Advanced Therapies Statement of Intent

This Statement of Intent provides a compelling vision for a strategic approach to harness the benefits from emerging and transformative therapies called Advanced Therapy Medicinal Products (ATMPs). The intention is to create a sustainable platform to enable NHS Wales to provide patients with equitable access to emerging ATMPs, explore how this sector can contribute to the objectives of the Welsh Government's *A Healthier Wales: Our Plan for Health and Social Care in Wales* and deliver our full potential in the international and UK development of ATMPs. Multiple expert groups and the UK Government's Life Sciences Industrial Strategy suggest development of the ATMP sector will provide key opportunities for investment and economic growth for the UK. ATMPs are set to transform current care pathways by potentially offering durable and curative outcomes where acute unmet medical need exists. Healthcare services are not currently configured to commission and provide these therapies as mainstream treatment. It is vital to translate the hope and potential of advanced therapeutics, with an immediate focus on cell and gene therapy, into reality to improve outcomes for the people of Wales. This framework will also support and foster strategic partnerships and collaboration between NHS Wales and our academic and industry partners. By working together we will harness the potential of ATMPs to improve health, well-being and prosperity for the people of Wales.

An ATMP can be either a:

- Gene therapy (i.e. the transfer of genetic material into the cells of a patient's body to treat the cause or symptoms of a specific disease).
- Cell therapy (i.e. the transfer of intact, live cells into a patient to help lessen or cure a disease). The cells may originate from the patient or a donor.
- Tissue engineered product (i.e. a regenerative medicine that replaces or regenerates human cells, tissues or organs to restore or establish normal function).

ATMPs offer significant promise for the long-term management and even cure of disease, especially in areas of high unmet medical need. The current clinical treatment approaches to cancer, heart disease, diabetes, stroke and other conditions will be changed by ATMPs. These therapies will impact many treatment pathways by exploiting techniques and methods to repair, replace, regenerate and re-engineer human genes, cells, tissues or organs in order to restore or establish normal function. Future plans will need to consider other advanced therapies and parallel healthcare innovations that will affect strategic implementation.

There will be major challenges to enabling the broad adoption of new ATMPs, especially around the production, transportation, and application of these products. Developing pathways to identify patients for treatment, aftercare and follow-up, will require consideration as will education, workforce, estates, quality and safety, research and innovation, informatics, commissioning, overall cost and partnerships.

ATMPs have the potential to alter patient outcomes radically for previously incurable diseases. The cost of these products will initially be high but their overall value will be higher due to the life-changing impact for patients compared to existing treatments. As these therapies move from clinical

trial to become available treatments the NHS will need to define, capture and quantify the cumulative value that they offer to inform commissioning decisions. NHS Wales needs to be able to deliver equitable and timely access to emerging ATMPs for all patients.

This area is rapidly developing with significant growth potential for the ATMP sector in Wales. Countries such as the USA, Canada, Japan, China and Australia have already taken a proactive strategic approach to capitalise on opportunities in this sector.

Alongside clinical adoption and aligned with wider Welsh Government ambitions, there is an opportunity to create a thriving and dynamic environment for ATMPs through strategic partnerships with industry and academia to increase prosperity alongside improving health and well-being for the people of Wales. To achieve this Wales will need to continue to be open to partnership and collaboration, at a national, European and international level, and play a significant role in this sector. This will require effective working with existing organisations (e.g. the Life Sciences Hub Wales, Health Technology Wales, Health and Care Research Wales, Welsh Health Specialised Services Committee, Health Education and Improvement Wales) national programmes (e.g. Value-based Healthcare, Genomics for Precision Medicine), academic and commercial partners, and the third sector. There will be unique opportunities to drive a "Once for Wales" approach to adoption and innovation at local, regional and national level meeting the aims of *A Healthier Wales: Our Plan for Health and Social Care*, and aspirations of the *Well-being of Future Generations (Wales) Act 2015,* within the philosophy of Prudent Healthcare. The Life Sciences sector, of which ATMPs form a part, is without doubt an industry of the future and the *Economic Action Plan for Wales* is a firm commitment to accelerating innovation and enhancing cross-cutting collaboration between the NHS, academia and industry.

This Statement of Intent outlines the challenges, opportunities and actions necessary to develop a sustainable strategic approach to developing the ATMP sector in Wales.

Key Priorities

1. Public Involvement and Engagement

The public are central to healthcare in Wales and will be at the heart of the development of systems and services to enable broad adoption of these treatments. Meaningful public involvement and engagement will allow the public and patients to contribute as equal partners to co-producing services for Wales that make a real difference. This will promote value-based medicines and approaches which prioritise achieving the outcomes that matter most to the people of Wales, rather than being over-focused on the service delivery process.

It will be necessary to continue to engage with and educate the public and patients around life-style related disorders, and their origin and management. Consequently there is a need to provide up-to-date accurate information, in an appropriate form and engage people in the debate around these potentially transformative therapies. It is essential that we enhance public understanding of the balance between cost, value and potential benefits that both experimental and developed ATMPs will have on patient outcomes and society as a whole.

ACTION

- NHS Wales will develop effective, targeted communication methods and maximise opportunities to work with the public to facilitate co-production of services and provide patients and the public with information to enable them to engage with decisions around commissioning, and the adoption or non-adoption of these treatments.

2. Clinical Pathways

Supply chains and treatment pathways are well-established for traditional small molecule medicines, but ATMPs require new systems to be designed, developed and implemented. These will include the treatments themselves, as well as manufacturing facilities, IT systems, logistics solutions, support services and companion diagnostics. There is close interconnectivity between ATMP pathways and developments in other specialties, such as genomics, pathology and imaging.

Ongoing programmes with industry, academia and service providers will supply an initial pathfinder approach for the development of clinical pathways and systems. This work will inform an understanding of the challenges of developing new ATMP pathways and potential solutions. This new knowledge will need to be shared across NHS Wales, and beyond. The requirements for ATMP delivery will include: estates, infrastructure and equipment; workforce and training; quality management and regulatory compliance; IT; and patient experience. ATMP pathways are complex in terms of production and patient administration, often requiring input from several medical teams. From patient identification, through treatment, and to short- and long-term follow-up, the existing clinical systems and processes within the health and care setting will require reconsideration. For cell-based ATMPs the nearest current clinical pathway is stem cell transplantation, and the expertise and standards required to deliver these treatments has been recognised as the basis for developing ATMP-related pathways in the NHS.

The patient care pathways for ATMPs will require a range of complementary services: timely access to diagnostics, preparatory treatments along with access to operating theatres and intensive care facilities. These pathways will span secondary and tertiary care, across active treatment and patient follow-up.

ACTION

- NHS Wales will establish a mechanism for coordinating and collaborating on a local, regional and national basis, including how to identify, map and share best practices for pathways.

3. Regulatory Compliance, Quality and Safety

There is a wide range of regulatory and quality standards for ATMPs that spans manufacturing, storage, transport, clinical facilities, quality management, policies, procedures, patient and product data, research activity, and patient care. For existing cellular therapies accreditation to FACT-JACIE (Foundation for the Accreditation of Cellular Therapy - Joint Accreditation Committee of the International Society for Cellular and Gene Therapies (Europe)-European Society for Blood and Marrow Transplantation) is standard and is typically mandated for the entire clinical pathway.

Whilst there are FACT-JACIE accredited facilities for cell-based therapies in Wales, there is a need to ensure the accreditation scope covers the future ATMPs that will be delivered through those centres. Furthermore, there is additional need to evaluate the specific requirements for other ATMPs that will be delivered through new centres in Wales. Regulations and quality standards are rapidly evolving and keeping pace with the rate of change and advancement in this sector. As such, it will be necessary to monitor, prepare for and dynamically react to these changes, along with those changes mandated by the *European Union (Withdrawal) Act 2018*. It is important to anticipate and prepare for all these new requirements to maintain compliance, and the expertise and systems to support these requirements.

ACTIONS

- NHS Wales' delivery and commissioning groups will review FACT-JACIE accreditation requirements anticipating short, medium, and long-term needs for [cell-based] ATMPs.
- NHS Wales will review broader regulatory and quality standards requirements (e.g. Human Tissue Authority, Human Medicines and Healthcare Products Regulatory Agency) for existing and future ATMPs.
- NHS Wales will develop a sustainable mechanism to support national adoption and compliance with emerging regulations and mandated standards and best practice.

4. Workforce Development

The initial adoption of ATMPs, and subsequent sustainable delivery and growth, will require new knowledge, skills, and competencies for each pathway, profession and partner. New workforce models will need to reflect the entire ATMP pathway, including the required phasing, scalability, cross-profession and multi-partner working. Professional bodies, academic centres, and staff in clinical practice will play a significant role in informing and developing new training and educational pathways. For the NHS in Wales, Health Education and Improvement Wales (HEIW) will lead on strategic workforce planning, education and continuing professional development. It will be important to ensure a close working relationship with NHS staff, professional bodies, commercial, trade and non-commercial/third-sector organisations to ensure training and education provision matches the evolving needs of this sector.

Many ATMPs are in an experimental phase and manufacturing processes are largely underdeveloped and niche. As a result, the skills and knowledge requirements associated with ATMPs are highly specialised (often post-doctoral). Until the industry matures, we will become increasingly reliant on highly trained professionals whilst processes are automated, mainstreamed and technician-controlled.

The commercial sector has identified proposals to increase the capability and capacity of the UK science talent pool to meet needs over the next decade. These include strengthening the link from academia to industry, STEM outreach, and promoting vocational and experiential training opportunities. The availability of skilled technical staff will be essential in the transition from small to large-scale production. Developing a detailed workforce and education strategy in Wales for advanced therapies will be a vital component of a future work programme.

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ACTIONS

- NHS Wales will work with HEIW and partners and will develop a workforce plan for ATMPs that reflects the evolution and emergence of new treatments.
- NHS Wales will work with HEIW, and other professional bodies, to review relevant undergraduate and postgraduate curricula as well as CPD provision for current and future workforce requirements to establish if they are fit for purpose.
- NHS Wales will work with Welsh Government to ensure the funding models will allow the delivery of a national approach to workforce training that reflects the evolving needs of ATMPs.
- NHS Wales and Welsh Government will work with industry, academia and other partners to support the growth, skills, competence and expertise of the workforce in Wales.

5. Estates

The adoption of ATMPs, including the establishment of clinical pathways, service specifications, and meeting regulatory requirements, will require timely access to the appropriate facilities. This includes the collection of components, materials and tissue from patient or donor, through to preparation, administration and post-treatment care. Near patient manipulation, storage and transport will need consideration, some approaches to which will be outputs from current programmes of work. In the short-term, there will be a need to adapt and upgrade existing facilities. In the medium to longer-term, further strategic planning that includes academia and industry will be required to inform investment decisions. Where possible, flexibility and future-proofing of infrastructure should be ensured to maximise value from capital-intensive investments, coupled with a phased implementation approach to ensure adequate capability and capacity at all times.

ACTIONS

- NHS Wales will review current infrastructure, resources and facilities necessary for the delivery of ATMPs in Wales such as clinical trials delivery, general wards, and laboratory and pharmacy services.
- NHS Wales will facilitate the development of a coordinated approach to identify, evaluate, and prioritise infrastructure needs based upon emerging ATMPs.
- NHS Wales will ensure that regional utilisation, workforce consideration, and facilities are considered in business cases and procurement decisions.
- NHS Wales and Welsh Government will work with industry and academic partners to develop a long-term strategic infrastructure plan, and bring consideration of ATMPs to wider NHS development planning.

6. Informatics and Information Governance

Developing a high quality and robust informatics ecosystem will be critical for delivering a world-leading, sustainable, effective and efficient ATMP service in Wales. *Informed Health and Care - A Digital Health and Care Strategy for Wales (2015)* and *A Healthier Wales: Our Plan for Health and Social Care in Wales (2018)* outline the vision for improving access to information and introducing new ways of delivering care with digital technologies. Effective planning and resource allocation will

be needed to support the development of the requisite connected IT environment for ATMP delivery.

A coherent vein-to-vein informatics network will be necessary to enable seamless sharing of necessary information between care setting and product supplier, to allow effective management of care pathways and follow-up, and for ensuring chain of custody and identity of the ATMPs.

An adaptive informatics infrastructure will be required to allow multiple NHS IT platforms to interface with ATMP supplier systems in order to maintain a reliable and seamless linkage through cell harvest, transport, manipulation and therapeutic delivery. A safe and effective product supply chain will require efficient exchange of information between the health provider and supplier, allowing appropriate patient data to be accessed and shared in a safe and secure manner that complies with the best standard of information governance.

An informatics ecosystem will need to enable improved understanding of patient demand, provide validated data for service modelling and benchmarking, and so inform demand management. Relevant and real-time key performance indicators will need to be developed to ensure the future ATMP service meets demand.

Healthcare informatics stakeholders (e.g. NHS Wales Informatics Service, Secure Anonymised Information Linkage Database, industrial partners, academia) will need to collaborate to develop an approach to compliantly access patient data and records for research purposes (e.g. meta-data analysis and clinical trials), identification of potential treatment cohorts, and to inform service planning and commissioning decisions. There is ongoing UK work to develop potential solutions to these needs. Consequently, all activities in Wales will need to be cognisant of such initiatives and where necessary aligned with UK outputs and international best practice.

ACTIONS

- NHS Wales will develop a plan for informatics, information governance, and business intelligence, and explore this with commercial partners.
- NHS Wales working with Welsh Government will ensure ATMP informatics requirements are included in strategic plans.
- NHS Wales will establish a sustainable mechanism that ensures relevant national and international informatics and information governance requirements are met.

7. Research and Innovation

7.1 Trial Delivery

Evidence indicates that patients treated in research-active environments have significantly improved outcomes. Due to this and the beneficial potential of ATMP treatments it is important that we ensure Wales maintains an active, credible and relevant clinical trials portfolio and platform.

Consideration will need to be given to physical infrastructure, collaborative and joint-working agreements, and in developing the necessary engaged, empowered and educated workforce. These are critical elements that will enable the sector to grow and develop and in turn will improve health, well-being and prosperity for the people of Wales.

Simplification of study set-up, contract management, and trial delivery will be important to attract and retain trial sponsors. Work is ongoing in Wales to streamline study set-up in alignment with wider UK processes, and to develop an all-Wales coordinated approach to contracting and costing of research. Additionally, opportunities exist to assist the identification and recruitment of patients for studies and subsequent trial delivery by learning from proven initiatives, such as the Bloodwise UK Trials Acceleration Programme.

Similarly, an opportunity exists to review financial considerations, such as adequacy of excess treatment and service support costs provided by Welsh Government for delivering non-commercial ATMP trials. The local support and delivery funding model supported centrally needs to be considered due to the complexity of ATMP clinical trials.

For the commercial ATMP sector to grow in Wales a single point of entry will be necessary. A national collaborative framework of organisations (e.g. The NHS in Wales, the Life Sciences Hub Wales, MediWales, Industry, UK and international partners, Health and Care Research Wales) could facilitate this.

7.2 Academic and NHS collaboration.

University status within the NHS in Wales provides an excellent environment and base for the development of expertise and new treatment approaches, products, services and clinical pathways. However, it is recognised that there are opportunities to improve and optimise the effectiveness of working partnerships. Translation of outputs and progression of ideas from academic and pre-clinical researchers, particularly to Phase I clinical trial, could be facilitated by identifying and connecting with relevant clinical counterparts. Differing priorities between NHS bodies and universities can result in a disconnect between service delivery and academic study that may be further impacted by factors such as the lack of access to procedural knowledge, accessible specialist equipment or funding to allow the translation of research into service provision.

Wales has a number of internationally recognised academic and clinical research clusters which undertake world class research and possess expertise in a number of fields. An opportunity exists to build upon this established academic and translational science base by further developing existing capabilities and capacities, retaining and attracting world-leading researchers and academics for Wales and developing Centres of Excellence.

Innovative funding solutions will be required to support the delivery of the above initiatives, the final approach to which will draw upon experience from both established centrally-funded and pathfinder models, such as the Life Sciences Bridging Fund. Regardless of the final route(s) to support that is adopted it is vital that Wales fully exploits the potential of our academic expertise.

Closer working and collaboration between academia, NHS Wales and other commercial and non-profit organisations will expedite bringing new products and innovations into a clinical setting. It is anticipated that this will lead to opportunities to generate and secure valuable, new intellectual

property (IP) in its various forms. Due to the complexity of the associated technologies (ATMPs and their production, deployment and adoption systems) careful oversight and management will be required to ensure that all opportunities are maximally exploited. Consequently, Research Offices

and Technology Transfer teams in NHS Wales and Universities may require additional speciality expertise and legal input that could be facilitated by organisations such as AgorIP

7.3 Horizon Scanning

Due to the fast pace of development of ATMPs and demands of associated clinical trials, horizon scanning will be essential to ensure that stakeholders are aware of new developments and opportunities in a timely manner. It is essential that the commissioning bodies, service providers, and professional directorates continue to assess new products and innovations promptly to improve planning, initiation and phasing of programmes. There is an opportunity to develop further the co-ordinated horizon scanning approach for this sector, bringing together intelligence and expertise, from additional interested organisations and stakeholders. These would include, the All Wales Medicines Strategy Group (AWMSG), Welsh Health Specialised Services Committee (WHSSC), NHS Directorates and Health Technology Wales; along with their UK counterparts and (trade) associations such as the ABPI.

ACTIONS

- NHS Wales, Welsh Government and Health and Care Research Wales will work to further support clinical trials of ATMPs in the short term.
- NHS Wales and Welsh Government will work with stakeholders to develop a strategic plan to ensure that research and innovation opportunities and current challenges for ATMPS are addressed (e.g. clinical trials, finance, strategic partnerships, Centres of Excellence) in order to improve health, well-being and prosperity for the population of Wales. This will include the link to adoption and commissioning.
- NHS Wales will work with stakeholders in order to develop an effective horizon scanning service for emerging ATMPs and related innovations to support strategic planning.
- NHS Wales and Welsh Government will work with stakeholders to develop a national network that will provide a strategic framework for ATMPs in Wales, which could include signposting and supporting academic and commercial research opportunities.
- NHS Wales will review funding for translational research in the advanced therapies sector to identify current opportunities and gaps, and explore new opportunities that build on successful models in other sectors.
- Health and Care Research Wales will actively consider the research, development and innovation of ATMPs in the development of its systems and processes for Wales, including its infrastructure support role.
- Welsh Government will work with NHS Wales to explore sector opportunities with higher education institutions in Wales.

8. Hosting and Commissioning.

The rapid emergence of new ATMPs, with high associated expenses and curative potential, will require the NHS in Wales to consider the suitability of its service planning and commissioning activities to enable the delivery of these therapies in Wales. Responsibility for a majority of the commissioning for ATMPs will reside with WHSSC, which is responsible for the joint planning of specialised and tertiary services on behalf of Local Health Boards (LHBs) in Wales. However, initially a national approach will be taken and WHSSC will commission all ATMPs delivered in Wales.

Consequently, ATMP developers will require clarity of the role and methods of co-ordination amongst stakeholders, service providers, commissioning and advisory bodies such as: Local Trusts and Health Board planning functions; AWMSG; Health Technology Wales; and WHSSC.

Conventional NHS therapy appraisal and reimbursement models are being challenged as they may not support commissioning decisions for ATMPs. Currently these treatments can be expensive per patient and are supported by a limited evidence base, but as they potentially offer substantial or transformative health gains and wider societal impacts they are worthy of careful consideration. Whether or not the current appraisal processes are the most suitable warrants further review as the sector matures and more ATMPs and relevant data become available. To find innovative solutions to these issues there is potential to engage with product suppliers, through collaborative working and co-production, and that builds on existing projects.

Given the differences between ATMP pathways, consideration will need to be given to how and where services are provided in Wales. Location, infrastructure, clinical delivery capability and capacity, and clinical governance will require significant consideration in order to support forward facing commissioning plans

ACTIONS

- WHSSC will work with NHS Wales, Welsh Government and relevant stakeholders to review the commissioning strategy to consider the emerging challenges related to ATMPs (e.g. costs and benefits, service providers).
- WHSSC, NHS Wales and Welsh Government will consider approaches to partnership working to develop new models of commissioning.

9. Strategic Partnerships

Due to the potential economic promise and healthcare benefits of ATMPs there is an aspiration for the UK to be a global leader in the development, delivery and commercialisation of ATMPs to attract a breadth of commercial organisations to the UK, stimulating sector growth. Welsh Government has an opportunity to ensure alignment of ambitions with those of the UK by building a stronger strategic agenda for science and innovation to support the economy with an effective translation through innovation to more high quality jobs. This approach recognises the links between the research and science-skills base and the processes that transform scientific outputs into economic advantage, improve health and well-being and benefit the Welsh population and economy.

Wales boasts clusters of genuine excellence from research to manufacturing and is well placed to exploit and develop opportunities in terms of scale, integration and access to markets. There is a growing ATMP sector, with an increasing number of commercial companies who benefit from close ties and strong support from the Welsh Government, NHS Wales and academia. These organisations address all aspects of the overall therapeutic supply chain including delivery, administration and follow-up pathways. This encompasses the design, implementation and support services for clinical trials; information technology systems; cold chain transport and logistics; storage and distribution solutions; as well as those developing therapies in a range of clinical areas (e.g. heart disease, tissue injury, blindness, and cancer).

Within the context of the global environment and supply chain, the UK-wide focus in this and the wider Life Sciences sector, Wales needs to create a strategic approach to cementing a position as a global player in ATMPs. In creating a strategic approach for Wales in this sector our specific potential, as well as the needs of healthcare systems and of our population must be recognised. There should be a focus on areas of strength where we can provide solutions and skills to support the development, delivery, equitable access and adoption of these transformative therapies and not seek to be world class at every element from conception to patient delivery. It is clearly recognised that benefits to the Welsh economy must be won in an international market. Wales' ability to work collaboratively to embrace and encourage innovation will drive new business investment and job creation in Wales.

Wales is well placed to deliver on these developments. The Life Sciences Hub Wales is positioned to be a key partner to accelerate economic development activity within the life sciences sector. Adoption of an open participation model, based on co-design and engagement between healthcare, industry and academia, will aid the identification of solutions which will meet health needs. Access to facilities and a well trained workforce are crucial elements in enabling partnership working.

Aligned to the above strategic commitments UK Government funding plays a key role in supporting development in the sector, including aspects of the research, translation, production, adoption and deployment of ATMPs. For example, in March 2018 competitive grant funding was secured to establish the Midland Wales-Advanced Therapy Treatment Centre. This consortium will explore a number of the challenges outlined above, and the outputs of this programme will be used to direct and inform subsequent strategic implementation plans.

ACTIONS

- Welsh Government will work with national, UK and international partners to provide strategic leadership for ATMPs in Wales.
- NHS Wales and Welsh Government will work with partners (e.g. Life Sciences Hub Wales) to develop a plan for strategic partnership working that increases new opportunities for ATMPs in Wales.

10. Next steps

A national Advanced Therapies programme and associated board will be formed to develop an implementation plan. A Programme team (currently hosted by the Welsh Blood Service) will support delivery of the plan and continue to act as a resource centre providing sector expertise and domain knowledge. The programme will engage with the public and other stakeholders and will report back to ministers in summer 2019. The implementation plan will be delivered in partnership together with and led by NHS Wales.