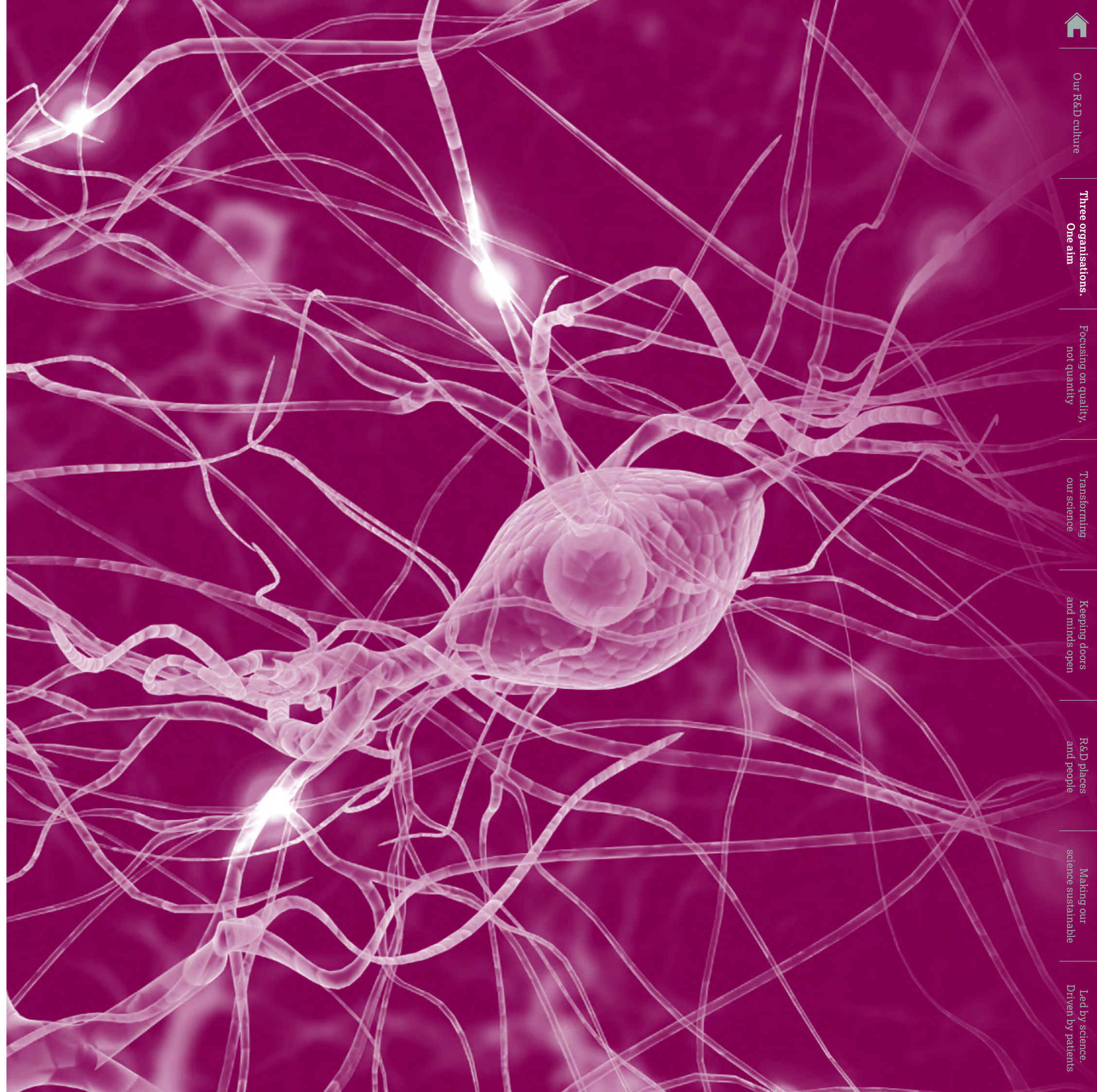
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## Our therapy areas – Neuroscience

We pursue opportunity-driven projects in Neuroscience. As a small, focused and agile group, we respond to new discoveries as they happen. Following observations that many neurodegenerative diseases have common mechanisms in which pathological proteins spread from neuron to neuron, we have invested in projects targeting alpha (α)-synuclein and tau, proteins involved in Parkinson's disease and Alzheimer's disease, respectively.

Our consistent commitment to high quality science aims to positively affect the lives of those living with neurodegenerative diseases, chronic pain, or psychiatric conditions. Our business model thrives on being dynamic and partly externalised, with a firm focus on driving science in our key areas of interest. Early, flexible partnering with the brightest and best in the world allows us to combine knowledge and progress clinical development, while managing the challenges associated with neuroscience research.



# Our expert functions

## Discovery Sciences

Discovery Sciences applies deep technical expertise in specialist technologies to support the delivery of targets and molecules to the early AstraZeneca pipeline. Targets are identified through our human genomics and functional genomics efforts, employing the latest technologies in genome editing and advanced cell model development. Once identified and validated, we work with therapy area project teams to identify novel small molecule effectors of these targets using our integrated sample management and platform screening groups.

## Biologics Engineering

Biologics Engineering focus on the discovery and engineering of novel biomolecules. The team build end-to-end capabilities in all aspects of biologics design, engineering, screening, analytics, and development, to create first or best-in-class therapeutics across all of our therapy. As well as monoclonal antibodies, we are pioneering complex modalities such as antibody-drug conjugates, multi-specific antibodies, circuits and engagers, nanomedicines, recombinant peptides and Cell/CAR T therapies. Our team is also developing novel antibodies for targeted therapies to the lungs and kidneys, and new biologics for engaging the microbiome.

## Precision Medicine & Biosamples

Our vision is to transform patients' lives through personalising treatment, delivering innovative diagnostics with external partners aiming to match AstraZeneca drugs to patients most likely to benefit. Over 90% of our clinical pipeline takes a precision medicine approach. Furthermore, our Biosamples team provides end-to-end expertise for the whole R&D portfolio across the Human Biological Samples lifecycle to meet our obligations to patients, including the lab analysis essential for safety.

## Clinical Pharmacology & Safety Sciences (CPSS)

CPSS provides non-clinical safety, clinical pharmacology and quantitative modeling support to the R&D portfolio, with expertise in mechanistic discovery safety, regulatory toxicology, pathology, animal sciences, clinical pharmacology and pharmacometrics, quantitative modeling and data sciences. Our work impacts molecule design, selection, clinical study design, dosing regimens, regulatory approval of new medicines and life-cycle management.

## Pharmaceutical Sciences

Pharmaceutical Sciences is responsible for key aspects of chemistry, manufacturing and control, from discovery to phase II trials. The function influences the intelligent design of medicines and delivery systems across all therapeutic areas, applying expertise in novel synthetic route and process design; data science and modelling; formulation and advanced drug delivery, as well as delivering to high standards from our drug substance and drug product manufacturing GMP facilities.

## Biopharmaceutical Development (BPD)

Working across all our therapy areas, BPD integrates cell biology, process science, molecular structure and function, solution and solid-state chemistry, advanced data analytics and engineering to create industry-leading technologies. These in turn facilitate efficient production of novel biologics, stable formulations for delivering new medicines, new drug delivery systems and patient-friendly devices. All of this helps us transform research into life-changing medicines.

## Development Operations

Development Operations is here to deliver science through a wide range of specialist expertise, operational excellence and data-driven innovation. These enable us to drive extensive clinical trial programmes from design to regulatory submission and approval. Providing the key connection between science and commercialisation, we deliver trials to the highest standards of quality, efficiency and ethics to thousands of patients globally.

## Data Science & AI (DS&AI)

DS&AI works across R&D to drive innovative data science and AI applications. By drawing actionable insights from our data, DS&AI acts as a data management and governance hub, helping bring transparency to discovery sciences and drug development. Together with our R&D and IT colleagues, we are harnessing new technologies to improve our disease understanding, accelerate the R&D process, and improve diagnosis with an ambition to bring new medicines to patients faster and more effectively.

## Digital Health R&D

Digital Health R&D leads the strategy and operational delivery of digital health solutions across R&D. Our aims are to help predict, prevent and treat patients' conditions more effectively. We do this using digital, data and analytics to improve and speed up portfolio development, improve patients' clinical trials experience and patient outcomes, and re-imagine the future of healthcare via partnerships and innovative digital solutions.

## R&D Information Technology (IT)

R&D IT uses technology to transform the speed and quality of our discovery and delivery of medicines to patients. The team helps optimise scientists' daily lives through the use of new IT technology, but are also committed to transforming R&D by creating and building new digital and data science platforms to increase R&D success and reduce timelines. Expertise includes automation, analytics-ready data, scaled engineering, high-quality digital applications, seamless integration and technology innovation.

## Business Development & Licensing

Business Development & Licensing's remit includes search and evaluation, transactions, and alliance management. Our role is to enrich the R&D pipeline and technological capability through external innovation from discovery to late clinical development by partnering with biotech companies, peer pharma and academic institutions. In this way, we can help ensure that both our science and portfolio are fit to meet future challenges by maximising the value of our strategic partnerships.

## Chief Medical Office (CMO)

The CMO works globally and is responsible for patient safety, regulatory excellence, quality assurance, clinical engagement and policy. Functioning across the enterprise, our priority is to continually improve the way we deliver our products and services. By creating opportunities for meaningful patient engagement, maximising access to medicines, and strengthening our commitment to a safe science culture, we aim to create better experiences and outcomes.

## Chief Operating Office (COO)

The COO's role is helping create world-class partnerships and work environments across all our sites, globally. We provide leadership in strategy, decision making, operational excellence, risk management, and specialist administration, as well as scorecards, reporting and publications compliance. We also nurture the pipeline of new scientists joining us through our global graduate, PhD and postdoc programmes, helping make great science possible.

## R&D Japan

R&D Japan has extensive capabilities in clinical development across all our therapy areas, driving studies from early development to life-cycle management. Supporting both local and global programmes, we are able to factor in local medical and regulatory requirements to help accelerate patient access, and lead global programmes for diseases prevalent in Asia, fostering partnerships and alliances to help create ground-breaking science.

## R&D China

R&D China also has clinical development expertise across small molecules and biologics, helping accelerate the development of innovative medicines for Chinese patients, and lead the delivery of global programmes in all our therapy areas. Our strategic investments in China include a pharmaceutical development hub and local manufacturing facilities, and R&D China drives our portfolio locally, as well as supporting the global development of our most promising medicines.



Development chemists in our labs in Maihara, Japan



# Focusing on quality, not quantity

Our drug discovery and development is guided by our 5R Framework, which champions quality over quantity, and has helped transform the culture of R&D and our business.

In the last decade, we have achieved an almost six-fold improvement in the proportion of pipeline molecules that have advanced from preclinical investigation to completion of Phase III clinical trials – from 4% to 23%. This improvement moves us well above the current industry average success rate of 14% in the 2018-2020 timeframe.\*



\*In-house data (2017-2021) and Centre for Medicines Research (CMR), a subsidiary of Clarivate (2018-2020).



## Circulating tumour DNA

AstraZeneca has pioneered the use of circulating tumour DNA (ctDNA) in the diagnosis of cancer. Pieces of DNA break off from a tumour and circulate in the bloodstream where they can be analysed to give genetic information about a patient's tumour. This allows healthcare professionals to determine the right treatment for the patient using a minimally invasive blood test.

## Precision medicine and developments in diagnostics

With 90% of our pipeline taking a precision medicine approach, compared to just 10% in 2009, we have been able to make significant steps forward in diagnostics. These include a broad range of cutting-edge technologies, such as tumour tissue diagnostics, molecular tests, and point-of-care diagnostics.

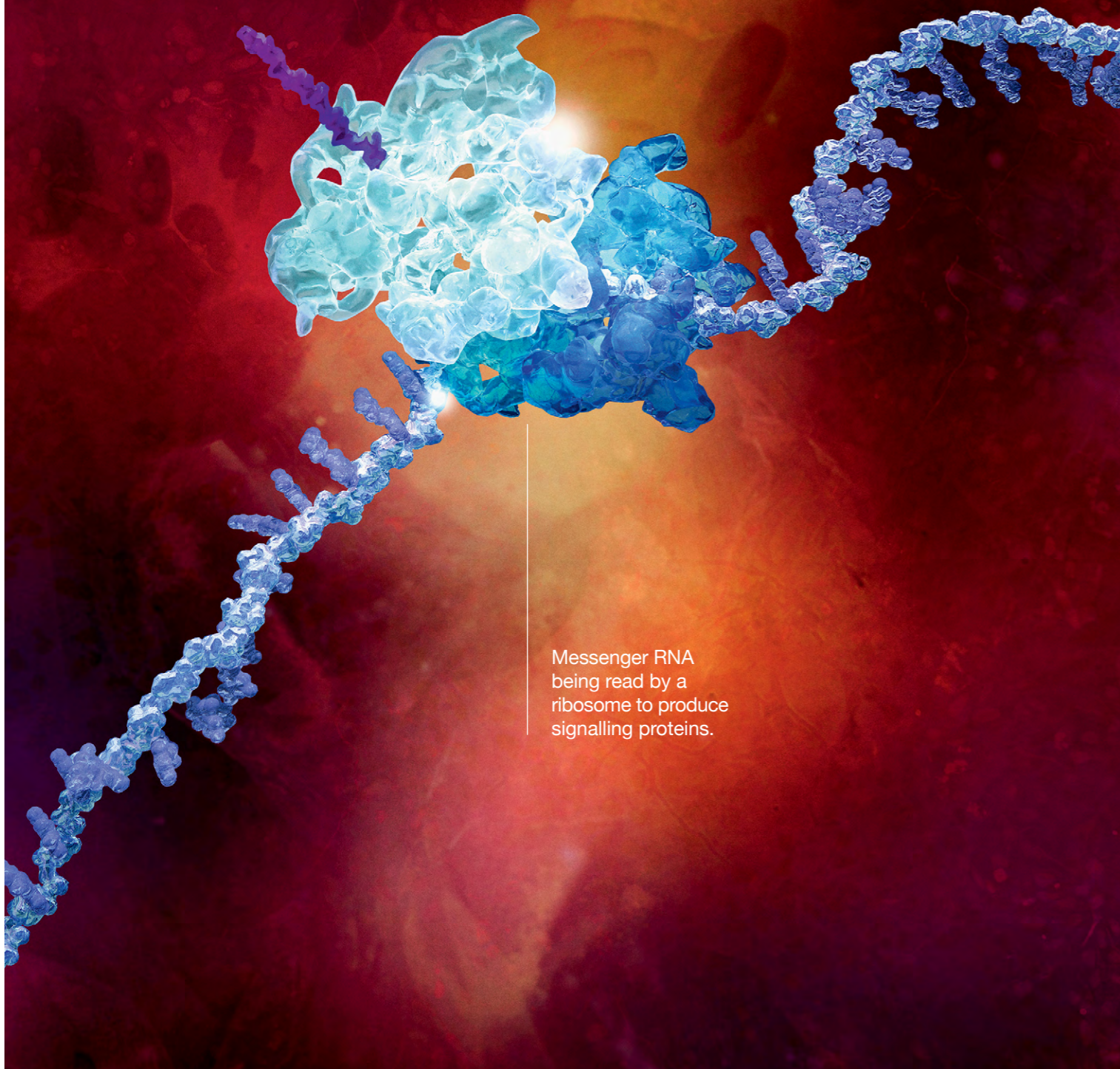
Since 2014, we have launched five precision medicine therapies linked to 53 different diagnostic tests, and are working towards developing technologies that can detect early disease. For instance, we are exploring tests based on circulating tumour DNA to measure minimal residual disease in colorectal cancer, which could lead to patients being treated with new therapies at an early stage, when response rates are higher.

Thinking beyond Oncology, we are collaborating with our partners to lead the way in a new era of precision medicines for chronic diseases; driving for better patient outcomes and a healthier and more sustainable future for patients and healthcare systems. We have developed point-of-care tests for respiratory disease measuring a biomarker for eosinophils with ChemBio Diagnostic Systems, and for inflammation measuring serum uric acid

with Nova Biomedical. We are also exploring tests based on measuring circulating free DNA (cfDNA) to understand inflammatory patterns or fibrotic levels in complex chronic diseases, such as idiopathic pulmonary fibrosis (IPF) and chronic obstructive pulmonary disease (COPD). In partnership with Gatehouse Bio we have studied microRNAs in a large IPF patient cohort to determine the link between whole blood patterns and disease progression. By understanding these connections we can include these biomarkers in future longitudinal clinical trials with the ambition of developing routine diagnostics and markers of disease.

In rare diseases, we remain committed to improving the diagnostic journey for rare disease patients, who often wait years to receive a proper diagnosis and many never receive one at all. In addition to collaborations with Rady Children's Institute for Genomic Medicine and The Manton Center at Boston Children's Hospital, we have entered into a collaboration with Genomenon to enhance its Mastermind® Genomic Search Engine used by genetic testing laboratories and medical centres across the globe.

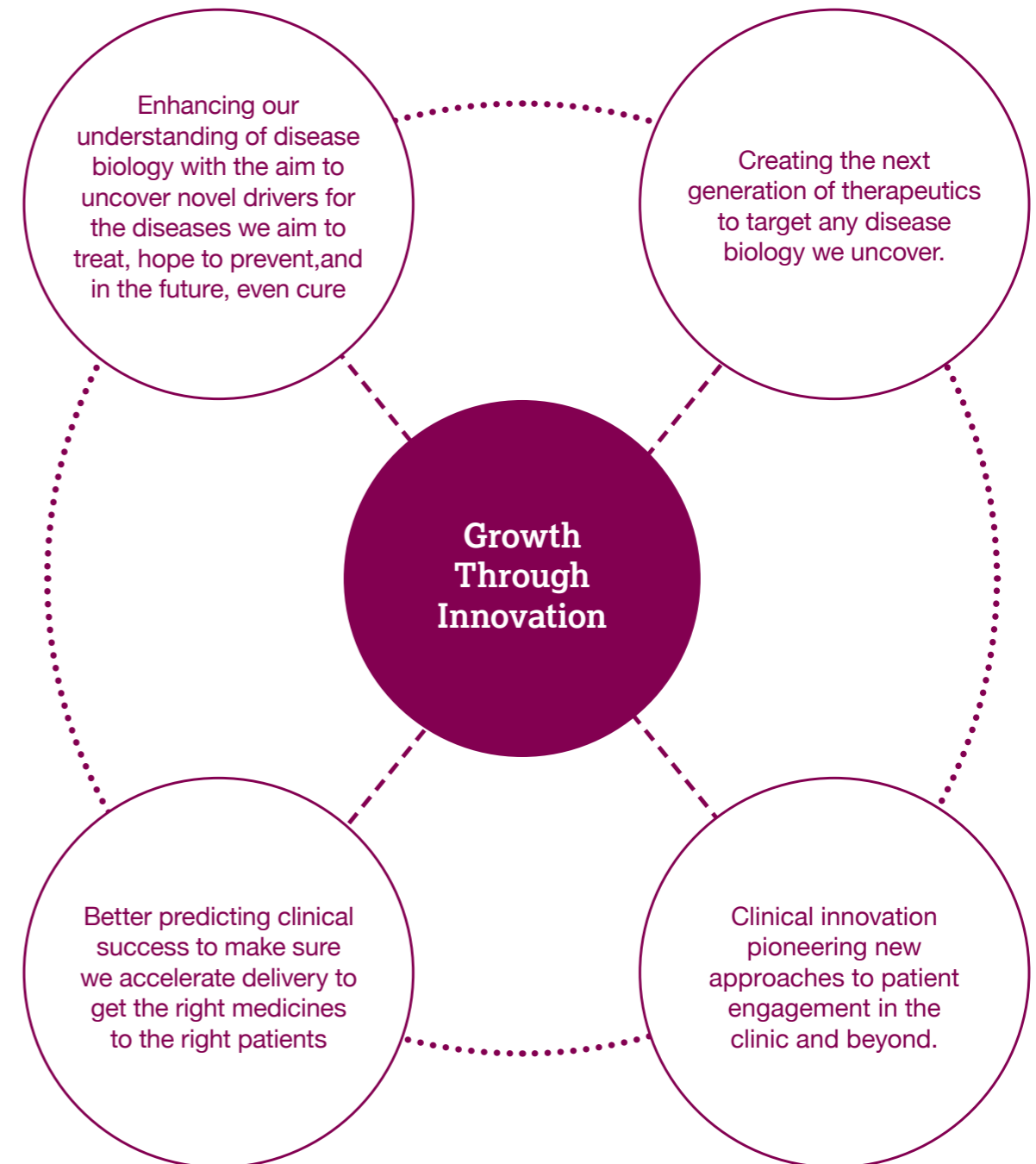
# Transforming our science



Messenger RNA being read by a ribosome to produce signalling proteins.

We are never complacent about scientific discovery and development, always pushing our R&D productivity, searching for new knowledge and the next breakthrough.

Our 'Growth Through Innovation' strategy will guide our business to 2030 and beyond, supporting us in advancing our scientific knowledge to extend the possible and helping shape the future of healthcare. We are committed to investing in and embedding four key areas, which will help us in our aspiration to create the greatest and swiftest impact on disease.



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# Data science & AI are transforming drug discovery and development

AI and machine learning is helping to transform the way we discover and develop new medicines. We hope to be able to increase the probability of success and reduce timelines in our drug discovery and development process by applying advanced AI and machine learning across R&D.

We are embedding AI across all of our R&D activities, from target identification to clinical trials to understand where we can harness new technologies and further automate processes. Our vision is one of freeing up more time for discovering and delivering as many new medicine programmes as we can from our innovative pipeline.

We are using AI to help us analyse and interpret huge quantities of data at all stages of drug discovery and development. We aim to gain a better understanding of the diseases we want to treat, identify new targets for novel medicines, speed up the way we design, develop and make new drugs, design and recruit for better clinical trials, and drive personalised medicine strategies.

For instance, in medicinal chemistry, we are augmenting traditional design and synthesis with sophisticated computational methods to predict what molecules to make next and how to make them. Today we use AI to help us deduce the best molecules to make in the shortest time, across 70 percent of our small molecule chemistry projects. AI is also helping us design and develop other therapeutic modalities including peptide or protein therapeutics, nucleotide-based therapeutics and cell based therapeutics. We are also using the power of machine learning to build algorithms that combine diverse data sets such as clinical trial data and real-world data, to identify patterns in disease progression or in how patients respond to different therapies. Their findings inform how we design clinical trials for our medicines.

## FAIR foundations, the right architecture and continuing investment

Today, we are generating and have access to more data than ever before. But the true value and transformational potential of scientific data can only be realised if it is 'FAIR' – Findable, Accessible, Interoperable and Reusable.

Making sure that we have the correct foundations for data science and AI is critical to our continued success. We have to get the data into the right shape, embed the right governance, implement the right analytical tools, and most importantly, get the right data into the hands of the right people to yield transformational benefits. This is why a concerted, cross-company effort around data and analytics is so important.

We are creating an enterprise-wide data and AI architecture. To achieve this, we are bringing the right people together – data scientists, bioinformaticians, data engineers and machine learning experts – to ensure that we are collecting, organising and using the right data, in the best way possible.

At the same time, we are also investing in internal training and education so that everyone in R&D understands our approach to data science and AI and can use or partner with the right experts to unlock data and apply it effectively.

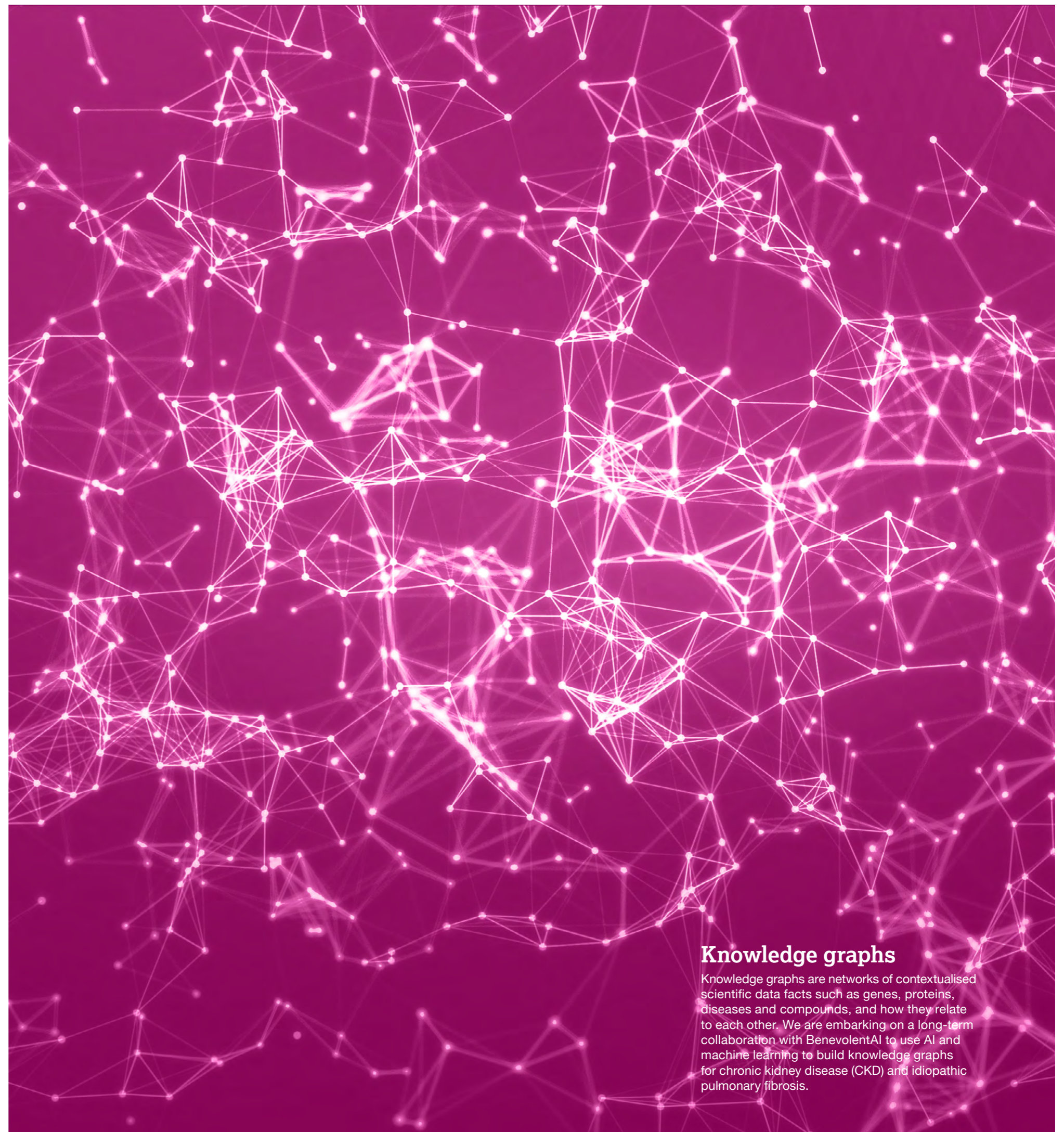


Visualisation of a data network

# Enhancing our understanding of disease biology

We are determined to advance our understanding of disease biology to uncover novel drivers for the diseases we aim to treat, prevent and in the future, cure. Selecting the right target remains the most important decision we make in the drug discovery process. We are investing in multiple approaches to improve this:

- Through our Genomics Initiative, we aim to analyse 2 million genomes by 2026 to identify rare genetic variants to uncover new targets and disease insights.
- We are investing in broader multi-omic technologies, such as transcriptomics, proteomics and metabolomics, to probe the more complex and transient molecular changes that underpin the course of disease and responses to drug treatment.
- Our use of precise gene and base editing technologies continues to help us create more relevant cell lines and animal models in a matter of weeks, as opposed to months or longer still.
- At our Cancer Research Horizons-AstraZeneca Functional Genomics Centre at the Milner Therapeutics Institute in Cambridge, in the UK, we aim to discover new targets by using CRISPR libraries to delete or upregulate every gene in the cell to understand the role of that gene in disease biology.
- We are combining these rich datasets with external data sources, and applying AI and machine learning to develop biomedical knowledge graphs to contextualise scientific data and the relationships between them in partnership with companies such as BenevolentAI and Tempus.



## Knowledge graphs

Knowledge graphs are networks of contextualised scientific data facts such as genes, proteins, diseases and compounds, and how they relate to each other. We are embarking on a long-term collaboration with BenevolentAI to use AI and machine learning to build knowledge graphs for chronic kidney disease (CKD) and idiopathic pulmonary fibrosis.

# Creating the next generation of therapeutics

In our quest to transform disease, we believe it is essential to target novel biology we uncover. We are continuing to design new ways to target the drivers of disease to help us create the next generation of therapeutics – going beyond traditional small molecules, monoclonal antibodies and peptides. Our medicines also consider improved formulations in ease-of-use oral tablets or capsules, injectable and inhalation devices, reducing the need for hospitalised infusions.

By combining our distinctive medicinal and peptide chemistry skills and technologies with those of other leading companies in highly specialised fields, we are working towards our goal of addressing the unmet medical needs of patients.

The diversity of technologies applied in our early pipeline is exemplified by the increased number of new modalities entering clinical development. Our early pipeline now consists of numerous new drug modalities, including oligonucleotides, mRNA, bispecific antibodies and antibody fragments, cell therapies and Anticalin® proteins.



**Next generation therapeutics**  
Advancements in biotechnology have expanded our toolkit of drug modalities. This provides an opportunity to design therapeutics for disease mechanisms previously considered difficult, if not impossible, to target and enables our scientists to pioneer new approaches to drug discovery.



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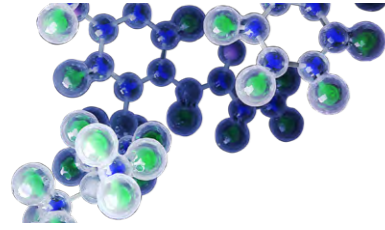
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# Drug modalities

## Pioneering new approaches to drug discovery



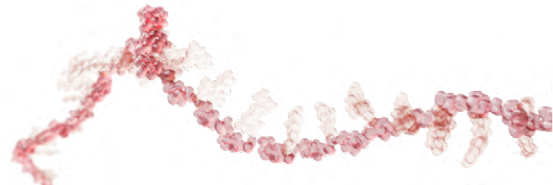
### Small molecule

A small molecule is a low-molecular weight (less than 900 daltons) organic compound.



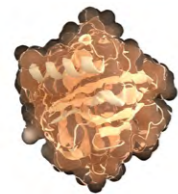
### Antibody platforms

Antibodies target proteins with exceptional specificity and can be engineered to: bind cancer and immune cells to redirect the immune system to attack cancer (T cell engagers), target multiple proteins (bispecific antibodies), combine with linker molecules (antibody drug conjugates), reduce in size or modify delivery via mRNA or DNA (in vivo expressed biologics) to improve specificity, potency and targeting.



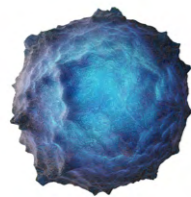
### Oligonucleotides

Oligonucleotides are short DNA or RNA molecules that interact with messenger RNA to prevent translation of a targeted gene. Targeted delivery can be achieved through conjugation to a homing ligand as well as encasing programmable therapies in lipid nanoparticles (LNPs) to improve cellular uptake.



### Anticalin® protein

Anticalin® proteins are artificial proteins derived from human lipocalins. They have a diversifiable amino acid sequence that results in four loops. These loops assemble into a cup-like structure that can bind both smaller and larger molecules.

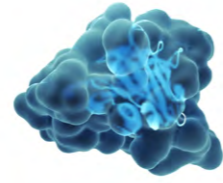
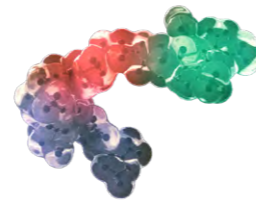


### Cell therapy

Cell therapies are currently in development with the aim to halt and reverse disease, restore damaged organs, and ultimately, cure many life-threatening conditions. We aim to do this by placing new, healthy cells into the body to replace diseased or damaged ones, or removing disease causing or dysfunctional cells using immune cells.

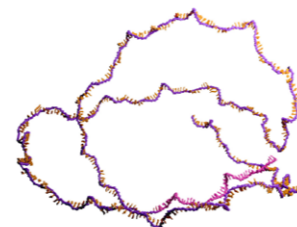
### PROTAC

A proteolysis-targeting chimera (PROTAC) is a hetero-bifunctional molecule containing two small molecule-binding ligands joined together by a linker.



### Therapeutic protein

Proteins consist of one or more chains of amino acids, linked together by peptide bonds. There are 20 naturally occurring amino acids that make up the building blocks of proteins. Antibody-based drugs are an example of a group of therapeutic proteins.



### Modified RNA

Modified RNA is a single-stranded RNA that conveys genetic information from DNA to the ribosome, where it is translated into protein products. Advances in RNA technologies to include replicase in the coding sequence allows the amplification of the number of RNA copies that can be produced. Self-amplifying RNA is the next disruptive mRNA platform.



### Bicyclic peptide

Bicyclic peptides are synthetic, highly constrained peptides, typically between 9 and 15 amino acids in size.



### CRISPR gene editing

CRISPR/Cas9 exploits a natural bacterial defense mechanism, to precisely edit the genome in somatic gene defects.

### Ionis Pharmaceuticals Antisense Technology Broadening our approach across therapy areas

Antisense oligonucleotides (ASO) are designed to bind precisely with specific RNAs thereby modifying the production of proteins potentially associated with disease. One of our molecules targets the mRNA for patatin-like phospholipase domain-containing 3 (PNPLA3) protein. Patients carrying a variant in the PNPLA3 gene leads to the production of a dysfunctional liver enzyme that is not only unable to digest fat itself, but impedes another type of enzyme from doing it too. If successful, this could be potentially the first precision medicine for non-alcoholic fatty liver disease (NAFLD).

### Pieris Pharmaceuticals Moving ahead with Anticalin® protein technology

The anticalin technology is designed to deliver engineered proteins which are significantly smaller than monoclonal antibodies, where each one is tailored to bind with antibody-like potency and selectivity to a drug target of interest. Their small size makes them strong candidates for direct delivery by inhalation to the lung.

The lead molecule is an engineered Anticalin® protein designed to bind to the interleukin-4 receptor alpha and block the action of two key cytokines responsible for lung inflammation in asthma. It is in continuing clinical development.

### Procella Therapeutics and the Karolinska Institute in Sweden Advancing regenerative medicine using stem cells

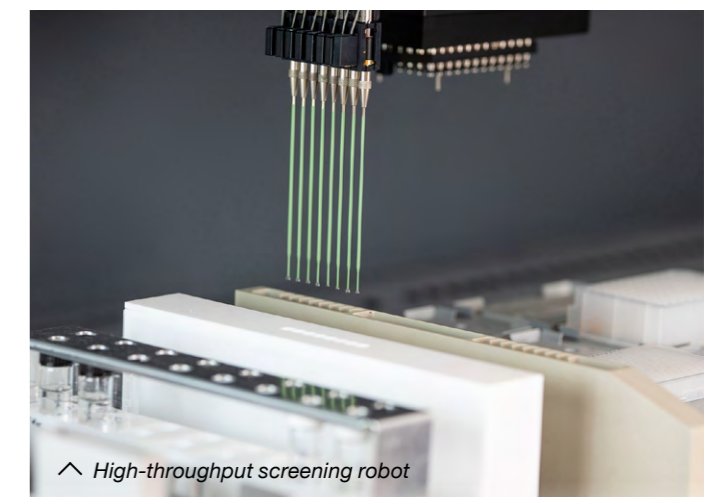
This highly selective approach is focused on developing new stem-cell based therapies aimed at repairing parts of the heart that have been damaged by a heart attack. Human ventricular progenitor cells are implanted in the injured heart to form new cardiac tissue that becomes vascularised, leading to improved cardiac function.

### Scorpion Therapeutics Enabling the discovery, development and commercialisation of novel cancer treatments against 'undruggable' targets

We aim to precisely target proteins that control gene expression, called transcription factors, to help develop therapeutics that can affect hard-to-target cancer proteins with the potential to transform oncology treatment. Many transcription factors have long been identified as important targets for new cancer treatments and as drivers of disease, but have previously been considered 'undruggable' using conventional drug discovery approaches.

### Zealand Pharma Building on our complement leadership with expansion into peptide therapies

Macrocyclic peptides offer a number of advantages. Their high selectivity and potency allow for low dosage volumes, improving ease of administration, and they have the potential to treat a broad range of complement-mediated diseases. We are exploring next-generation peptide therapies with the aim to help more patients with complement-mediated diseases.



High-throughput screening robot



# Better predicting clinical success

In our efforts to improve our ability to predict the clinical success of our candidate drug molecules, we are adopting a range of cutting-edge technologies.

## Humanised models

Humanised models bridge the gap between animals and humans and are a big step forward compared to the conventional human cell cultures which have been in use for many years. These models provide an environment in which human cells behave more like they would in the body, generating data about toxicity, efficacy and other key effects that are more relevant to patients than previous methods.

- Organ-Chips help us to recreate what happens in full-size tissues and organs. Recently published research in collaboration with Emulate, Inc. and the Wyss Institute at Harvard University, demonstrates the ability of the Liver-chip to model the liver toxicity of eight previously-studied compounds, and the Bone marrow-chip to effectively replicate drug-induced toxicity responses observed in human patients at clinically relevant doses.
- 3D bioprinting and organoid models are helping us create complex structures for research into kidney and respiratory disease where pre-clinical to clinical translation is a challenge. Our collaboration with Harvard University created human vascularised renal proximal tubules to study cellular crosstalk and the behaviour of our compounds in the kidney. To support our emerging research and assess our drug candidates in COPD and IPF, we have developed 3D organoids to help mimic the complex cell interactions in the lung and provide many advantages compared to simpler models, such as monocultures and 2D models.
- In the development of 'miniature organs' to recreate the mechanical and electrical properties in a beating heart, we are working with Novoheart, using their 3D human ventricular cardiac organoid chamber. This 'heart-in-a-jar' technology is designed to reproduce key characteristics of heart failure with preserved ejection fractions.

## CRISPR-Cas9 genome editing

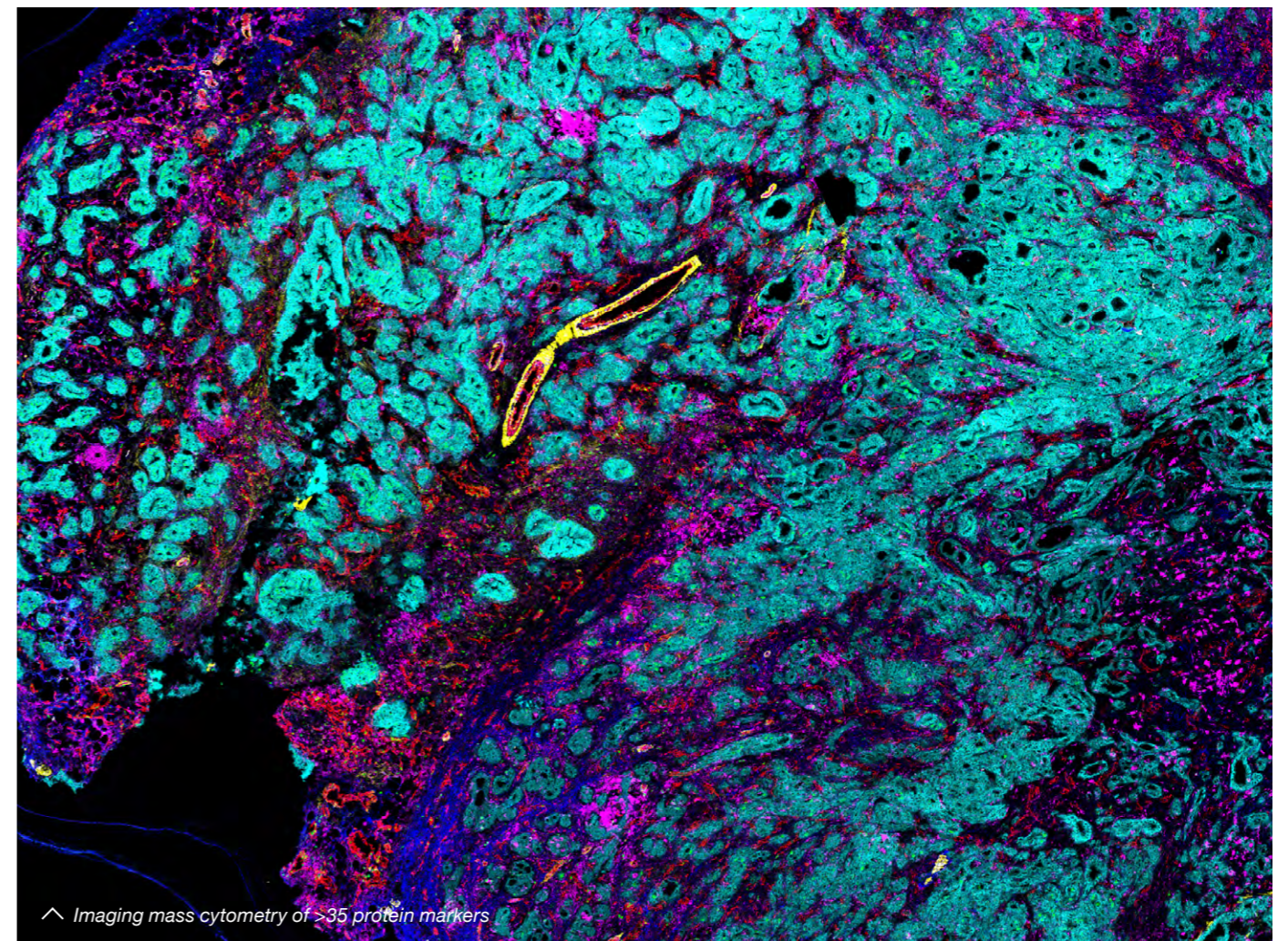
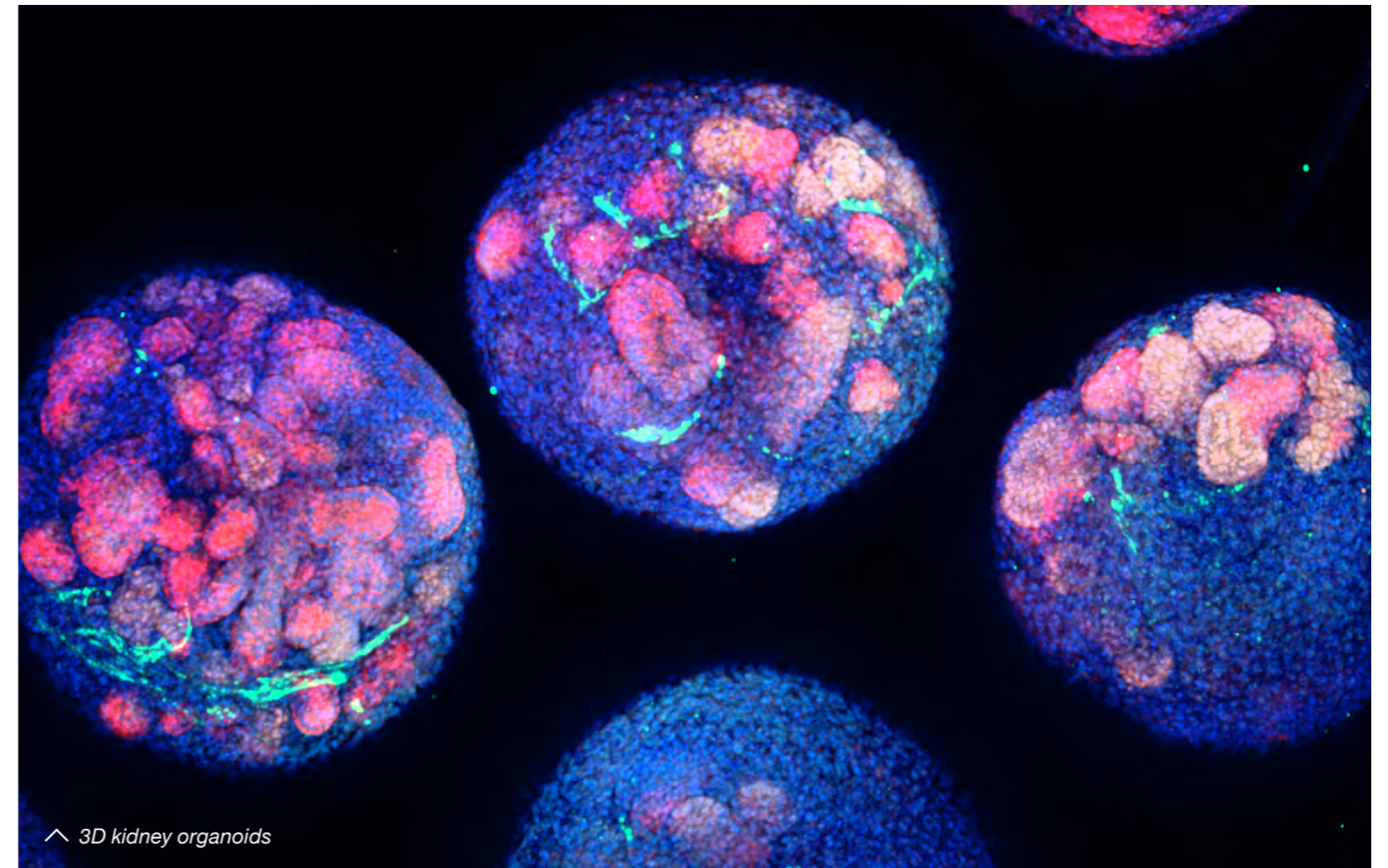
CRISPR is a powerful tool in target selection and validation. It can be used to create precise genetic disease models, often involving the change of a single nucleotide. We have applied CRISPR to create over 120 cellular disease models in which we have deleted or introduced single nucleotide changes to genes to examine the effect of specific genes on disease pathways. We are also actively working to use CRISPR technology to correct genes, such as the HTT gene in Huntington's disease as well as advance CRISPR technology, by developing Prime Editing Nuclease approaches to enhance specificity and potentially enable future therapeutic use.

## Mass spectrometry imaging

Mass spectrometry imaging helps us to capture, at a molecular level, the exquisite cellular interaction that can both define a disease, and also monitor for effective treatment. By retaining the spatial complexity in a tissue sample, we can monitor the modulation of biomarkers in tissue in response to drug treatment, while simultaneously also quantifying drug biodistribution and immune cell populations. With the Cancer Research UK-funded Grand challenge consortium, we aim to use this imaging to create 3D maps of tumours for the first time, including the whole tumour and its microenvironment. Along with new advances that allow us to analyse larger molecules and protein-drug complexes, these technologies can give us a holistic view to help inform pre-clinical decision making.

## Patient-derived xenograft models

Patient-derived xenograft models are helping us recreate the complexity and heterogeneity of a tumour for studying late-stage cancers, and model the mechanisms by which tumours become resistant to current therapies. With the University of Colorado in the US, we are continuing to show how different patient-derived xenograft models can help define new combination therapies in oncology.



# Model-informed drug development

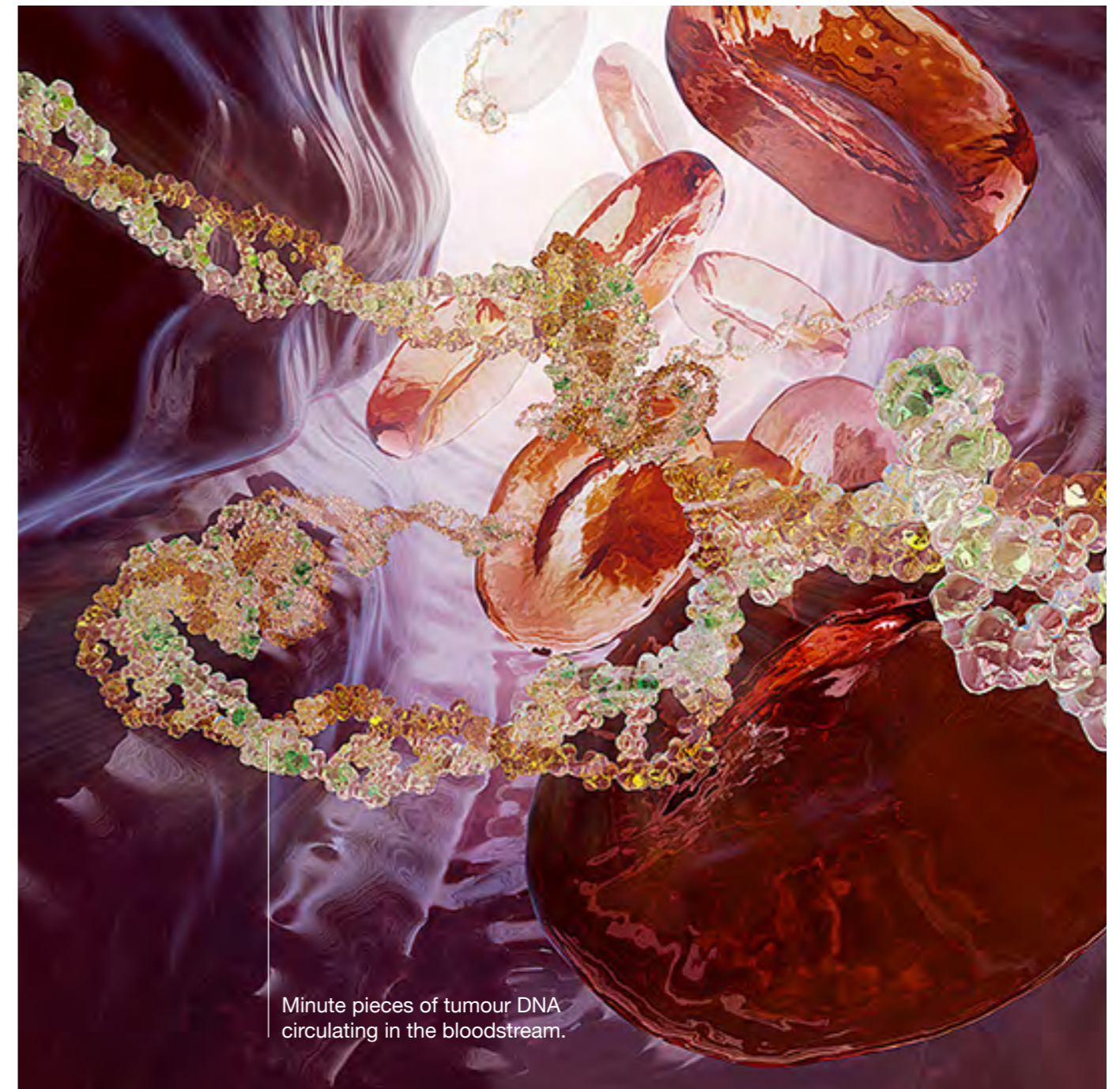
Quantitative pharmacology uses advanced analytical modelling to generate new and vital insights on drug efficacy and safety across the entire drug discovery and development continuum. Through modelling, simulation, systems pharmacology and advanced bio-analytics, we are interrogating how drug candidates interact within the human body to help inform decisions about the optimal balance between efficacy and safety. Working collaboratively with partners across AstraZeneca and beyond, we provide unique insights and expertise to ensure we deliver the right dose to the right patients.

With an extensive skill-base in clinical pharmacology, pharmacometrics, statistics and biometrics, our collective of expert scientists are pioneering new ways to extend our predictive modelling capabilities. By combining the latest computational technologies with the diverse expertise of our people, we deliver clinical programmes with greater speed, quality and efficiency.

Using extensive clinical pharmacology data, our teams are designing drug development models to simulate virtual trials that:

- Examine how the benefit-risk profile of a potential drug candidate is impacted by real world variables such as age, sex or comorbidities.
- Offer insight into how a potential drug candidate may perform against current treatments or in combination with other therapies.
- Predict outcomes for efficacy and safety across different patient profiles, helping expand the reach of our drug candidates to additional patient populations who may benefit.

By providing these approaches, Quantitative Pharmacology is an important complement to the traditional toxicology and animal science methods in drug safety studies, and is key to helping better predict and deliver clinical success for AstraZeneca and the patients we serve.



Minute pieces of tumour DNA circulating in the bloodstream.

## Circulating tumour DNA (ctDNA) in Oncology

Circulating tumour DNA (ctDNA) are small DNA fragments that often leak from cancer cells into a patient's bloodstream. The detection and analysis of ctDNA may provide valuable insights about a patient's prognosis or information on how well a treatment is working.

In collaboration with GRAIL, we are using a novel approach to detect ctDNA to identify patients with high-risk, early-stage disease who could benefit most from treatment. Through this collaboration, we aim to accelerate the adoption of ctDNA across clinical trials and make our cancer medicines available at an earlier stage of disease when there is greater potential to transform patient outcomes.

Researchers are investigating whether ctDNA measurements can identify patients with minimal residual disease (MRD) who may be at higher risk for disease recurrence post-surgery or post-adjuvant therapy.

Identifying MRD may enable physicians to intervene earlier and to offer personalised, effective treatments that could increase survival and improve quality of life. We are collaborating with diagnostics experts like ArcherDX to generate highly sensitive, personalised ctDNA assays to test for MRD, which has the potential to inform patient prognosis and to tailor individualised treatment options.





## Clinical innovation pioneering new approaches to engagement in the clinical and beyond

We are transforming how we conduct our clinical research, improving the patient experience and providing clinical evidence of the safety and effectiveness of new treatments more quickly and effectively.

In a typical year, we conduct over 240 global clinical trials, involving more than 123,000 patients, in around 60 countries. Digital technologies enable us to improve design and reduce set-up time. Electronic health records will help improve delivery, and more accurately forecast drug supplies, avoiding waste and delays. Trials will be more patient-centric, with less burden on the patients, and the value of the information we get from these trials will be greater, helping us to make faster and more effective decisions.

### Accelerating and improving patient recruitment

We have started using Patient Registries to help us identify patients quickly and reach a broader demographic of patients. We have also recently launched eConsent, a new digital tool that enables remote sharing and review capabilities of the informed consent with patients to get new trials underway safely and at speed.

### Reduced patient and investigator burden

Digital is helping patients optimise medication use, connect with medical staff, and manage or prevent adverse events during trials. Unify, a patient application and clinical trial support tool was developed with patients and medical professionals to virtually connect all study participants to create an optimal participant experience before, during and after a trial. Unify also generates quality real-time data that can enable novel endpoints, provide optimal healthcare and improve patient outcomes. In addition, invasive monitoring is being replaced with digital alternatives. Finger prick glucose monitoring, for example, is being replaced by patches that give continuous readings. It is also helping us improve disease understanding and patient outcomes, and in early trials, we are exploring new digital markers - for instance, determining the relevance of fractional exhaled nitrous oxide (FeNO) as a biomarker in assessing lung inflammation.

### Patient centric and clinically relevant endpoints

In our early clinical trials, we are using more adaptive designs, adopting biomarker-guided patient selection and including novel imaging techniques and biomarker endpoints, to inform outcomes earlier and guide trial design. We are also establishing novel composite endpoints as surrogate measures of longer-term outcomes to be able to assess our drug candidates in smaller, shorter trials. For example, in severe asthma and COPD trials exacerbation rates are rare events meaning large, lengthy trials are required to assess efficacy. Our scientists developed CompEX, a composite endpoint of exacerbations through diary event capture which could measure for severe exacerbations with substantially fewer patients, in less than half the time of previous trial designs, promoting faster decision-making in early clinical development.

### Digital therapeutics

As our digital capabilities grow, we are able to explore how we can help patients prevent, manage or treat their condition with evidence-based, digital therapeutic solutions. For instance, with Voluntis and the National Cancer Institute, we are developing a digital therapeutic for women being treated for recurrent platinum-sensitive high-grade ovarian cancer. Currently in clinical trials, this aims to support patients through tolerability and management of adverse effects - recently winning the Prix Galien award for best patient engagement technology.

# Our R&D response to COVID-19

Our R&D response to the COVID-19 pandemic highlights our commitment to science, collaboration, and delivering life-changing medicines to the people who need them most. When the true scale of the crisis became clear:



^ We continued our clinical trials around the world and delivered medicines to patients



^ We kept our employees safe through testing and bolstered the UK's national testing effort



^ We mobilised our own research to advance the development of a long-lasting antibody therapy, recognising that not everyone could receive a vaccine



^ We partnered with Oxford University in a united endeavour to develop a vaccine made for the world at no profit during the pandemic

## Keeping our employees safe globally

We established our internal COVID-19 testing programme in just 18 days in March 2022. Initially set up to safeguard those working on-site and maintaining our supply of medicines, we quickly expanded the programme to include regular PCR and antibody testing to employees at our key sites and out in the field. Over the pandemic, we switched from nasal swabs to saliva sampling to make testing easier and less invasive, developed a bespoke web platform to enable quicker, simpler testing, achieved external accreditation for our UK and US COVID-19 testing labs, and introduced pop-up, mobile PCR testing to improve accessibility for all.

## We rose to the call

In April 2020, we answered the call from the UK government to help bolster the national testing effort. In collaboration with the University of Cambridge, GSK and Charles River Laboratories, we helped to set up the Cambridge Testing centre in just five weeks turning a few empty rooms into a high-throughput testing facility. In just 12 months, the centre delivered over 3.25 million samples.

In addition to delivering the testing required, we also innovated and streamlined the process. Together with our partners, we reduced the amount of testing reagent required by half, partnered with BiologIC and Electrolux Professional to make samples safer and testing more scalable and sustainable, developed a new direct-to-PCR approach alongside Primer Design reducing time-to-results by two hours, and deployed a pooled testing approach, enabling more people to be tested with fewer samples to support mass testing.

## Our commitment to finding new treatments...

Since 2018, we have been working on a novel platform to discover and manufacture therapeutic antibodies of an unknown viral pathogen in less than 60 days. The platform uses microfluidics to screen antibodies from individualised B cells, and enabled us to move our potential long-acting antibody (LAAB) combination from discovery to clinical trials in less than 3.5 months. Our expertise in antibody discovery also enabled us to extend the lifetime of the LAAB in the body from 3 months to potentially up to a year.

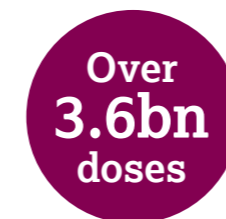
LAABs could potentially treat or prevent disease progression in patients already infected with the virus, or be given as a preventative measure prior to exposure for those people for whom a vaccine may not be appropriate.

## ...and developing a vaccine made for the world

We partnered with Oxford University to develop a COVID-19 vaccine made for the world at no profit during the pandemic. To deliver the vaccine to as many countries as possible, we set up more than 25 new supply partners in over 15 countries, and heavily invested in our existing facilities to increase their productivity. Overall, we cut our supply chain distribution time down from 6 years to 300 days.

AstraZeneca was the first global pharmaceutical company to join the COVAX facility in June 2020. We and our partners are the largest contributors to COVAX, providing over two thirds of all vaccines supplied so far. We are committed to the global mechanism to develop and produce new tools to tackle COVID-19, and enable equitable access to them across the world, for all participating countries, regardless of income level.

We continue to follow the science and develop new solutions and strategies to respond to the evolving SARS-CoV-2 virus, to help safeguard the health and wellbeing of communities around the world.



More than 2 billion doses supplied so far...



...to over 170 countries worldwide.



Two-thirds of the vaccine supplied in the first half of 2021 went to low and middle-income countries.



We test over 35,000 employees, contractors and partners for COVID-19 weekly...



...by processing saliva samples from 38 sites across 5 countries.



We run 93 weekly sample collections and 29 courier routes, covering over 25,000 miles.

Our R&D culture  
 Three organisations. One aim.  
 Focusing on quality, not quantity.  
 Transforming our science  
 Keeping doors and minds open  
 R&D places and people  
 Making our science sustainable  
 Led by science. Driven by patients.

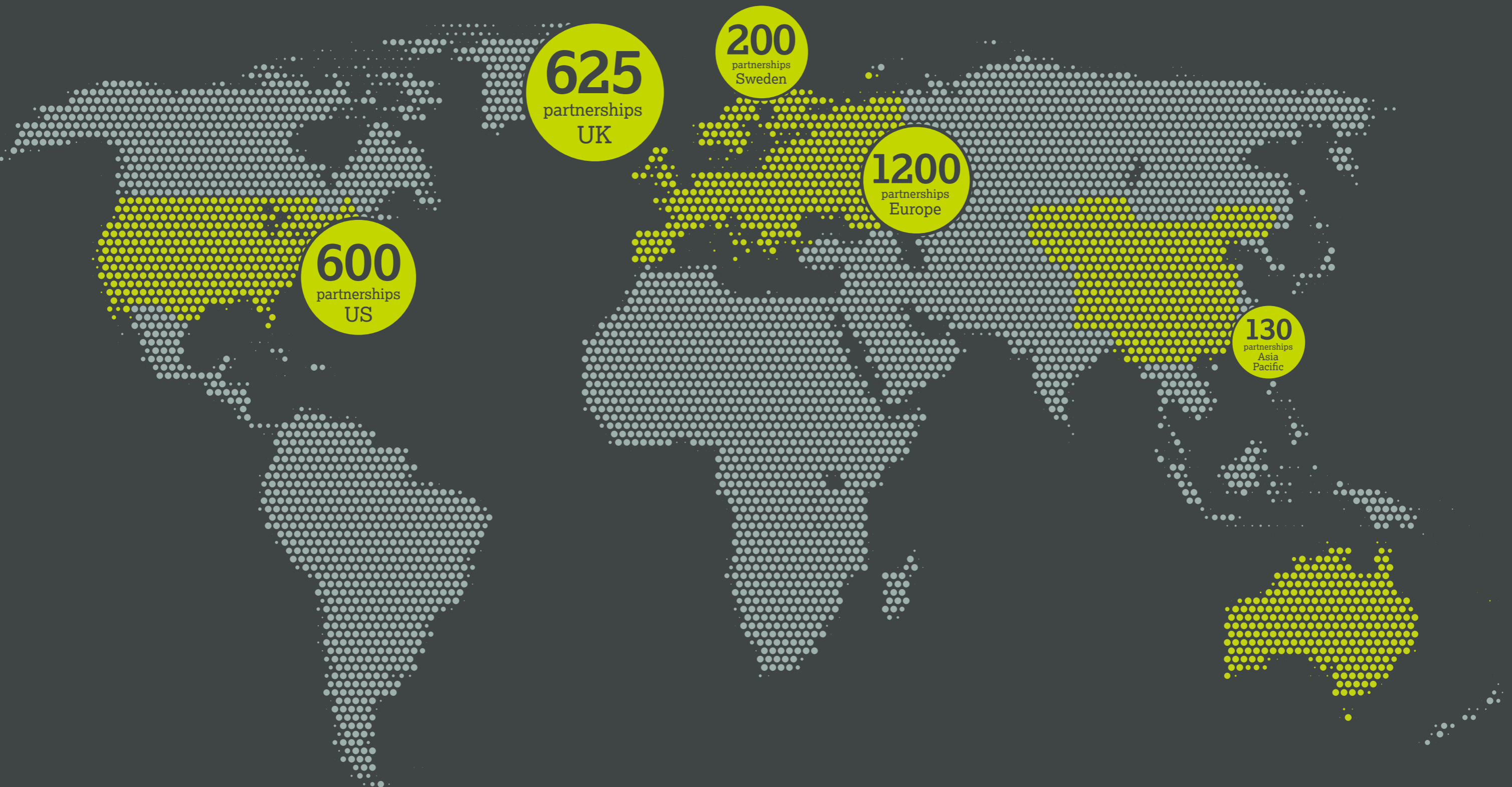
# Keeping doors and minds open

We know that however innovative our science is, however effective our medicines and delivery methods are – if we are to achieve all we want to achieve, we cannot do it alone.

To address all the issues facing healthcare and achieve the scientific breakthroughs we aspire to, we need to work together, collaborating among ourselves and with others, bringing the best talent together to tackle the toughest problems.

As a business, our teams are leading the way in creating open research environments that go beyond the usual collaborative models, with academia, biotech companies, industry peers, healthcare systems and governments.

We have over 2000 active partnerships and aim to lead the industry in partnership building over the coming years, because this is a powerful source of transformational potential.



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science sustainable

Led by science.  
Driven by patients

## Working side-by-side with academic institutions

Our scientists work in collaboration with others in dedicated laboratories in universities and research institutions, aiming to generate high-impact science to support possible future advances in life-changing medicines.

These institutions include the AI Innovation Centre and the Karolinska Institute's Cardio Metabolic Centre in Sweden, the Max Planck Chemical Genomics Centre III in Germany and in the UK, the Francis Crick Institute, the Functional Genomics Centre at the Milner Institute, the Antibody Alliance Laboratory with Cancer Research UK, the Medical Research Council Laboratory for Molecular Biology (MRC LMB), the Respiratory Hub at Imperial College and the University of Cambridge.

In addition, we have established a collaborative research initiative that brings together seven of the world's foremost oncology medical centres, each with strong translational research capabilities, to expedite research in some of the hardest-to-treat cancers. The partner institutions include: Institut Gustav Roussy (France), Johns Hopkins Medicine and Memorial Sloan Kettering Cancer Center (US), Universidad de Navarra and Vall D' Hebron Institute of Oncology (Spain), Peter MacCallum Cancer Centre (Australia) and Princess Margaret Cancer Center (Canada).



^ Bioscientists in our labs in Wuxi, China

## Open Innovation

Our Open Innovation programme is designed to offer a permeable research environment where scientists both inside and outside of AstraZeneca can share their ideas and collaborate on projects.

Since the programme was launched in 2014, we have reviewed more than 1000 proposals from scientists in 40 countries across six continents. Our Open Innovation collaborators have been awarded \$75 million in grant funding to support their research projects using our assets, and our Open Innovation portfolio now features 35 ongoing or planned clinical trials and more than 425 pre-clinical studies.

Our Open Innovation portal makes it easy for external scientists to access all the collaborative opportunities we offer to help find ways to advance medical science together:



^ Preclinical research  
Breaking new ground in modern drug discovery



^ Clinical research  
Translating innovative ideas into the next generation of medicines



^ CoSolve  
Finding bold and innovative solutions to transform patients' lives



^ Idea incubator  
Catalysing collaborations to drive healthcare innovation



# R&D places and people

**AstraZeneca is profoundly committed to its purpose of pushing the boundaries of science to deliver life changing medicines, and we have built our business around it.**

We have an active R&D presence in more than 60 countries across the globe with strategic R&D centres including The DISC in Cambridge, Gaithersburg, Maryland in the greater Washington, D.C. region in the US, and Gothenburg in Sweden, together with the recently announced centre to be located in Kendall Square in Boston, MA, and the acquisition of Alexion added a Rare Disease R&D Centre of Excellence in New Haven, Connecticut, US.

We have integrated R&D teams and accelerated decision making processes, and are using our unique scientific capabilities to deliver one of the most productive pipelines in the industry.

Of our 80,000 employees, more than 13,000 work exclusively in R&D. In 2021, our scientists published a total of 871 manuscripts, with 169 in high impact peer-review journals (impact factor exceeding 15 according to Reuters five-year rating), compared to one in 2010.

Our business and scientific culture is diverse, inclusive and collaborative, and we do everything in our power to enable all of our people to be the best they can be.

## Strategic science centres

### Gaithersburg

A unique, innovative and inclusive modern campus, just a short drive from Washington DC, our Gaithersburg facility is home to a diverse community of more than 4,000 people, with the capacity to discover, develop, manufacture, and commercialise life changing medicines – all on one site.

With a team of world-renowned scientists, cutting-edge technology, and a collaborative, interactive and cross-functional scientific culture, it's a great place to work and an exciting place to be. Our outstanding facilities and amenities promote wellness and a positive work-life balance, helping us attract and retain the best talent, while contributing to our business's values-led and sustainable approach to R&D.



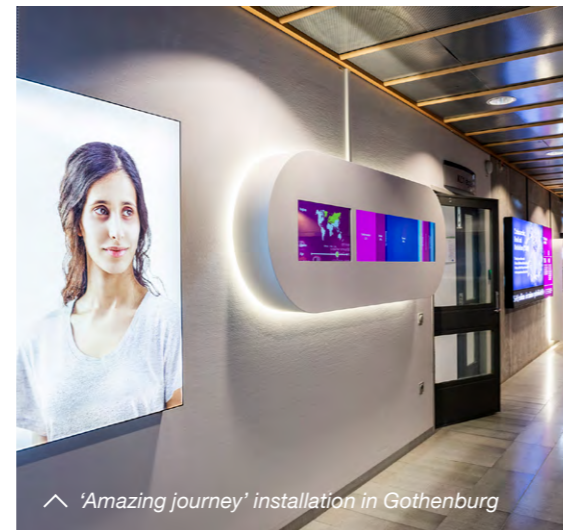




∨ R&D centre in Gothenburg



∧ CoffeeLab meeting space in Gothenburg



∧ 'Amazing journey' installation in Gothenburg

## Gothenburg

With more than 2,600 employees from 70 countries, our vibrant Gothenburg site helps support the entire life-cycle of AstraZeneca medicines, from drug discovery and clinical trials, through to global commercialisation and product maintenance. In 2017, we launched Lab4Life, creating an open and truly shared research environment that goes beyond the usual laboratory model. By breaking down traditional lab walls, automating processes and driving state-of-the-art IT, we are creating novel ways of working to speed up delivery of new medicines.

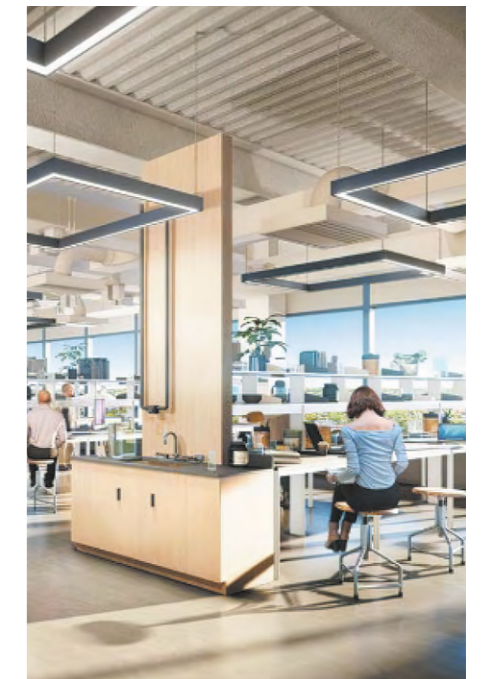
Looking to the future, Gothenburg has initiated the creation of a new, global cluster for health and life sciences, as part of the GoCo Health Innovation City project, which includes the Gothenburg BioVentureHub. There are currently more than 30 external companies and one academic group co-locating with AstraZeneca at the heart of the Gothenburg site. By facilitating interactions between drug, device, diagnostics and digital health companies, we are creating a dynamic, creative and fertile environment to help unlock the power of what science can do.



## Boston

Located in Kendall Square, Cambridge, Massachusetts, at the heart of the greater Boston life science ecosystem, the new AstraZeneca R&D centre will support approximately 1,500 R&D, commercial and corporate colleagues in a vibrant new space, designed to encourage collaboration and innovation.

The site, scheduled for completion in 2026, will bring together our Boston area AstraZeneca and Alexion teams and contribute to our aim of building bridges across our Alexion and AstraZeneca networks. Optimised for both internal and external collaborations, our Boston centre will play a large part in our next chapter of success to show the powerful results of what science can do when we come together to collaborate and learn from each other.



Our R&D culture

Three organisations. One aim

Focusing on quality, not quantity

Transforming our science

Keeping doors and minds open

R&D places and people

Making our science sustainable

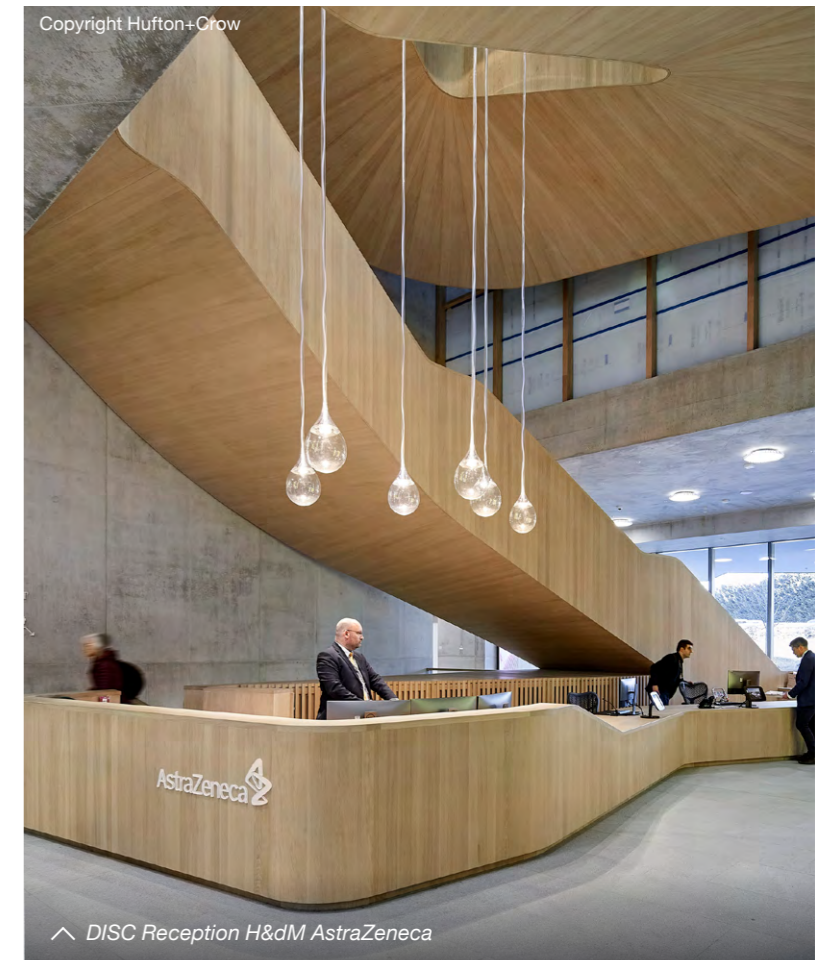
Led by science. Driven by patients.

## Cambridge

Cambridge is home to one of our global strategic R&D sites – The Discovery Centre (DISC), which is a state-of-the-art research facility and our corporate headquarters. The DISC is designed to play a central role in enabling the delivery of our science-led strategy, turning science into medicine. It is located at the heart of the Cambridge Biomedical Campus, one of Europe's leading life sciences clusters.

With access to world-class talent and opportunities for collaboration, being in Cambridge enables us to continue to focus on innovative science in our chosen therapy areas. At the same time, we're committed to ensuring our company is a great place to work for the more than 4,000 AstraZeneca employees located here.

The scale of our collaboration with local partners is significant for our company and for patients. Currently we're involved in over 200 partnerships across the Cambridge life sciences ecosystem and more than 130 active collaborations with the University of Cambridge. And here – as well as globally – partnerships and collaborations like this are pointing the way to the future, as we focus on the discovery, development and delivery of the next generation of life-changing medicines.



# Inspiring great scientists

Our ambition to take and sustain scientific leadership rests on our ability to attract and retain the best scientists. And nowhere is our determination to do this more evident than in the way we recruit, develop and inspire our people.

It's vital that we continue to attract the brightest minds, the best talent and the boldest innovators. People who share our passion for science and our belief in its potential to re-define the possible.

In return, we offer a working environment that truly reflects our ambition to push the boundaries of science. A place that empowers and inspires. Where curiosity, innovation and collaboration flourish, where drive and determination are rewarded, and where great science comes alive.

We believe that the best science almost always comes from teams with diverse backgrounds, different skills and a broad range of experiences, and as a business, we are committed to maintaining a culture that is not only diverse and inclusive, but genuinely inspirational.

✓ *AstraZeneca at the Pride in London event*



**Our people impress and inspire us.  
Our values define and guide us.**

- We follow the science
- We put patients first
- We play to win
- We do the right thing
- We are entrepreneurial



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^ Scientist in our labs in Macclesfield, UK



^ Cell biologists in our labs in Gothenburg, Sweden

## Women as Leaders

Our Women as Leaders programme supports our aim of increasing the number of female colleagues in senior scientific roles, and brings women together to discuss issues like career progression and personal development.

In the last decade, we have increased the number of women in senior roles from 25% to 48%. And in January 2019, AstraZeneca was the only major pharmaceutical company included in the Bloomberg Gender-Equality Index, which distinguishes companies committed to transparency in gender reporting and advancing gender equality.

## AZPlus

Gender equality is also supported by AZplus, our employee resource group which aims to empower LGBTQIA+ colleagues to reach their full potential. With AZPride and the #thisisAZ campaign, AZplus has promoted inclusivity both internally and externally to encourage the recruitment of a diverse talent pipeline.

Its voluntary work led the launch of a groundbreaking cross-sector initiative, the Proud Science Alliance (PSA), which promotes LGBTQIA+ inclusion in life science and healthcare through a new website and social media channels, reaching thousands of scientists globally.

## Development assignments

Providing our people with ready opportunities for development is high on our agenda and the majority of this comes from direct, on-the-job experience. From our Development Marketplace to cross-team secondments and shadowing opportunities, our programmes set out to make sure that we can continue developing the skills and capabilities to equip everyone in R&D to be the best they can be. And throughout 2019, we saw more than 80 colleagues take up assignments outside their core role to broaden their learning and experience.



^ Protein engineer in our labs in Cambridge, UK

## Chief scientist programme

As part of our drive to continue creating great science, we are keen to work with the best scientists, both within and outside of the pharmaceutical industry. To make sure that we attract top science talent from academia, we have developed our flexible and versatile Chief Scientist Programme.

By tailoring individual arrangements to enable scientists to work with AstraZeneca R&D full-time, part-time, or on assignment from university, we promote a permeable research environment, designed to meet the needs of both individuals and institutions.

Being flexible in our approach enables scientists of the highest calibre to stay connected to their research and their universities, and work flexibly between commitments. This empowers them and us, enabling us to connect with the best scientific minds to work together in accelerating the discovery and development of life changing new medicines.

## Early talent programmes

We have a portfolio of high-quality early career programmes supporting a diverse range of scientific talent. Every year, we support more than 500 young scientists – including apprentices, undergraduate and graduate placements, PhDs and post-doctoral scientists.

### Postdoctoral programme

Our postdoctoral programme brings together motivated and innovative postdoctoral scientists who have a passion for ideas and a real desire to make a difference through an academic-style postdoctoral position in a global pharmaceutical setting.

The two to three-year programme funds postdoctoral projects originating with AstraZeneca scientists and clinicians from across our many different scientific disciplines and areas of research. These projects address fundamental scientific challenges that underpin drug discovery and development.

In addition, each postdoctoral scientist receives a tailored training and development programme, encompassing key skills such as presentation delivery and publication writing. This is a very valuable and well-rounded experience.

### Graduate programme

Our graduate programme offers graduates the opportunity to complete three different placements in two years across R&D, focusing on delivering breadth and depth of experience. Graduates are supported in each placement by a line manager and by a mentor who remains with them throughout the programme, providing career counselling and guidance.

As well as developing technical skills by working with world-class scientists using state-of-the-art facilities, all graduates are enrolled into our Global Graduate Development Programme, where the focus is on the softer skills that are required to successfully transition into industry.

# Making our science sustainable

We are a scientifically driven business with a strong global presence and as such, believe that we have a duty of care to help improve people's health and do as much as we can to contribute to the health of the planet.

Our approach to sustainability is built around three pillars: access to healthcare, environmental protection, and ethics and transparency.

## Environmental protection

We set science-based emissions reduction targets to contribute to the global fight against climate change. We are among the first seven companies globally to have our targets verified by the Science-Based Targets initiative as being in alignment with their new Net Zero Standard, the world's first science-based certification of companies' net zero targets in line with the Paris Agreement's goal of keeping planetary warming to 1.5°C.

## Environmental protection

We appreciate the interconnection between our business and the wider world and strive to find innovative ways to make the most efficient use of resources and help protect our environment – aiming to manage our environmental impact across all our activities and products.

- For instance, we work in collaboration with the not-for-profit organisation, My Green Lab, to run a globally organised, locally delivered initiative, called Green Labs. Its aim is to improve the sustainability of our research labs, starting with surveys among people working in the lab environment to benchmark our current sustainability efforts. The initial phase began in 2019, with nearly 900 scientists across six different sites. Currently, all of our labs at our core R&D sites have now been certified to at least Gold level, which has already resulted in reduced energy and water use. Specifically, 61% of our total electricity use is sourced or generated from renewable sources and we have reduced our water use by 8% since 2015.

- Our chemists have devised several new techniques that can make drug design and discovery more sustainable, without sacrificing safety or effectiveness; using light as a catalyst, exploring new ways to create the 'building blocks' of chemical reactions, finding 'shortcuts' in the number of synthetic steps to make a medicine reducing by-products.
- We are also pioneering new approaches to reduce our dependence on natural resources and minimise the environmental impact of our products. Our Lab Plastics Recycling initiatives in Cambridge, for example, will save over 4.5 tonnes of plastic from incineration or landfill each year.



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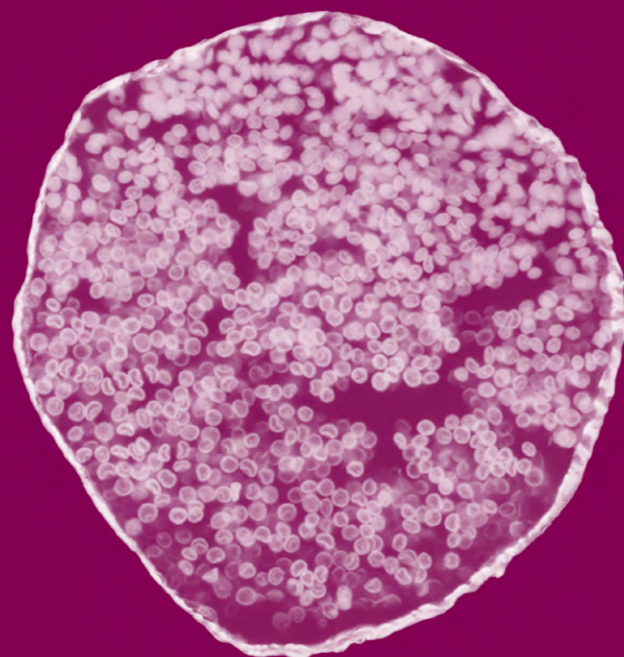
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Driven by patients

### Access to healthcare

Patients and healthcare professionals have a deeper understanding of the connections between products, waste, and pollution. We have created an innovative Green Chemistry tool to facilitate solvent selection, allowing our scientists to consider environmental properties alongside physical properties and regulatory needs.



## Access to healthcare

We are committed to improving access to healthcare by removing barriers, addressing the burden of disease across R&D, and via our ambition to make our medicines more accessible and affordable, and enable improved disease prevention and treatment.

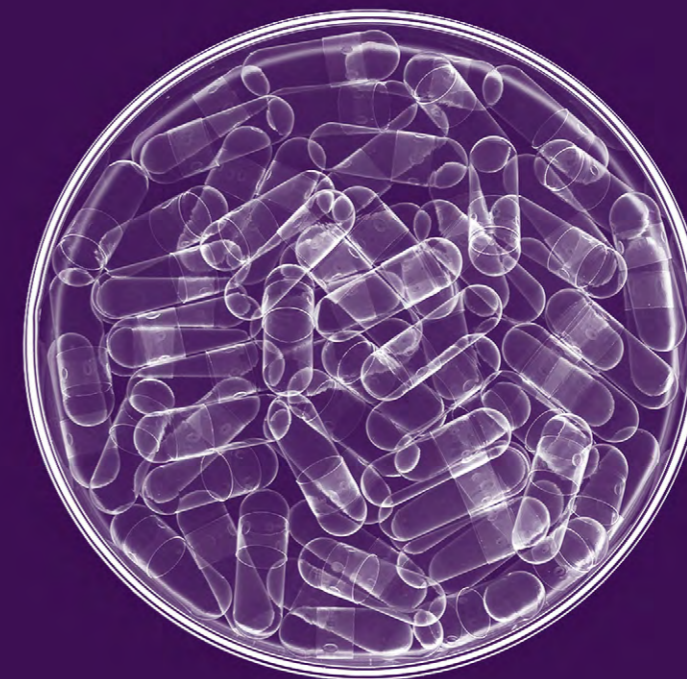
- By maximising the value of health-related data we are moving towards accelerating our clinical trials and the delivery of potential new medicines. For example, through the adoption of Electronic Health Records (EHRs), we can access a vast and highly relevant data source with huge potential to refine or replace many clinical trial processes including patient identification, selection, trial conduct, and capture of data.
- Our ground-breaking DISCOVER CKD study uses real-world data from more than 100,000 chronic kidney disease patients across six countries to better understand the patient journey. This three-year study will analyse data which includes treatment patterns, quality of life and diet that are not captured using traditional tools. The study will help us identify gaps we may one day address with our emerging portfolio of renal therapies, shaping the future of care and reaching a broader number of patients.
- Another example of helping increase access to healthcare is the [Emerging Markets Health Innovation Hubs](#) (EMHIs): integrated, open science ecosystems, operating in partnership with academia, entrepreneurs, industry, medical professionals, governmental partners and venture capitalists. EMHIs are designed to improve access to

resources and technology, improve capacity for local R&D, and boost AstraZeneca's capabilities to address local needs. The first Hub in Emerging Markets opened in Russia in July 2018, followed by Hubs in Brazil, Argentina, India, Singapore and the Gulf Cooperation Council countries, as well as mainland China, Taiwan, and Hong Kong. The Hubs have already produced tangible results, such as key cross-sector partnerships, and innovative new products, solutions and research opportunities. The connected ecosystems have also accelerated innovation by collaborating with local start-ups, complemented by a partnership with Slush – a global community of start-ups, entrepreneurs and investors.

- Our Global, multi-award winning New Normal, Same Cancer campaign brought together patient advocacy groups, medical societies and governments from around the world to urge patients back into care during the COVID-19 pandemic. The campaign was in direct response to the needs of the cancer community, developed and delivered with and for patients and the broader cancer community in 68 countries around the globe. In addition, our award-winning, best-in-class Patient Partnership Programmes enable us to consult and collaborate with patients and caregivers to better understand their needs and co-create solutions that matter to them.

### Clinical trial transparency

The clinical trial phase is essential in the development of new medicines. As an ethical and transparent company, we apply our global policies and standards wherever trials take place and require all our sponsored trials to include patient engagement practices.



## Ethics and transparency

We are building trust in our business and our science by continuing to pursue ethical practices and by bringing a high level of integrity to everything we do.

- Our research sites and bio-hubs are inclusive and dynamic centres for innovation, designed to enable science to thrive. A good example of this is the new, global cluster for health and life science that we created in Gothenburg as part of the GoCo Health Innovation City project (see 'R&D places and people' on page 40), which includes our pioneering BioVentureHub. Numerous different companies and an academic group have joined us on the site, offering opportunities for cross-fertilising disciplines and ideas, and fostering progressive and holistic ways of working.
- A critical ethical issue for us is animal welfare, firstly because caring for animals' welfare is the right thing to do, and secondly because good science depends on it. We have signed the Concordat on Openness on Animal Research in the UK, and apply the principles of openness and transparency globally. And we also follow the '3Rs' – Replacement, Reduction, and Refinement – meaning that, wherever possible, we replace the use of animals with non-animal alternatives, reduce the number of animals we use by designing animal studies optimally, and refine conditions for animals to maximise their welfare.

- We promote life-long learning and development across our employees, ensuring our workforce is equipped for the future. Our multi-year, multi-country investment in STEM (Science, Technology, Engineering and Mathematics) outreach programmes aims to inspire the next generation of scientist leaders and promote an understanding of the value and importance of global R&D towards creating a better, more sustainable society.



## Some facts about R&D sustainability

Approximately

# 90%

of our pipeline has a precision medicine approach

We have the

# largest R&D pipeline

for diseases in the scope of the 2018 Access to Medicine Index

# 61%

of our total electricity use is sourced or generated from renewable sources

We have achieved an

# 8%

reduction in our water use since 2015

# 93%

of active pharmaceutical ingredient discharges from our suppliers has been demonstrated as safe

Our Open Innovation programme has over

# 250,000

compounds available from our screening library

As well as iDREAM hubs in Russia, Taiwan and Brazil, we now have them in

## China, Argentina, India and Hong Kong,

all designed to help improve the local capacity for R&D through collaboration



^ Solar panels on the roof of AstraZeneca Macclesfield



^ Electric car chargers at AstraZeneca Gothenburg



^ Our corporate beehive at AstraZeneca Gothenburg



Our R&D culture

Three organisations. One aim

Focusing on quality, not quantity

Transforming our science

Keeping doors and minds open

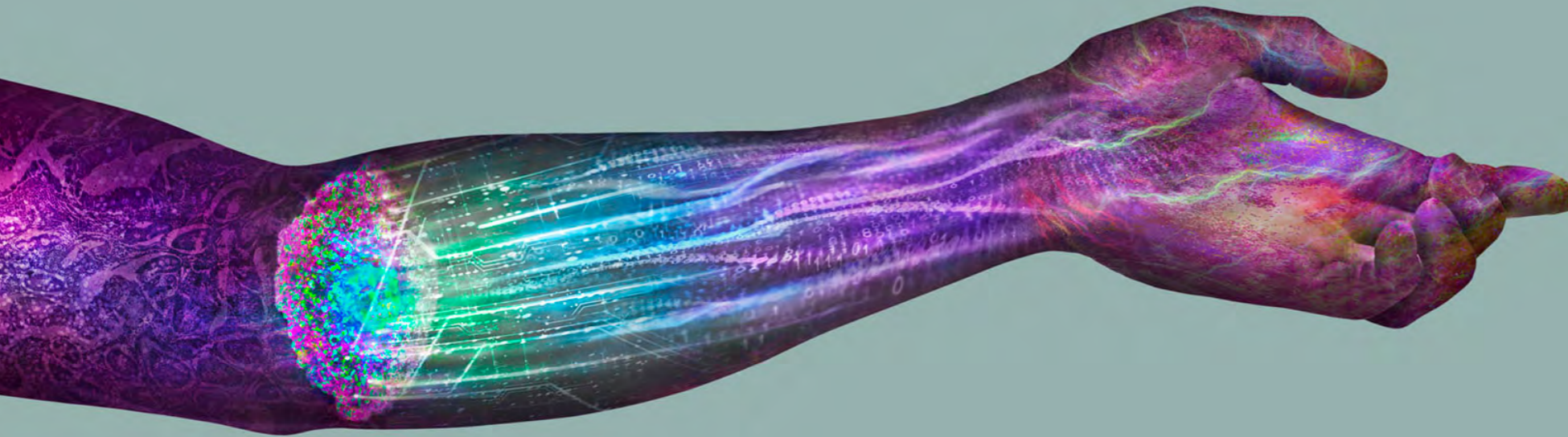
R&D places and people

Making our science sustainable

Led by science. Driven by patients.

### Predicting clinical success

Humanised preclinical models are bridging the gap between animals and humans, from traditional cell cultures. AstraZeneca is adopting a range of cutting-edge technologies combined with advanced imaging to improve our ability to predict the clinical effectiveness of our candidate drug molecules.



# Led by science. Driven by patients

The pace of change in healthcare is moving more rapidly than ever before, as patient populations and expectations rise, science advances, and data and technology dramatically accelerate progress.

We have always put patients first and are creating a patient-centric culture in every aspect of our work, from discovery to clinical trials, treatment delivery, and beyond. This is helping us achieve our aim of getting the right medicines to the right patients, faster than ever before.

We are transforming our business by using data, digital technologies and AI to increase the probability of success, and to discover new medicines more efficiently and deliver them more effectively.

At AstraZeneca's R&D, we will continue to build our business's reputation for scientific leadership by inspiring people with curious minds, harnessing data and technology, working seamlessly and inclusively, and always learning from patients.

This in turn is how we'll attract and retain the best people and partners, to help us deliver life changing medicines. Building a diverse, inclusive, listening and inspiring culture, and making a real and sustainable difference to patients, healthcare and our wider society.

Our ambition is to transform the lives of patients with improved outcomes and a better quality of life, through more effective treatment and prevention, ultimately working toward a cure for some of the world's most complex diseases.





