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Horizon Scan for Advanced Therapy Medicinal Products

October 2021

Disclaimer:

This project is funded by the National Institute for Health Research (NIHR) [HSRIC-2016-10009/Innovation Observatory]. The views expressed are those of the author(s) and not necessarily those of the NIHR or the Department of Health and Social Care.

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Background & Objectives

NIHR Innovation Observatory

- We are the national horizon scanning and intelligence research centre hosted at Newcastle University

- Funded by the NIHR, we provide national stakeholders with timely intelligence that support the delivery of the most valuable/useful innovation into the NHS to benefit patients

- We share intelligence to enable
  - regulatory processes, HTA & market access
  - industry to innovate
  - NHS to implement & adopt
  - citizens needs to support innovation
  - NIHR to research

Background

- Advanced Therapeutic Medicinal Products (ATMPs) are novel therapies based on cells, genes or tissues with the potential to address the underlying cause of the diseases. They come with potentially significant implementation requirements, high costs & regulatory/assessment uncertainties
- In November 2019, the NIHR Innovation Observatory undertook a rapid horizon scan for 'potential' ATMPs that were within a ~5 year timeframe to obtaining a product licence (Marketing Authorisation) in the EU/UK
- Since then, NHSE/I's commercial medicines and the Specialist Pharmacy Service (SPS) have enhanced this scan to develop Therapeutic Product Profiles (TPPs) for ATMPs due to be launched in the NHS from 2021-22
- A number of AAC Early Stage Product (ESP) workstreams (WS3, WS4, WS5 and WS7) are focussed in the ATMP landscape, requiring a longer runway to plan for the smooth adoption of these technologies in the NHS

Objectives

- The aim of this scan was to provide a ‘spine’ of data and intelligence on ATMPs in the clinical development pipeline with a potential product licence/launch in the NHS, up until ~2026
- The scan will help AAC partners plan for the introduction of these products into the NHS and will complement NHSE/I and SPS enhanced horizon scan which will be worked up into TPPs closer to the products being licenced/launched (0-3 years)
- The scan includes additional data fields (‘core dataset’) as agreed by the AAC working group consisting of colleagues from the NIHR Innovation Observatory, Catapult, NHSE/I, ABPI, MHRA and NICE
- The scan also includes additional analyses (reported separately) that will provide high-level, emerging trends from the ATMP dataset in order to proactively identify key innovation areas and/or unmet needs in the ATMPs development pipeline

Scope

- For the purpose of this work, the NIHR Innovation observatory included advanced therapy medicinal products (ATMPs) that are **likely** to meet the EMA or MHRA designation of an ATMP. These include:
  - Gene therapies
    - product has to be a biological medicinal product and contain recombinant nucleic acid(s);
    - and the recombinant nucleic acid(s) should be directly involved in the mechanism of action (and hence therapeutic action of the product)
  - Somatic cell therapies
    - engineered cells or tissues that have undergone substantial manipulation (e.g. expansion, genetic modification, differentiation/activation of growth factors or have a different essential function);
    - and intended function is to prevent, diagnose and or treat disease via pharmacological, metabolic actions
  - Tissue engineered therapies
    - somatic cell therapies that have the intended function to "repair“, "regenerate“, or "replace"
  - Combined therapies
    - incorporate an active substance i.e. a cellular or tissue part consisting of viable or non-viable cells or tissues and of one or more medical devices or one or more active implantable medical devices as an integral part of the product

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Method

Scanning Criteria

- The NIHR Innovation Observatory undertakes routine horizon scanning as part of its core function, utilizing a robust methodology to identify and track innovative health technologies
- It maintains a comprehensive database - MIND ('Medicines Innovation Database') - of these innovative medicines, focusing on those with potential UK/EU licence/launch within ~5 years
- The NIHR Innovation Observatory's MIND contains individual 'Technology Records', defined as innovative medicine(s) + indication(s). Key data fields are collated for each Technology Record, including 'potential' and 'actual' ATMP status
  - '**Potential**' ATMPs are those that are contain products that are likely to meet the EMA's (or MHRA) definition of an ATMP
  - **'Actual'** ATMPs are those products that have received the EMA's designation of an ATMP
- In addition, we consolidated the phase III data obtained from an ongoing scan and analysis of the global ATMP pipeline being undertaken by the ABPI

Inclusion/Exclusion Criteria

For this scan, the following criteria were applied:

- Inclusion
  - All technology records that are tagged as either ‘potential’ or ‘actual’ ATMPs on the Innovation Observatory’s MIND
  - All technology records in phase II trials onwards. Technologies in phase I studies were also included where there is intelligence or positive signals from the trial suggesting regulatory progression in the UK/EU
  - All clinical areas are included
  - Clinical trial locations in the UK/EU/North America. Other locations were included where additional intelligence suggested that the company may seek to launch in the UK/EU
  - Line extensions of a product that are already registered/approved for other indications were also included
- Exclusion criteria
  - Small interfering – RNA molecules (siRNAs) and other synthetic oligonucleotide-based products

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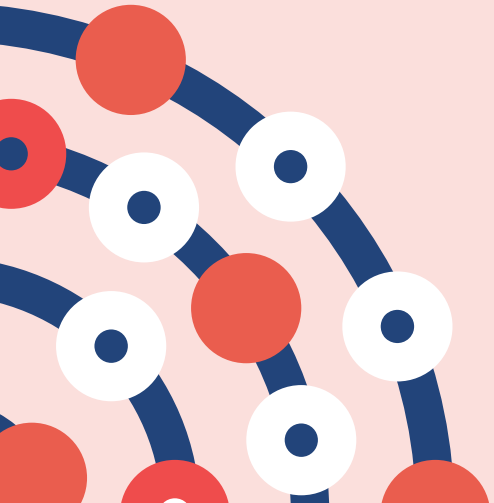
Summary of Data Collected*



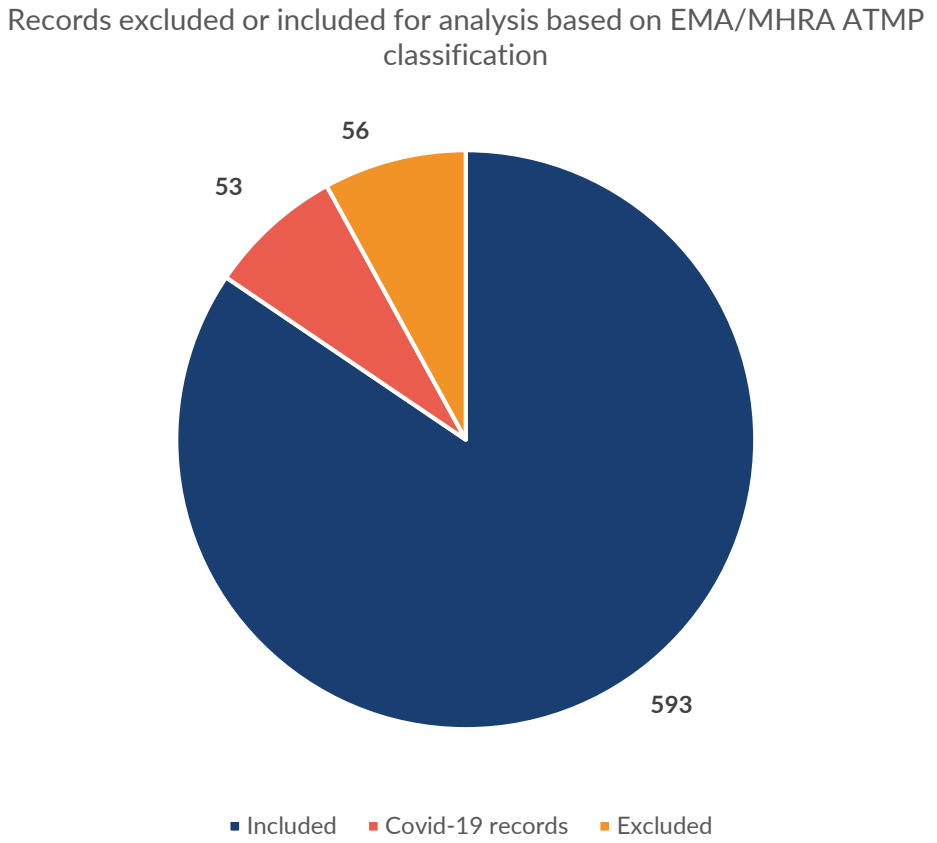
*To be viewed/interpreted with the dataset provided

Overview of the ATMP dataset

- An initial scan on the Innovation Observatory's MIND returned 691 technology records tagged as **potential** ATMPs
  - siRNAs and discontinued technology records (n=56) excluded
  - COVID-19 related technology records (n=53) excluded

- 11 additional technology records were added from the ABPI Phase III scan

- In total, 593 technology records consisting of 459 unique ATMPs and associated with 733 clinical trials* are included in the dataset (as of 16th of July 2021)



*By clinical trial identification number

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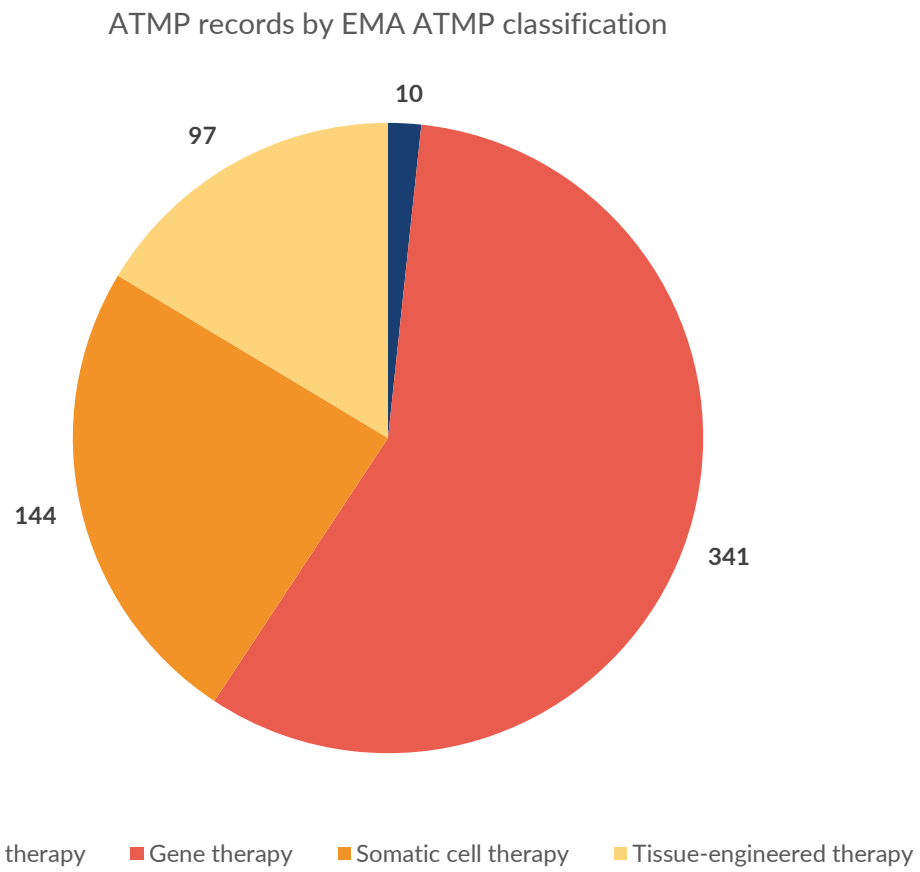
Description of selected data fields

Data field	Description	Additional notes/comments
NICE TSID	Technology records have been notified to NICE Topic Selection	~86 records have been notified to NICE, although their current status in the NICE process is not included in dataset
Intervention(s)	Interventions listed on the technology record, i.e the ATMP and other non-ATMP product (if applicable)	~84% of technology records list a single intervention (ATMP); non-ATMP interventions on the clinical trial record are included in the data field
Available on NHSE/I ATMP profiles?	Technology records checked against NHSE/I ATMP profile (September 2021 update)	All products listed in the NHSE/I ATMP profiles are included in this dataset with the exception of Gliovac
Added from ABPI Phase III subset?	Technology records that have been retrieved from the 59 phase III candidates shared by the ABPI	11 new records added from ABPI data: six tissue engineered, four gene therapies & one somatic cell therapy
Rare diseases?	Technology records' main indication against A-Z list of Rare/Orphan diseases (08/2020) from the Orphanet database	Records classed as 'unclear' include broad indications that have a subgroup identified as a rare/orphan disease on the orphanet database
Regulatory status	Technology records checked for the current status of regulatory development (in development, EU licence, others)	Majority of the technology records (~ 94%) are still in clinical development – the highest clinical trials phase of development is captured in the dataset (trial phase)
Single or multi trial record?	Multi trial records are those that have more than one clinical trial attached to it	
Primary clinical trial	While all trials associated with each technology record (trial IDs) are included in the dataset, a single (pivotal) trial was identified for each technology record	Prioritised according to: - Highest phase of development, i.e. phase III > phase II > phase II/I > phase I - Status, i.e. active > completed > suspended - Trial location i.e. UK > EU/USA > ROW

To be viewed with dataset

EMA definition of ATMPs

- What percentage of records potentially meet the EMA classification for gene, somatic cell, tissue engineered or combined therapy?*



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* Records were tagged for EMA/MHRA ATMP classification according to the EMA/MRHA definition for each ATMP type, and according to information publicly available regarding the technology. Source: https://www.ema.europa.eu/en/documents/scientific-guideline/reflection-paper-classification-advanced-therapy-medicinal-products_en-0.pdf

To be viewed with dataset

Therapy/clinical areas being targeted by ATMPs

- Which therapy areas are most often pursued?*

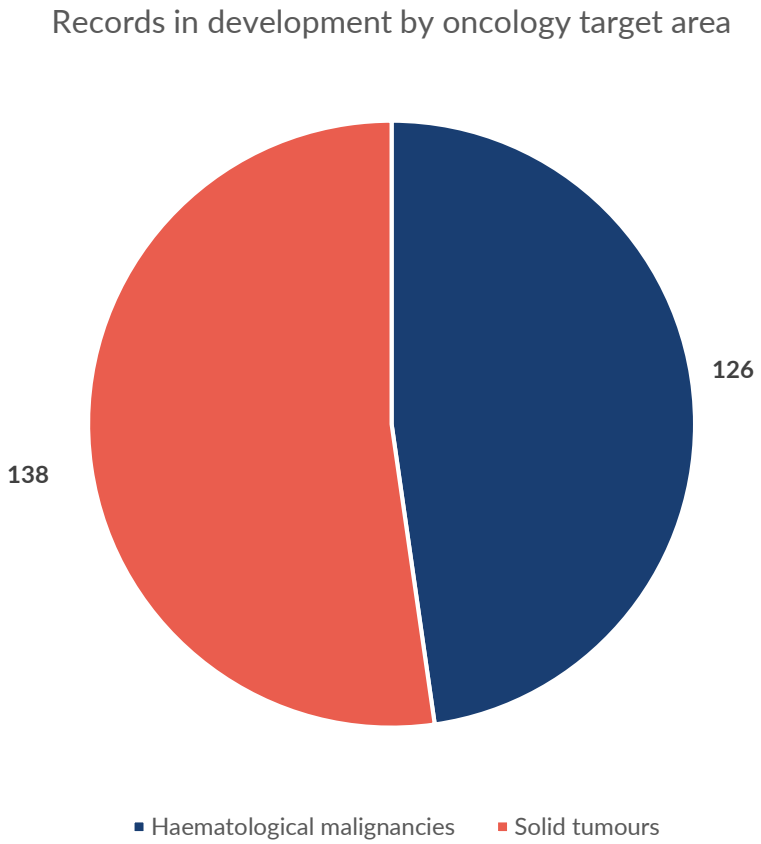
Top 5 therapy areas by # of records	Gene therapy	Somatic cell therapy	Tissue engineered therapy	Combined therapy	Total records
Haematological cancers and lymphomas	95	27	2	1	129
Genetic disorders	53	1	5	0	59
Endocrine, nutritional and metabolic disorders	42	5	3	2	52
Cardiovascular/cardiovascular system	10	14	20	4	48
Ophthalmology	26	3	11	1	41

*Top 5 therapy areas (N=329) of the 593 records identified in the scan, according to therapy areas as listed on MIND

To be viewed with dataset

Oncology indications targeted by ATMPs (~45%)

- Which cancer indications are most often pursued?



Indication	Number of records (n)	Solid tumour or haematological malignancy
Multiple myeloma	28	Haematological malignancy
Acute lymphoblastic leukaemia (ALL)	17	Haematological malignancy
Diffuse large B-Cell lymphoma (DLBCL)	13	Haematological malignancy
Glioma	13	Solid tumour
Melanoma	13	Solid tumour
Non-small cell lung cancer (NSCLC)	12	Solid tumour
Solid tumours	11	Solid tumour
Acute myeloid leukaemia (AML)	10	Haematological malignancy
Breast cancer	9	Solid tumour
Colorectal cancer	9	Solid tumour

Non-oncology indications targeted by ATMPs (~55%)

- Which non-cancer indications are most often pursued?

Top 10 Indications by # of Records	Number of records (n)
Retinitis pigmentosa	11
Haemophilia A	10
Heart failure	9
Osteoarthritis	9
Duchenne muscular dystrophy	7
Sanfilippo A Syndrome	7
Parkinson's Disease	6
Age-related macular degeneration	6
Type 1 diabetes	6
Limbal stem deficiency	6

To be viewed with dataset

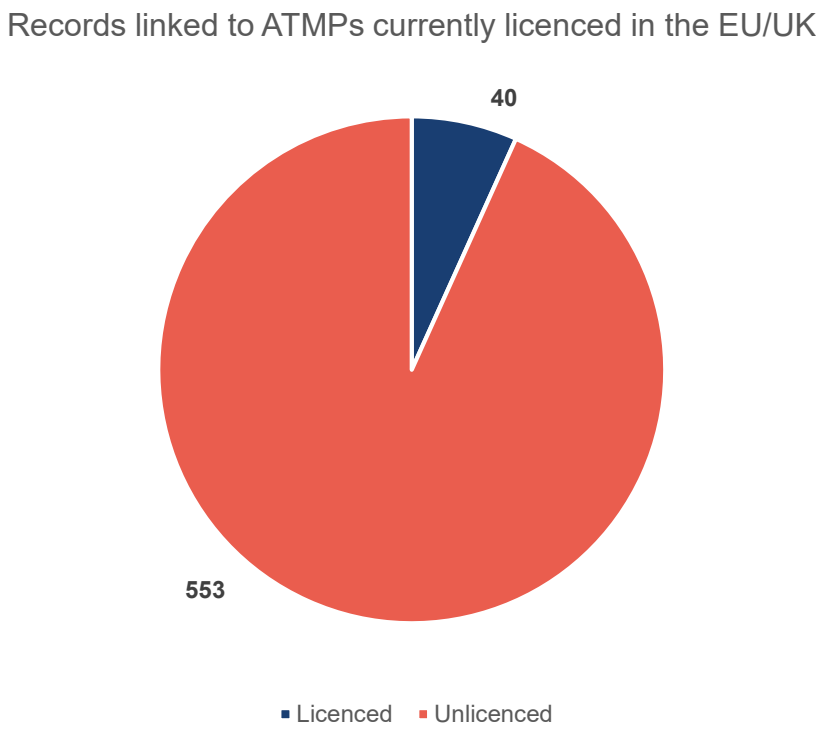
Regulatory status of ATMPs

- How many technologies have regulatory approval (product licence) for use in other indication(s)?

A total of 40 technology records include products that are already licenced for various indications in the EU/UK

These include the following 6 unique ATMPs in development as significant licence extensions:

- Axicabtagene ciloleucel (Yescarta)
- Darvadstrocel (Alofisel)
- Holoclar
- Onasemnogene abeparvovec (Zolgensma)
- Talimogene laherparepvec (Imlygic)
- Tisagenlecleucel (Kymriah)

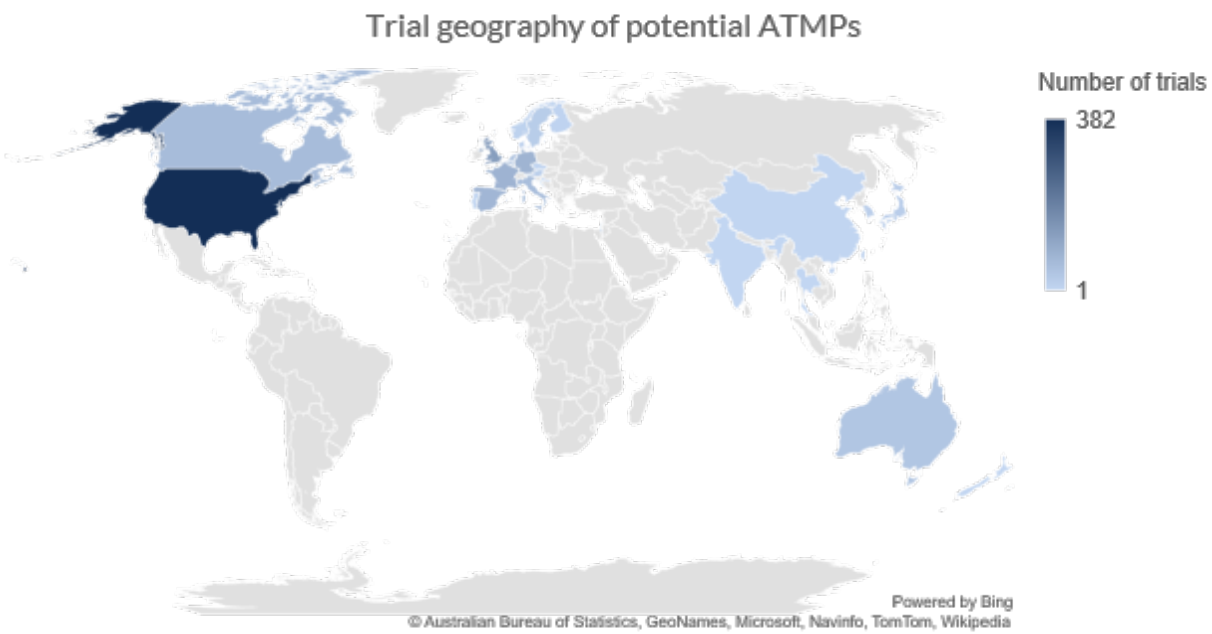


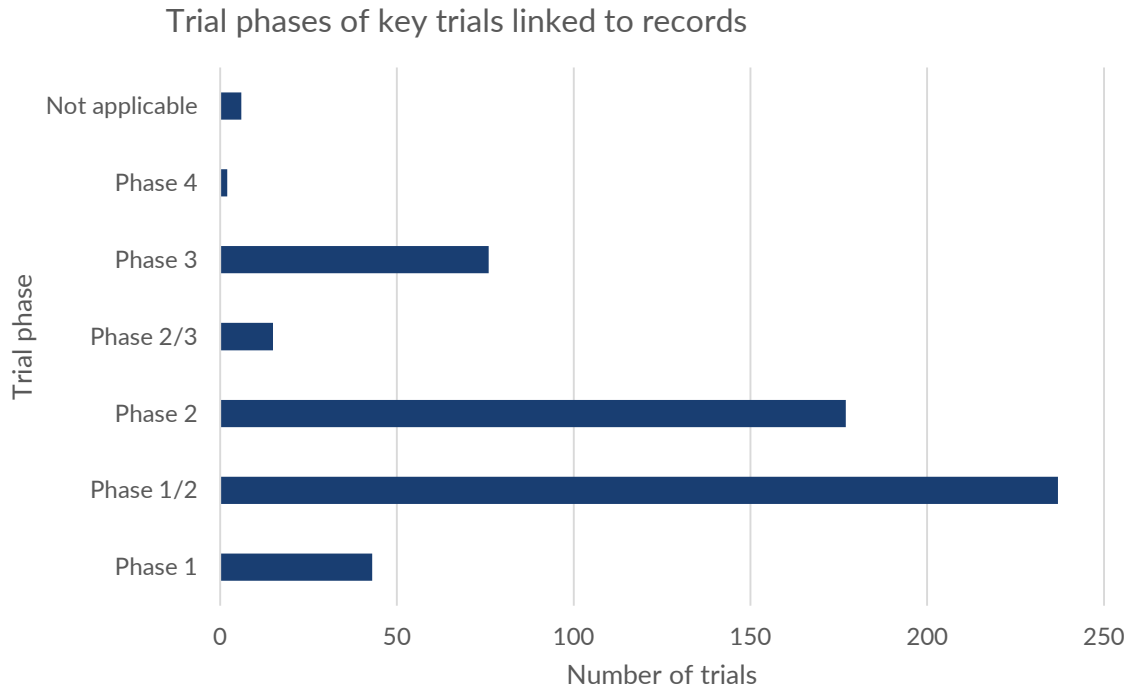
*Intervention names from all records had license status checked on eMC. Source: https://www.medicines.org.uk/emc#gref

To be viewed with dataset

Clinical trial activities of ATMPs: Geography & Phase

- What do we know about the associated 'primary' clinical trials?





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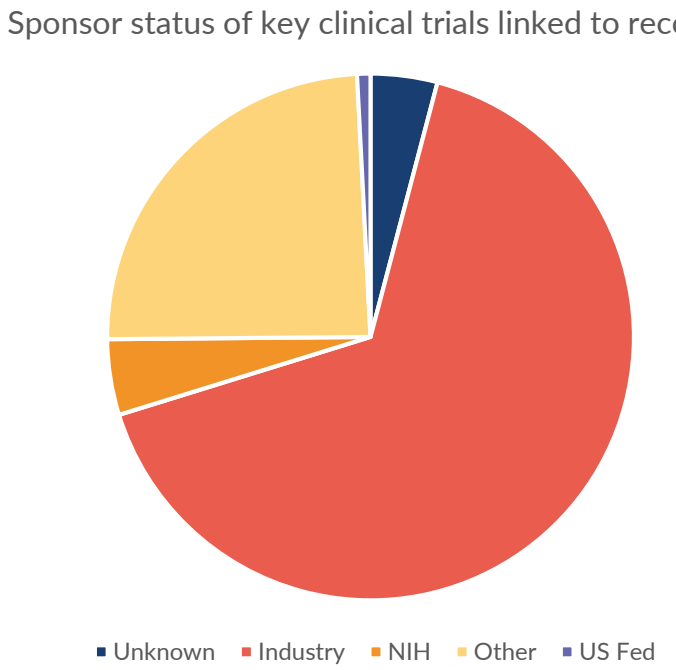
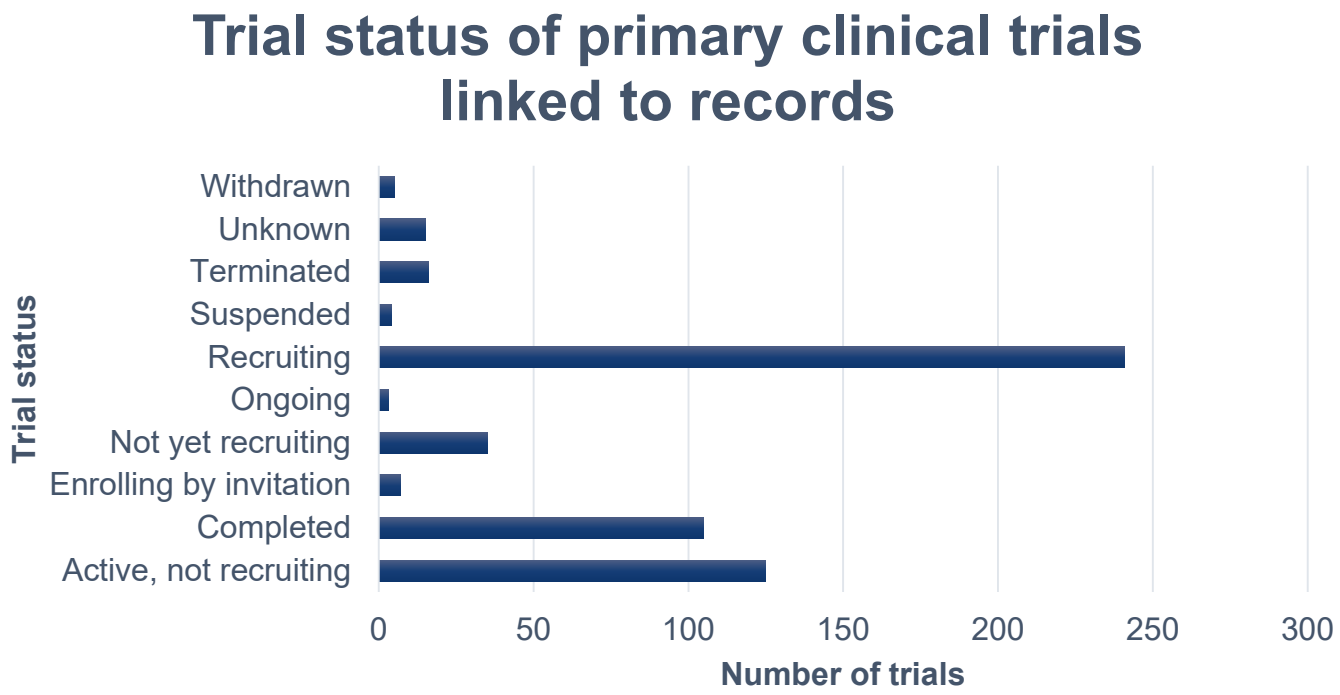
To be viewed with dataset

Clinical trial activities of ATMPs: Sponsor & Status

- What do we know about the associated clinical trials?





Conclusion

Summary

- Summary of the dataset
  - The ATMP dataset consists of 593 technology records that includes 459 unique ATMPs that are associated with 733 clinical trials
  - Data relating to ATMPs in development for COVID-19 (n=53) are included as a separate sheet in the dataset
  - Haematological malignancies (~40%) and genetic disorders (18%) are the most commonly targeted therapy areas
  - 13% of the technology records (n=78) have estimated product licence dates suggesting potential for a UK/EU licence and/or launch in the next 3 – 5 years
- Data validity & uncertainty
  - The ATMPs were identified primarily from trials registries during routine scanning with additional information (e.g. classification, product description, etc) obtained via extensive manual searching by Innovation Observatory's analysts
  - Regulatory information (estimated filing, licence and launch dates) came directly from the companies/commercial developers via UKPS or direct engagement with the Innovation Observatory
  - The dataset aimed to capture ATMPs with a potential product licence/launch in the NHS up until ~2026 (5 years), but this comes with a high level of uncertainty given the rapidly changing landscape of development and regulatory processes

Limitations

- Every effort was made to ensure the accuracy and completeness of the data but this cannot be guaranteed
- Clinical and regulatory pathways for ATMPs are not always straightforward and the data provided comes with some degree of uncertainty around the progression of the ATMPs identified
- Data sharing - estimated product licence (Marketing Authorisation) dates are commercial-in-confidence data and have not been included in the scan dataset
- Information around certain areas (e.g., point of care manufacture, dosing, required diagnostics, and NHS preparedness) fell beyond the scope & capacity of this scan
- ATMPs in development in certain locations (e.g. China-only) have not been systematically captured in this dataset given the location remit of the Innovation Observatory
- The scan was performed by NIHR Innovation Observatory staff who are not subject matter experts in the field of ATMPs. Some of the specific product type data (i.e., the ATMP classification) may require further verification

Recommendations/future work

- This dataset provides an initial 'spine' of data intended to support the different work streams of the AAC Early Stage Product (ESP); further stakeholder (e.g. clinical, commercial) and enrichment activities of the dataset may be required
- The dataset is also intended to support the NHSE/I and SPS horizon scanning for ATMPs closer to market (0 – 3 years); future work will be needed to enrich the data for products that are not yet on NHSE/I radar which can be identified from the dataset
- This dataset has been consolidated with phase III data obtained from the ABPI's global ATMP scan. Additional work is required to align the analysis (e.g. potential innovation/impact, phase II data, etc) and improve interpretation
- Opportunities to align the data in this scan with those from the Catapult Cell and Gene therapy's clinical trials database have been raised
- Further analyses of this dataset to identify emerging trends and innovation is ongoing, following the recommendations and ongoing discussions with the AAC working group

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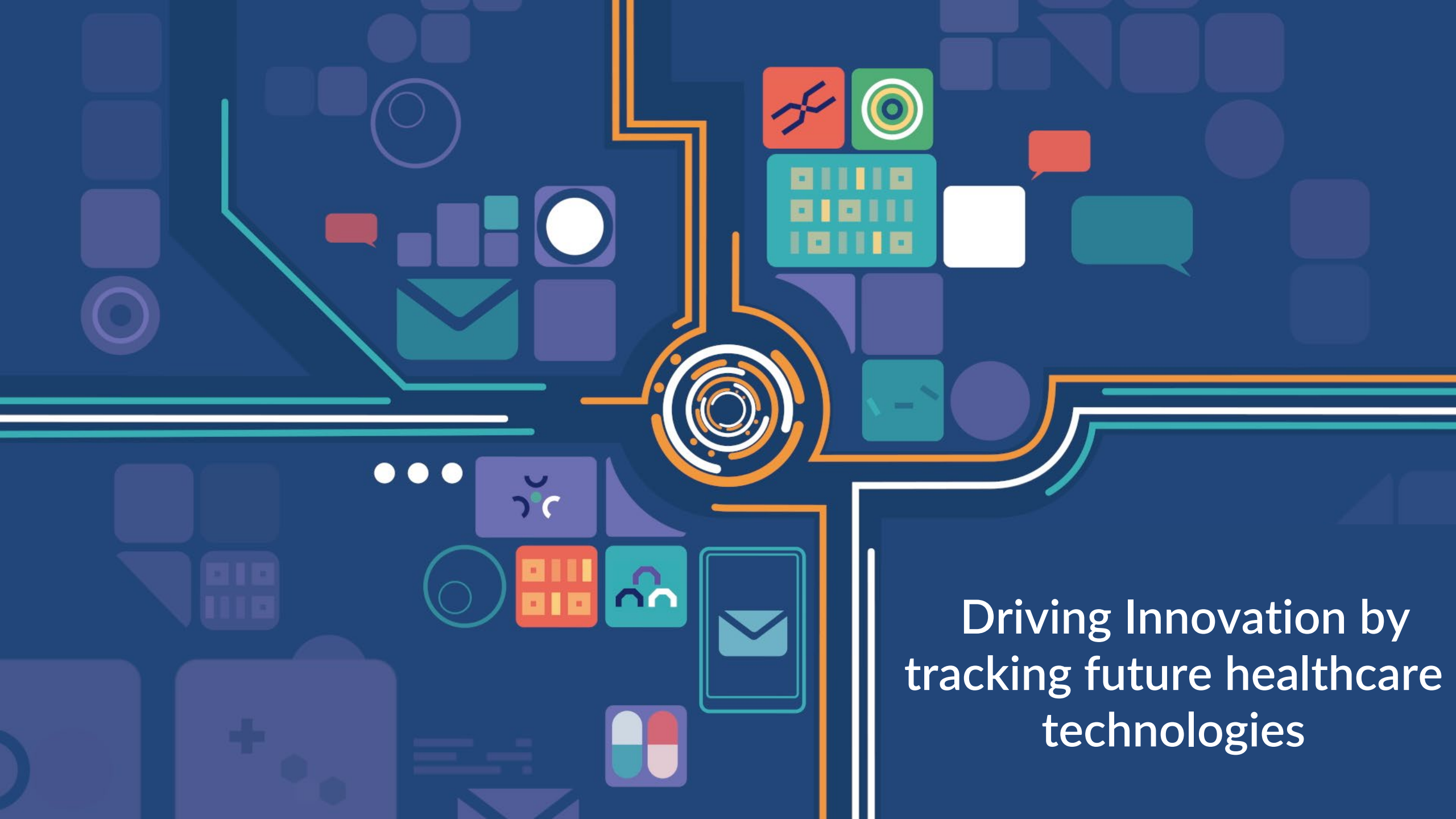
Driving Innovation by tracking future healthcare technologies