

Advanced Therapy Medicinal Products Project

Perspectives on preparedness: healthcare system readiness for adoption of disruptive innovative technologies

October 2019

The project



Having led the NHS service development work for the first two chimeric antigen receptor T-cell (CAR T) therapy products in England, I became interested in how the wider system would prepare for the next generation of Advanced Therapeutic Medicinal Products (ATMPs). I wanted to hear from partners about what they thought it would take for patients to get access to ATMPs in future. So, working as part of the Cell & Gene Therapy Catapult, I led this project to progress the agenda and my leadership as part of the Health and Care Leaders Aspiring Director Programme.

We discovered that whilst affordability is a key issue, it can crowd out other factors, reducing the adoption debate to price setting and reimbursement between companies and health service payers. Through our interviews with industry, regulators, policy makers and others, we heard about many other important issues for ATMP adoption. We asked partners about their contribution to this agenda and about their perceptions of the roles, responsibilities, actions and constraints of others. We found many points of alignment as well as significant differences in perspectives.

In 2019, the NHS Long Term Plan recognised the importance of expanding the frontiers of medical science and innovation. In September, NICE recommended access to another ATMP on the NHS. There can be no better time to build greater understanding and collaboration. Working as partners, we can ensure the right actions are taken forward at the right time. Individually and together our efforts can secure benefits for patients, healthcare, industry and the UK.

I hope you enjoy reading the report as much as I enjoyed researching it!



Claire Foreman

Executive summary: What we heard from partners

Perspectives on

roles &

responsibilities

to enable ATMP

adoption



POINTS OF ALIGNMENT

Standardisations to support efficiency of adoption processes

We all have to plan early, together

CAR T adoption has been a huge success

Strong end to end infrastructure and logistics We need to adapt ways of working

Huge potential to transform outcomes for patients

Flexible commercial approaches

Data is the key to value assessment, uptake and reimbursement

POINTS OF DIFFERENCE

NHS needs to create more investment headroom e.g. use of generics

NICE approval should guarantee market access & reimbursement

> Industry ignores system affordability constraints

UK needs to be more inviting to industry

Unlimited patient access

UK uptake is 'low and slow'

Value assessment processes must change

Systems need to pay now for value and innovation

Specificity of treatments can leave some patients behind

NHS needs to do more to support research & innovation



Objectives of the project and report



In this project, we set out to learn from partners what they think needs to happen to support ATMP adoption in the UK. With our focus on perspectives and partnership, we did not attempt to comprehensively assess adoptions activities in the UK or to compare arrangements with those in place internationally. Instead, we aimed to:

- Work across organisational boundaries to hear and understand some of the issues and perceptions of partners in relation to healthcare system readiness for adoption of treatment innovation. These are set out in the 'deep dive' sections.
- Contribute to environment shaping by sharing insights, increasing understanding and enhancing engagement by producing a report of the ideas and issues identified by partners.
- Set out areas for further exploration and collaboration to progress healthcare system readiness to accommodate technological innovation in therapeutics, particularly when the innovation is disruptive as opposed to incremental and about a class of treatments, not individual therapies.
- Set out a range of potential partner actions to optimise the 'ecosystem' for adoption of cell and gene therapies, and potentially other innovative medicines development.

Advanced Therapy Medicinal Products (ATMPs)



ATMP can include any of the following medicinal products for human use:

 a gene therapy medicinal product



 a somatic cell therapy medicinal product



 a tissue engineered product



The full definition of ATMPs is found in Directive 2001/83/EC as amended by the ATMP Regulation 1394/2007.

Adopting innovation: what makes ATMPs different? CATAPULT



Well understood features of treatment innovations (e.g. heart transplant)			Novel features of treatment innovations (e.g. ATMPs)		
Extreme efficacy	Durable outcomes	High upfront cost	Complexity	Rate of innovation	Volume of innovation and speed of obsolescence
Disease modifying and potentially "curative".	A single administration may lead to many years/ a lifetime of improved health.	Potentially high cost manufacture, administration and/or hospital care. High healthcare value.	ATMPs are often complex in their: • Biology/action • Manufacture • Administration	Scientific advances; industry corporate agendas; progressive regulators; and extreme efficacy combine to drive shortened development times to a few years.	Huge amount of innovation taking place, encouraged by clinical results and corporate investment. Next generation products are rapidly superseding existing technologies.

The ATMP pipeline



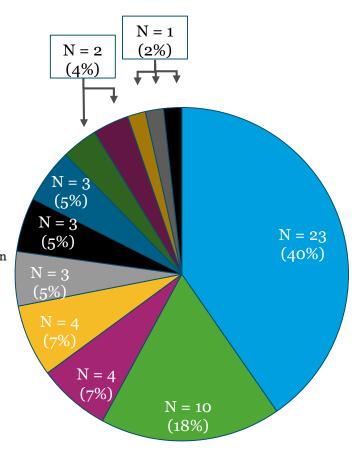
Reimbursement status of approved ATMPs in the EU

Product	Date of MAA approval	Reimbursed in Member States	Reimbursement status
Zynteglo (bluebird bio)	03/06/19	-	Pending
Luxturna (Spark/Novartis)	23/11/18	UK	Due to start January 2020
Yescarta (Kite/Gilead)	27/08/18	UK	Through the UK Cancer Drugs Fund
Kymriah (Novartis)	27/08/18	UK	Through the UK Cancer Drugs Fund
Alosifel (Takeda)	23/03/18	-	Rejected by NICE Aug 2018
Spherox (CO.DON AG)	10/07/17	Germany, UK	UK - restricted beyond its regulatory label
Zalmoxis (MolMed)	18/08/16	France, Germany, Italy	
Strimvelis (GSK)	26/05/16	Italy, UK	Use is limited in one centre in all of Europe
Imlygic (Amgen)	16/12/15	Germany, UK	UK - restricted beyond its regulatory label
Holoclar (Chiesi)	17/02/15	France, Italy, Spain, UK	Restrictions applied to the indication and/or the level of reimbursement

Number of cell and gene therapies in Phase 3 development (with US and/or EU trial site)

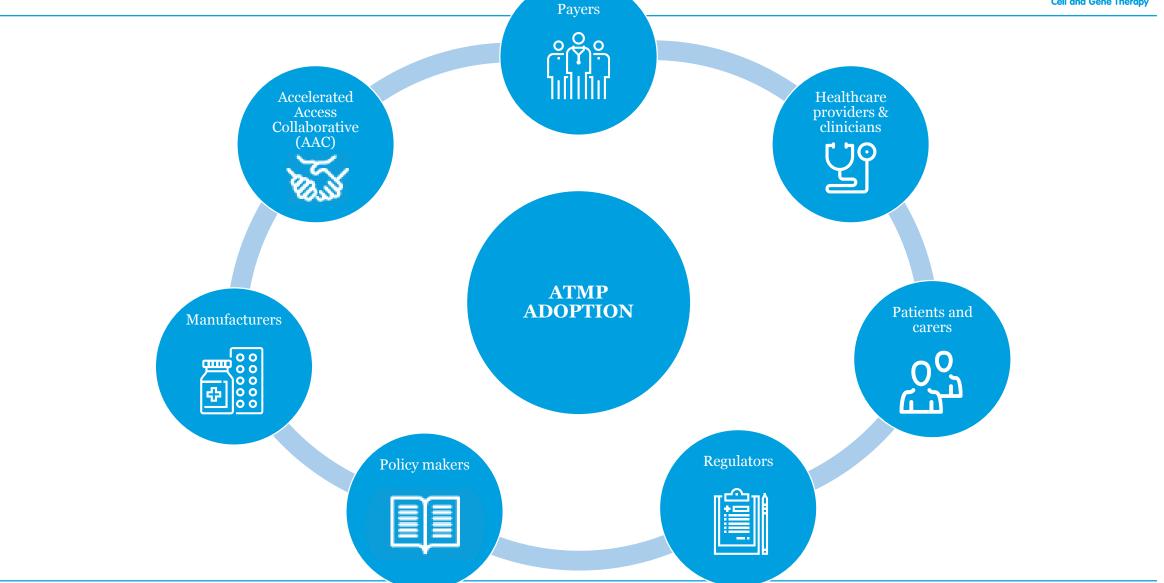


- Cardiovascular Diseases
- Musculoskeletal
- Ophthalmology
- \blacksquare Central Nervous System
- Immunology and Inflammation
- Genitourinary Disorders
- Haematology
- Infectious Diseases
- Dermatology
- Gastroenterology
- Immunodeficiency



The Partners

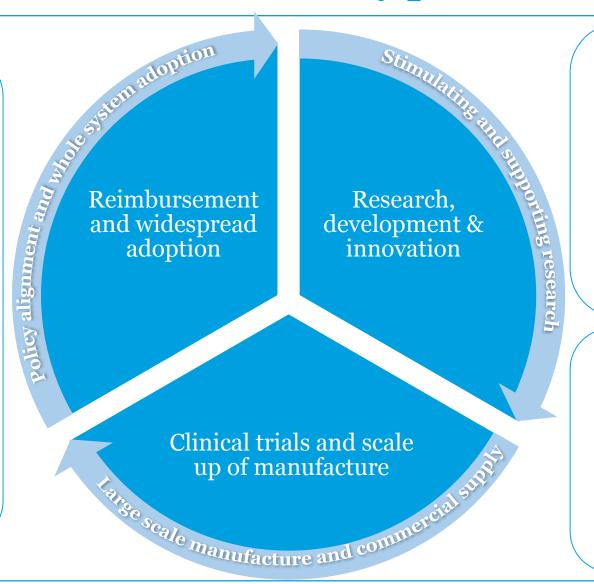




ATMPs: Headline issues raised by partners



- Quicker licensing
- Supply chain development
- Manufacturing capacity close to patients
- Reimbursement and ongoing investment
- Clinical services engagement
- Commissioning, infrastructure and training requirements
- 'Steady state' capacity requirements
- Estimating patient uptake
- Clinical follow up / data collection



- Academic collaborations
- Balancing efficacy and efficiency in product development
- Innovation investment which supports public finances
- Intellectual Property (IP) and the potential for generics
- Sufficient clinical trials infrastructure and ethics committee capacity to support UK ambitions
- Policy and infrastructure support for UK manufacturing
- Company commitment to manufacturing in the UK
- Supporting patient recruitment
- Training and education
- Meeting different international regulatory and health assessment approval processes

Partner perspectives deep dive: Macro (policy) & micro (product) level planning



Industry goals rely on prioritisation of innovation investment beyond health policy

ATMPs adoption brings economic and commercial as well as health benefits

Horizon scanning and quality data required to improve micro and macro planning efforts

ATMPs change relationships between the manufacturer, care provider, patients and payers

Micro planning involves all partners in timely preparation for the adoption of individual ATMPs

Macro planning is a multipartner function, not for the payer alone. This is not understood by other partners

Macro planning needs to focus on system adoption, expanded use of ATMPs and ongoing implementation The planning challenge is about timing and scale

Greater visibility of the issues facing each other is required

The definition of 'good' micro and macro planning differs by partner

The AAC is key to macro planning considerations

ATTCs / providers / commissioners / industry are key to micro planning ATMPs approval and uptake has been via adjustments to existing processes so far. This is unlikely to be feasible in the long term

Impact of other factors – currency markets, EU exit

NHS capacity for clinical trials and routine service delivery is a critical issue

What are the opportunity costs of not supporting ATMP adoption?

Partner perspectives deep dive: Clinical and cost effectiveness



Is the relationship between cost, price and value fully understood? What is the value proposition of ATMPs?

Healthcare systems must buy the greatest amount of health gain – where there is uncertainty, how optimistic should we be? NICE is not the payer: value assessment and reimbursement are different

ATMPs may displace other high cost drugs, be transformative for daily life or offer treatment for the first time

Social, economic and psychological impact of ATMPs

Precision medicine means higher grade outcomes at a greater upfront cost. Can this be accommodated, mitigated or challenged? The debate continues as to whether existing processes for value assessment are fit for purpose for ATMPs

Early company engagement with NICE on value assessment is critical

Managing value assessment and affordability / funding are separate processes, although this is not well understood 'Sticker shock' of ATMPs - high upfront costs but potentially cost saving over an extended time period

cost more competition, efficiency,
data and ATMP
improvements can
reduce cost / price

Consensus needed amongst partners on the construction, collection and validation of metrics

Partner perspectives deep dive: <u>Investment, price and reimbursement</u>



Issue of linking payment and effect is not new. What options do we have in ATMPs?

Pricing approaches remain a key priority for industry

Is the research, health and industrial policy environment sufficiently positive to assure ongoing investment and innovation?

Need pricing and reimbursement models to address different challenges and expectations

NHS should help create headroom in existing budgets for ATMP investment e.g. widespread adoption of generics

Does it make a difference that 'big pharma' brought the first 2 CAR Ts? Small ATMP-only companies rely on approval and product adoption to achieve profitability

What is to be reimbursed cost or value of this
treatment; innovation of the
next; or UK manufacturing?

High expectations of companies, investors and shareholders for reimbursement and cash flow now and in the future.

Venture capital funding frames market expectations

What is the role of wider government policy levers?



UK needs to 'book' its share of supply and onboarding capacity in a global market to ensure patient access



Investors expect high patient uptake of ground-breaking science. What does this mean for planning assumptions?



Access with evidence arrangements exist in cancer (CDF). What do we have and need for non-cancer indications?

Partner perspectives deep dive: Individualisation vs standardisation



Striving for appropriate standardisation in research, manufacture, service requirements, and pricing for performance approaches What difference could genomics and gene testing make?

Are ATMP 'centres of excellence' or integrated speciality pathways the best way to organise services to support adoption?

Company resources are limited – what process efficiencies can the system require and support?

Chain of custody requirements for autologous products represent a high value and high cost part of ATMP pathways

Could allogenic 'off the shelf' ATMPs deliver improved efficiency and price without compromising extreme efficacy of autologous products? Is a standardised adoption approach at UK or international level feasible or desirable in efforts to accelerate adoption?

There are different views about whether a move away from single batch autologous to more 'off the shelf' allogeneic products could improve cost and efficiency

Is there an opportunity to integrate collection of cells for ATMP manufacture e.g. apheresis capacity, closer to patients?

What does the work of ATTCs tell us and what role can they play?

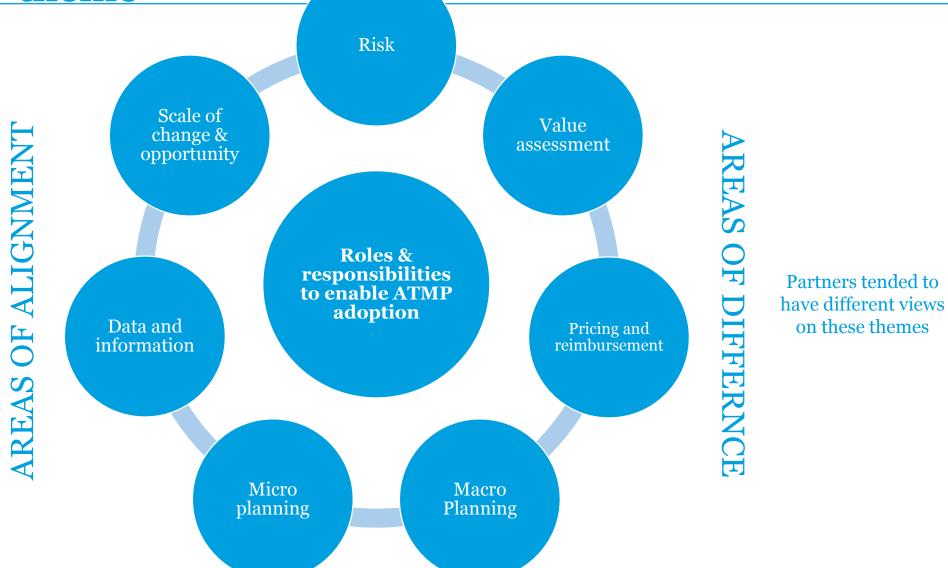
What is the role of the AAC?

Patient groups are cautiously optimistic about ATMPs - do we understand what matters most to patients and carers?

Partner Perspectives: Mapping by theme



Partners tended to have similar views on these themes



What did we learn?



- There is huge passion and excitement amongst partners about UK-led academic and commercial ATMP innovation. The UK already boasts great science, flagship companies, a GMP manufacturing centre, ATTC test beds, positive health technology assessments, healthcare adoption and market access.
- More is required to support ATMP adoption and all partners have views about their role and the role of others. This is not always aligned, often due to misconceptions about the responsibility, imperatives, beliefs or behaviours of others.
- No one partner can solve the challenge of ecosystem preparedness and adoption. It relies on multiple partners, not on the healthcare payer alone. Creativity and leadership will be required by all partners.
- So far, adoption has occurred with adaption of existing processes. It is unlikely that this will be sufficient to optimise ATMP adoption in future.
- Despite a growing understanding of ATMPs, these are early days and the potential impact of ATMPs for individuals, healthcare, industry and the economy is not yet fully understood. This is an immature ecosystem, learning as we go.
- To learn from experience so far, build on best practice and avoid duplication, we need data and tools to help organise how we consider, plan and act for ATMP adoption.
- It remains unclear which critical factors research and clinical trials; company profiles and investment; health technology appraisal; pricing and reimbursement; manufacturing; supply chain and logistics; clinical service capacity and readiness; patient uptake will be the key to unlocking ATMP adoption.

Opportunities



The healthcare opportunity

- Harness the power of the NHS and The Long Term Plan to make UK the best in the world at ATMP adoption
- Enhancing research capacity and capability to promote clinically and cost effective treatment innovations
- Step change in outcomes, experience and healthcare for patients
- Systematic service readiness for innovation uptake

The industrial opportunity

- Industrial growth for the sector and the UK role in therapeutic innovation
- Translate excellence in innovation to excellence in manufacturing
- Enhanced GMP UK
 manufacturing supported by
 the Cell and Gene Therapy
 Catapult
- Developing industry NHS interface and relationships

The ecosystem opportunity

- Harness actions of all partners through the AAC
- Collaborative action to map out opportunities for greater alignment on strategic planning, including horizon scanning
- Alignment of regulatory processes to support adoption at approval
- Communication and patient engagement

Project team





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About the project



Between January 2019 to August 2019 over 20 meetings were held with companies, regulators, policy makers and patient groups to explore issues, ideas and perceptions. Thematic analysis was undertaken to identify areas of alignment, areas of difference and areas for further engagement and action. This report summarises the outputs of Claire's 'connecting' leadership project.

- Co-sponsored by NHS England and Catapult Directors.
- 'Connecting experience' project to build leadership as part of the Health and Care Leaders Aspiring Director Programme https://www.leadershipacademy.nhs.uk/programmes/health-care-leaders-scheme/
- Qualitative project, focusing on views and insights of senior leaders in a range of sectors and organisations to deepen understanding.
- Identifying gaps and emergent themes, as well as well known issues.
- Signalling the potential direction for further organisational and system exploration and action.
- The outputs of this project are being shared with participants, partners and the Accelerated Access Collaborative to help current and future work on ATMP adoption.

Participating organisations

Achilles

Alliance for Regenerative Medicine

Autolus

Bellicum Pharmaceuticals

Bloodwise

Blue Bird Bio

Cell and Gene Therapy Catapult

Cell Medica

Gilead

HM Treasury

NHS England

NICE

Oxford Biomedica

Office of Life Sciences

Pfizer

Retina UK

RNIB

Syncona